БОЛЕЗНИ ХИРУРГИЧЕСКОГО ПРОФИЛЯ

MICROSTRUCTURE OF THE INNER WALL OF RETINAL ARTERIES CHANGES WITH AGE IN ANAMNESTICALY HEALTHY PERSONS*

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Arteriosclerosis involves the whole human vascular system with a somewhat patchy appearance. Although typical arteriosclerotic lesions are confined to major arteries, vessels of microcirculation are affected as well. Retinal vessels are part of the microvascular bed. They can be assessed in non invasive ways by rather simple optical methods and are similar to cerebral vessels in their structure and function. Retinal vessels are not straight tubes with a constant lumen, but rather possess narrower and wider diameters in different segments. The aim of the present work was to study functional and morphological age-related alterations in retinal vasculature as well as to determine quantitative parameters which could characterize these changes. Changes in longitudinal vessel section of retinal arterial segments were examined clinically by Retinal Vessel Analyzer (IMEDOS, Germany) in 35 anamnesticaly healthy persons at the age of 21—27 years, 40—60 years and 60—85. A monochromatic flicker of 12.5 Hz was applied for 60 s. Arterial diameters were measured in vessel segments of 1 mm in length in order to obtain the longitudinal arterial profiles. Differences in amplitude and frequency of arterial widths change were characterized by the parameter 'spectral edge frequency' (SEF). The rate of microirregularity of retinal arterial inner walls along a vessel increased significantly in anamnesticaly healthy volunteers with increasing age. SEF was significantly different between the young and senior age groups in each phase of the arterial reaction to flicker ($p < 0,05$, Mann-Whitney-Test). No significant difference within any age group was found in each phase of the arterial reaction. No significant difference between the middle age and either young or old volunteers was found at baseline. However following stimulation the middle age group displayed a significant difference to the young

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group with values resembling the old age group. It is concluded, that retinal arteries in the elderly sustain significant microstructural changes of their longitudinal profiles, which might be of either functional or irreversible nature and might be an expression of endothelial damage, the instability of vessel wall or partial degradation of smooth musculature of vessel wall.

Key words: aging, arterial structure, microcirculation, retina, arterioles, arteriosclerosis.

Arteriosclerotic changes occur in blood vessels with age even in the absence of arteriosclerotic risk factors [1]. The border between physiological aging and pathological arteriosclerosis is not well defined. Both undergo similar biochemical processes and result in similar changes in the vasculature [2].

Arteriosclerosis involves the whole vascular system in a somewhat patchy appearance. Although typical arteriosclerotic lesions are confined to large conduit arteries, vessels of microcirculation are affected differently. In arteriosclerosis endothelial function seems to be attenuated as demonstrated by altered vasodilatation to demand.

Retinal vessels are part of the microvascular bed and posses some special properties [3]. The non fenestrated endothelium creates the blood-retina barrier, similar to the blood brain barrier of cerebral vessels the difference in vessels being that retinal arteries possess no adrenergic innervations. The transparency of the optic media allows for direct observation of this microvascular bed. It also enables us to use an elegant non-invasive functional provocation of vessel dilation, namely light application to the retina. Dilation of retinal vessels can be achieved by changing the flicker illumination of the retina. This effect is called neurovascular coupling and has been studied extensively in the ophthalmic community. The most effective stimulus for the human retina consists in the application of a rectangular flicker light with a frequency of 8—20 Hz [4]. By using the Retinal Vessel Analyzer (RVA, IMEDOS Ltd., Jena) it is possible to observe retinal vessels before, during and after a defined monochromatic flicker stimulus application of 12,5 Hz for any chosen time.

Neurovascular coupling is also well known in the central nervous system (CNS). It is defined by neuronal activity evoking local change in blood flow. In the CNS neurovascular coupling has been shown to be unaffected during normal aging [5]. The effect is highly dependent on glial cell activity as has been shown in mammalian retinal mounts [6].

