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HISTORY OF SONOGRAPHY IN OPHTHALMOLOGY

ABSTRACT

Since first reports in 1949, the application of sonography have been expanded in medicine and ophthalmology.Starting from A-mode ultrasound used for differential diagnosis of retinal detachment and choroidal melanoma, to advanced corneal epithelial thickness measurement using Very High Frequency enabling more accurate outcome for refractive surgery. In our paper we describe a historical development of ultrasound technique as a diagnostic tool in ophthalmology. We conducted database research, using Pubmed and Google Scholar. As a result we present historical beginnings and current interests in ophthalmic ultrasound.

KEYWORDS: ultrasound, ultrasound biomicroscopy, very high frequency ultrasound, clinical applications, ophthalmology

Ultrasounds are defined as acoustic oscillations distributed in a medium with frequency higher than 20 KHz, that are inaudible for humans [1]. First reports considering use of ultrasound in medicine are from 1949 and consider use of reflectoscope, an apparatus generating frequencies between 1-2.5 MHz for assessment of the quality of industrial metal . George Ludwig employed the reflectoscope for measurement the acoustic impedance of gallstones, by comparing them to human muscle tissue and beef tissue. He defined impedance as a product of density and velocity of sound in the substance. The differences between different tissue impedances allowed for differentiation between gallstone and muscle tissue. Additionally the author concluded that wavelength should not exceed the diameter of a visualized object [2]. In 1951, John Wild and John Reid built the first B-mode scanner [3]. In 1956 Henry Mundt described the first application of ultrasound in distinguishing between retinal detachment and choroidal melanoma in humans. Studies performed before on calves' eyes using different parameters of ultrasound machines resulted in secondary cataracts after 20 minutes exposure [4]. Before performing exams on patients, authors examined pigs eyes in order to determine output signal and complications. Using reflectoscope authors were able to differentiate between retinal detachment and choroidal melanoma, the two diagnoses that appear similar in clinical examination, however differ significantly in treatment and prognosis [5]. Higher frequency transducers provide finer resolution of more superficial structures, whereas lower frequency transducers provide greater depth of penetration with less resolution. Nowadays ophthalmic ultrasound is particularly useful when the visual pathway is unclear, due to corneal opacities, cataracts or vitreous hemorrhage (image 1). It provides a cheaper, faster and complications-free alternative to other imaging methods such as CT or MRI. Current indications for ophthalmic ultrasound have been summarized in table 1[6].

In our paper we present historical and modern aspects of application ultrasound in ophthalmology. As per methodology, we searched Pubmed and Google Scholar using keywords: ophthalmic ultrasound, ultrasound ophthalmology, b presentation ultrasound ophthalmology, a presentation ophthalmology. We cite newest articles as well as historically significant papers.

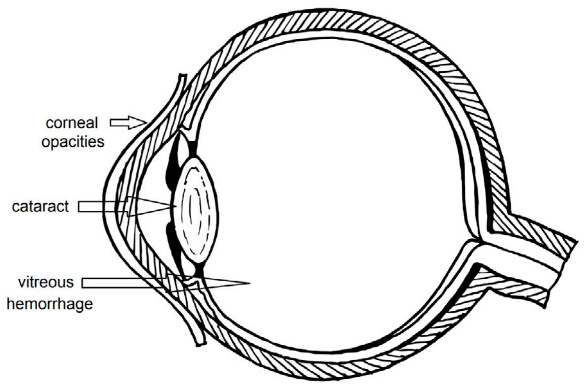

Image 1. Causes of unclear visual pathway

An A-mode (amplitude) is a two-dimensional method of presenting the acquired signal in time. Ultrasound probe generates acoustic waves that are reflected back to the probe, then the signal is plotted on screen as a function of depth. The first applications of ultrasound in ophthalmology in 1956 used that mode for diagnosing choroidal melanoma. The output was a linear chart with waves that correspond to the distribution of acoustic waves passing through consecutive parts of the eyeball (image 2). Authors also made an observation that the length of the record depends on the length of the eyeball and is significantly shorter

