New technologies in diabetic retinopathy.

Chapter · January 2016

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New technologies in diabetic retinopathy

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In 2013, 382 million people around the world were diagnosed with diabetes. It is estimated that this number will most likely increase three fold until 2035. Over 60% of people with type 2 diabetes and almost all patients with type 1 diabetes will develop diabetic retinopathy within 20 years of diagnosing the disease. Diabetic retinopathy is still the major cause of blindness and worsening vision all over the world, and is associated with significant costs for healthcare system and society. This happens despite the fact that diabetic retinopathy can be completely prevented through primary prevention, related to strict control of metabolic risk factors or prevention through early detection and treatment of early retinal lesions. However, the cooperation between the general practitioner, diabetologist and ophthalmologist is not always appropriate in terms of providing care for a diabetic patient. In industrial areas, where ophthalmologist availability is high, approximately 40-50% of patients do not report for recommended annual ophthalmic examinations. This largely results from the lack of knowledge and non-adherence to recommendations [1].

The gold standard in ophthalmology for diabetic patients, according to Early Treatment Diabetic Retinopathy Study (ETDRS) recommendations, is to perform 7-field stereoscopic 30° fluorescein angiography of the eye fundus, performed by trained personnel, both in terms of examination technique and result analysis. Digital photography in pharmacological mydriasis conditions seems to be a more practical, faster and easier alternative to screening the eye fundus lesions [2]. A report prepared by American Academy of Ophthalmology showed that single-field eye fundus photography may serve as the appropriate examina-

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Telemedicine is a solution for screening tests in the case of retinopathy in diabetic patients treated by general practitioners and at diabetology outpatient clinics. A trained technician taking a digital photo of the eye fundus in diabetic patients and sending the images using electronic methods to reference center means that the percentage of detected patients with proliferative diabetic retinopathy has increased to about 80% [4,5]. The European Union financed the TOSCA program concerning digital screening tests in a few European countries (Germany, Denmark, Great Britain, Ireland) [6]. Pilot studies in different countries such as India and Peru, have also confirmed the reliability of digital screening test techniques in ophthalmology [7,8]. The market for telemedicine products and technologies is currently making continuous progress in terms of generating new systemic solutions, applications and diagnostic devices.

IRIS Okulistyka Software

IRIS Okulistyka (Ophthalmology) is a professional computer software for medical data and image archiving, creating a patient registry. IRIS Okulistyka software is meant for registering patient visits and examinations. It has an advanced database in which it is possible to store all results and diagnoses, view medical histories, register and archive images (e.g., from a slit lamp) and digital video sequences (e.g., from a surgical microscope) in a simple way. Moreover, IRIS Okulistyka software allows to take planimetric measurements, print and record (on a CD/DVD) reports from visits, and search the database using selected criteria. Medical data stored in the software can also be used in presentations and scientific publications (Fig. 1).

Fig. 1. Visualization of IRIS software's operating screen
IRIS Okulistyka software can register and save an image from any diagnostic device equipped with standard signal input (GDX, tonometer, auto refractometer) or equipped with an optic path with a camcorder/digital camera (e.g., slit lamp, microscope, fundus camera). IRIS Okulistyka software will automatically archive data on a chosen storage device, protecting it from data loss. This will save the system from lack of storage space on the hard drive, and will allow the user to store his/her work results on external storage devices.

**Angio-OCT**

OCT devices are commonly available in everyday ophthalmic practice and are the most ordered examinations in macular disease diagnostics. Conventional OCT allows detailed assessment of retinal structure, whereas fluorescein angiography (AF) has been the 'gold standard' in assessment of retinal circulation for 50 years. The introduction of OCT-based angiography in the autumn of 2014 (OCT angiography – Angio-OCT, OCTA) is considered to be the next milestone in ophthalmic diagnostics. Angio-OCT is the latest method allowing for visualizing the blood flow in retinal vessels and choriocapillaries without using a contrast agent.

SSADA (Split Spectrum Amplitude Decorrelation Angiography) is the base of Angio-OCT, identifying the retinal vessels through detection and measurement of blood cell movement in the vessels. It allows for distinguishing solid tissue from blood flow. OCTA allows for assessment of the histologic vascular structure of the retina. The blood flow is visible in the superficial vessel plexus, deep vessel plexus, at the external retinal layers' level and in the choriocapillaries. All these layers are visible simultaneously, but they can be analyzed separately, which is not possible in the case of AF (Fig. 2).

Superficial plexus is constituted by large and medium vessels, visible through an ophthalmoscope in the nerve fiber layer. Their branches form juxtafoveal, regular networks around the additional foveal avascular zone (FAZ). The deep plexus is formed by vessels located in the internal part of the inner nuclear layer.
and the external part of the external plexiform layer, visible as a single vascular plexus and creating the so-called **internal-external** complex. This thick network of vessels contains numerous horizontal and vertical connections which become congested in the FAZ area. In both plexuses, the normal vessels are characterized by a constant thickness and homogeneous signal. The external retina in a healthy eye is avascular, therefore this layer is most frequently visible as a homogeneous, dark background (no flow). The vessels in this layer can be observed only in pathologic conditions, such as neovascular membrane.

Contrary to AF, which is a dynamic method (contrast agent flow results in image differing depending on examination duration), Angio-OCT is a static method – flow in the vessels is visualized at any given time. Angio-OCT is part of a routine OCT examination. Thanks to using Angio-OCT, one can obtain three-dimensional images; in the case of AF this is impossible. The limitations of this method are the same as in standard OCT: lack of translucency obstructs a precise assessment of the retinal circumference. It is currently possible to use scans with the dimensions of 3x3 and 6x6. With good patient cooperation and appropriate fixation, it is possible to assess the average retinal circumference. Angio-OCT is an examination that includes both angiography and high-resolution OCT. It allows for early detection of pathologies within the vessels at different retinal levels. Moreover, it is a non-invasive examination, it can be safely repeated several times, and the short measurement time favors its use in patients with lower cooperation levels as well as in children.

