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Teleophthalmology image-based navigated retinal laser therapy for diabetic macular edema: A concept of retinal telephotocoagulation

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Abstract

Background: To determine the feasibility and efficacy of a retinal telephotocoagulation treatment plan for diabetic macular edema.

Methods: Prospective, interventional cohort study at two clinical sites. Sixteen eyes of ten subjects with diabetic macular edema underwent navigated focal laser photocoagulation using a novel teleretinal treatment plan. Clinic 1 (King Khaled Eye Specialist Hospital, Riyadh, Saudi Arabia) collected retinal images and fundus fluorescein angiogram. Clinic 2 (Palmetto Retina Center, West Columbia, SC, U.S.A.) created image-based treatment plans based on which macular laser photocoagulation was performed back at clinic 1. The primary outcome of the study was feasibility of image transfer and performing navigated laser photocoagulation for subjects with diabetic macular edema between two distant clinics. Secondary measures were change in best- corrected visual acuity (BCVA) and central retinal thickness (CRT) by spectral-domain optical coherence tomography at 3 months after treatment.

Results: The teleretinal treatment plan was able to be successfully completed in all 16 eyes. The mean logMAR BCVA at baseline was 0.49±0.1, which remained stable (0.45±0.1) 3 months after treatment (p=0.060). The CRT improved from 290.1±37.6 µm at baseline to 270.8±27.7 µm 3 months after treatment (p = 0.005). All eyes demonstrated improvement in the area of retinal edema after laser photocoagulation and no eyes demonstrated visual acuity loss 3 months after treatment.

Conclusion: This study introduces the concept of retinal telephotocoagulation for diabetic macular edema, and demonstrates the feasibility and safety of using telemedicine to perform navigated retinal laser treatments regardless of geographical distance.

Key Words: telemedicine; teleophthalmology; navigated retinal photocoagulation; diabetic retinopathy; macular edema;

Introduction

Telemedicine in its broadest definition is the assessment and review of patient information (history, examination, or investigations) by a health professional who is separated temporally and/or spatially from the patient.[1] Based on this concept, teleophthalmology has evolved from being a research tool to a useful clinical service in many areas of ophthalmic diagnostics and care. Teleophthalmology has been shown to be a valuable means for extending care to larger populations of high-risk patients with diseases such as diabetic retinopathy, glaucoma and/or retinopathy of prematurity.[2-8]

Laser photocoagulation is one of the most well-studied methods of treating retinal diseases in ophthalmology. The navigated laser photocoagulator, also known as the NAVILAS laser system (OD-OS GmbH, Teltow, Germany), has been shown to be more accurate and provide better visual gains compared to conventional focal laser therapy for diabetic macular edema.[9,10] It allows for registered image overlays and motion-stabilized laser delivery with image tracking to treat retinal lesions both in the posterior pole and periphery. Treatment plans (on either fundus photo, fundus fluorescein angiogram or optical coherence tomography thickness map) are overlaid onto a real-time, in vivo image of the patient's retina.

The transfer of images and its subsequent analysis is the basic concept of telemedicine/teleophthalmology. The NAVILAS laser system uses retinal images as the template for treatment, making it an ideal system to use for distant planning and retinal telephotocoagulation. In this study we assess the feasibility and efficacy of retinal telephotocoagulation, which involves image transfer, registration, and fluorescein angiography based treatment planning as well as execution of navigated focal laser treatment, between two distant clinics. Thus, we aim to introduce the concept of retinal telephotocoagulation.

Methods

King Khaled Eye Specialist Hospital Institutional Review Board approval was obtained for the study protocol and procedures. All study conduct adhered to the tenets of the Declaration of Helsinki and written informed consent was obtained for each subject at baseline. Inclusion criteria consisted of subjects with diabetes mellitus and diabetic macular edema. At all visits, subjects underwent visual acuity testing at 4 meters, slit lamp and dilated ophthalmic examination, and spectral domain optical coherence tomography (SD-OCT) imaging using the Heidelberg Spectralis

HRA+OCT (Heidelberg Engineering, Heidelberg, Germany). The central retinal thickness (CRT), which is the average retinal thickness of the central 1 mm around the fovea, and the area of non-central retinal edema was measured at baseline and at each study visit. Fluorescein angiography, using the NAVILAS laser system, was performed at screening and these images were used for focal laser treatment planning. The primary outcome measures were change in mean best-corrected visual acuity (BCVA) and CRT from baseline to 3 months.