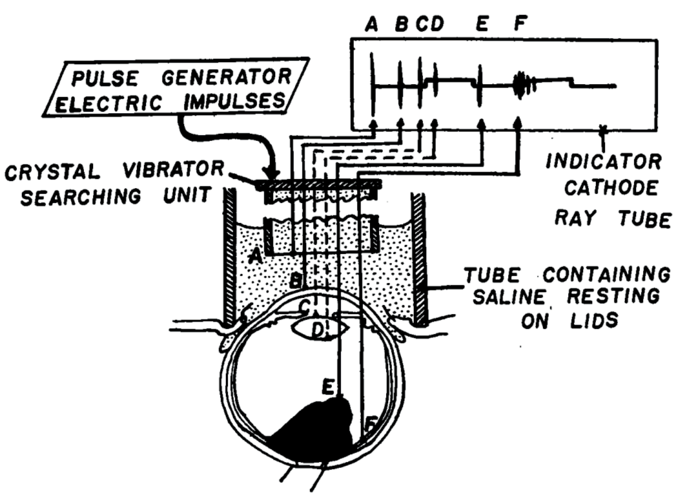

Image 2. Interpretation of a-mode ultrasound in relation to the eye

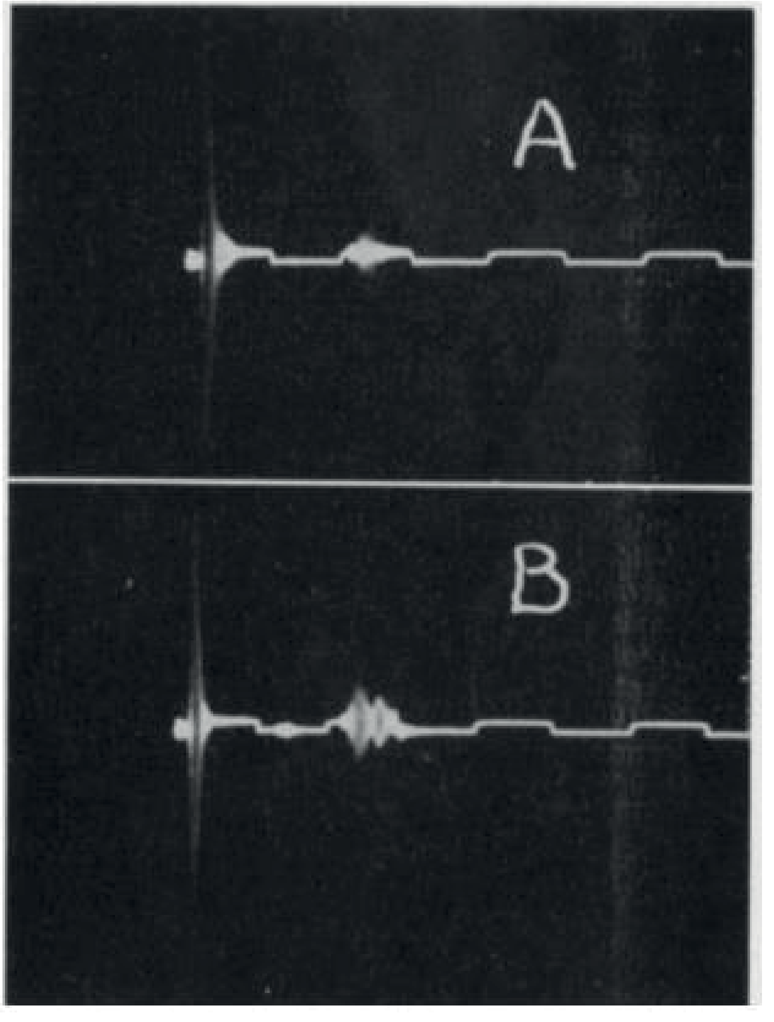

Image 3. A-mode scan of healthy eye (A), a-mode scan of eye with retinal detachment, scans are similar

in children with microphthalmos (congenital small eyeball), also the posterior pole tumor creates bigger reflection in the A-mode scan when the probe is directly above the tumor. They proved that A-mode ultrasound is a suitable method for qualitative differential diagnosis of retinal detachment and choroidal melanoma. (image 4). Limitations of that method were uncomfortable patients' position - an eye had to be immersed in saline solution, long exposure time and inability to demonstrate differences between tumor and subretinal hemorrhage [5]. The ultrasound

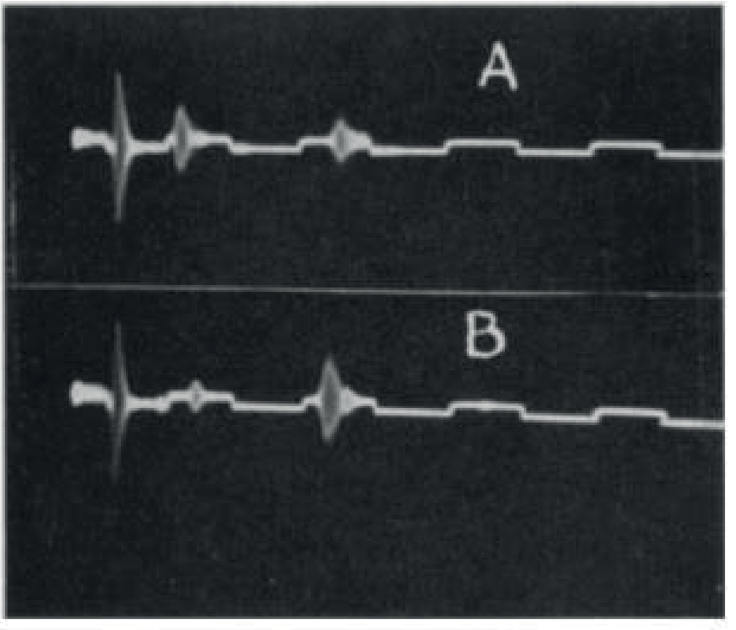

Image 4. A-mode scan of a healthy eye (A), a-mode scan of an eye with melanoma, posterior reflection is stronger (B)

projection A machine was presented in Boston in 1972 and it used a 10 MHz head. The camera was handheld and could be held directly to the eye. The device allowed to obtain images with a resolution of 0.3 mm. [7]

