Optical Coherence Tomography Fast versus Regular Macular Thickness Mapping in Diabetic Retinopathy

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Abstract

Objective: The purpose of the study was to investigate if absolute values and reproducibility of thickness maps obtained from 2 optical coherence tomography (OCT) scanning protocols, regular high-resolution and fast low-density mode, differ in patients with diabetic macular edema. **Methods:** A total of 26 consecutive patients undergoing fluorescein angiography and Stratus OCT scanning for the evaluation of diabetic macular edema at the Departments of Ophthalmology in Munich and Vienna were included. **Results:** Retinal thickness of the central field of the thickness map measured by fast retinal thickness protocol was 287 ± 97 and 290 ± 113 μm by the regular protocol. This difference as well as that for all other fields was not statistically significant. Three times repeated measurements applying both OCT scanning modes in 10 patients yielded very good intrasession correlation coefficients between 0.70 and 0.99, with corresponding intrasession standard deviations ranging between 6 and 16 μm. The fast mode yielded slightly less reproducible values than the regular mode. Visual acuity did not influence the results. **Conclusion:** In practice both scanning modes can be interchanged and absolute values can be compared directly. Best reproducibility is obtained with higher sampling density even in patients with reduced visual acuity due to diabetic macular edema.

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Introduction

Diabetic retinopathy is a leading cause of severe visual impairment and blindness in the developed countries. The incidence and prevalence are high and continue to increase [1]: it is estimated that currently alone in the USA 10.2 million adults aged 40 years or older have diabetes mellitus. Besides proliferative disease diabetic macular edema is the major vision-threatening retinal change [2]. For its treatment the Early Treatment Diabetic Retinopathy Study (ETDRS) has defined distinct criteria and shown the effectiveness of focal laser coagulation [3, 4]. In addition several new medical treatment options have become available recently, such as anti-VEGF agents or PKC inhibitors [5, 6]. Therefore appropriate and timely detection of macular edema has increasing importance in order to offer patients the best possible treatment and prevent vision loss.

Besides stereoscopic, biomicroscopic fundus examination [7], over the last years new objective methods were

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established to quantify the retinal thickness of the posterior pole. Optical coherence tomography (OCT) is most frequently applied and allows objective measurements of macular thickness. With several scans it can generate detailed retinal thickness maps covering the posterior pole. The instrument allows to reliably detect such small increases of retinal thickness of <10 μm [8–10], while stereoscopic fundus examination usually only detects retinal thickening of approximately 100 μm [11]. OCT therefore is believed to be superior to clinical examination for detecting small amounts of retinal thickening in diabetic macular edema [12, 13]. However, the currently most frequently applied OCT, the Stratus OCT (Carl Zeiss Meditec, Jena, Germany), offers 2 modes for measuring macular thickness maps: a regular high-resolution mode and a fast mode. Although the resolution in the x-y plane and scanning times differ significantly, both modes are applied and interchanged in clinical practice, to date without proper validation. Knowledge about any possible differences between the 2 scanning modes is especially of importance for cases where only the fast mode gives results due to patient disability or compliance. Therefore, the aim of this study was to investigate if absolute values and reproducibility of these 2 OCT scanning modes differ in patients with diabetic macular edema.

Table 1. Patient characteristics

	Distribution	Statistical significance p
Gender	18 male (69) 8 female (31)	0.07
Eye	10 right (38) 16 left (62)	0.33
Age, years	64 ± 20 [24–77]	–
Diabetes type	9 IDDM (35) 17 NIDDM (65)	0.17
Duration of diabetes, years	14 ± 14 [1–26]	–
Hemoglobin A_{1c}, %	7.0 ± 0.6 [5.7–7.7]	–
Retinopathy level	2 mild NPDR (8) 13 moderate NPDR (50) 5 severe NPDR (19) 6 PDR (23)	0.02*
Visual acuity (logMAR of Snellen)	0.40 ± 0.41 [0–2.0]	–

Given are the median with interquartile range in square brackets or number of patients with percentages in parentheses. * p = 0.02: significant difference. IDDM = Insulin-dependent diabetes mellitus; NIDDM = non-insulin-dependent diabetes mellitus; NPDR = nonproliferative diabetic retinopathy; PDR = proliferative diabetic retinopathy.

