Aus der Klinik für Augenheilkunde
der Medizinischen Fakultät Charité – Universitätsmedizin Berlin

DISSERTATION

The Apply of Spectral Domain Optical Coherence Tomography in Retinal Vessel Assessment of Diabetic Retinopathy

zur Erlangung des akademischen Grades
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Abstract

Purpose: To evaluate spectral domain optical coherence tomography (SD-OCT) based methods to differentiate retinal vessel types and measure retinal vessel diameters, and compare these findings with the reference from infrared reflectance (IR) images and/or fluorescein angiography (FA); then, evaluate the retinal vessel diameters in relation to different severity grades of diabetic retinopathy using SD-OCT.

Methods: Patients who underwent circular OCT-scans centered at the optic disc with or without non-proliferative diabetic retinopathy (NPDR) were retrospectively reviewed. Individual retinal vessels were identified on IR and given unique labels both on IR and SD-OCT. Vessel types (artery, vein or uncertain) and vessel width obtained by IR and/or FA were documented as ground truth. From OCT, presence of the hyperreflective lower border reflectivity feature and measurements of each vessel, including horizontal vessel contour diameter, vertical vessel contour diameter, horizontal hyperreflective core diameter, and reflectance shadowing width, were assessed.

Results: A total of 398 vessels with documented vessel type were included for vessel type assessment. Using SD-OCT, 338 vessels were assigned a final grade, of which, 86.4% (292 vessels) were classified correctly. When using only IR based ground truth for vessel type, the SD-OCT based classification approach reached a sensitivity of 0.88/0.93, and a specificity of 0.93/0.88 for arteries/veins, respectively.

194 vessels larger than 40 μm were documented for diameter measurements. The mean vessel width obtained from IR was 107.9±36.1 μm. A mean vertical vessel contour diameter of 119.6±29.9 μm and a mean horizontal vessel contour diameter of 124.1±31.1 μm were measured by SD-OCT. Vertical vessel contour diameter did not differ from vessel width in all subgroup analysis. Horizontal vessel contour diameter was not significantly different from vessel width for arteries and had strong (r=0.88m) or very strong (r=0.91) correlation with vessel width for veins.

Of 59 eyes from 45 patients examined, 30 (50.2%) had mild NPDR and 29 (49.8%) had severe NPDR, respectively. Eyes with mild NPDR had wider mean arteriolar vertical vessel inner diameter (89.8±12.1μm), vertical vessel outer diameter (120.9±12.9μm), and vessel shadow width (81.3±15.3μm) than patients with severe NPDR (87.9±10.8μm,

119.1±9.7μm, 78.8±10.9μm). However, the differences were not statistically significant (p=0.53, 0.55, 0.47). In contrast, wider venular diameters were associated with increasing severity of NPDR (p=<0.001, <0.001, 0.007).

Conclusion: Retinal vessel type assessment and diameter measurements can be achieved with the current generation of SD-OCTs and be routinely implemented in the clinic. Wider retinal venule diameter was significantly associated with the severity of NPDR by SD-OCT assisted measurement.

Abstrakt

Ziel

Auf der Spectral-Domain optischen Kohärenztomographie (SD-OCT) basierend sollen retinale Gefäße differenziert und die Gefäßdurchmesser ermittelt werden.

Infrarot-Bilder (IR) und/oder Fluoreszeinangiographie- (FAG-)Bilder dienen als Referenz. Darüber hinaus sollen die Durchmesser der retinalen Gefäße im SD-OCT in Beziehung zu dem Schweregrad der diabetischen Retinopathie gesetzt werden.

Methode

Auf die Papille zentrierte circuläre OCT-Scans von Patienten mit oder ohne nichtproliferativer diabetischer Retinopathie (NPDR) werden retrospektiv ausgewertet. Einzelne retinale Gefäße wurden im IR-Bild identifiziert und ihnen wird eine ID sowohl im IR-Bild als auch im SD-OCT zugeordnet. Die verschiedenen Gefäßtypen (Arterie, Vene oder nicht bestimmbar) wurden klassifiziert und die Gefäßbreite im IR-Bild und/oder FAG gemessen und als Referenzwert festgelegt. Im SD-OCT wurden das Merkmal der hyperreflektiven unteren Grenze bestimmt und die einzelnen Gefäße gemessen. Dabei wurde der Durchmesser der horizontalen und vertikalen Gefäßkontur, der horizontale hyperreflektive Kerndurchmesser und die Breite des Reflexionsschattens bestimmt.