The A-mode ultrasound was also used in quantitative measurement of axial length, lens thickness and vitreous chamber depth. The velocity of ultrasound in temperature of 37 degrees Celsius was found to be 1536 m/s in artificial aqueous humor and 1532 m/s in the vitreous [8, 9]. Knowing the distance between two waves in ultrasound transcript (image 5) – one from the cornea and other from the lens – the depth of the anterior chamber can be calculated. For practical reasons, the velocity in the anterior chamber and vitreous have been approximated to 1532 m/s. The ratio of the distance traveled by ultrasound in one medium (a1) to that in another medium (a2) is the same as the ratio of the velocity in the first medium (V1)to that in the other medium (V2) when the passing time is the same in both. The formula is:

$$a1/a2 = v1/v2$$

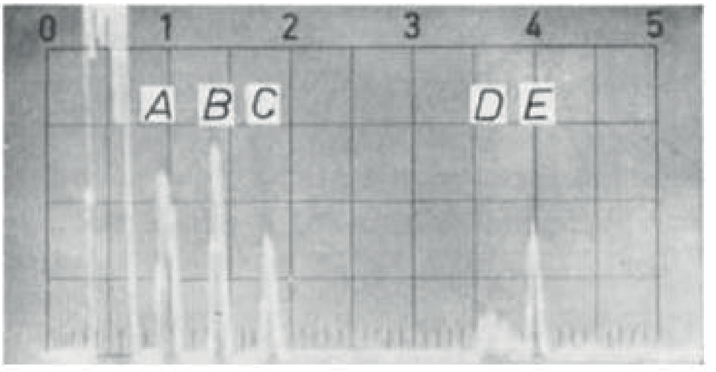

Image 5. A-mode scan A - anterior corneal surface, B - anterior lens surface, C- posterior lens surface, D - posterior wall, E- interferometer

The passing time between cornea and anterior lens surface is the same as the passing in the distance of water (d1) between echo A and B in the ultrasound transcript. The velocity of ultrasound in water in temperature = t is 1557 - 0.0245 $(74 - t)^2$, so the formula for the depth of the anterior chamber (d2) is

anterior chamber depth = $1532 * \mathrm{d1}/1557 - 0.0245(74 - \mathrm{t})^2$

When that formula was created, the anterior chamber depth could be alternatively assessed with an optical apparatus manufactured by AB Visus, Gothenburg, Sweden using Stenstrom's method [10], authors of the study obtained similar results from both methods. In order to determine lens thickness one needs to determine the velocity of ultrasound in healthy lenses, it was tested to be 1641 m/s [8,9]. The formula for the lens thickness is

lens thickness = $1641 * \mathrm{d2}/1557 - 0.0245(74 - \mathrm{t})^2$

where d2 is the distance of water between the interference position of echo B and echo C. Similarly, the velocity of ultrasound in vitreous chamber was determined 1532 m/s in temperature +37 degrees Celsius [7,8] and the apparent position of vitreous was defined as the distance between echo C and D (d3)

length of the vitreous = $1532 * \mathrm{d3}/1557 - 0.0245(74 - \mathrm{t})^2$

The average anterior chamber depth in the age group 40-49 years old was 3,58 mm for men and 3,45 mm for women and the number decreased with age. Results were similar to those acquired by optical device. The lens thickness in the age group 40-49 years old was 4,189 mm for men and 4,098 mm for women and the number increased with age. The vitreous chamber length in the age group 40-49 years old was 15,79 mm for men and 15,38 for women and the number decreased with age. The axial length was calculated as the sum of the values above and corneal thickness as well and totalled 24,00 mm for men and 23,13 mm for women [11]. Similar results were reported by Stenstrom in 1946, he determined using roentgen rays that axial length was 24,04 mm for men and 23,89 mm for women. Additionally in the study the correlation between axial length and refraction was found: subjects with longer eyeballs were myopic and those with shorter eyeballs were hypermetropic [12]. Similar finding was reported by Franken in 1961 using the ultrasound (image 6) [11, 13]. Knowledge of the length of those structures allows for calculating the power of the intraocular lens implanted into the eye during cataract surgery. Nowadays A-mode ultrasound in applanation technique has been declared safe and is still used