Methods

Patients

A total of 26 consecutive patients undergoing fluorescein angiography and Stratus OCT scanning for the evaluation of diabetic maculopathy at the Departments of Ophthalmology in Munich and Vienna were included in this study. From each patient only 1 eye was randomly selected for further analysis. Inclusion criteria were acceptable metabolic control defined by a hemoglobin A_{1c} of <8%, acceptable control of blood pressure (<140/90 mm Hg) and some degree of clinically significant diabetic macular edema according to the ETDRS criteria [14] on clinical stereoscopic slit lamp examination. Both proliferative and nonproliferative diabetic retinopathy were included and no previous surgery to the posterior segment was allowed, while mild focal laser therapy was. Further exclusion criteria were neovascular glaucoma, no visual function (stability of fixation was no inclusion or exclusion criteria), vitreous hemorrhage and all other eye diseases, especially those involving the macula. A full ophthalmological examination including a dilated (1% tropicamide) stereoscopic fundus exam (biomicroscope, 78-dpt lens) was performed by retinal specialists (A.S.N., N.M.). In all patients both fluorescein angiography and OCT were carried out after informed consent. All research was conducted in accordance with institutional guidelines and board approval and conformed to the tenets of the World Medical Association Declaration of Helsinki.

OCT Measurements

OCT (Carl Zeiss Meditec) was performed with a commercially available unit of the Stratus OCT-III. The principles of OCT have been described in detail elsewhere [15, 16]. In this study software version 4.04 was applied to measure retinal thickness applying a scan length of 6.0 mm. Internal fixation of the OCT was used. Six radial scans every 30° were performed and the instrument's built-in, automatic mapping algorithm was applied to automatically calculate the retinal maps. Retinal thickness in the 9 ETDRS fields was analyzed. In each patient, 2 maps were generated: 1 consisting of scans in the regular scanning mode applying 512 A scans and 1.28 s per scan and 1 with the fast macular scanning applying less dense 128 A scans in 0.32 s per scan. The 2 scan protocols were performed in random order. Additionally, in 10 randomly selected patients the 2 mapping protocols (fast and regular) were applied 3 times in random order to determine the intrasession reproducibility.

Statistics

Data were collected and analyzed using SPSS 13.0 for Windows (SPSS Inc., Chicago, Ill., USA). On all statistical tests $p < 0.05$ was considered significant. Multi- and univariate analyses were applied. Paired testing and nonparametrical methods (e.g. Spearman correlation) were chosen where appropriate, which was especially the case for the not normally distributed OCT thickness data.

Results

Patients

The demographic characteristics of the 26 patients included are summarized in table 1. Visual acuity ranged from logMAR 0–2 with a median of 0.40, corresponding to Snellen 20/50 (range 20/2,000–20/20).

OCT Macular Map Comparison

The median retinal thickness of the central field measured by the fast retinal thickness protocol was 287 ± 97 and 290 ± 113 μm (median ± interquartile range) by the regular macular retinal thickness protocol. This difference as well as that for all other fields was not statistically significant. A sample patient illustrating the good concordance of the results is shown in figure 1. The details of the measurements are listed in table 2. The correlation coefficients of the values obtained by the 2 scanning modes were very good, ranging between 0.72 and 0.95.

OCT Macular Map Reproducibility

The 10 patients with repeat measurements had a median visual acuity of 0.52 logMAR ranging from 0 to 1.3,

Fig. 1. Patient with diabetic macular edema. **a** Color fundus photograph of the left eye of a patient with mild clinically significant diabetic macular edema. **b** Early phase of fluorescein angiography. **c** Late phase of fluorescein angiography. **d** Corresponding regular macular thickness map computed from high-density scans (1.28 s/scan). **e** Corresponding fast macular thickness map computed from low-density scans (0.32 s/scan).

Table 2. Comparison of fast and regular OCT maps in diabetic macular edema

OCT field	Regular map μm	Fast map μm	Significance of median difference	Correlation of regular and fast map values	Significance of correlation p
1 (center field)	290 ± 113	287 ± 97	n.s.	0.95	<0.001
2 (central superior)	315 ± 105	324 ± 98	n.s.	0.92	<0.001
3 (central temporal)	314 ± 97	313 ± 118	n.s.	0.84	<0.001
4 (central inferior)	317 ± 97	307 ± 81	n.s.	0.95	<0.001
5 (central nasal)	295 ± 90	306 ± 75	n.s.	0.72	<0.001
6 (peripheral superior)	284 ± 109	276 ± 111	n.s.	0.90	<0.001
7 (peripheral temporal)	271 ± 92	283 ± 106	n.s.	0.88	<0.001
8 (peripheral inferior)	272 ± 77	276 ± 86	n.s.	0.88	<0.001
9 (peripheral nasal)	270 ± 66	275 ± 69	n.s.	0.85	<0.001

Values are medians ± interquartile ranges. n.s. = Not significant.