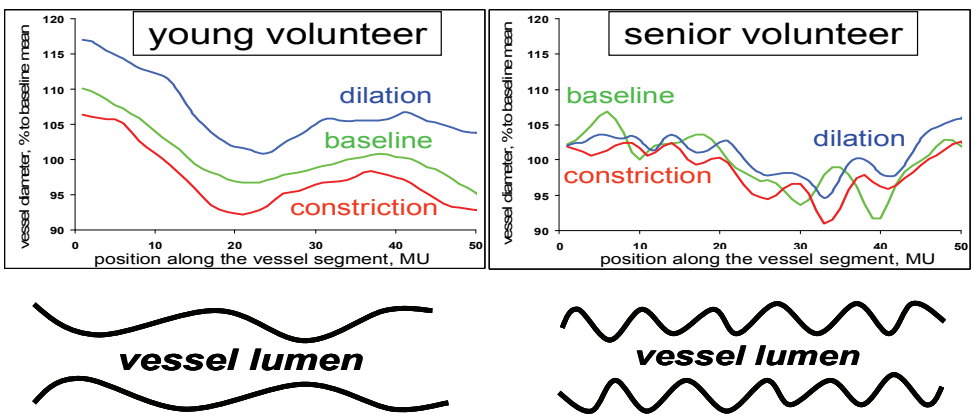


Fig. 1. Schematic illustration of our hypothesis: in healthy young persons the longitudinal profile is smoother than in healthy seniors. This effect is persistentalso if the vessel is constricting or dilating

We suppose that age induces changes in the configuration of the arterial wall of vessels of the microcirculation. Our hypothesis is that in young persons the longitudinal profile is smoother and this effect is persistent also if the vessel is constricting or dilating (Fig. 1).

In order to assess changes in microvasculature due to age, we examined healthy volunteers of different age groups and the behavior of their retinal vessels to flicker. From the obtained data of the blood column within the retinal vessels before, during and after stimulation a longitudinal vessel profile was determined and vessel wall irregularities calculated thus defining a measure for vessel wall characteristics depending on age.

Materials and methods. *Subjects*. 12 healthy volunteers according to their general practitioner in each age group of 21—27 years (5 males, 6 females, age 24,9 ± 1,9 years) and 60—85 years (4 males, 7 females, age 68,6 ± 7,6 years) as well as 11 healthy volunteers of 40—60 years (3 males, 8 females, age 50,2 ± 5,3 years) were entered into the prospective clinical study. They had not used regular medication for 3 months prior to examination.

Patients with any eye disease or the following systemic affections were excluded: acute myocardial infarction; diabetes mellitus; blood pressure higher than 150/95 mm Hg; heart disease state III and IV (NYHA). At the beginning of every test a clinical ophthalmic examination consisting of measurement of visual acuity, objective refraction, keratometry, applanation tonometry and funduscopy was carried out. We administered tropicamide eye drops to induce mydriasis.

Informed consent was obtained from the subjects after explanation of the nature and possible consequences of the study. The study design has been reviewed and approved by the ethics committee of the Medical Clinic (Klinikum rechts der Isar) of the Munich University of Technology and has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

Measurements. 20 min after pupil dilation with one drop of Mydriaticum Stulln® (Pharma Stulln Ltd, Germany) continuous measurement of retinal venous diameter was performed using the RVA. Measurements of the arterial reactions were taken later offline from video tape. Properties of RVA and its measurement principles have been described before [3]. Briefly, the device allows non-invasive on-line assessment of the vessel diameter depending on time and location along the vessel. Before, during and after provocations arterial and venous diameters can be assessed. For that purpose the RVA consists of a retinal camera (Zeiss 450 FF), a CCD-camera for electronic online imaging and a PC for system control, analyzing and recording of the obtained data.

For each examination a segment of an approximate length of 1 mm of a retinal vessel one to three disc diameters away from the optic disc was investigated. The vessel longitudinal section within the region of interest was scanned 25 times per second. The automated algorithm allows to compensate for eye movements and obtains data along the vessel over time thus creating a 3D matrix of values obtained during a functional measurement. The RVA measures vessel diameters in relative units (MU). These arbitrary units are equal to 1 micron if the measured object corresponds to the normal eye of Gullstrand.