Ergebnis

Insgesamt sind 398 Netzhautgefäße mit dokumentiertem Gefäßtyp (IR/FAG) in die Klassifikation der Gefäße im SD-OCT eingeschlossen worden. Im SD-OCT sind 338 Gefäße endgültig klassifiziert worden, davon waren 86,4% (292 Gefäße) korrekt. Wenn nur die IR-Bilder als Referenz hinzugezogen worden sind, lag die Sensitivität im SD-OCT bei 0,88 bzw. 0,93 und die Spezifität bei 0,93 bzw. 0,88 für Arterien bzw. Venen.

194 Gefäße mit einem Durchmesser von >40µm wurden für eine weitere Messungen im SD-OCT zugrunde gelegt. Der mittlere Gefäßdurchmesser im IR-Bild war 107.9±36.1 µm. Der mittlere vertikale Durchmesser der Gefäßkontur betrug 119.6±29.9 µm und der mittlere horizontale Durchmesser lag bei 124.1±31.1 µm im SD-OCT. Der vertikale Durchmesser wies keine Unterschiede in allen Subgruppen auf. Der horizontale Durchmesser war nicht signifikant unterschiedlich für die Arterien, wies jedoch eine starke (r=0.88) bzw. sehr starke (r=0.91) Korrelation mit der Gefäßweite der Venen auf.

Bei 59 Augen von 45 Patienten zeigten sich in 30 Augen (50,2%) eine milde und in 29 (49,8%) Augen eine schwere NPDR. Bei milder NPDR war der mittlere vertikale innere Gefäßdurchmesser der Arterien (89.8±12.1µm), der vertikale äußere Gefäßdurchmesser (120.9±12.9µm) und das Ausmaß des Gefäßschattens (81.3±15.3µm) größer als bei Patienten mit schwerer NPDR (87,9±10,8µm, 119.1±9.7µm ,78.8±10.9µm). Allerdings waren diese Unterschiede nicht statistisch signifikant (p=0.53, 0.55, 0.47). Im Gegenteil dazu, waren größere Durchmesser der venösen Gefäße mit zunehmendem Schweregrad der NPDR signifikant assoziiert (p=<0.001, <0.001, 0.007).

Schlussfolgerung

Mit dem aktuellen SD-OCT Geräten können arterielle und venöse retinale Gefäße unterschieden und die Gefäßdurchmesser zuverlässig gemessen werden. Diese Methode kann im klinischen Alltag eingesetzt werden.

Die Durchmesser der venösen Gefäße von der SD-OCT unterstützten Messung waren signifikant mit dem Schweregrad der NPDR assoziiert.

Introduction

Diabetic retinopathy (DR) is the most common microvascular complication of diabetes mellitus and the leading cause of visual loss in the working-age individual [1]. Systematic risk factors such as glycosylated hemoglobin (HbA1c), blood pressure, and duration of diabetes have been shown to be associated with severity and progression of DR [2]. Now that DR is a vascular disease process, assessment of the retinal vasculature itself is still the fundamental basis for grading of the severity of the disease. More detailed descriptive parameters have been proposed to be included in risk models for disease progression and visual loss, with the developments of retinal imaging and image analysis. As an exemplary parameter, retinal vessel diameter can provide additional information, independent of retinopathy severity, hyperglycemia, hypertension, and other factors, regarding the risk of DR progression [3].

Several methods such as fundus photography, computer-assisted image analysis, and fluorescein angiograms [4], have been described for the measurement of retinal vessel diameters in DR. Even optical coherence tomography (OCT) has been found useful for vessel analysis despite initial reservations more recently [5]. Therefore, the final aim of this study was to examine the association of retinal vessel diameter changes as measured on SD-OCT with severity of DR in patients with type 2 diabetes mellitus. Before doing this, we wanted to establish a method to classify and measure retinal vessels with the current commercially available SD-OCT.

In recent years, researchers have found that alterations in the arterial or venular tree of the retinal vasculature are also associated with generalized vascular problems, such as diabetic retinopathy [6]. Since arteries and veins are differently affected in these disease processes, a prerequisite for assessment of the vascular change is to separate those vessels from each other. Thus, the first step of this study was aimed to evaluate SD-OCT based methods to differentiate retinal vessel types and measure retinal vessel diameters, and compare these findings with the reference from infrared images and/or FA.