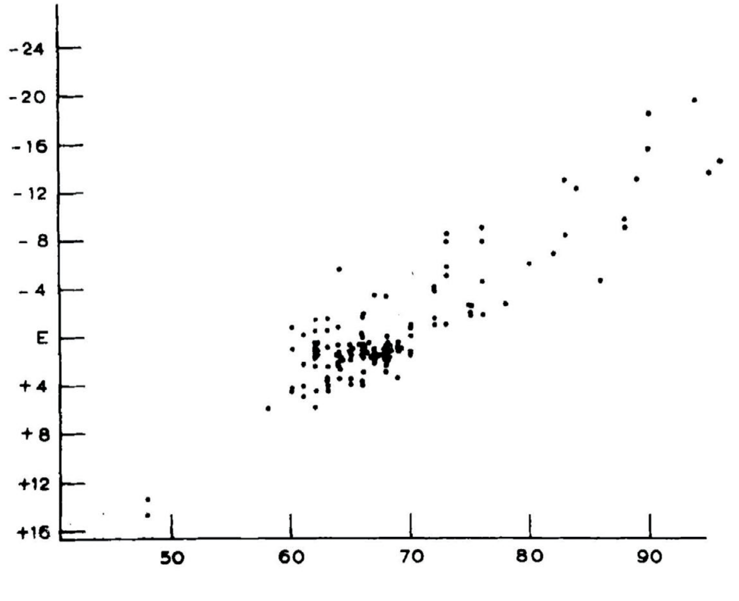

Image 6. Correlation between length of optic axis and refraction; x-axis: length of optic axis expressed in scale divisions; 50 = 16.7 mm, 60 = 20.0 mm, 70 = 23.3 mm, 80 = 26.7 mm, 90 = 30.0 mm; y-axis the refraction

before cataract surgery, however new techniques have been introduced [14]. Partial coherence interferometry (PCI) is an optical method of axial length measurement used in IOL Master 700 (Carl Zeiss, Jena, Germany). PCI uses a projection of 6 light spots of an infrared laser (780 nm) illuminating the cornea (projected radius of 2.3–2.5 mm) [15]. The light source separates into two beams then both of them are reflected from separated ocular interfaces at different times. If the delay of these two light beam equals an intraocular distance within the coherence length of the light source, an interference signal (called partial coherence interferometry signal) is detected, similar to that of ultrasound A- scan, but with a very high resolution (approximately 12 um) and precision (0.3 to 10 um) (image 7). In biometry, PCI based measurements resulted in fever refractive errors compared to ultrasound (applanation) biometry, however it cannot be used in patients with dense cataracts, or with motor disabilities such as tremor [16]. Optical low coherence reflectometry (OLCR) is another optical technique used in apparatus LENSTAR LS900 (Haag-Streit, Bern, Switzerland). It uses a superluminescent diode (wavelength: 845 nm, coherence length: ~30 μm) to mea-

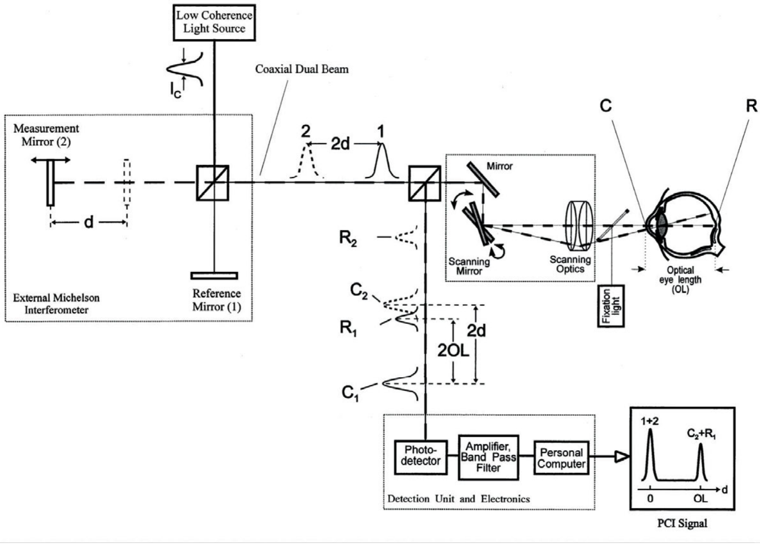

Image 7. Sketch of the partial coherence interferometer. The eye is illuminated by the interferometer, then reflected signals, for example C1, C2, R1, and R2, are superimposed on and detected by a photodetector.

sure coherence of the light source [17]. In comparison to applanation biometry OLCR is similar to PCI and it produces more accurate results, however it has the same limitations as PCI – when the cataract is dense the beam of light cannot penetrate through the tissue, hence there is no result. When comparing listed methods of measurement the axial length, the smallest magnitude of mean and SD of difference in AL (0. 01 mm±0.03 mm) was in the IOLMaster-LENSTAR comparison, followed by the LENSTAR-applanation comparison (0.18 mm±0.23 mm; −0.52 D±0.93 D). It means that PCI and OLCR offer the resolution 10 times better that A-mode ultrasound biometry (10 micron vs 100 micron), nevertheless due to the limitations of optical methods there are still some indications for A-mode biometry, such as dense cataract, lack of cooperation with the patient or general diseases such as parkinson disease or tremor in general.