Retinal Telephotocoagulation Process

Image registration and transfer are two essential components of retinal telephotocoagulation. Image registration is the process of transforming images acquired at different time points, or with different imaging modalities, into the same coordinate system. It is an essential part of any surgical planning and navigation system because it facilitates combining images with important complementary structural and functional information.[11] Briefly, once imported into the navigated laser system (NAVILAS®, OD-OS Inc. Berlin, Germany), a registration tool accesses the image to be aligned with a reference image, which was previously acquired by the navigated laser system. The semiautomatic registration uses landmarks identified by the operator in both images to calculate a multidimensional transformation matrix for registration. Correct registration can be achieved with only three corresponding landmarks, depending on the source images. Any additional landmark would provide the software with more information to recalculate and would potentially improve the image transformation to compensate for image distortions. Five landmarks spread over the entire image area typically result in an accurate overlay. Nine registration points is the theoretical optimum. A transformation and warping algorithm in the application scales and rotates the resultant layered image, providing both visual and internal confidence scales to determine adequate alignment.[12]

Patients underwent initial retinal imaging including fluorescein angiography at King Khaled Eye Specialist Hospital (KKESH - clinic 1) in Riyadh, Saudi Arabia. The fluorescein angiography images were registered to the subject’s fundus image using NAVILAS Contact registration software and then transmitted in an encrypted format to the Palmetto Retina Center in West Columbia, South Carolina, U.S.A. (clinic 2). One of the investigators (JFP) created off-line treatment plans using NAVILAS Contact software. The plans consisted of targeting leaking microaneurysms and placement of computerized grid patterns in areas of diffuse leakage. The treatment plans were then transmitted back to clinic 1 and navigated focal laser treatment was performed (IK) using the same NAVILAS system.

Statistical Analysis

Univariate descriptive analysis was performed using Statistical Package for Social Studies (SPSS 22; IBM Corp., Armonk, NY, U.S.A.). The mean and standard deviations were calculated for continuous variables. Snellen visual acuity values were converted into logarithm of the minimum angle of resolution (logMAR) for statistical analysis at baseline and the last follow-up. Student’s paired t-test was used for comparison and p-value <0.05 was considered statistically significant.

Results

Clinical outcomes

Ten patients (16 eyes) with diabetic macular edema entered the study with the mean age was 55.31±4.31 years (range 46-67 years). The mean duration of diabetes mellitus was 11.18±4.43 years (range 4-26 years). The mean logMAR BCVA and CRT at baseline were 0.49±0.1 and 290.1±37.6 µm, respectively. The BCVA remained stable at 0.45±0.1 (p=0.060) but the CRT improved to average of 270.8±27.7 µm (p=0.005) three months after treatment. Nine eyes (56%) had CRT >250 µm at month 3. Table 1 shows the baseline demographics as well as the visual acuity and anatomic outcomes for all 16 eyes in this study.

Retinal Telephotocoagulation Outcomes

All images taken at clinic 1were sent to clinic 2 for creation of treatment plans and all treatment plans were successfully transmitted between two clinics without registration error. On average, 5 corresponding anatomic points were necessary for accurate overlay of imported image. Treatment site (clinic 1) did not make any modifications to treatment plans from clinic 2. Four eyes received pattern grid laser, four eyes focal laser only and eight eyes combined focal/grid photocoagulation. The mean number of laser spots per treatment was 58.3±26.5 (range 19-121 spots), whereas the mean power used was 104.7±7.1 mW (range 90 - 140 mW). The mean laser duration was 98.6±5.6 milliseconds (range 90 – 120 milliseconds). All patients were successfully treated at clinic 1 according to the treatment plans from clinic 2 and all laser applications after accurate power titration were placed according to the plan. Figures 1and 2 show examples of the treatment plan as well as the baseline and follow-up SD-OCT images. The patients were compliant with treatments and no adverse events occurred during photocoagulation.

Discussion

Telemedicine uses information and communication technologies to provide health care services to patients from a distance.[13] There are two broad categories of telemedicine depending on the technology used: store-and-forward (asynchronous, ie. transfer of images) and real time (synchronous, ie. videoteleconferencing). Teleophthalmology mostly adopts the store-and-forward method, followed by interactive services and remote monitoring methods. Alternatively, a hybrid method including both store-and-forward and real-time teleexamination can be used for the provision of efficient teleophthalmology services.[13-16]

In this study we confirm previously described and validated safe retinal image transfer[12] between two clinics. The images generated at clinic 1 were used to create treatment plans at clinic 2, and these treatment plans were subsequently used for treatment back at clinic 1. Consideration of key optical parameters such as color bit depth, white balance, focus and magnification is usually important in image transfer. Using the same system in both clinics minimizes this issue compared to image transfers with similar but not identical imaging instruments or systems.[17] Transmission of navigation information including surgical planning has also been accomplished over long distances in other specialties.[18] Images such as preoperative computerized tomograms, intraoperative video, 3-dimensional models and a surgical plan were transmitted in real-time over the Internet during neurosurgical procedures.[18]

The majority of the current teleophthalmology services concentrate on patient screening and appropriate referral to experts.[19-21] Published literature reporting real-time telemedicine, particularly within the field of ophthalmology, is scant. The concept of retinal telephotocoagulation introduced in this study is a successful example of real-time teleophthalmology application. However, it can also be used as store-and-forward application depending on agreement of involved clinics.