Methods

Data collection

Patients with or without non-proliferative diabetic retinopathy (NPDR) at the Charité department of ophthalmology were retrospectively reviewed. A circular OCT-scans centered at the optic disc using a Spectralis OCT + HRA (Heidelberg Engineering, Heidelberg, Germany) was performed to each patient. Information regarding age, gender, history of ophthalmic diseases or surgeries, ophthalmic diagnoses, lens status, and visual acuity were collected. Only patients with type 2 diabetes mellitus were included in this study. The Early Treatment Diabetic Retinopathy Study (ETDRS) protocol was used to assess the presence and severity of DR. For patients with NPDR, arterial hypertension and other ocular comorbidities, including retinal arterial or venous occlusion, neovascular age-related macular degeneration, glaucoma, and uveitis were excluded. NPDR patients, who underwent previous panretinal photocoagulation laser treatment, were also excluded [7]. Approval for data collection and analysis was obtained from the institutional review board of the Charité-University School of Medicine in Berlin. Written consent was given by the patients for their information to be stored in the hospital database and used for research. The research adhered to the tenets set forth in the Declaration of Helsinki.

The OCT scanning protocol consisted of a circular scan with 3.42–4.04mm diameter centered on the ONH. The high resolution OCT mode with a mean number of 30 averaged scans (ART = 30) was used to scan the eyes. Images with good quality, for both OCT and IR, with FA performed on the same day, were reviewed and analyzed using Spectralis viewing software (Heidelberg Eye Explorer, version 1.7.1.0).

Grading methodology [7-9]

One grader first reviewed IR images for every eye. A circle representing the OCT scan was superimposed on IR images using the Spectralis Software. Each vessel included by IR was given a unique identity number (ID) for subsequent grading. The corresponding vessels on OCT were labeled with the same ID. This strategy allowed each vessel from different imaging modalities (IR or OCT) to be assessed in an independent, masked fashion without knowledge of its relationship with other vessels or

eye.

Two graders independently assessed the vessel type using IR and/or FA images by randomly selecting the vessel ID after the initial vessel selection. Also, the OCT images were covered during this step. By the maximum findings from IR and FA, vessel types were labelled as “Artery”, “Vein” or “uncertain”, and considered as ground truth for further analysis. Additionally, vessel width obtained from IR, which is defined as minimum vessel diameter, measured vertically to the vessel axis with the caliper tool from the Spectralis software at the crossing point of vessel and OCT scanning line, was also evaluated for further analysis. The brightness and contrast settings for IR images were used as follow: “black on white” for color table, “medium” for sharpen and “none” for noise reduction. The graders assessed each frame generated from the OCT images independently by randomly selecting the vessel ID. A vessel contour was recognized in the inner retina for each vessel. A hyperreflective core presented as equal or hyperreflective structure in comparison to the surrounding retinal tissue within the contour. The reflectivity feature at the lower border of the hyperreflective core (lower border reflectivity feature, LBRF) was used for SD-OCT assessment. The presence or absence of hyperreflective LBRF (HLBRF) was then documented as present (Y), absent (N) or cannot grade (NA). Due to the difficulty to interpret the true reflectivity features, vessels with a lower border right at the boundary of hyperreflective and hyporeflective retinal layers or small vessels without distinguishable lower border reflectivity were excluded for this feature. Other features of each vessel, including maximum horizontal vessel contour diameter, maximum vertical vessel contour diameter, and maximum reflectance shadowing width were assessed from OCT. These features were assessed preferably with the brightness and contrast of “white on black” for color table.

Statistical analysis

The difference of each OCT parameter with the referenced vessel width was tested with a paired t-test. Correlation of OCT measurements with the corresponding vessel width obtained by IR was assessed by pairwise correlation analysis (Pearson correlation), Multivariable models were constructed to examine the association of vessel diameters with severity grades of NPDR. Models were adjusted for age, gender, and

cataract surgery. Area under the receiver operator characteristic curve (AUC) was used to evaluate the prediction ability of vessel parameters. A two-sided p value of <0.05 was considered to be statistically significant.

Results

Characteristics and classification of vessel types by SD-OCT

Of 26 eyes from 18 patients, a total of 452 vessels with adequate image quality and without pathology within the OCT scan area were labelled in the study. By using the maximum finding from IR and FA, 51 vessels among them were documented with unknown vessel type. Due to bifurcation at the intersection of the OCT scan, three more vessels were excluded. As a result, a total of 398 vessels were included in the study, among which, 302 (75.9%) were classified by IR and additional 96 were only identifiable by FA.

