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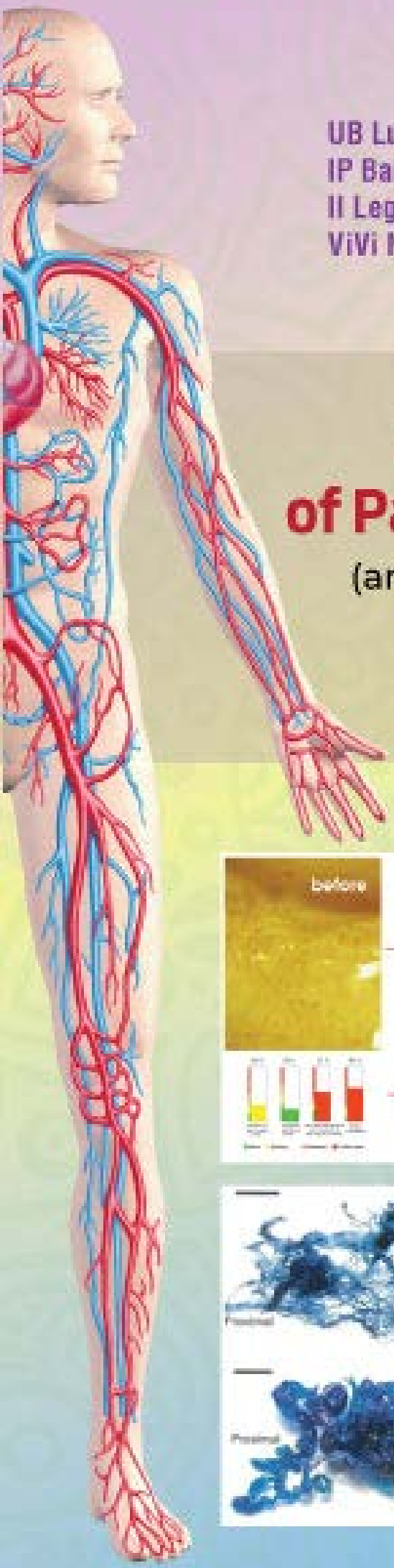
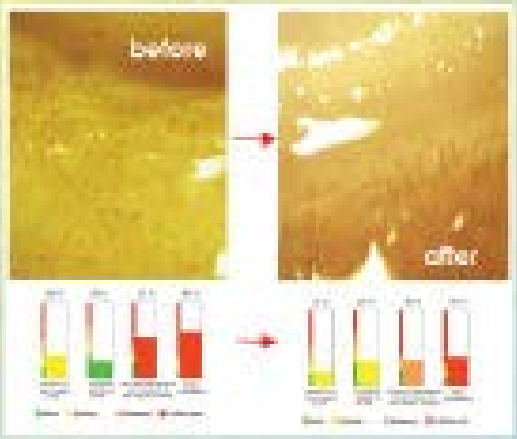
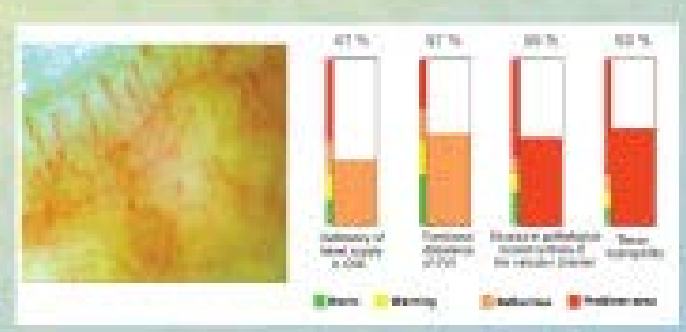
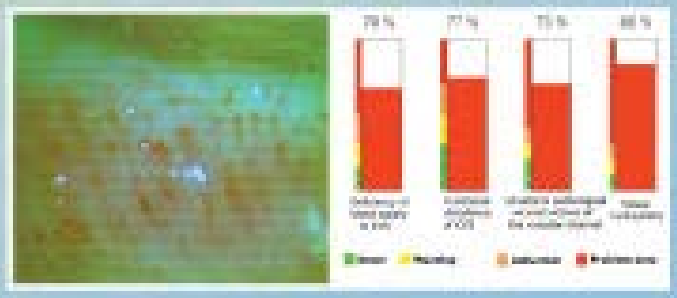


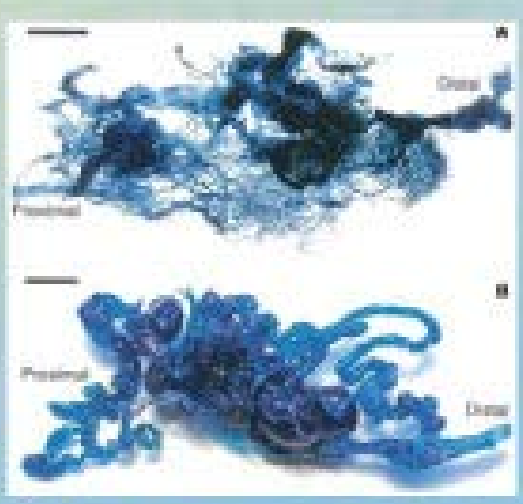
VASCULAR SCREENING of PathoNeoAngioOncogenesis

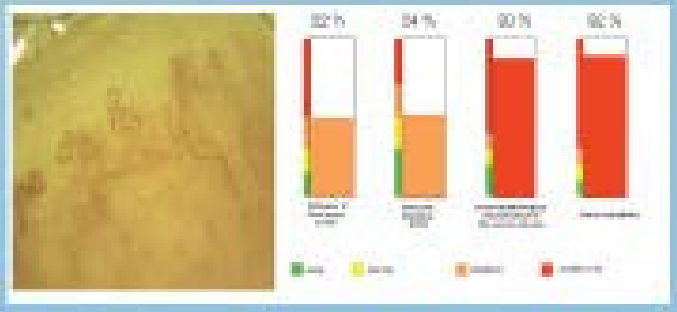
(analytical approach to an early diagnosis of pathological ArterioVenous angiotransformations at the micro- and macrovascular levels)











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Review Article

Vascular Screening of PathoNeoAngioOncogenesis. (Analytical Approach to an Early Diagnosis of Pathological ArterioVenous Angiotransformations at the Micro- and Macrovascular Levels)

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Review

Relevant research of the vascular factor in the process of uncontrolled tumor growth

The oncopathology together with the vascular pathology occupies a leading place among mortality and disability among the workforce [1- 4], and in recent decades patients with this pathology are younger: teenagers, children, and even newborns with tumors [5-8]. In Ukraine, there are recorded cases of tumors in the fetus and attempts of intrauterine resection of such tumors [9]. The Chernobyl accident in 1986 may provoke an environmental disaster in Ukraine with the gradual growth of cancer pathology of various locations [10-13]. In 2013, WHO adopted the Global Plan of Action on the prevention of non-communicable diseases and fight against them during 2013-2020, which provides for a series of actions aimed at reducing by 25% premature deaths from oncology and cardiovascular disease, diabetes, and acute respiratory diseases [14]. This is a quite good intention that requires adequate technologies.

On the other hand, for the last decade, some surgical treatment methods and chemotherapy [15-20], local cryodestruction of the tumor applying the ischemization technologies in the reservoir of the vascular pedicle of the tumor as an artificial suspension of tumor vascularization [21] are becoming more and more popular. Also, there is a theory of oncoangiogenesis [22-24] about the need for vascularization at the micro- and, moreover, at the macrovascular level of an organ or a system with tumor size greater than 2 mm.

As for the therapeutic management of neoangiogenesis, some pharmaceutical companies are trying to make antiangiogenic drugs - blockers for angiogenesis and neovascularization (cancer neovascular): (Avastin, Zolendronate, etc.) that slow down the process of uncontrolled growth in the vascular bed in situ [25-27]. However, each case requires proof for the existing vascular pathology and the dynamics of the personalized treatment result with neoangiogenesis blockers.

At the same time, vascular screening technologies should be used in the cancer patient management as informative tools of evidence-based medicine in applied angiology of the microcirculatory bed [28] for verification, monitoring, and dynamic monitoring of the effectiveness of neoangiogenesis blockers. This will prolong life

expectancy and, under all favorable conditions, improve the quality of life by angiocorrection of concomitant subjective complaints of vascular discomfort, as well as monitor the condition of cancer patients during the disease and have objective data on sanogenic or pathological changes in the body.

Today oncopathology in general remains extremely difficult and less curable since there are no effective technologies for tracing and predicting the positive course of the disease [1,4,7,15].

Current optimistic data on the life expectancy of a patient up to 5 years since the oncopathology diagnosis are not at all pleasing, taking into account the suffering of the patient [1,4,7,15]. In this unhappy background, a program sounds optimistic to reduce the cancer incidence by 25% in the next 20 years (2017-2037) in the United States [29] and the tendency to find effective tumor markers for detecting a condition prior to the disease or early stages of the oncoprocess [30,31].

Therefore, we believe that it is not proper to talk about the psychological comfort and quality of life in this period. Even with the best possible prospects, the patient's frustration with the possibility of recovery and the lack of real criteria for the objectification of the fact that the oncoprocess is suspended is virtually absent.