**RETeval**

A device for performing screening electrophysiologic examination in patients with diabetes. RETeval performs electroretinographic measurements with flashing stimulation with a frequency of 30 Hz. A skin electrode and manual mea-
susement camera are used when performing the examination (Fig. 3). RETeval's advantages include: faster examination time in both eyes – about 3 minutes, no need to use pharmacological mydriasis, obtaining reliable measurements with cloudy lenses, easy use and non-invasiveness.

Traditional cameras for eye fundus photography are expensive, difficult to use, large and stationary. Contrary to that, the smartphones now available are inexpensive, easy to use and compatible with different Internet platforms and operating systems which makes them perfect for use in screening examinations in telemedicine. Since 2010, there are more and more market-available possibilities for using smartphones for both photographing and documenting the eye fundus images, while using various adapters and functional eye examination using appropriate applications.

**iExaminer**

A form of ophthalmoscope attached to an iPhone, it allows for performing complete eye fundus imaging and saving images. With no pharmacologic mydriasis, one can obtain an image with 25 degrees of view field. The small area of the obtained image is a definite disadvantage of this technique (Fig.4).

![iExaminer adapter and obtained photo of the eye fundus](image)

**D-EYE**

S14, an Italian and American research and development laboratory, developed D-EYE – an innovative smartphone accessory – as an inexpensive replacement for the traditional ophthalmoscope. The mobile camera for the eye fundus
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examination, together with the appropriate D-EYE Care application operating on Android and iOS systems, is compatible with the Apple iPhone 5/5s/6 and Samsung Galaxy S4/S5 smartphones. D-EYE allows for taking photographs and recording videos of the eye fundus in HD quality. The attachment's ease of use provides a clear image of the anterior and the posterior eye segment, allowing qualified medical personnel to conduct diagnostic examinations and perform assessment of various eye diseases, such as diabetic retinopathy, glaucoma and cataract.

According to the inventors and creators from S14, D-EYE, together with the application, allows for:

- easy and ergonomic diagnostics of seriously ill patients, children and infants;
- problem-free observation of the optic nerve disc (even without pupil-dilating drops) in order to diagnose glaucoma;
- diagnostics and assessment of cataract progress;
- examination of the age-related macular degeneration (AMD);
- diagnostics and assessment of diabetic retinopathy stage;
- diagnostics and assessment of hypertensive retinopathy stage;
- detection of neurological disorders, blood vessels' malformations, presence of retinopathy or maculopathy symptoms (retinal edema, cotton wool spots, effusions) and other eye diseases (Fig.5).

Fig. 5 Adapter and obtained photos [11]
Peek Retina (Portable Eye Examination Kit)

An adapter attached to the smartphone's camera, allowing for performing a retinal examination under any conditions. The device has a small size, hence it is easy to fit in a pocket, and can be installed on a smartphone at any time to change it into a functional ophthalmoscope (Fig.6).

The hardware operation is based mainly on taking a photo of the patient's eye. Next, by using special software, it is subjected to processing, allowing for diagnosing e.g., cataract, glaucoma and other eye diseases. Over the last two years Peek Retina was tested in Kenya and other parts of the world, and it has also passed clinical trials which have confirmed the device's reliability.

Eye examination system called Peek is a mobile application and a special hardware accessory, changing an Android smartphone into a mobile examination and diagnostics center. This solutions contains many useful functions, one of which includes geotagging, making patient localization easier; however, it is not the main part of the set. The device can be used to perform a basic eye examination: vision acuity, visual field, sensitivity to contrast, color vision, cataract examinations, visualization of the retina and classification of vision acuity. In addition, there is on-going further development aimed at improving the solution by adding additional applications for extended examinations. The project is based in London, and the application and smartphone accessory testing are conducted in Kenya. It is also the location of preparations to adapt the idea to local conditions.
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Fig. 6. Peek Retina [12]
By using the capabilities of mobile device, such as smartphones and tablets, both the patient and physician can make use of better information access, easier communication and faster diagnostics. Online application stores contain numerous free and paid applications for unaided examination of vision acuity, color vision, Amsler test and contrast sensitivity. Some examples include: Badanie oczu (‘Eye Exam’), Eye Handbook, Eye Trainer Pro, EyeChart (Dok LLC, Austin, TX), and EyeChart RandomEyes (Dok LLC).

**SightBook App.**

DigiSight Technologies developed and application for Apple Inc. software which provides patients and physicians with the quick and reliable ability to perform functional eye screening, through near and far visual acuity, color and contrast vision, and Amsler test (Fig. 7). The patient can also define the sequence of tests on their own and set regular time intervals. The results are displayed instantly and saved on the device. By logging into the DigiSight network, both the patient and physician can create a virtual patient report with the vision test results and appointment dates for checkups at the ophthalmologist’s office. The application also allows for exchange of specific information between physicians treating a particular patient, e.g., diabetologist, ophthalmologist, endocrinologist.

By observing the enormous progress over the last few years, in terms of improving and simplifying the patient examination techniques concerning diagnostic devices, software, as well as applications, it can be assumed that when it comes to diabetic retinopathy screening, telemedicine will gain even more enthusiasts and it will result in reducing the number of patients with undiagnosed diabetic retinopathy.

![Fig. 7. SightBook](Visualization 13)
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