Among the 398 included vessels, 27 vessels were documented as “NA” for the HLBRF due to their lower border right at the boundary of hyperreflective and hyporeflective retinal layers. Because of the small size of the hypercore feature, additional 33 vessels also failed to have a differentiable reflectivity feature in the lower vessel contour. Thus, 338 vessels were assigned a final grade for HLBRF in the study and differentiated into arteries and vein, of which, 86.4% (292 vessels) were classified correctly. 43 vessels (15 arteries and 28 veins) that IR failed to differentiate were correctly recognized by SD-OCT. 23 vessels crossed over one another at the point of the OCT scan intersection and 21 (91.3%) of them were correctly classified.

Characteristics and correlation of vessel diameters

A total of 194 vessels with measurable vessel width from IR were included in the study for diameter measurements. Among them, 88 arteries and 65 veins were documented. When all vessels were included, vertical vessel contour diameter in OCT correlated strongly with vessel width measured by IR image ($r=0.9812$, $p<0.0001$). There was no statistical difference between their mean values ($p=0.6775$, paired t-test). Similar results were found when only arteries, only veins, or only vessels larger than 85 μm were included for the analysis.

When only arteries were included, horizontal vessel contour diameter did not differ statistically from vessel width (p=0.1941 for all arteries and p=0.3020 for arteries≥85 μm). However, the difference between vessel width and horizontal vessel contour diameter became statistically significant when only veins were included (p=0.038 for all veins and p=0.0103 for veins≥85 μm). When all vessels were included in the analyses, this difference was persistently significant (p=0.002 for all vessels and p=0.0038 for vessels≥85 μm). More interesting still, in these same cases, the correlation of horizontal vessel contour diameter and vessel width was strong (r=0.8856 for vessels≥85 μm and r=0.8803 for veins≥85 μm) or very strong (r=0.9109 for all vessels and r=0.9107 for all veins). Similarly, when only arteries were assessed, horizontal vessel contour diameter did not differ from vertical vessel contour diameter, but differed when only veins or all vessels were included.

Characteristics and correlation of vessel parameters in NPDR patients

59 eyes from 45 patients were examined. Among them, 30 eyes (50.2%) had mild NPDR and 29 eyes (49.8%) had severe NPDR, respectively. A total of 535 vessels (271 arterioles and 264 venules) were included in this study. Patients with mild NPDR had wider mean arteriolar vertical vessel inner diameter (89.8±12.1μm), vertical vessel outer diameter (120.9±12.9μm), and vessel shadow width (81.3±15.3μm) than patients with mild NPDR (87.9±10.8μm, 119.1±9.7μm, 78.8±10.9μm). However, the differences were not statistically significant (p=0.53, 0.55, 0.47). The mean venular vertical vessel inner diameter, vertical vessel outer diameter, and vessel shadow width were 122.8±11.4μm, 152.7±12.7μm, 109.8±15.1μm in mild NPDR, and 136.2±12.9μm, 165.9±12.7μm, 120.4±14.2μm in severe NPDR.

Wider venular diameters (vertical vessel inner diameter, vertical vessel outer diameter, and vessel shadow width) were associated with increasing severity of NPDR (p=<0.001, <0.001, 0.007, respectively). After multivariate adjustment for age, gender, eye, and cataract surgery, the association remained (p=0.04, 0.01, 0.007, respectively).

The mean differences between mild and severe NPDR in retinal venules were 13.4±3.2 μm for vertical vessel inner diameter, 13.2±3.3 μm for vertical vessel outer diameter, 10.6±3.8 μm for vessel shadow width, and 1.89±2.9 μm, 1.78±2.9 μm,

2.51±3.5 μm in retinal arterioles, respectively.

The AUCs were 0.78 for venular vertical vessel inner diameter, 0.76 for vertical vessel outer diameter, and 0.69 for vessel shadow width, respectively.

Discussion

Vessel type assessment [8]

In SD-OCT, retinal arteries have clearly distinctive hyperreflective lower borders but retinal veins do not. With help of this feature, our study successfully differentiated retinal arteries from veins with a commercially available SD-OCT instrument.