The Covid-19 pandemic in 2020 has strengthened the importance of early diagnosis of oncopathology and minimization of clinical signs of oncopathology in patients [32,33]. Covid-19 mortality statistics among cancer groups indicates a high risk of morbidity and mortality from complications after Covid-19. Therefore, a tool is needed to visualize the process of neoangiogenesis and neooncogenesis differentiation in the initial stages of pathological transformation of the microvascular bed.

From the point of view of process-management, the process of treating cancer is transformed into the continuous and uncontrollable, which is more likely a work with force majeure problems as new cancer forms are detected. Today there are no preventive technologies for the objectification of the body condition regarding onco-risks, as well as the dynamics of the reverse sanogenic reorganization in the patient's body.

Our experience of long-term care of oncological patients with concomitant psychoneurological pathology has shown that even with the existing psychological support of specialists and relatives, the patient's doubts in the possibility of cure for oncological diseases remain dominant in despair in the possibility of complete recovery and in the subconscious block of their future and the choice of death as an option for salvation from long-term and hopeless struggle against the serious illness. Therefore, the process of managing cancer patients also requires visualization of the dynamics of the microvascular transformations as evidence-based medicine:

1. primarily for physicians as a tool to verify the fact and dynamics of structural changes in the microvascular bed and NeoAngioOncogenesis,
2. to minimize psychological and depressive disorders in patients of oncopathology risk groups and verified cancer patients,
3. for the population - vascular disorders are early and reflect restructuring of microcirculation both at the level of the regional vascular reservoir of the oncoprocess localization and at the level of systemic hemodynamics.

It is to demonstrate the visualization process and to support the patients' belief in their recovery and to find and create evidence-based technologies for monitoring the oncoprocess course in the patient's body.

Angiology as a science about the nature of the vascular bed in normal and in pathological conditions

Numerous studies devoted to the study of the hemodynamic features at norm and pathology led to the appearance of a special field of science – *angiology* [28] which summarizes the information on the structure of the vascular tree - regional angioarchitectonics, the structure and functions of various regional reservoirs of the human vascular system (brain, lungs, heart, liver, kidney, small pelvis, limbs, etc.) at normal and pathology, about blood supply and blood circulation at various pathological conditions [34,35].

However, angiology as a science is relatively young and its development became possible due to non-invasive instrumental diagnostic devices for dynamic monitoring and modeling of various situations in the restructuring of the bloodstream.

Since the cardiovascular system is a dynamic system with variable hemodynamic parameters, recent static studies of fixed images of vascular segments (CT, MRI in angiomode) did not obtain enough information to understand the pathogenesis of vascular reconstructions.

On the other hand, the recommendations of recent years for the use of MRI-contrasting angiography for early detection of oncogenesis [23,24,36,37], reaffirm the need for a study of the vascular bed at the microlevel. Therefore, for the last 30 years the angiology gradually changed the emphasis on the fixation of vascular pathology in local segments (ultrasound scanning, rheovasography (RVG), MRI in angiomode) on the global approach as an integral system of closed tubes - the theory of vascular blood circulation [28,35,38], which enables not only to study hemodynamic parameters, to distinguish the macrolevel of the vascular bed (major and peripheral segments of the arterial and venous channels) and the microlevel - the microcirculation level - arterioles, venules, and capillaries but also to analyze the relationship between pumping-sucking function of the heart, arterial and venous interconnection links, the influence of

microcirculation changes on vascular resistance in an integral cardiovascular system.

Current methods for visual diagnosis of dynamic changes - ultrasound scanning and dopplerography of major arteries and veins, MRI in angiomode, X-ray contrast angiography perform local examination of regional vascular reservoirs using different objectification methods. The microcirculation level is investigated by methods of laser flowmeter of surface tissues, capillaroscopy of the nail bed locally on the skin surface, or by CT-MRI contrasting angiomodes to visualize the angioarhitectonics of the vascular link locally at the tumor area, which tissue can still not be structurally differentiated [36,37,40,41].

As the cardiovascular system is the most dynamic system with numerical once-a-second changes in hemodynamic parameters in a certain norm range, and the number of hemodynamic parameters important for the formation of adequate blood supply can reach 50-100 within the CVS as a vascular blood flow [28]. Therefore, the static image of CT-MRI, even in the angiomode, gives a global picture of angioarchitectonics, and dynamic diagnostic methods complement the information on the CVS function and play a crucial role in the verification of vascular dyshemia.

Therefore, the best methods for assessing vascular disorders are vascular screening technology (microvascular level) and duplex scanning with dopplerography for peripheral and main arteries and veins (macrovascular level), which can be regarded as highly informative methods of evidence-based medicine in applied angiology [28,35,42].

Numerous hemodynamic parameters have been developed for the assessment of vascular disorders within the regional vascular reservoir or for the assessment at the system level, which work synchronously within the optimal corridor of hemodynamic parameters of the norm; require in-depth knowledge of hemo- and hydrodynamics, and may be subject to analytical evaluation and quantitative-qualitative analysis thanks to current vascular innovative analytical technologies - **AngioSmart Vascular Innovative Analytical Technologies** (VIAT Angiosmart) with expert clinical conclusions. This approach is devoid of subjectivism, and the software package contains the knowledge and large experience of a doctor-scientist-expert [42].

Microcirculation may play a leading role in the formation of uncontrolled angiogenesis, in the vascularization of tumors by forming a vascular glomus with primitive undifferentiated blood vessels that often detect pathanatomas in the tumor [41,43-45].

Investigation of the vascular bed in angiology is a special new direction, which concerns not only the visualization of the vascular reservoir but also the study of the functions of hemodynamics in the formation and development of sanogenic and pathogenic transformations [28,35,40].

Terminology

The logic approach to terminology in angiology to describe the processes of angiogenesis and vascularization

For the easy perception of various terms in applied angiology, we propose physiological processes named with simple terms.

Physiological vascular processes, but stimulated by the organism in response to the problem (skin damage, bone fracture, etc.), of angiogenesis and vascularization processes aimed at temporarily localizing the vascular network in the projection of wounds, ulcers, and inflammation are presented with a prefix **neo + term**.

All **pathological processes** of angiogenesis, vascularization, and pathological alterations in the vascular channel are presented with a prefix **patho + term**.

Angioarchitectonics is a structure of the vascular tree and various types of its branches, which are hereditary and influence the change in hemodynamic parameters of blood flow in regional reservoirs and can serve as risk factors for the development of vascular pathology at certain pathological caliber, branching types and branching angles of the arteries and veins [46].

Angiotransformation is a change in the vascular bed structure at the micro- and macrolevels as a result of hemodynamic reconstructions, which leads to formation of a pathological type of angioarchitectonics involving oncocapillaries in structurally and functionally distorted hemodynamics in the microcirculatory channel [25,45-50].

Physiological and pathological angiogenesis

Angiogenesis (neoangiogenesis) - as an option for the formation of a vascular network in a fetus and a physiological process of some new vessels' development controlled by the body in the life process [23,24,43].

Physiological angiogenesis is a process of new blood vessels' formation in an organ or tissue. Normally, the angiogenesis processes occur in the body with moderate intensity and are activated only in the regeneration of damaged tissues, sewerage of blood clots, the elimination of inflammation foci, the appearance of scars and similar processes of recovery, as well as in the growth and development of the organism [44,45,52,53].

Judah Folkman is a pioneer in the study of angiogenesis, who in 1970 published the oncoangiogenesis theory [54,55].

PathoNeoAngiogenesis is a pathological formation of new blood vessels and vascular networks uncontrolled by the organism

[25,52,56].

OncoNeogenesis - the process of tumor formation with possible malignancy [23,24,47,48].

PathoAngioOncogenesis (NeoAngioOncogenesis) is a pathological uncontrolled angiotransformation and neovascularization, which begins at the level of change in the regular loop-shaped structure of the capillaries into the abnormal – oncocapillary [24,57], forms arteriolar vascular networks that are not characteristic for patients in adolescence and adulthood, and promotes the development of a tumor at the micro level [47,48]. Such networks develop progressively and uncontrollably, grow in volume, do not differentiate into peripheral and major vessels, but only arterioles and venules expand in volume, arteriolar-venular shunts for the formation of a vascular lace of a tumor and its growth with the collateral type of blood supply [40,48,58]. In 2012 U. B. Lushchyk proposed a term «**PathoNeoAngioOncogenesis»** [59].

We intentionally use the term **«PathoNeoAngioOncogenesis»**, but not oncoangiogenesis, because we are convinced that the vascular channel and the uncontrolled process of vascularization is a basis for tumor development and the background for the risk of tumor developing.

PathoNeoAngioOncogenesis as a sign of pathological uncontrolled angiogenesis with the formation of the vascular network for tumor growth. In tumor tissues, especially in tissues of malignant tumors, angiogenesis proceeds constantly and very intensively. This is probably one of the causes for the rapid growth of malignant tumors since they are very well supplied with blood and receive far more nutrients per unit mass of tumor than normal tissue, thus robbing healthy tissues of the body. In addition, enhanced tumor angiogenesis is one of the mechanisms of its rapid metastasis since tumor cells can create metastasis along the blood vessels (along the walls) or spread around the body with blood flow [24].