Presentation B enables two-dimensional imaging of the posterior segment of the eye, and therefore allows the detection of bleeding into the vitreous chamber, retinal detachment, and intraocular tumors. Since ophthalmic examination is based on visual structural assessment in direct examination,during a vitreous hemorrhage visual inspection of the fundus is not possible. Ultrasound allows to differentiate between fresh haemorrhages and old lesions, also to assess the degree of blood absorption.

In B-view ultrasound, the presence of tears, detachments, or clinically insignificant retinal dissections can be detected. The detachment itself can only be diagnosed by an experienced ultrasound specialist in the A projection – however, it is not used in clinical practice. Ultrasound examination in a patient with a retinal detachment allows to plan the scope of the operation and the location of possible scleral support, which is a surgical technique used in retinal detachment. It allows to assess the safety of vitrectomy – vitreous removal. [18] The diagnosis of subretinal bleeding is largely based on ultrasound. It enables to assess the coexistence of a retinal tear at an early stage, requiring lasering. The ultrasound determines further treatment. [19] Nowadays, ultrasound examination in B presentation allows for the diagnosis of vitreous haemorrhage [20] and retinal detachment with high sensitivity and specificity. [21]

Projection B combined with the measurements made in the A projection and subjected to their evaluation based on a predefined algorithm allows for the improvement of the efficiency of the diagnosis of eye cancerous tumors. [22] In some cases, ultrasound is more useful than other imaging methods, such as MRI, in diagnosing tumor infiltration of surrounding tissue. [23] Projection B is not free from limitations. The higher the resolution (frequency), the shallower the signal penetration [21]. In a general sense, a useful ultrasound machine is one allowing to image structures as large as 1 mm to a depth of about 150 mm. Ultrasound travels through the tissues at a speed of about 1500 m/s. [24] Wavelength is one of the factors that determine the final resolution of the image generated by an ultrasound scanner. The depth of the imaging depends on the signal frequency used. Signals with a frequency of 10 MHz can penetrate to a depth of 50 mm, and signals with a frequency of 60 MHz to about 5 mm. Unfortunately, the opposite is true with the resolution of the image obtained. Higher frequency waves give a higher resolution image, but allow for shallower structures to be imaged. [25] This is reflected in practice. Ultrabiomicroscopy uses high-frequency waves to obtain high-resolution images. In the case of an ophthalmic examination, it is used to assess the angle of infiltration, the depth of the anterior chamber or the condition of the ligamentous apparatus [26]. The ideal ultrasound transducer features a high-performance transmitter and a highly sensitive receiver. Its acoustic impedance is similar to that of the human body. Currently, the heads use synthetic ferroelectric ceramic zirconate titanate (PZT) as an ideal material for the construction of the transducer [26]. Tissues absorb ultrasound according to the 0.2-0.5 dB per cm per MHz rule. The attenuation increases with increasing frequency and distance. For some time, the sensitivity of the head is too low to effectively receive and analyze the signal – it does not penetrate the background echo [24].

An interesting issue is ultrasonic computed tomography, which uses ultrasound to obtain transverse scans and then merge them into a three-dimensional image. The expectations regarding this technology are high. The first studies, however, do not show promising results.

Due to the problem of deflection of sound waves on heterogeneous tissue, the image produced on the basis of the scans differs significantly from the real one. [27] In the case of an ophthalmological examination, the lack of hard bone structures obscuring the viewed image may give hope for the development of this technology and its use in the future in ophthalmic diagnostics.

The highest frequency of ultrasound in medicine in general is used for imaging the anterior segment of the eye. The ultrasound biomicroscopy (UBM) is a contact, non-invasive method that requires topical anesthesia and uses frequencies from 35 to 60 MHz. It was first described in 1992 by Pavlin et al [28]; authors used 50–100 MHz transducers that produced 4 x 4 mm filled within 4 mm depth with 512 images lines at scan rate 5 frames per second. The probe was immersed in a cup that was placed on the cornea and was filled with methylcellulose solution. The used value for the speed of sound in ocular media was 1540 m/s. Average anterior chamber depth was 3,128 ± 0,372 mm. Contrary to the A-mode measurement the distance was obtained from the posterior surface of the cornea to the lens surface [image 8], hence the results were more accurate. Since the study was designed to assess the capabilities of new diagnostic methods, the study group was relatively small (9 subjects), so the