Assessment of longitudinal vessel profiles. Temporal assessment of retinal vessel behavior in response to stimuli is the most common feature of the device already published by different authors [7]. For this feature changes in vessel segment diameter mean over time are traced by the intelligent algorithm. The obtained data however additionally allows to observe spatial changes in vessel diameter along a chosen segment and thus obtain a longitudinal profile of the vessel segment at chosen time intervals. Through this feature it is possible to assess in vivo non invasively dynamic variations in longitudinal vessel profile in humans during different states of stimulation. The method of data acquisition for local vessel analysis with RVA was explained in detail before. Differences in diameter along the vessel segment during a defined time period can be assessed. For each pixel (point of the segment) the mean of all measurements in this location during the chosen time interval is calculated. We termed the result "longitudinal vessel profile". It reflects the configuration of the vessel-blood interface in the longitudinal vessel section when assuming the vessel to be axially symmetrical (fig. 2). Profiles obtained at different time intervals can be compared.

Fig. 2. Explanation of the concept "longitudinal vessel profile": vessel diameter is continuously assessed between points A and B; vessel diameter varies at different locations forming the "longitudinal vessel profile"; the latter reflects the configuration of the vessel-blood interface in the longitudinal vessel section when assuming the vessel to be axially symmetrical

In order to describe the longitudinal profile of a vessel and its caliber changes we need to characterize the frequency in those changes. Waves along a curve (temporal or a spatial) can be defined by their frequency and amplitude. Applying these principles to the longitudinal retinal vessel profile waves of different frequency can be determined, namely high frequency waves (HFW) including waves in the longitudinal vessel profiles with 10—20 oscillations per 1 mm of the vessel segment and a magnitude between 1,5—15 μm and low frequency waves (LFW) defined as 0,2—5 oscillations per 1 mm of vessel segment and a magnitude of 15 μm — 40 μm.

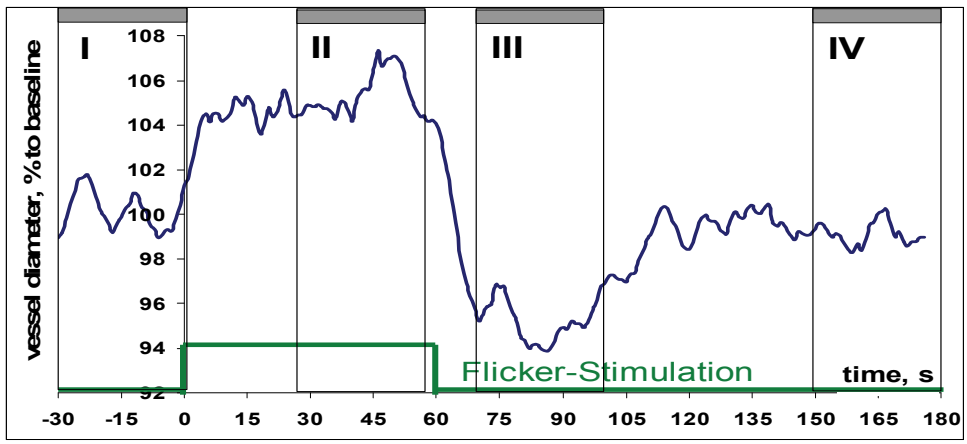
Stimulus. During examination retinal vessels were stimulated with flickering light relying on the principles of neuro-vascular coupling. This vascular stimulation and its underlying principles were described in detail previously. Briefly, an optoelectronic shutter is inserted in the retina camera in place of an additional optical filter. The shutter interrupts the observation light (530—600 nm) with irradiance at the fundus of approximately 1.96×10—4 W/cm^2 over the entire 30° visual field of the retinal camera The chosen frequency of 12,5 Hz of rectangular light interruption provides a sequence of one normal illuminated and one dark single frame at a video frequency of 25 Hz.

Measurement of the baseline vessel diameter for 100 seconds was followed by two cycles of 60 s flicker provocation and 150 s observation. Total duration of the measurements including baseline and observation between flicker provocation amounted to 9 min.