On the other hand, the anaerobic type of the metabolism [23,24,60] in the tumor and the extremely rapid division of atypical cells receive additional “favorable” conditions for the progression of the pathology under conditions of hypoxic-ischemic background for PathoNeoAngioOncogenesis in the predisease stage. Recently there were publications on the affinity of vascular and oncopathology [61], diabetes and oncopathology. Therefore, in our study, we also tried to make certain correlations between cardiovascular disorders and pathoneoangiogenesis.

In patients with breast cancer, we observed the presence of a capillary modified structure in the finger nail bed of homolateral irrelevant lesion of the mammary gland.

Physiological and pathological neovascularization

Physiological neovascularization is a physiological, controlled by the organism, process of development of vessels and the formation of the vascular bed locally at the injured area, or globally in the development of the embryo, the growth of the infant.

Ophthalmology distinguishes corneal neovascularization and choroidal neovascularization [44,45].

Pathological neovascularization (pathoneovascularization) is pathological vasodilatation in places where they should not normally occur, or the emergence of new vascular networks locally and their uncontrolled progressive growth [44,50,53,62].

Infectious mutagen is a compound hypothetical concept that reflects the combination and mutation of bacteria and viruses that are adsorbed on a fungal basis and interact in a conglomerate, provoking oncogenesis (carcinogenesis).

Infectious marsh is a term proposed by Lushchyk U.B. (2005) to describe the pattern of venous congestion of the hypervolemic type of different genesis, where there are optimal pathological conditions for blood stasis, the formation of the primary infectious focus at the microlevel with the absence of signs of sanogenic turbulence and cavitation of pathological cells - viruses, bacteria, fungi [40].

AngioSmart Vascular Innovative Analytical Technologies (VIAT AngioSmart) are up-to-date innovative approaches to diagnosis, modeling, process and risk management in CVD treatment. **VIAT AngioSmart** enables to create unique diagnostic and monitoring tools for medical practice assistance since they combine technological complexes for obtaining images and information, as well as analytical IT technologies for image processing, clinical interpretation of received images, with the formation of an expert-level automated conclusion for minimizing time for a clinician to obtain detailed, reliable information and avoiding subjective inferences with minimal knowledge in the field of applied hydrohemodynamics, MacroMicroAngiology, rheology and clinical angiology [63].

New terms in treatment of vascular disorders - angiocorrection and angiotherapy.

Vascular innovative technologies - analytical technologies – enable to assess changes of many hemodynamic parameters (at least 35-50 parameters of blood flow evaluation in arterial and venous vascular beds at macro- and microlevels), in contrast to the estimation of generally accepted parameters of blood flow (volume and linear velocities of blood flow, vascular diameter), and there is a need for correction of these parameters by medicinal means [28,34,35].

Therefore, new terms like **angiosurgery** and **angiotherapy** have been gradually introduced as a basis for restoring the bloodstream permeability and the adequate blood supply to an organ [34].

In turn, over time, there was a need to differentiate the medicinal process of restoring only hemodynamic parameters of the blood flow in the vascular bed - angiocorrection and restoring the level of adequate blood supply for optimal organ function - angiotherapy.

Angiocorrection [28,34,38] is a process of correcting hemodynamic parameters at the level of the main, peripheral, and microcirculatory beds to restore adequate, physiological blood supply for an organ or system that is responsible for the structure and hemodynamic parameters of the age pattern of the arterio-venous balance and the corresponding structure of the regional angioarchitectonics in one or another local vascular reservoir by drug or operational means.

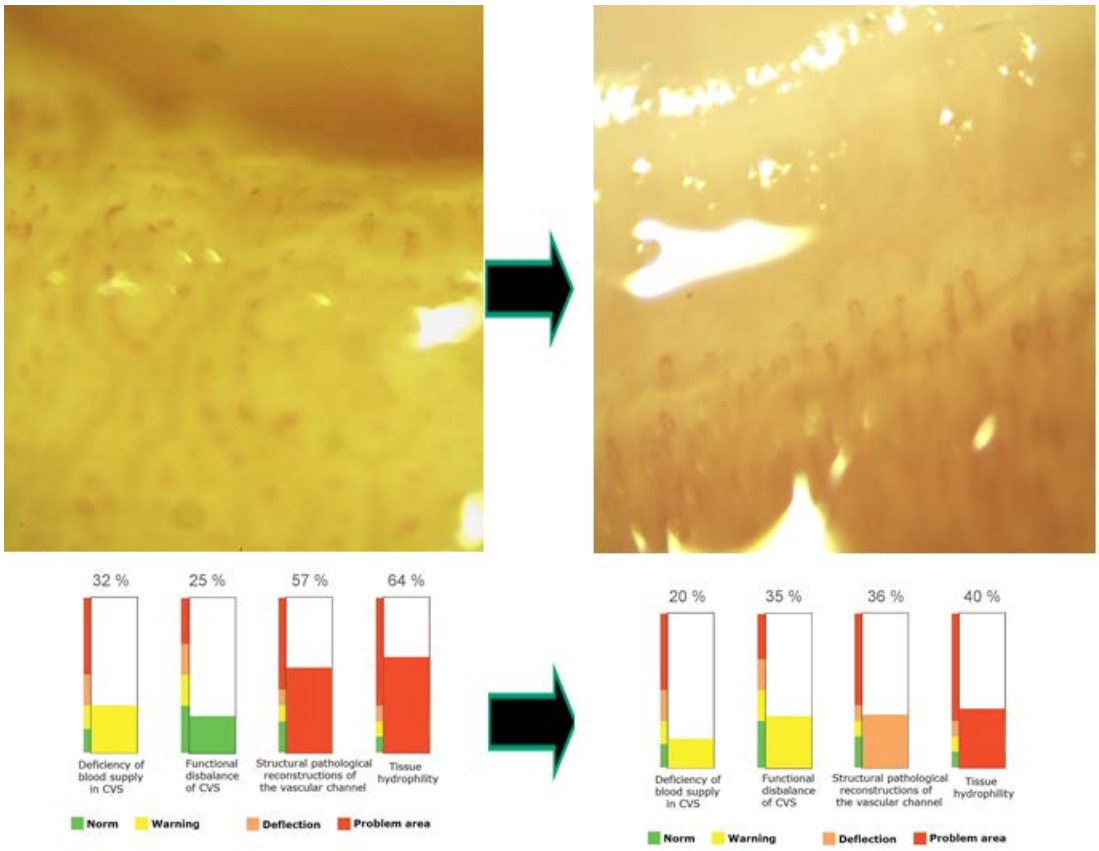
Angiotherapy [28,34,38,47] is a process of restoring a deficient blood supply for an organ and / or organism in certain regional vascular reservoirs to the level of the age-old physiological norm by applying the medicinal sanogenic effect on the logical redistribution of blood volume in the vascular system in the organism, the formation of blood supply adequate to the organism's needs and the elimination of ischemic-hypoxic conditions at the level of microcirculation locally in a separate organ and in the organism as a whole, avoiding formation and use of the effect of the stealing syndrome at the interregional vascular level [42].

Angiogenesis in norm

Angiogenesis [22,52] is a universal process of development of vessels in tissues of different genesis, which is balanced by the action of pro- and antiangiogenic factors or signals [23-26, 43-45,48-51,53,56,57,60,62,64].

Angiogenesis is physiological and is associated only with embryogenesis, reparative, regenerative, inflammatory processes etc. in normal cells [44,45,65,66].

In this article we have used materials from **the VIAT AngioSmart** database for clarity of microvascular processes. The analytical software displays hemodynamic indices of norm and pathology in different colored scales according to the traffic light rule: **orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm.**



Figures and histograms 1 and 2. Positive effect of physiological neoangiogenesis of regenerative type with sanogeneous vascular reconstruction and hemodynamic parameters for 6 months of vasoactive treatment (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

In pathological conditions, PathoAngiogenesis accompanies the growth of solid and hematological tumors, rheumatoid and autoimmune diseases, diabetes, psoriasis, atherosclerosis, endometriosis [25,26,43-45,48-51,53,56,57,60,62,64] and reflects the loss of control or failure in the regulation of angiogenic factors for one or another reason [24,25,26,43,48,50,53].

However, today the risk factor itself remains unknown, which can provoke pathological angiogenesis – PathoAngiogenesis and PathoNeoVascularization [49,50,51,53,56,57].

There are already some attempts to create drugs that would stimulate local physiological NeoAngiogenesis for tissue regeneration and apply them to treat ulcers, wounds at diabetes, and to restore brain substance in vascular dementia and Parkinson's disease [41,67,68,69].

Theoretical bases of angiogenesis and NeoAngiogenesis in oncogenesis

It is generally known that tumors have their vascular system, which can often resemble a vasculature [23,24,70]. Unlike normal blood vessels, the tumor's blood vessels have structural and functional anomalies. Quite often, pathomorphologists have focused on immature vessels in wounds and tumors [23,24,71,72]. Such immature arteries do not have pericytes - cells that are functionally linked to the vascular endothelium - and their presence is important for stabilization and maturation of the vascular structures [72].