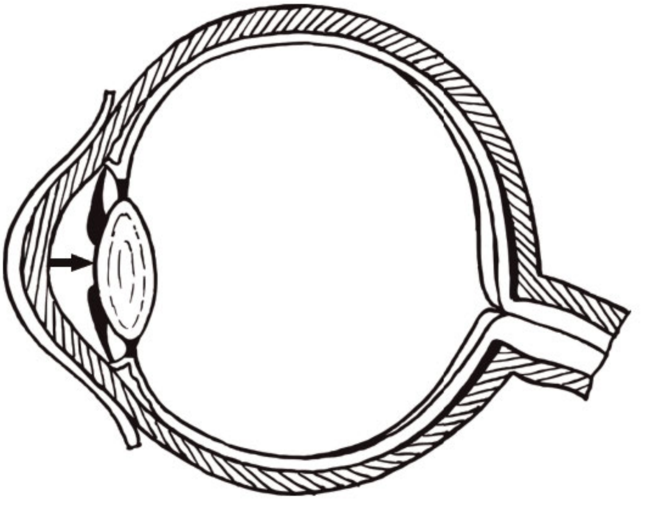

Image 8. Anterior chamber depth

authors did not observe narrowing the anterior chamber with age. UBM also for quantitative measurement of iridocorneal angle, the structure that can be visually examined via gonioscopy exam. The gonioscopy is the gold standard for iridocorneal angle examination, however it is a qualitative method that requires patient cooperation. Using ultrasound the angle (θ1) was measured with the apex in the iris recess and the arms of the angle passing through a point on the trabecular meshwork 500 um from the scleral spur and the point on the iris perpendicularly opposite [image 9]. UBM can be used in evaluation of iridocorneal angle, especially when rubeosis iridis is observed. In this condition new pathological blood vessels are formed on the surface of the iris as well as in the filtration angle, causing block and spike in intraocular pressure [image 10]. Other pathology visualized by UBM is angle recession, the implication of ocular trauma [image 11] [29]. Modern units operate at frequency of 50 MHz and obtain a resolution between 25 and 50 um, with tissue penetration 4-5 mm. Nowadays the technique is used for assessment of the iridocorneal angle, before a cataract surgery or when diagnosing nodules of the iris. When assessing the width of iridocorneal angle it is a golden standard for patients that do not cooperate during gonioscopy exam. Narrowing of the iridocorneal

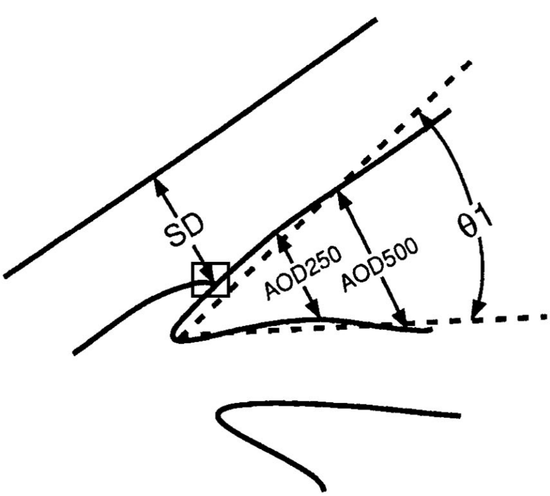

Image 9. Iridocorneal angle (θ1) measurement made from ultrabiomicroscopy imaging, ▫ - scleral spur

Image 10. Anterior synechiae — visual representation of blood vessels forming in iridotrabecular angle

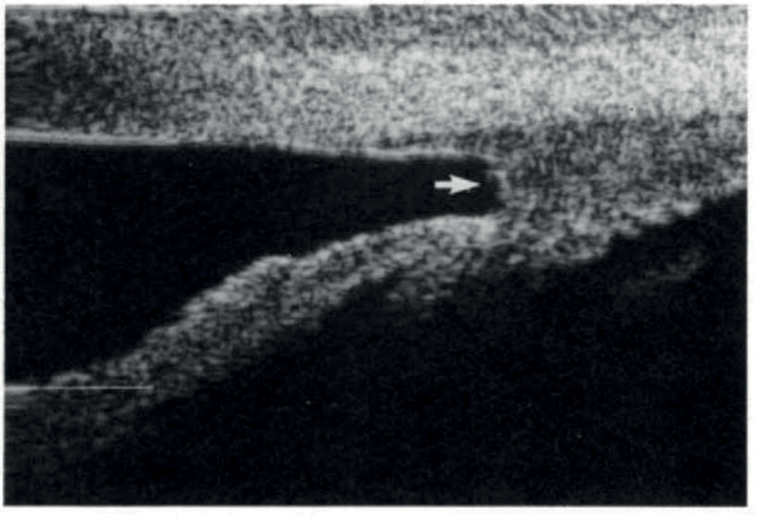

Image 11 Angle recession - loss of continuity of ciliary body post-trauma

angle can cause angle closure glaucoma [image 12] Scleral spur position is used as a marking point because it is easily distinguished from iridocorneal angle's anatomy repetitively. The evaluation of Zinn ligaments, the structures that hold the eye's lens in position, is essential before cataract surgery among patients who experienced head trauma in the past [30,31, 32]. If the ligaments are elongated or torn, there is higher risk of lens luxation