Traditional concept of teleophthalmology is to have a person in remote area who acquires and transmits images to a reading center. A decision is then made at reading center whether the patient needs to be referred for detailed ophthalmic examination. Automated imaging systems in screening large populations at risk for blinding diseases have also been used. They use evaluation algorithms such as pattern recognition or machine learning classifiers to perform primary triage of eye condition.[22-24] This may eliminate the need and workload for reading centers and can be used to directly referred the patient to an ophthalmologist or retina specialist. Retinal telephotocoagulation, as presented here, is a therapeutic rather than diagnostic application of teleophthalmology where an external expert transmits treatment plans to local practitioners for patients in remote areas.

We believe that retinal telephotocoagulation can have broad applications in both patient care and clinical research where central reading (planning) centers can standardize laser photocoagulation across all participating sites. All treatments in this cohort were safe and clinical outcomes comparable to previous reports.[25] Previous studies including randomized clinical trials have shown dramatic inter-operator variability in conventional laser photocoagulation, which might have impacted comparison to other treatments such as intravitreal pharmacotherapy.[26] It is also possible that retinal tele-navigation could be useful in vitreoretinal and robotic surgery where image-based navigation information guides surgical treatments.

In summary, we introduce the concept of retinal telephotocoagulation. To the best of our knowledge, this is the first study using telemedicine-based therapeutical rather than diagnostic approach in ophthalmology. This study demonstrates the feasibility and safety of using telemedicine to perform navigated retinal laser treatments regardless of geographical distance.

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Conflict of Interest: MW is an employee of OD-OS, GmbH. All other authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all individual participants included in the study.

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Figure Legends

Figure 1. **A.** Image of treatment plan (blue dots) on fundus fluorescein angiogram in an eye with diabetic macular edema. **B.** Post-treatment color fundus image showing hard exudates (yellow) and laser burns (blue circles). **C.** Spectral-domain optical coherence tomography B-scan before laser treatment demonstrates hard exudates (intraretinal hyper-reflective bodies) and macular edema. **D.** Spectral-domain optical coherence tomography B-scan following laser treatment demonstrates reduction in both hard exudates and the amount of macular edema.

Figure 2. **A.** Image of treatment plan (blue dots) on fundus fluorescein angiogram in an eye with diabetic macular edema. **B.** Post-treatment color fundus image showing hard exudates (yellow) and laser burns (blue circles). **C.** Spectral-domain optical coherence tomography B-scan before laser treatment demonstrates hard exudates (intraretinal hyper-reflective bodies) and foveal cyst/macular edema. **D.** Spectral-domain optical coherence tomography B-scan following laser treatment demonstrates reduction in both hard exudates and the amount of macular edema.

Table 1: Baseline demographics as well as visual acuity and anatomic outcomes of subjects treated with teleretinal photocoagulation for diabetic macular edema.

Study Eye	Age (yrs)	Duration of DM (yrs)	Treatment Plan (Focal/Grid)	Baseline BCVA	Follow-up BCVA	Baseline CRT (µm)	Follow-up CRT (µm)
1	49	5	Grid	0.22	0.22	243	239
2	55	7	Grid	0.3	0.3	267	242
3	56	4	Focal/Grid	0.3	0.22	275	251
4	62	13	Focal/Grid	0.8	0.7	415	330
5	46	6	Focal	0.3	0.3	255	257
6	63	17	Grid	0.92	0.7	445	312
7	56	13	Focal	0.7	0.6	303	290
8	67	26	Focal/Grid	0.6	0.6	296	290
9	53	11	Focal/Grid	0.4	0.3	277	265
10	56	12	Focal	0.6	0.6	323	289
11	51	8	Focal/Grid	0.3	0.3	256	240

12	60	16	Focal/Grid	0.6	0.7	268	288
13	52	7	Focal	0.4	0.4	260	241
14	49	6	Focal/Grid	0.22	0.22	221	224
15	57	14	Grid	0.6	0.5	278	256
16	53	14	Focal/Grid	0.6	0.6	302	279

BCVA: Best corrected visual acuity; CRT: Central retinal thickness; DM: Diabetes mellitus; yrs: Years; µm: Microns