Besides, the vascular network of the tumor is tortuous and becomes chaotic in form, since it does not hold the skeleton of the vessel [41]. Quite often, the vascular wall of the vascular coil in tumors has increased permeability, which contributes to tumor growth. On the other hand, there is a theory of non-moistening of a vascular wall in norm and a sharp violation of its permeability - with pathologically altered porosity [73,74].

Today there is no doubt the fact that the course of tumor depends on many pathogenic mechanisms that promote progression or inhibit malignant growth [23,24,75,76].

NeoAngiogenesis should be considered as an integral link of tumorigenesis (ontogeny) among recent factors as the vascular network is a trophic part of tumors, which provides its viability and thus tumor progression, recurrence and metastasis process of tumors [23,24,77]. Therefore, pathological angiogenesis (PathoNeoAngioOncogenesis) plays an important role in the proliferation and metastasis of cancer.

PathoNeoVascularization and PathoAngiogenesis as signs of the pathological uncontrolled process of new vascular networks formation at the microlevel

PathoAngiogenesis is a pathological process of the new microvessels' formation based on the existing vascular network in the changed tissue and its transformation into tumor (PathoNeoAngioOncogenesis).

In pathological conditions, such as tumor production of proangiogenic growth factors, PathoNeoAngioOncogenesis causes the formation of an own vascular network that helps the tumors to grow [40].

With a lack of blood supply, the tumor receives oxygen and nutrients only by diffusion, while its size cannot exceed 1-2 mm in diameter [23,24,78].

The tumor remains in a "sleeping" condition until blood vessels become growing from closely situated capillaries (PathoNeoAngioOncogenesis) with gradual involvement into this vascular network of arterioles, peripheral arteries and major arteries, thus gradually the vascular pedicle of the tumor is forming [23,24,56]. For the most part, all authors focus on the arterial vascular stem [23,24], without attaching significant importance to the signs of venous stasis at the microcirculatory level and the involvement of the venules in the PathoNeoAngiogenesis process with subsequent transformation into PathoNeoAngioOncogenesis [40,69,70].

The launching of PathoNeoAngioOncogenesis ("angiogenic switching") results in fast growth and metastasis of the tumor. Of course, it is important at an early stage to diagnose such switching and block it at the level of minimal abnormal angiotransformations avoiding the tumor growth at the macrolevel of blood supply to an organ or a system. Unfortunately, current technologies are aimed at detecting the tumor structure and mostly at the 3rd-4th clinical stage of the oncoprocess [23,56]. Assuming that the tumor is developing on average for 5-7 years [23,24,56], it is easy to imagine how much time the medicine loses for timely detection and radical treatment [23,57] and preserving life quality and capacity.

If we compare the experience of different countries, the success of the Japanese system in combating the predominant gastric cancer in them is the diagnosis of oncology process at 1st stage by organizing a dispensary examination and detection at the early preclinical stages of the onset of the disease [23,57].

NeoVascularization and tumor growth

Along with a term of NeoAangiogenesis also a term of NeoVascularization is distinguished as a fact of the formation of a new vascular network. Physiologically, NeoVascularization usually performs a protective function in the body. In case of trauma, it promotes acceleration of a wound healing, after surgical transplant - its good engraftment.

However, pathological NeoVascularization can also have a negative shade - a pathological growth of blood vessels where they should not be in the norm.

In tumors, osteoarthritis, and diabetic retinopathy, PathoNeoVascularization leads to an unfavorable prognosis of the disease course as it causes its progress.

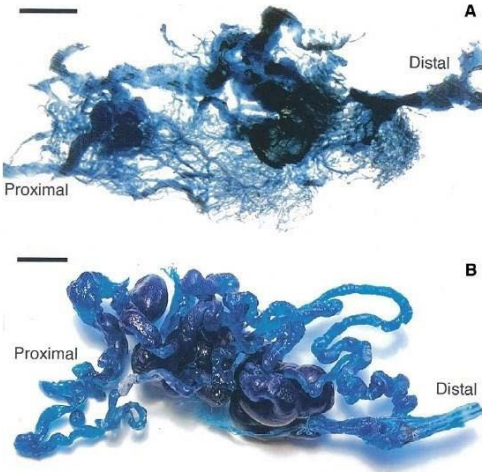


Figure 3. Picture of NeoVascularization as a vascular net of immature and mild-differentiated vessels with a sharply altered structure [79].

Angiogenesis reflects more the essence of the pathogenetic mechanism of vascular reconstruction (angiotransformation), and NeoVascularization reflects the result of this reorganization in the form of new vascular networks' formation under the action of NeoAngiogenesis, which today can be visualized by methods of X-ray CT, MRI in angiomode, by digital optical capillaroscopy and ultrasound color angioscanning with the application of certain intellectual technologies for the identification of these angiotransfromations [28,40] and clinical interpretation.

Current technologies for life-time non-invasive and X-ray visualization of processes occurring in the human body require new knowledge of doctors for clinical interpretation. Often, this information for clinical conclusions should be taken from non-medical sources - applied mechanics, hydrohemodynamics, ultrasound physics, optics, X-ray visual imaging.

In this stream of information, a physician does not have time to replenish the stock of medical knowledge. Therefore, software with the possibility of primary image processing and secondary analytical processing of the received images is urgently necessary for the formation of an objective conclusion and clinical expert-level interpretation in order to prevent subjective interpretation and twisting fantasies of amateurs around little-known topics [63].

Investigation of the vascular factor in the process of uncontrolled tumor growth

Oncogenesis in most cases is accompanied by a pathological vascular reconstruction [23,24,57,78]. It is established that compensatory-adaptive alterations of the vascular bed happen (PathoNeoAngioOncogenesis and PathoNeoVascularization) constantly in tumors, which are aimed at ensuring the growing demands of the tumor in the increased blood supply. Therefore, in recent years, the number of studies related to the study of mechanisms of PathoNeoAngioOncogenesis is constantly increasing [23,24,74,80].

At present, the problem of diagnosing disorders in the structure and functioning of the vascular system is of great scientific and practical importance, since modern diagnostic systems allow in a new way - in the dynamics, and not in the statics - to visualize the functions of those or other vessels, to conduct life-time non-invasive modeling of detected pathological conditions in a living organism, individually determine risk factors and predict the course of vascular pathology, as well as influence these processes during treatment on the evidentiary basis of modern vascular innovative technologies [63].

On the other hand, the search for technology that is sensitive to the objectification of PathoNeoAngiogenesis can help the medicine solve the problem of oncogenesis in the embryo - that is, at the stage of angiotensification in the neovascular microlayer and significantly improve the cancer statistics in the world, extend the life of cancer patients and provide them with an adequate quality of life but ideally the possibility of a complete recovery.

Today there are isolated cases of 15-20-year-old catamnesis of oncopathology in patients who died of metastases, and the pathomorphological study discovered that the primary cancer in situ (for example, in the Ukrainian clinic "Feofaniya"(2010) at the pathoanatomical conference was considered the 15-year-old case of death of a patient with breast cancer that had been cured (posthumously it was pathohystologically and pathomorphorphologically confirmed the absence of signs of oncogenesis in situ, and

estimated metastases in the liver were primary liver cancer that developed after 15 years of transmission of primary onco-debut). These facts are encouraging prospects for possible cure cancer pathology and identify factors of oncogenesis on the other, preclinical stages, possibly as immune failure or hemodynamic background is favorable for PathoNeoAngioOncogenesis.

Pathological angiogenesis in oncology - PathoNeoAngioOncogenesis

J. Folkman - a founder of the angiogenesis theory - has distinguished avascular and vascular phases in the progression of tumor growth [24,54,55].

The tumor in the avascular phase is in a "drowsy state," which can last indefinitely, without clinical symptoms, such as in situ with carcinoma [23,24].

The transition to the vascular phase in PathoNeoAngioOncogenesis is induced by hypoxia, which triggers a series of cascading reactions that modulate the level of expression of hypoxia-dependent transcription factors (hypoxia-inducing factor, etc.), mutations of tumor suppressor genes and cause rapid tumor growth [23,24].

All of this contributes to the synthesis of proangiogenic cytokines (growth factor of endothelial vessels, fibroblast growth factor, platelet-derived growth factor, etc.) that stimulate proliferation of endothelial cells and, as a consequence, progression of tumor disease.

The key regulator of NeoAngiogenesis is recognized as the growth factor of vascular endothelial cells - VPF (vascular permeability factor also known as vascular endothelial growth factor or VEGF) [23,24,57].

VEGF

The phenomenon of circulation of angiogenic factors, in particular, the vascular endothelial growth factor (VEGF), is interesting in terms of its biological and pathophysiological importance and intriguing in identifying it in order to further use the information obtained to diagnose the malignant process and predict the disease course [24,57].

World literature actively discusses the role of VEGF signaling pathways in the development of tumors such as breast cancer and soft tissue sarcoma [49,57].