Table 3. Reproducibility of fast and regular OCT maps in diabetic macular edema

OCT field	Fast maps ICC	Fast maps intrasession SD, μm	Regular maps ICC	Regular maps intrasession SD, μm
1 (center field)	0.97	10.71	0.99	7.23
2 (central superior)	0.93	10.63	0.95	9.43
3 (central temporal)	0.94	11.12	0.98	8.83
4 (central inferior)	0.93	8.32	0.90	13.23
5 (central nasal)	0.71	14.47	0.85	13.90
6 (peripheral superior)	0.70	13.85	0.88	8.49
7 (peripheral temporal)	0.84	15.93	0.97	9.97
8 (peripheral inferior)	0.95	6.47	0.91	8.44
9 (peripheral nasal)	0.71	16.13	0.96	5.69

which corresponds to Snellen 20/50 with a range from 20/400 to 20/20. Table 3 gives the intrasession correlation coefficients (ICC) and the intrasession reproducibility for those patients. Very good ICCs between 0.70 and 0.99 are obtained, the corresponding intrasession standard deviations range between 6 and 16 μm. The session standard deviations did not correlate with any other factor included in the study, especially not with visual acuity.

Discussion

OCT has become a valuable imaging modality in the evaluation and management of various macular diseases, particularly with regard to diseases that result in abnormal macular thickness, such as macular edema. The Zeiss Stratus OCT allows not only good axial resolution of ap-

proximately 10 μm but also faster scanning than previous time domain models. This may be used for increasing the number of A scans as with the 'regular' macular map mode or allow faster scanning with a lower number of A scans as with the 'fast' macular thickness mode. Faster scanning should theoretically reduce motion artifacts and might therefore be beneficial in patients with reduced visual acuity. On the other hand due to less lateral resolution after the instrument's software processing the resulting thickness measurements may yield higher variability. The current study showed in patients with diabetic macular edema that no large differences exist between the 2 scanning modes. The variation of the OCT macular maps acquired in a longer time but with high lateral resolution was consistently lower (see table 3) than for the fast mode. Differences were, however, small. As absolute measurements did not differ between the 2 map-

ping modes, this means that in practice both scanning modes can be interchanged. Still, the best reproducibility is obtained with higher sampling density even in patients with reduced visual acuity such as in diabetic macular edema.

These results are in concordance with a paper investigating reproducibility in normal subjects [17], where also good reproducibilites were found for both scanning modes with some advantage for the high-density scans. It is remarkable that the same is true for the patients with diabetic macular edema investigated in our study, although they have reduced visual acuity and ability to fixate. It appears important that in those patients the 2 scanning modes were applied in random order to avoid any bias, e.g. by getting tired. When comparing in detail the values reported for the normal subjects in Paunescu et al. [17], the diabetic patients in our study show between 2 and 3 times higher session standard deviations for the same 3 times repeated measurements. This is believed to be related to a reduced ability to fixate due to diabetic macular edema. Another possible explanation is that scan quality may be impaired by less fixation causing higher variance of scan analysis [18]. Interestingly, no correlation between OCT session variability and the patients' visual acuity could be shown in our study – fixation itself was not measured in this study. When transferring our results it should also be considered that the retinopathy level distribution in patients mostly represented more advanced retinopathy levels, while for instance in screening settings lower levels are to be expected. In comparison to the previous OCT 2000 version, where a reproducibility for macular thickness measurements of <20 μm was found in diabetic retinopathy [19], our current

study observed a better reproducibility with the Stratus OCT. This may be related to the increased sampling density and axial resolution – and only to some minor degree to the higher speed of image acquisition with the Stratus OCT.

In summary, in patients with diabetic macular edema, fixation loss appears to be less of a concern, as image resolution is compromised in a fast macular scan protocol as compared to the regular, slower protocol. This regular scan protocol provides more data points and may therefore be more indicative of changes in the macula [20]. On the other hand differences in map repeatability are small and the absolute thickness values do not differ. Therefore the values of both protocols can be directly compared. This implies that in cases where regular scanning is difficult one can use the fast macular map, which yields similarly reliable results as the slower high-density mode. In summary, with the current study in a first attempt the comparability of slow and fast scanning has been shown in diabetic retinopathy. The results should be confirmed in a larger number of patients with time domain OCT and with other imaging technology applied in macular edema, such as spectral domain OCT.

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