With a sensitivity of 0.7929 (unclassified vessels included) or 0.8758 (unclassified vessels excluded) comparable with the methods from other groups, and a specificity of 0.93, higher than that reported by Saez et al. and Relan et al. [10, 11], our method achieved both high sensitivity and specificity for detection of retinal arteries. For arteries, the positive predictive value was 0.9371, and the false positive rate was 0.0677 or 0.0703, which was also lower than in previous reports [10]. Furthermore, for arteries, our system results in a higher positive likelihood ratio of 11.7173 or 12.4561 and equivalent negative likelihood ratio of 0.2221 or 0.1336 as compared to Saez et al. and Relan et al. [10,11], which confirms the high reliability of our proposed classification technique. Moreover, for arteries, the percentage of correct classification by our system was similar to those reported [11]. This good performance also held true for retinal veins. In all, our approach has shown high classification accuracy and specificity for both arteries and veins, which is at least analogous to the certified classification systems reported in the literature.

Several potential advantages have been shown in the current method. The current SD-OCT based technique could correctly classify both large and small vessels, while the classification method based on IR, which is vessel width dependent, is most likely to correctly classify larger vessels. The same point could be made from the descriptive data where the OCT based classification failed: vessels as small as 44 μm and as large as 168 μm were interpreted with a wrong vessel type. Therefore, the current SD-OCT based method is more scanning angle or feature dependent. In addition, with the current

method, the classification of vessel types is not compromised at retinal vessel crossings. In general, it is still a challenging task to correctly classify the retinal artery/vein at a crossing point [12]. The current method was able to achieve 91.3% correct classification rate for the crossing vessels.

Vessel diameter measurements [9]

In our study, vertical vessel contour diameter measured from SD-OCT demonstrated no difference with vessel width in all subgroup analyses. Albeit with some differences, horizontal vessel contour diameter also showed very strong correlation with vessel width. The diameters of the retinal vessel could be determined accurately and is comparable to measurements from non-tomographic images with the help of SD-OCT.

Utilizing the current scanning protocol, no difference was found between vertical vessel contour diameter obtained by SD-OCT and vessel width measured by IR images in all subgroup analyses. Horizontal contour diameter presented with some variation of agreement with vessel width or vertical contour diameter depending on whether veins or arteries were included for the evaluation. The limitation of the current methods may explain this result. As previously mentioned, the manual grading for vessel width by IR images largely depends on the contrast of the retinal vessel with the background. Previous report showed that arteries usually have a different contrast from the background compared to veins [13]. This may have resulted in the variation of measurements between arteries and veins. The other explanation could be that, although a vertical scan to the vessel axis was attempted with OCT, the cross-section of the scan that displayed as the horizontal vessel contour is slightly larger than the vertical scan to the vessel axis. Other factors could also have affects on the measurement on horizontal vessel contour diameter. For example, the horizontal contour diameter is often not applicable, as an atypical vessel contour structure was seen. While strong correlation between two imaging methods seems clear now, the direct link to true morphology is far more complex. As yet, we still don’t know if the vessel contour on OCT represents the exact anatomical vessel boundary [14]. Since there are ultrastructural differences between the vessel walls of arteries and veins, which in turn may affect appearance on OCT, exact measurements on OCT alone remain questionable. Thus, the limitations of

the current methods along with potential anatomic differences resulted in the larger variation of horizontal vessel contours compared to vessel width or vertical contour diameter.

Vessel analysis in NPDR patients [7]

Retinal vascular diameter changes might be associated with progression of DR in people with type 2 diabetes [3]. A SD-OCT assisted method was used in our study to measure the retinal vessel diameters in patients with NPDR. Retinal vessel parameters including vertical vessel inner diameter, vertical vessel outer diameter, vessel shadow width, and vessel wall thickness were measured and documented from each eye for further analysis in this study. Measurements of vertical vessel inner/outer diameter, and vessel shadow width were used to represent the diameter of retinal vessel.

Our study suggested that wider retinal venule was significantly associated with the severity of NPDR, but narrower retinal arteriole not. A study of 996 people with type 1 diabetes showed both larger arteriolar and venular diameters were associated with progression of retinopathy after multivariate analysis controlling for confounding factors [4]. Another population-based cohort study suggested that larger retinal venules but not arterioles were independently associated with a greater risk of progression to severe DR in people with type 1 diabetes. Our findings would support the latter study. Widening venular in association with increasing severity of retinopathy is likely to be caused by more general pathogenetic factors of DR such as endothelial dysfunction, inflammatory changes, and hyperglycemia [15].