Pulse and blood pressure. During the examination time blood pressure measurements by Riva-Rocci (RR) were taken once a minute. From those data we calculated the mean systemic arterial blood pressure as: mean RR = RR diastole + 1/3*(RR systole – RR diastole) mmHg.

Data evaluation and statistical methods. Definition of observation time intervals. The time course of vessel diameter change in all subgroups was plotted. The ensuing slope of the temporal response was consistent in all subjects and corresponded to results in healthy subjects reported by other authors. This time response was not the subject of the present study. However since it represents the basis for the definition of time segments in our study design it is briefly described.

Average arterial diameter over time demonstrated a diameter increase during provocation; a reactive vessel constriction was observed after releasing the stimulus with an ensuing return to initial baseline values (fig. 3). These temporal phases were observed in all groups. Four time intervals for examination were defined as shown in fig. 3.



I — baseline (before the flicker-stimulation): 30 s
II — dilation during the provocation: 30 s (individually)
III — constriction (vessel regulatory reaction): 30 s (individually)
IV — relaxation (150—180s after start of flicker): 30 s

Fig. 3. An example of individual temporal arterial vessel reaction to flicker provocation in the measured cohort and introduction of time intervals used for longitudinal vessel profile assessment

Start of time segments II and III (fig. 3) was assigned individually. For each subject an individual time interval included the point of maximal dilation or constriction and was chosen so that changes in vessel diameter during the interval were minimal.

Longitudinal vessel profiles during selected time segments were assessed (fig. 3), at defined time intervals and compared with each other within one subject.

To characterize the longitudinal vessel profile we used Fast Fourier Transform, an algorithm to compute the Discrete Fourier transform and its inverse. DFT is widely employed in signal processing and related fields to analyze the frequencies contained in a sampled signal, which is expressed in terms of a sum of sinusoidal components [8]. DFT determines amplitude, frequency and phase of each component. One of the results

of Fast Fourier Transform application, the distribution of frequencies in the analyzed signal can be represented in form of a power spectrum.

Power spectra of longitudinal vessel profiles of all subjects in each phase of vessel reaction were obtained by Fast Fourier Transformation. Each power spectrum was reduced by dividing each value in the frequency distribution by the whole area of the power spectrum as described in detail elsewhere. For each type of spatial curves and for each age group average power spectra were derived from these reduced individual power spectra by calculation of the median value in the group for each point of frequency distribution as suggested by other authors for brain vessels [9].

The parameter Spectral Edge Frequency (SEF) was introduced and calculated for each subject for the time intervals: I. local baseline, II. dilation, III. constriction, and IV. relaxation. SEF is a quantitative parameter to describe the presence of high frequencies and to characterize high frequencies. It is derived from the power spectrum of the vessel profile, created with Fast Fourier Transformation [9]. SEF divides the whole area under the power spectrum in two non equal parts: 95% and 5%. In general high SEF-values describe a more wavy curve (higher sinus frequency) and accordingly for low values. SEF may reflect variations of HFW for a subject at different time intervals and variability of HFW between subjects.

A program was created in MATLAB 6.1 in order to plot power spectra and evaluate the chosen parameter. The length of vessel segments was measured in RVA in measurement units (MU). 1 MU equals to 12,5 μm in a normal Gullstrand eye.

The spatial frequency parameter SEF is represented in reciprocal measurement units: MU-1. In order to simplify matters, we termed this unit “Hz” as well, since it represents an analogue of temporal frequency for spatial curves, which is usually measured in Hz. One spatial Hertz corresponds to one oscillation in a MU. Consequently, for example the value of 0,1 spatial Hz corresponds to one whole oscillation of a vessel profile in 10 MU.

A template with corresponding macros in MS Excel was created for each subject in order to filter, process and analyze the numerical data from the RVA. Since it was impossible to prove the normal distribution of measurement data, Mann-Whitney Test for independent samples was used in order to assess statistical differences of the evaluated characteristics. Since comparing three groups of volunteers regarding 1 parameter, necessary adjustment for multiple comparisons were considered by the Dunnet method [10] with a coefficient of 3. Because of the small number of subjects the non parametric tests were applied on the level of significance of $p = 0,05$ for each evaluated parameter. Non parametric statistical analysis was performed in SPSS 11.0 for Windows.