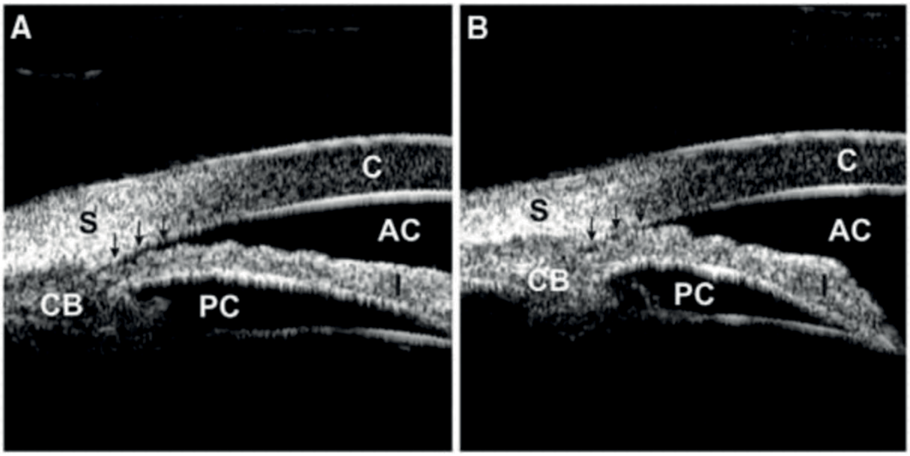

Image 12. Narrowing of the iridocorneal angle in a provocative test in the dark, s-sclera, C - cornea, CB - cillary body, AC - anterior chamber, PC - posterior chamber. Arrows mark iridocorneal angle that narrows in dim lighting

during the procedure (image 13, image 14). Patients with subluxed lens require experienced surgeon or different implantation technique. UBM is useful also in differentiating solid from cystic lesions of the iris [30]

In 1993 a very-high frequency (VHF) ultrasound was introduced in corneal layers imaging. Corneal surface poses a challenge for the ultrasound imaging due to its curvature and superficial location. Conventional A-scan imaging is made from rectified echo and as each echo contains peaks and null, the obtained image has a grained structure. In contrary, the VHF uses deconvolved analytic signal (DAS) which is a representation of echo change over time, thus it produces image resolution of 49 um, enabling it to visualize and measure the epithelial thickness (image 15) [33] Modern VHF units allow to create corneal epithelial thickness map, particularly useful in post refractive