In this study, we also found that, the mean differences in retinal venules between mild and severe NPDR were 13.4±3.2 μm for vertical vessel inner diameter, 13.2±3.3 μm for vertical vessel outer diameter, 10.6±3.8 μm for vessel shadow width, respectively. In support of our results, Falck A et al. found that patients with >10 μm retinal venular widening during the follow-up period were more likely to progress to severer DR than patients with less or no change in venular diameter in type 1 diabetes [15].

The AUCs of retinal venular diameter in this study demonstrated that widening of retinal venule could be a potential predictive factor for progression of DR. Klein and colleagues added the changes of retinal venular diameter to the model including

traditional risk factors for progression of DR (such as age, gender, diabetes duration, smoking, HbA1c, cholesterol and body mass index). For inclusion of changes in retinal venular diameter in the model, the increasing AUC showed that widening of retinal venule may provide additional information to predict progression of DR [5].

Conclusion

Retinal vessel type assessment and diameter measurements can be achieved with the current generation of SD-OCTs and be routinely implemented in the clinic. Wider retinal venule but not narrower retinal arteriole was significantly associated with the severity of NPDR by SD-OCT assisted measurement. Further longitudinal study would be needed to evaluate whether change in retinal venule could be used as a clinical predictor of DR progression [7-9].

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Affidavit

I, Qing, Shao, certify under penalty of perjury by my own signature that I have submitted the thesis on the topic [The Apply of Spectral Domain Optical Coherence Tomography in Retinal Vessel Assessment of Diabetic Retinopathy] I wrote this thesis independently and without assistance from third parties, I used no other aids than the listed sources and resources.

All points based literally or in spirit on publications or presentations of other authors are, as such, in proper citations (see "uniform requirements for manuscripts (URM)" the ICMJE www.icmje.org) indicated. The sections on methodology (in particular practical work, laboratory requirements, statistical processing) and results (in particular images, graphics and tables) correspond to the URM (s.o) and are answered by me. My contributions in the selected publications for this dissertation correspond to those that are specified in the following joint declaration with the responsible person and supervisor. All publications resulting from this thesis and which I am author of correspond to the URM (see above) and I am solely responsible.

The importance of this affidavit and the criminal consequences of a false affidavit (section 156,161 of the Criminal Code) are known to me and I understand the rights and responsibilities stated therein.

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Date Signature

Declaration of any eventual publications

Qing, Shao had the following share in the following publications:

Publication 1: Qing Shao, Florian M. Heussen, Yanling Ouyang, Annette Hager. Retinal vessel diameter changes in different severities of diabetic retinopathy by SD-OCT. Eur J Ophthalmol. Sep 29, 2015.
Contribution in detail: Qing Shao carried out the collection, analysis and interpretation of data; participated in drafting the manuscript.

Publication 2: Yanling Ouyang, Qing Shao, Dirk Scharf, Antonia M. Joussen, Florian M. Heussen. Retinal vessel diameter measurements by spectral domain optical coherence tomography. Graefes Arch Clin Exp Ophthalmol. August 17, 2014.
Contribution in detail: Qing Shao carried out the collection, analysis and interpretation of data; participated in drafting the manuscript.

Publication 3: Ouyang Y, Shao Q, Scharf D, Joussen AM, Heussen FM. An easy method to differentiate retinal arteries from veins by spectral domain optical coherence tomography: retrospective, observational case series. BMC Ophthalmol. May 15, 2014.
Contribution in detail: Qing Shao involved in data collection, analysis and revision of the draft.

Signature, date and stamp of the supervising University teacher

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Shao, Q, Heussen FM, Ouyang Y, Hager A,:
Retinal vessel diameter changes in different severities of diabetic retinopathy by SD-OCT
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DOI: http://dx.doi.org/10.5301/ejo.5000694

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Retinal vessel diameter measurements by spectral domain optical coherence tomography
Graefes Arch Clin Exp Ophthalmol 2015 Apr;253(4):499-509
DOI: http://dx.doi.org/10.1007/s00417-014-2715-2

Ouyang Y, Shao Q, Scharf D, Joussen AM, Heussen FM.

An easy method to differentiate retinal arteries from veins by spectral domain optical coherence tomography: retrospective, observational case series.

BMC Ophthalmol. 2014 May 15;14:66
DOI: http://dx.doi.org/10.1186/1471-2415-14-66

Lebenslauf

"My resume will not be published for privacy reasons in the electronic version of my work."

Publications

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