Results. *Circulation parameters.* The mean systemic blood pressure did not vary significantly between groups at the beginning of the examination and did not change significantly within any group during the whole examination period.

Measured retinal vessel reactions. In fig. 4 HFW expressed by SEF is demonstrated according to the phase of arterial reaction. SEF was significantly different between the young and senior age groups in each phase ($p < 0,05$, Dunnet test). SEF was also significantly different between the young and middle age group in dilation, constriction and re-

laxation ($p < 0,05$). No significant difference could be found between the young and middle age group for baseline tonus.

The statistically significant increase of HFW with age in arteries is demonstrated for each phase of the vessel reaction in fig. 5.

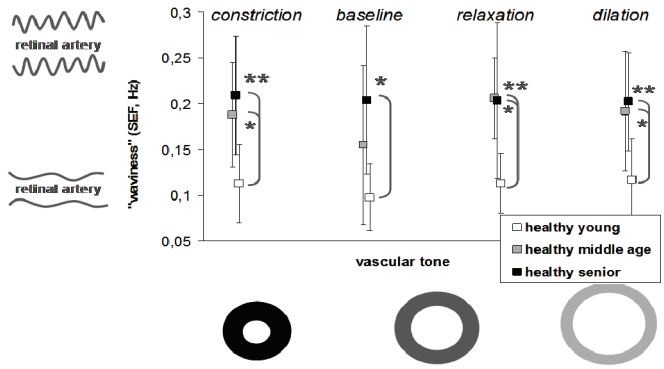


Fig. 4. High frequency waviness of longitudinal arterial profiles, expressed by SEF dependent on vascular tone. Cartoons along the axes illustrate "waviness" and "tone". Note, that the SEF — values are comparable within each age group. However they are higher in both older groups. This shows significant difference of longitudinal arterial profile structure between the youngest and two older groups.

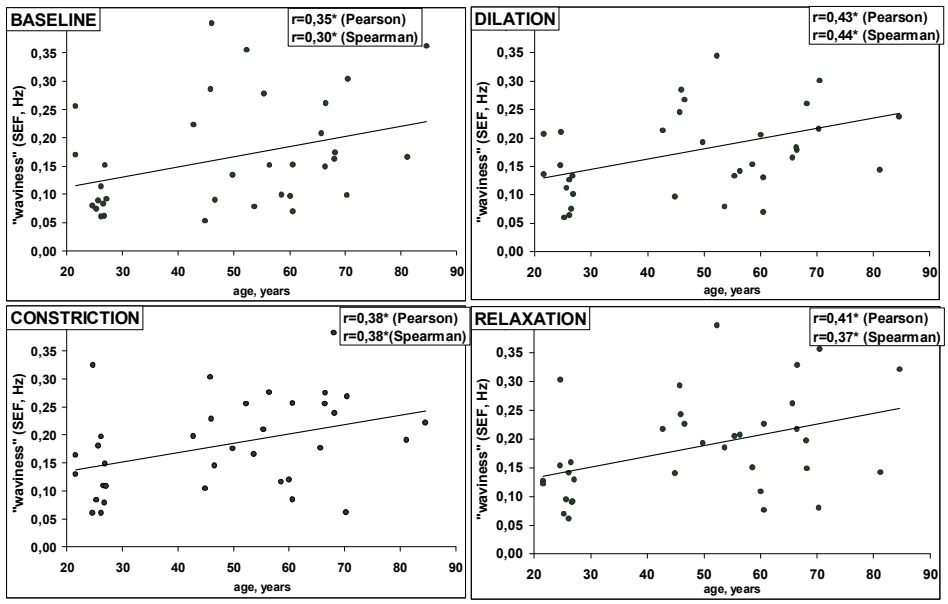


Fig.5. High frequency waviness of longitudinal arterial profiles expressed by SEF dependent on age at the 4 phases of vessel reaction during flicker stimulation assessment. Each subject is represented by a black point. Corresponding correlation coefficients and their significance (*) are represented.