Providing the correlation of this factor with the aggressiveness of the malignant process and metastasis, it is logical to look for control of PathoNeoAngioOncogenesis, which may be the basis for the pathogenetic methods of treating cancer patients [24].

The search for means of influencing PathoNeoAngioOncogenesis of tumor tissue in clinical trials became the subject of serious discussion only in recent years [23,24,56,57,60,75,76,77,81].

New antiangiogenic drugs are being actively studied and developed, which will enable the tumor process to be transferred from poorly predicted and practically uncontrolled to a chronic, therapeutically predictable disease [23,76,77,78]

Clinical studies have shown that PathoNeoAngioOncogenesis in breast cancer can be a new prognostic marker that allows predicting the disease course and assessing the response to treatment. It has been established that VEGF is an independent prognostic factor in patients with esophageal cancer, uterine neck, neuroblastomas; this marker correlates with poor prognosis in patients with ovarian cancer, prostate [24,57].

Pathological angiogenesis and stages of NeoVascularization in the oncogenesis - PathoNeoAngioOncogenesis and PathoNeoOncoVascularization

According to the theory of "natural history" of tumor growth, the formation of metastases begins with the onset of PathoNeoAngioOncogenesis, that is after the number of tumor cells exceeds 10^3, and the diameter of the tumor is 0.5 cm [23,24].

The terms of clinical signs of metastases are individual, they depend, first of all, on such an indicator as the time of doubling the tumor volume [23,24].

It is determined that 10 years after treatment in patients who had a tumor up to 0.5 cm in diameter, the frequency of development of remote metastases may be 9% [23,24].

It has been established that regional lymph nodes are not a mechanical barrier for tumor cells, as previously thought, but lymphogenous and hematogenous dissemination occur simultaneously [23,24,72,73].

Stages of PathoNeoOncoVascularization

At the current stage of the scientific development, it is known that angiogenesis is a complex of processes that consistently provide interaction between cells of vessels, mitogens and components of the extracellular matrix [24].

Regardless of the nature of angiogenesis (embryonic, inflammatory, reparative, tumor), **PathoNeoOncoVascularization has several successive stages [24]:**

- expansion of existing vessels with increased permeability;
- rupture of the basal membrane;
- migration of endothelial cells into the perivascular stromal tissue towards the source of the angiogenic stimulus (in the form of a sprout consisting of cells with weakened intercellular contacts);
- proliferation of endothelial cells at the top of the sprout;
- formation of the vessel with the formation of a canal inside the formed sprout, synthesis of a new basal membrane, fusion of newly formed vessels and initiation of blood flow.

PathoNeoAngioOncogenesis and apoptosis

NeoAngiogenesis and tumor apoptosis are considered as two of the most important prognostic markers for disease and sensitivity to antitumor therapy [23,24,56,57,60,75,76,77, 81].

PathoNeoOncoVascularization often correlates with biological aggressiveness and malignancy of tumors, it depends on the kinetic features of the tumor [23].

The greatest activity of PathoNeoAngioOncogenesis is observed in the transition of the pre-cancer into cancer. The number of blood vessels in the tumor correlates with the disease progression: the higher vascularization, the worse the prognosis [23,24].

Currently the results of the conducted research give grounds for planning antitumor therapy taking into account factors of vascularization of a malignant neoplasm, and applying antiangiogenic therapy [23,24,57].

The conducted experimental and clinical studies of recent years [23,75,76,78] have confirmed the importance of antiangiogenic therapy as an important component in antitumor treatment.

Thus, today many scientists have confirmed the significant influence of the vascular factor in the development and progression of tumor growth.

Somehow it has historically become evident that PathoNeoAngioOncogenesis is associated with arterial link that logically forms the vascular leg [24] for blood supply and “feeds” the tumor. The venous system, as always, remains in the shadow of scientific research since itself remains largely underestimated [28,35,40,66,67,82].

However, very few authors pay attention to the venous bed and its role in PathoNeoAngioOncogenesis and in the formation of a pathological neovascular phenomenon of oncogenesis [23,24]. Mainly, concentrating on signs of the vascular pedicle of the tumor as the main pathway for vascularization of the tumor, virtually no one considers the essence of hemodynamic conditions for tumor growth and the pathogenesis of pathohemodynamic transformations in situ [23,40,54].

Results of own researches and observations of pathological angiotransformations in cancer patients

For the last 20 years, Veritas Research Center and the Clinic of Vascular Innovations have been investigating vascular deregulatory changes at various pathologies. The main Clinic’s contingent includes patients of psycho-neurological profiles, with cerebrovascular and cardiovascular pathology. However, episodically, we treat patients with verifiable diagnoses who complain of concomitant neuropsychiatric symptoms and require specific symptomatic treatment of vascular dyshemia.

Therefore, according to the algorithm of the clinic, all patients undergo a comprehensive instrumental check-up of all organs and systems, mainly by ultrasound methods; further, if necessary, the medical staff monitors the disease course and conducts dynamic monitoring of hemodynamic changes in the process of their specific treatment by the oncologist according to standard international protocols and, if necessary, conducts the personalized correction of vascular dyshemia in cases of severe imbalance of the regional arteriovenous vascular reservoir, the threat of thrombus formation and thromboembolism.

First years, we were very cautious about the need for correction of the vascular bed, adhering to the generally accepted principle of the prohibition of using vascular medications and methods of exercise therapy, massages in oncopathology [83].

Gradually life made us very carefully start to apply our schemes for personalized angiocorrection under instrumental control in cases where we were sure that our treatment would not hurt the patient. So, initially, as a necessity, some venotonizing therapy was used aimed at reducing the severity of venous stasis in organs of the small pelvis, perineum and the head under the instrumental monitoring by vascular screening for microcirculation and angiomarker technology for ArterioVenous macrocirculation. Even small doses of vascular medications led to a significant subjective improvement in patients confirmed by ultrasound and capillaroscopic examinations [28,34,84]. Then we have developed some technologies for the analysis of ultrasound scanning, ultrasound dopplerographic and capillaroscopic images, which were improved for the analytical technologies of MacroAngioMarkers and microvascular screening [46,85-93].

This study uses the materials of dynamic observation of the vascular status of major arteries and veins in the brain, limbs and regional vascular reservoirs in the liver, kidneys and small pelvis using the method of vascular biomarkers - MacroAngioMarkers and MicroAngioMarkers (vascular screening technology) in patients with an officially confirmed form of the cancer [28,87,88].

The purpose of this study was stipulated by treatment of the oncology patients with concomitant vascular pathology - headaches, feeling of cold in the body and limbs, dizziness, resistant arterial hypertension, nosebleeds, sleep and memory disorders, limb edema, nausea and vomiting, convulsive seizures, diencephalic crises, general weakness, etc.

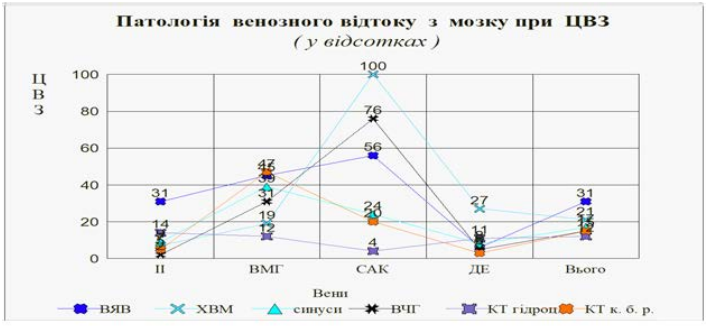
Results brief overview of the correction of angiotransformations in the vascular system of cancer patients

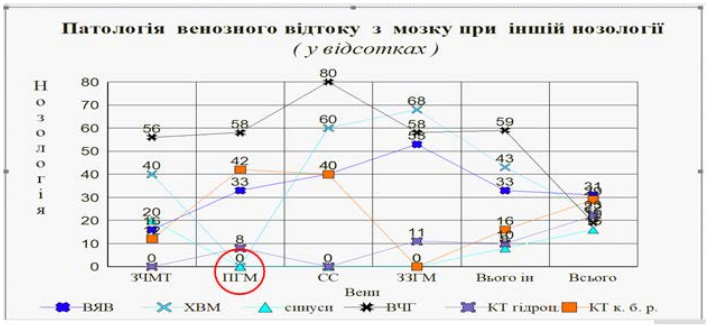
These studies cannot qualify for a full-fledged research, but episodic cases that we observed in the dynamics of each patient are noteworthy, they have the right to establish the fact of specific vascular pathological alterations and require a full-scale project to study PathoNeoAngioOncogenesis.

1. An example of a patient with a confirmed diagnosis of thyroid cancer of 1st st.

One of the first variants of positive verification of our assumptions was the case of diagnosis of thyroid cancer 1st st. in 1996 in a 25-year-old girl with a clinic of venous DE 1st st. and USDG-patterns of unjustified high arterial blood flow in one of the thyroid arteries and thyroid-carotid stolen, expressed by extravasal compression of homolateral internal jugular vein without ultrasound structural changes in the thyroid gland. Complaints on headaches, dizziness, weakness, darkening in vision, tearfulness and psycho-emotional instability as siggns of cerebral dyshemia well fit into the clinical picture of thyroidopathy. Biopsy of the thyroid gland confirmed 1 st. of the oncoprocess. Further thyroid rejection allowed radical treatment tactics and saved the life of the young girl, a successful catamnesis of her life for over 20 years until now.