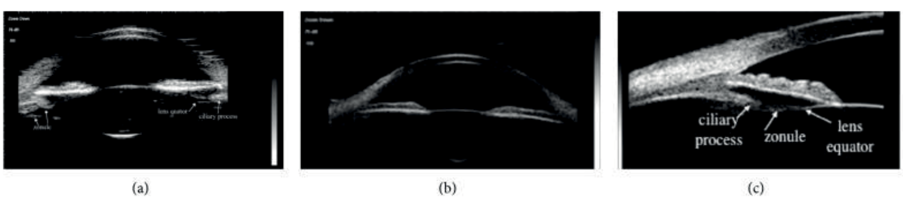

Image 13. Physiological position of the lens

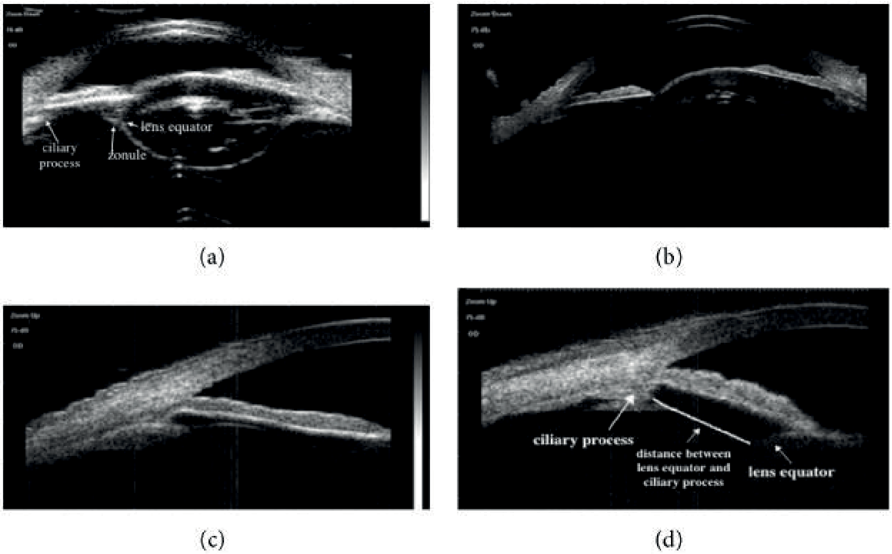

Image 14. Lens subluxation

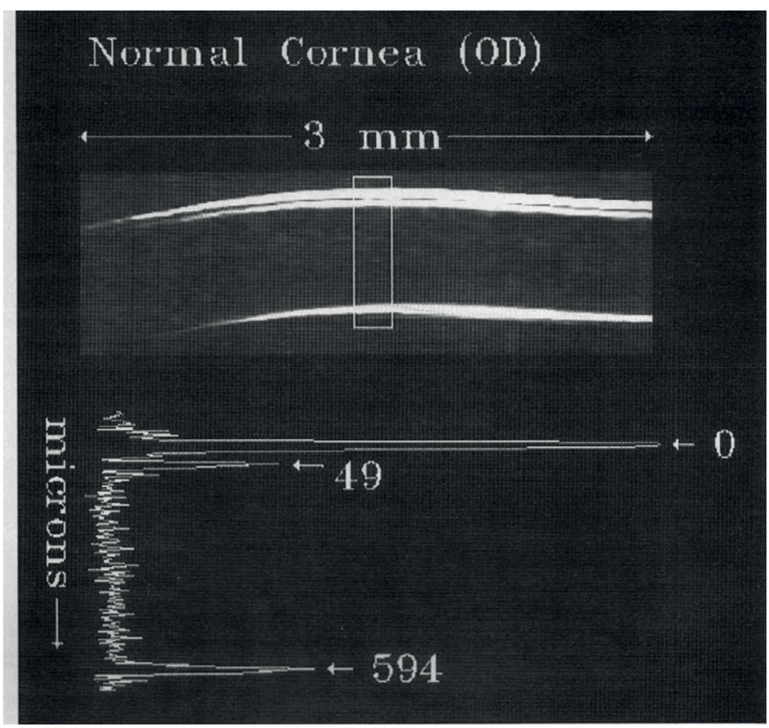

Image 15. Corneal epithelial thickness measurement using VHF

surgery observation. In superficial refractive surgery a laser beam is used in order to remodel the surface of the cornea and achieve the emmetropia, meaning the state of vision in which a faraway object at infinity is in sharp focus with the eye lens in a neutral or relaxed state (image 16) [34]. Accurate laser depth allows for stable outcomes, however abnormal thickness or distribution of epithelial thickness might interfere with the refraction, so the assessment of epithelial thickness becomes a standard procedure preoperatively. Using arc-B VHF unit for corneal epithelial mapping and pachymetry creates accurate and reproducible images [35]. When calculating ACD both UBM and VHF give similar results [36]

In summary, although sonography is a relatively dated technique and despite the introduction of new optical methods, it is still valuable in everyday diagnosis. Among the advantages are a wide imaging field, unit's mobility, real-time examination and a broad range of diagnostics that one can perform using only one unit. Despite having Optical Coherence Tomography (OCT), Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) only with ultrasound the central and peripheral retina can be examined when the visual pathway is obscured. The exam can be performed at the bedside, and is relatively safe for all patients, including pregnant women. Using different transducers allows for visualizing anterior and posterior segments of the eye. In the anterior part anterior chamber depth can be measured and iridocorneal angle assessed, especially when primary angle clo-

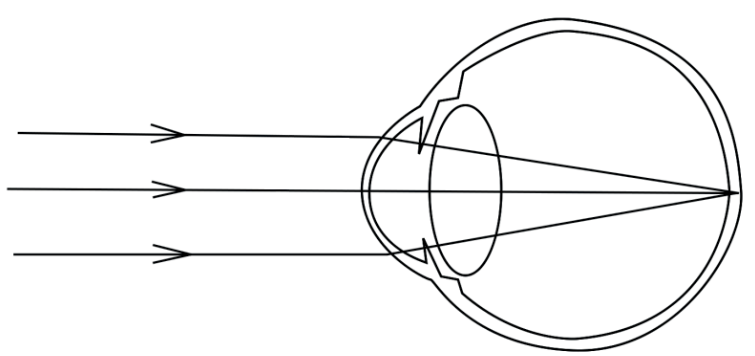

Image 16. Emmetropia, a state when light beams traveling from infinity through an eye focus on the surface of the retina

sure glaucoma is suspected. Sonogram is also used in diagnosing cancerous lesions of the iris and ciliary body. It is worth mentioning that it is the only technique allowing the examiner to visualize behind the iris. This region is unreachable for optic devices because laser beam cannot penetrate through the iris. When using a transducer for the posterior portion of the eye vitreous detachment, retinal detachment and tears and choroidal tumors such as melanoma can be detected. Among the disadvantages there is lower resolution and operator dependency, meaning that the conclusion of the exam and the description can be made only after performing it, not just by looking at obtained images.

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