Discussion. The present study investigated, whether changes in vascular configuration of retinal vessels can be observed in different age groups. We used a non invasive functional method measuring the blood column within a vessel segment. The functional

stimulus applied here was flicker light, using the effect of neurovascular coupling and observing dilation and constriction of the vessel following stimulus application.

Our main finding is that is that the blood column diameter of retinal arteries shows a significantly higher degree of irregularity in older subjects than in younger subjects. The irregularities are likely due to microirregularities of the inner arterial wall. Such age dependent findings have been reported in larger conduit arteries such as the carotid artery for the intima media thickness. Technology to investigate this phenomenon in much smaller arteries in the microcirculation has not existed so far.

Since retinal vessels are easily observable and are part of the microvasculature they could be used as a substitute for assessment of small vessel disease.

The primary functional characteristic of vessels is their lumen diameter. The diameter determines their resistance. The diameter is determined by the active properties and structural properties of the vessel. The effectors for displaying the active properties of a vessel are the smooth muscle cells, their number, their arrangement and their state of contraction. The latter is massively influenced by the endothelial cells and their mediators.

Functional endothelial changes are seen in atherosclerosis, arterial hypertension, diabetes mellitus, ischemia and cardiovascular disease [11]. Several studies indicate that aging and endothelial dysfunction progress in parallel. Vascular tone depends upon a balance between vasodilators (e. g. endothelial derived nitric oxide) and vasoconstrictors (e.g., endothelin) with reduced formation of vasodilators resulting in vasoconstriction. Endothelial cells play an important role in modulating the microvascular tone and autoregulation. In neurovascular coupling vessel dilation is caused by local increase of endothelium-derived nitric oxide triggered by the application of light to the retina. The effect can be blocked by L-NMMA, which highlights the importance of nitric oxide and regular endothelial function for a normal neurovascular coupling effect.

In aging Ferrari et al. [2] described migration or proliferation of vascular smooth muscle cells infiltrating the subendothelial space, increased deposition of collagen, elastin, and proteoglycans, in conjunction with an increase in blood cells. Lundberg and Crow [12] showed impaired signal transduction pathways in vascular smooth muscle cells when examining the ability of older cells to respond to inhibitors. If these changes were non-uniformly distributed along an artery these pathologic processes could cause irregularities in the longitudinal vessel profile.

In our study we found a statistically significant difference in the arteriolar longitudinal vessel profile between the young and senior age group regardless of the dilation state. In older healthy persons more small undulations were found. The younger group demonstrated lower frequency diameter changes. Interestingly this pattern was undisturbed by stimulation and was kept constant in the dilation and constriction states caused by neurovascular coupling.

It is known that the relationship between arteriolar and venous diameter changes with age [13]. In older age arteries possess a smaller diameter in relation to the retinal veins independently from any other arteriosclerotic risk factors. This could be an effect occurring in addition to the more irregular structure of the vascular profile, caused by the same pathophysiology.

The middle age group also showed interesting findings. At baseline longitudinal vessel profile amounted to values inbetween the young and old age group without reaching statistical significance. However during all functional stimulated states (dilation, constriction and relaxation) the middle age group differed significantly from the young one and was almost identical to the old age group (fig. 5). Although we did not find significant differences in the arteriolar longitudinal vessel profile during the stimulation in the middle age group, this means that in the unstimulated state the vessel wall in middle age is still similar to the one encountered in young persons. However when metabolic demand by stimulation via mediators causes a muscular reaction this pattern changes to the one encountered in older age. So in middle age there is already some functional impairment in vascular reaction following flicker light stimulation. Previously we investigated longitudinal arterial profiles in glaucoma using another type of functional provocation and found a similar phenomenon. In a group of glaucoma patients baseline SEF values were not different from age matched controls, however in dilation there was a significant change in SEF with even more irregular values. This underlines the fact that early age related and pathologic changes in longitudinal arterial structure might be discovered only in the dynamic vessel behavior following provocation.