We published the theory of vascular oncogenesis - PathoNeoAngioOncogenesis for the first time in 2005 in the book "The Blind Doppler for clinical intellectuals'' [40] and it was based on the 15-year experience in the examination of patients with ArterioVenous dyshemias and oncopathology in the form of a chemodectomas of the carotid artery, thyroid gland tumors and brain tumors [84,94]. This theory is based on the ultrasound examination of the main arteries of the head and neck and the diagnosis of PathoNeoOncoVascularization patterns and the formation of the vascular pedicle or several vascular pedicles in cerebral arteries, which vascularized a volumetric new growth, provoked intravascular syndrome and determined the significant effect of venous dyshemia on the formation of a pattern of pathological NeoOncoAngiogenesis (PathoNeoAngioOncogenesis). It should be emphasized that only in the group of patients with brain tumors, venous collaterals were not included in the compensation of venous congestion even with subdecompensated signs of intracranial hypertension [84]. It was the only group of patients where venous collaterals were not included in the compensation of venous congestion.





Figures 4 and 5. Pathology of venous outflow in the brain in CVD and other pathology - ПГМ - brain tumors, blue triangle and cross - venous collaterals are absent) (materials of doctoral dissertation by Lushchyk UB, 1998) [84].

At the same time, we noticed that it was possible to objectify the vascular pedicle of the pathological NeoOncoVascularization of the organ long before the ultrasound-structural changes in the tissues of the organ. On the other hand, in case of brain tumors, objectivation of the vascular pedicle was mainly in patients with confirmed oncoprocess of 3-4 clinical groups and was accompanied by unusual audio signals from the projection of the vascular pedicle of the tumor that resembled the sound of a motor, a motorcycle [84].

Therefore, we tried to investigate the microcirculatory channel by the capillaroscopy method with the ability to visualize and analyze the structural and functional changes in the projection of the nail bed of fingers [28,63,87,88,95].

The primary information processing - native non-invasive images of microcirculation (interpretation of capillaroscopic images) was carried out according to the copyrighted technique of Dr. Lushchyk UB, patented as *Method of evaluation of microcirculation disorders within the norm and pathology in people of all ages with the help of the capillaroscopy: State Patent of Ukraine*. No. 67709A; 31.12.2003 [85,87,88].

It is well-known that the microcirculation "picture" in norm indicates the adequate functioning of CVS in a single link "heart - major arteries – arterioles - capillaries - venules -main veins - heart". However, detecting pathological abnormalities (orange and red scale zones in histograms of vascular screening technology) we expand the spectrum of CVS research into all parts of the vascular blood stream - heart, major and peripheral arteries and veins, ArterioVenous and hydrodynamic balance [28,35,63].

The next development of smart capillaroscopy technology allowed to correlate macrovascular ArterioVenous [40,86] and microvascular arteriolarvenular disorders in patients with oncopathology [28,87,88].

The most revealing was a group of 97 patients who came to the dispensary overview after a surgery on the breast. This sample was spontaneous - during the dispensary observation at the Cancer Institute of the Academy of Medical Sciences of Ukraine 97 patients underwent vascular screening, the purpose of which was to get acquainted with the state of microcirculation on the nail bed of the fingers of both hands in patients with breast cancer of various stages.

All patients have expressed structural changes in the microcirculatory channel of the nail bed of the fingers, in 68% - homolateral to the side of breast cancer, in the remaining 32% - bilateral changes in the microcirculation in the nail bed of both hands. 80% of the surveyed have significant structural changes in the capillaries - the dilated venular segments of the capillaries and in 46% there was a venular net, the capillary tortuosity and anomalous forms of capillaries in 67% of patients, perifocal edema in 48% was moderately expressed, isolated, perivasal, in 12 % - a tendency to continuous edema in the form of a hydrophilic perivasal strip, in the remaining 40% - intense, drainage perivascular edema around the group of capillaries with compression of the arteriolar segment of the capillaries, 72% - signs of severe deficiency of blood filling of arteriolar capillary segment, 45% - signs of the rheology disorders with microthrombing. It should be emphasized that all these changes took place on the background of venular dilatation (80% of patients).

Figures and the histograms 4.1. and 4.2 present normal vascularization and hemodynamic characteristics obtained with vascular screening technology. The green color of histograms reflects a variant of the norm.

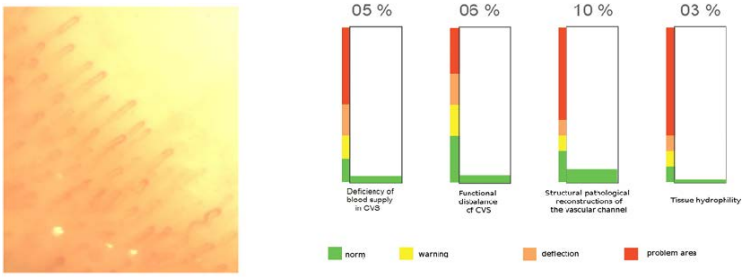


Figure and histogram 4.1 (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

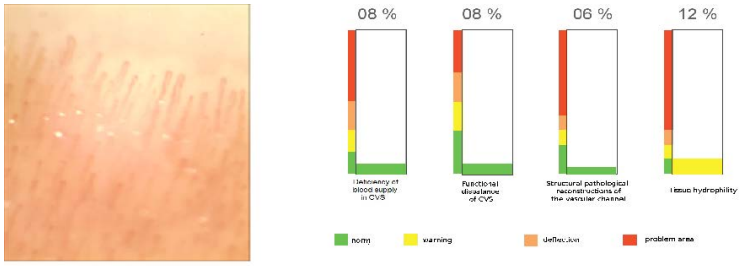


Figure and histogram 4.2. (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation

pattern, yellow-green histograms reflect the range of microcirculation norm).

Figure and histogram 5.1-5.15 show pathological MicroNeoVascularization in patients with breast cancer

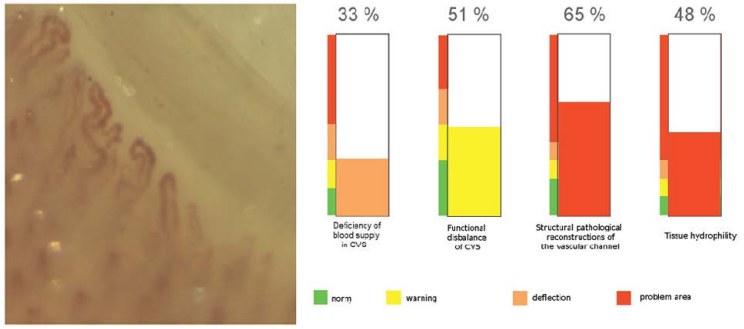


Figure and histogram 5.1. (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

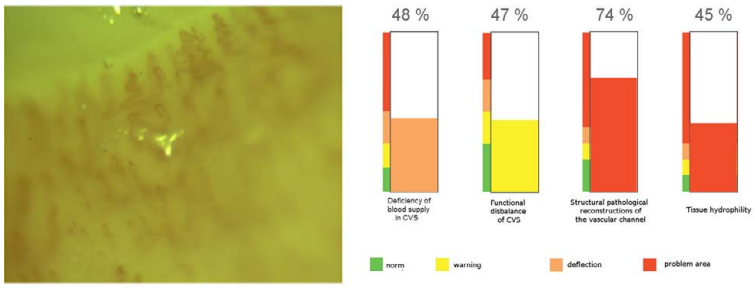


Figure and histogram 5.2. (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

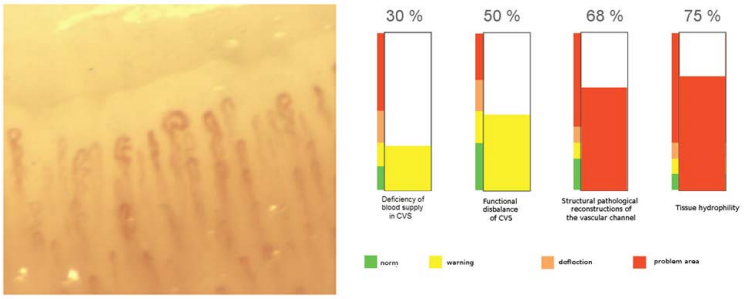


Figure and histogram 5.3. (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

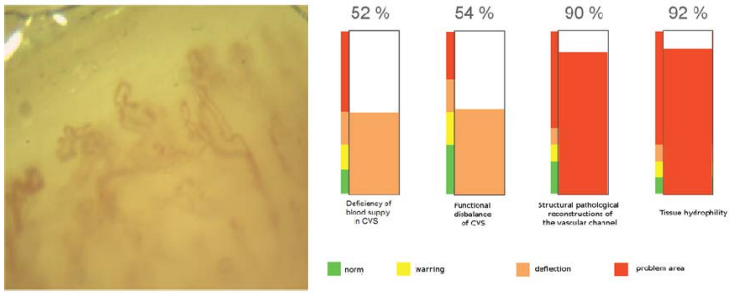


Figure and histogram 5.4. (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

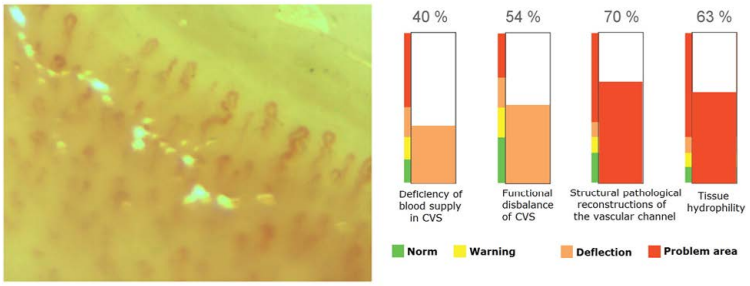


Figure and histogram 5.5. (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

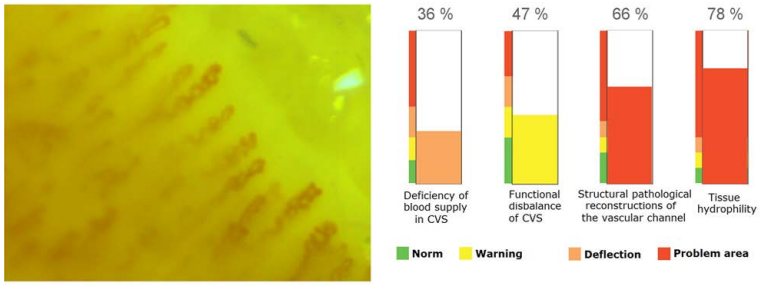


Figure and histogram 5.6. (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

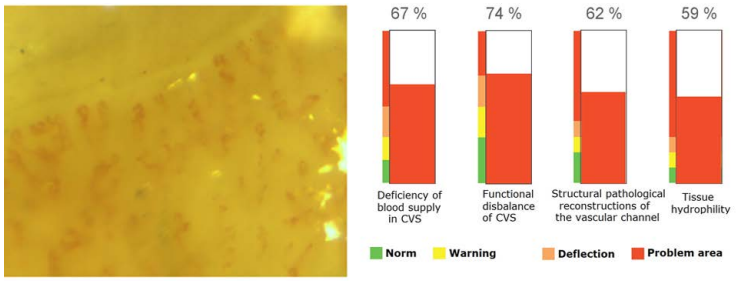


Figure and histogram 5.7. (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

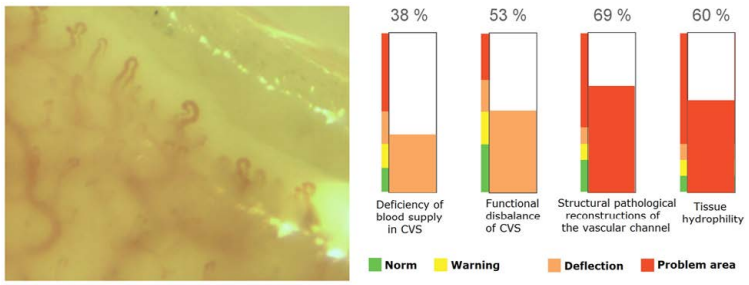


Figure and histogram 5.8. (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

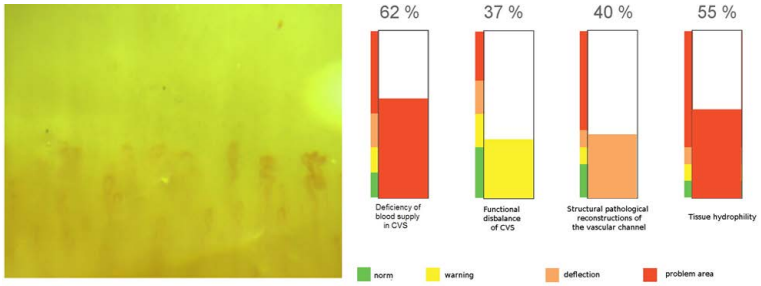


Figure and histogram 5.9. (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

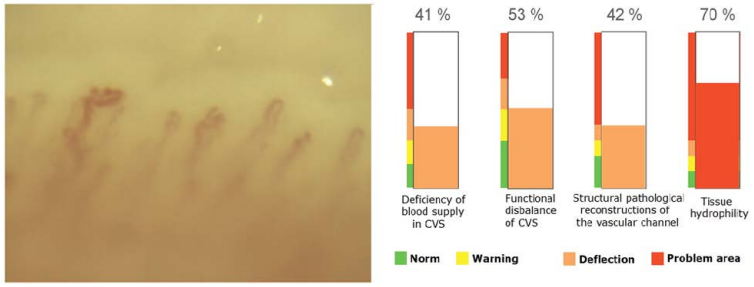


Figure and histogram 5.10. (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

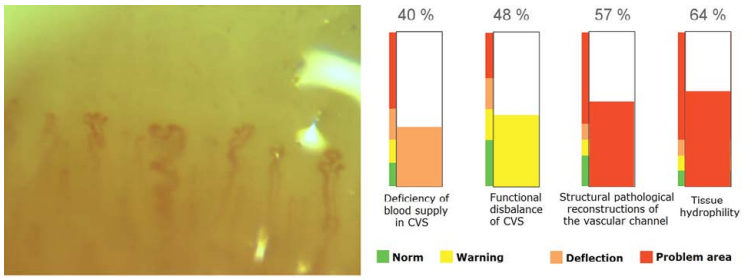


Figure and histogram 5.11. (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

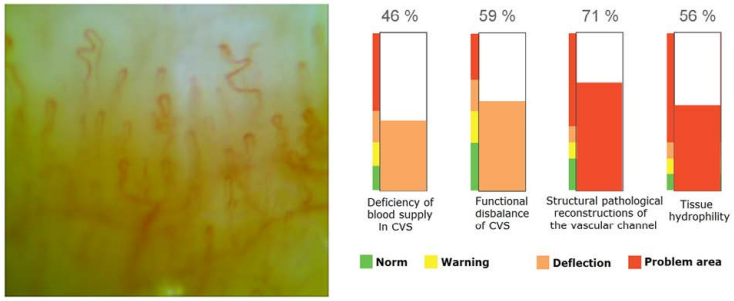


Figure and histogram 5.12. (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

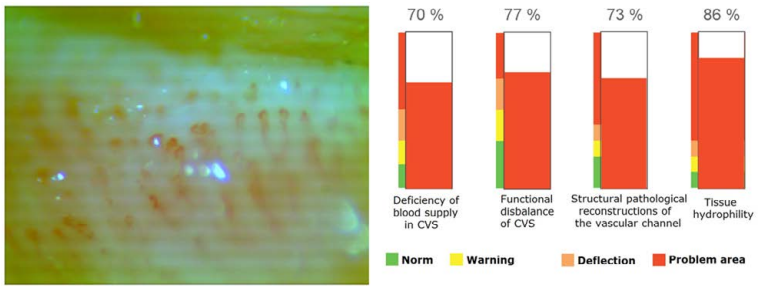


Figure and histogram 5.13. (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

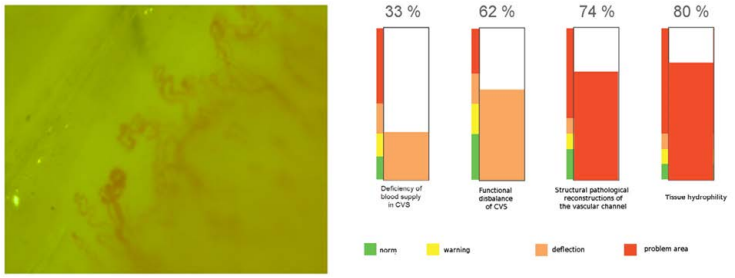


Figure and histogram 5.14. (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

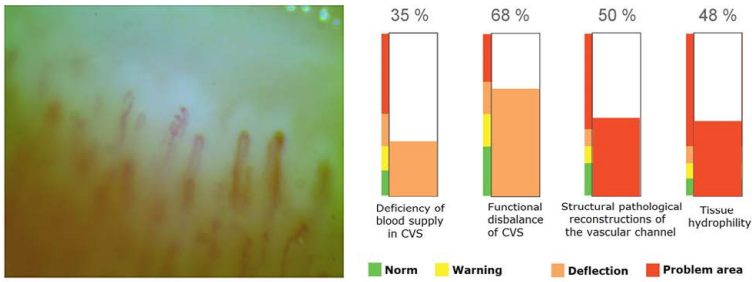


Figure and histogram 5.15. (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

It should be emphasized that in most cases, patients had the course of specific treatment intravenously with the use of a "sick" hand. We assume that with such structural changes in the microcirculatory channel of the hand, it is not desirable to use the veins of this hand for intravenous infusions since the risk of thromboembolism and hematogenous spread of mutagenic factors is quite high.