An explanation for our findings and the reduced arterio-venous relation in older age could be a functional one with smooth muscle cells exhibiting a more pronounced constriction during baseline with increasing age. This might be due to endothelial dysfunction with may have several effects:

1) defective dilation even though the endothelium is intact, which may contribute to increases in vasoconstrictor response [14];

2) vasodilation is attenuated or reversed to vasoconstriction, in response to vasoactive products released by activated platelets [15];

3) impaired endothelium dependent relaxation may contribute to augmented vasoconstriction by serotonin released by platelet aggregation [16];

4) increased destruction of nitric oxide may play an important role in impairment of endothelium-dependent relaxation thus nitric oxide formation may be normal or even increased but increased degradation of nitric oxide may result in impaired vasodilatation [15].

Impaired production or impaired reaction to mediators could explain a more irregular appearance of the wall depending on local expression of the changes.

Another explanation for our findings of more high frequency and more irregular longitudinal vessel profiles with age could be a structural one implying that in older age, similar to the state in hypertension, a smaller lumen exists with normal sized and functioning smooth muscle cells. Since the diameter of the lumen is reduced even small irregularities in smooth muscle cell status are reflected in a more pronounced way. Research from gerontology by Ferrari et al. [2] demonstrated that although arteries of healthy elderly subjects have no endothelial lesions or discontinuities, endothelial cells can be irregular in shape and have increased height. This fact might also be part of the age-related irregularity we found in the longitudinal arterial profile.

As mentioned above the pattern of wall irregularities did not change during stimulation in the young or old age group. With the middle age group demonstrating a functional

difference in the stimulated states we think that the feed back mechanism: endothelial cell — smooth muscle cell in a healthy population is different in different age groups. Whether is able to react ideally to physiologic stimuli in an adequate way even in older age seems questionable.

The question remains, whether those more irregular and higher frequency of vessel wall diameter change have any implication. We have learnt from fluid mechanical simulations in Newtonian fluids that irregular rough structure of the internal vessel wall lead to increased resistance to flow [17, 18], which primarily will lead to decrease in blood flow. Consistent peripheral demand could in consequence lead to an increase in blood pressure to supply the need. Our findings might therefore be an explanation for increase in blood pressure in older populations. Also the adherence of cellular blood components might be increased by more irregular structures.

There is one further point to consider in the interpretation of our data: RVA data acquisition is performed by assessing grey values in an image. RVA therefore measures what it detects optically, in our case it is not the inner diameter of a vessel but the thickness of the red blood cell (RBC) — column without the blood plasma layer. The irregularity of measured RBC- column profiles might be related to the microirregularities of the inner arterial wall as described above. The low frequent waviness of the vessel longitudinal profile is obviously a property of the vessel wall configuration. For high frequency waves a fluid mechanical effect might also be considered. A mathematical model for non-Newtonian media published by Khantuleva et al. [19] describes self-organization and self-regulation effects in open systems. It explains systems adapting to varying conditions and models the changes during transitions due to the interacting underlying mechanisms. For blood flow in small vessels it includes the possibility of a random local formation of small vortex pulsations near the vessel wall (at the border of the plasma layer), dependent on flow parameters, rheological conditions and geometrical configuration of the vessel. Consequently the effects on microirregularities of the RBC- column found in our clinical experiments could also be due to these self-regulated non-Newtonian hemodynamical effects in the blood flow, and not only to changes in the vessel wall. This needs to be validated in further experimental and numerical studies.

Assessment of microirregularities of the vessel lumen applying contemporary methods of image analysis is now widely performed in clinical medicine. Characterization of microirregularities of the arterial inner wall using mathematical methods including frequency analysis has been recently published by several groups analyzing intima media configuration in the carotid artery [20]. Labropoulos [20] reported that “with increased age and number of risk factors present, the wall/blood interface in the a. carotis became more irregular”. However those attempts have been mostly limited to large vessels using parameters such as e. g. intima media thickness (IMT) or pulse wave velocity. Microcirculation plays an important role in tissue metabolism. Vascular characteristics of microcirculation so far are difficult to examine non invasively in vivo. The retina is unique in the body. Its vasculature resembles the one in the central nervous system (CNS) and is easily accessible by non invasive optical methods. Our findings in retinal arteries represent the central microcirculation and complement the knowledge acquired for microirregularities in large vessels.

In ***summary***, evaluation of functional retinal arterial vessel reactions is possible, characterization of microirregularities feasible and a difference in older age is seen in healthy volunteers compared to a younger age group in our set-up. The validity of this measure and clinical implications of our findings remain to be evaluated. Especially a study in a hypertensive population would be very helpful in understanding the value of irregular vessel wall formation.

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МИКРОСТРУКТУРА ВНУТРЕННЕЙ СТЕНКИ АРТЕРИЙ СЕТЧАТКИ ИЗМЕНЯЕТСЯ С ВОЗРАСТОМ У АНАМНЕСТИЧЕСКИ ЗДОРОВЫХ ЛИЦ

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Артериосклеротические изменения охватывают всю сердечно-сосудистую систему человека и выражены по-разному в различных ее отделах. Считается, что артериосклероз поражает, в основном, крупные артерии, однако патологические изменения происходят также и в сосудах микроциркуляции. Сосуды сетчатки глаза являются частью центрального микроциркуляторного сосудистого русла. Они могут быть зарегистрированы неинвазивно простыми оптическими методами, а по своим структурным и функциональным особенностям схожи с сосудами головного мозга. Сосуды сетчатки имеют сужения и расширения в различных отделах, а их поперечное сечение непостоянно вдоль сосуда. Цель исследования состояла в изучении функциональных и морфологических возрастных изменений структуры внутренней стенки артерий сетчатки, а также в определении количественных параметров, которые могли бы характеризовать эти изменения. Изменения продольного профиля участков ретинальных артерий регистрировались у 35 анамнестически здоровых испытуемых разного возраста с помощью динамического анализатора сосудов сетчатки (Retinal Vessel Analyzer, IMEDOS, Йена, ФРГ), который позволяет изучать динамическую реакцию сосудов сетчатки прижизненно неинвазивно и в реальном времени. На основе этого прибора был разработан и применен новый количественный метод прижизненного исследования продольных профилей внутренней стенки сосудов сетчатки. В ходе исследования сосуды сетчатки стимулировались мигающим светом частотой 12,5 Гц, вызывающим реактивную вазодилятацию. На участках артерий сетчатки длиной 1 мм регистрировались продольные профили внутренней сосудистой стенки. Степень неровности внутренней сосудистой стенки (НВСС) артерий сетчатки характеризовалась параметром конечная частота спектра (КЧС). НВСС артерий сетчатки анамнестически здоровых испытуемых не менялась при реактивном изменении тонуса сосуда. На всех стадиях сосудистой реакции НВСС артерий значительно увеличивалась с возрастом. В частности, КЧС значительно отличалась в младшей (21—27 лет) и старшей (60—85 лет) группах испытуемых ($p < 0,05$; критерий Мана—Уитни). Значимые различия между КЧС в этих двух группах и в средней возрастной группе (40—59 лет) не были обнаружены в исходном состоянии сосуда. После стимуляции КЧС в средней возрастной группе приблизилась к значениям старшей группы и значительно отличалась от КЧС в группе молодых ($p < 0,05$). Таким образом, меняющийся вдоль сосуда сетчатки внутренний диаметр образует нерегулярный профиль сосуда с микронеровностями. Внутренние стенки артерий сетчатки с возрастом претерпевают существенные морфологические и функциональные микроструктурные изменения, которые могут быть обусловлены различными причинами: биомеханической неустойчивостью тонкой сосудистой стенки, частичным патологическим нарушением функции сосудистого эндотелия, а также фокальными изменениями ригидности или нарушениями функции гладкой мускулатуры сосудистой стенки.

Ключевые слова: старение, сосудистая структура, микроциркуляция, сетчатка, артерии, артериосклероз.