Taking into account the expressed pathological microcirculatory patterns of "PathoNeoAngioOncogenesis", which mostly reflected the picture of venous stasis at the microcirculatory and peripheral levels, we can assume the important role of venous stasis and microthrombosis in the pathogenesis of the onset and progressive development. [40,88,97-100].

Hydrodynamic perivasal conflict on the background of expressed structural changes of onco-capillaries as a result of pathological "wetting" of the vascular wall and gradually increasing deficit of arteriolar blood supply on the background of structural changes of the microcirculatory tract actually complete the terminal stage of death of the cancer patient. [101].

Similar patterns we now observe at patients after Covid-19 and already allocate in separate post-Covid-19 vascular syndrome with specific patterns of sudden pathological structural transformation of microvessels with a microthromboangiopathy. (See Figure 13)

The microvascular imbalance actually goes into an uncontrollable stage, when an adequate blood volume cannot regularly enter into one or another part of the sick organism, which enhances the processes of hypoxia and stimulates the anaerobic type of metabolism. In 78% of cases, these hemodynamic changes correlated with the clinical picture of lymphostasis in one and / or both upper extremities, and in 90% of cases it was accompanied by a feeling of cold and / or palpitations of the fingers [28,40].

Single attempts to use the traditional personalized course of intensive angiocorrection were accompanied by unusual, unexpected pathological paradoxical reactions of the organism, accompanied by expressed vascular chaotic meteotropic pathological reactions and

an unstable psycho-emotional background of oncologic patients. Often, these reactions led to the transition to a "light" chemotherapy or radiation therapy scheme, which did not allow for the desired outcome of treatment. As a result of such an organism's reaction, small doses of radiotherapy resulted in accelerated, radio-stimulated progressive tumor growth.

Capillary reactivity to functional tests (orthostatic tests) was reduced with inert reactions of the vascular bed after a 7-10 second pause in 76% of patients, accompanied by subjective feelings of dizziness, darkening in the eyes, the need to lie down, sit down, etc., that testified to the extremely unbalanced system of cardio-vascular autoregulation and the inability of the body to effectively manage the cardiovascular system, especially when changing the body position (orthostatic reactions).

Over the last 8 years, the clinic had a unique experience of vascular correction and supervision of "non-curable" oncopatients, who applied for medical aid with concomitant vascular pathology.

Clinical examples of the dynamics of the microcirculation picture in cancer patients

1.1. Patient J. 63y. Diagnosis: Non-Hodgkin's Lymphoma.

Clinical history 2 years after diagnosis. The debut of the disease from sudden mechanical obstruction of the intestine and resection of the intestine (summer 2011). The period of supposed well-being lasted about half a year after the resection was carried out.

However, 2 months after the operation, we conducted a microcirculation study and hirudotherapy of the perineum. (November, 2011)

Vascular screening technology (VST): capillary-cells with black component and expressed microcirculatory deficiency, which indicated a sediment adsorbent in the intercellular environment after oral intake.

In the dynamics of receiving the minimum angiotherapy, the black sorbent "came out of the capillaries".

In 2 months after resection of the intestinal tumor, the patient complained of a feeling of heaviness in the perineum, "shots" in the inner thigh, periodic twisting pains in the middle of the perineum. A 2-week course of angiocorrection was performed to restore blood supply to the body with periodic sessions of hirudotherapy in the perineal projection.

Hirudotherapy of the perineum - the received blood is black, like a resin. This color of blood indicated a deeply pathological process that took place. Despite recommendations for further examination by an oncologist, the patient felt well and refused chemotherapy and any further medical treatment. He chose the methods of folk medicine to further support his life.

He received 3 sessions of hirudotherapy of the perineum about the signs of an expressed venous stasis in the small pelvis long before the appearance of the mortem clinical picture of lesion of the horse tail. No specific angiotrophytic treatment was given.

The disease course was characterized by a multifocal symptomatology with a sharp decrease in visual acuity, then with the problems of movement on the background of symptoms of lesion of the horse tail.

He died of thromboembolism 1 year after the onset of the disease.

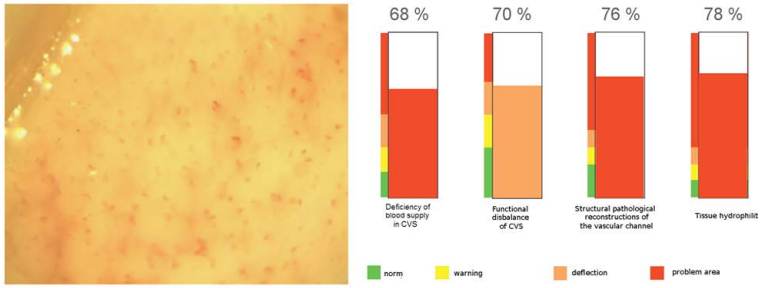


Figure and histogram 6.1 Dot-type visualization of capillaries with virtually no blood flow and signs of microthrombi at the time of the debut of the illness in the patient J. (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

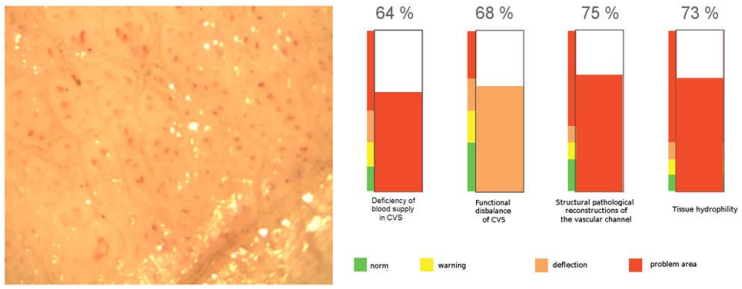


Figure and histogram 6.2. Patient J. Expressed hydrophility with the formation of local cells. This phenomenon needs further research for proper interpretation. (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

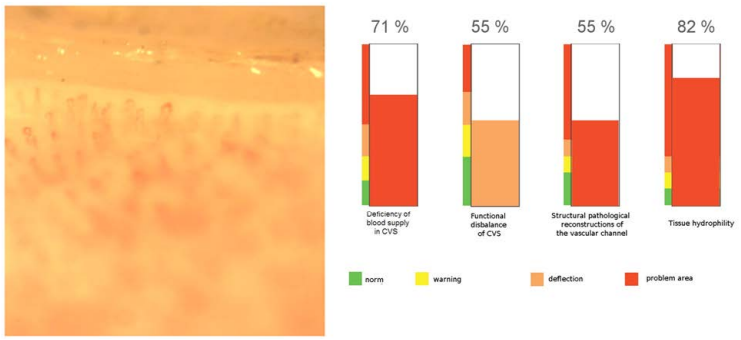


Figure and histogram 6.3 Patient J. After a few daily courses of minimal vascular therapy. Insignificant improvement of the microcirculation due to improved blood flow to the capillaries and the change of the dot- type of capillaries for the visualization of short capillaries. (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

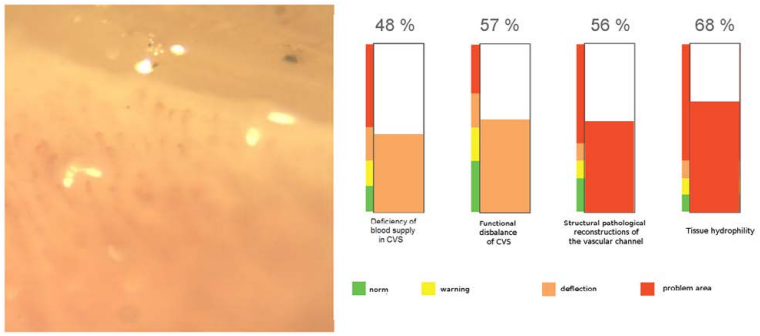


Figure and histogram 6.4. Patient J. Positive dynamics of a two-week course of angiocorrection. The histogram reflects a significant improvement in blood supply and a decrease in the severity of microcirculation deficits and reduction of functional disorders in the vascular blood stream. (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

1.2. Patient A. 60y. Diagnosis: Cr. Mammae sinistra, TNM: T2B N1 M0 (2012)

Diagnosis in 2012. Operated in 2012: Mastectomia sinistra totalis. Chemotherapy + radiotherapy for 1 course + hormone therapy (axastrol).

She applied at our clinic after the completion of a specific treatment of oncopathology with complaints of general weakness, dizziness, depression, difficulty of moving, palpation of the fingers and toes, memory loss, blunting of emotions, sleep disturbances.

The patient had a three-month course of individual angiocorrection and angiotherapy by copyright technology of Acad. Lushchyk U.B.

In connection with certain home conditions, the treatment was conducted by intramuscular injection under the monitoring of vascular innovative technologies weekly.

In the dynamics of 3 months of vascular treatment (angiocorrection) it was managed to level almost all complaints.

The Patient A. herself spoke about her condition: "They stopped giving up seats to me in subway" (Ukrainians give up seats at general transport to the sick, pregnant women and the elderly as it is a cultural tradition).

A month after the course of treatment the patient A. returned to her work and continues working at present time, regardless of retirement age. She feels good.

Observation: Oncocontrol 1 time per year. In 2017 there is no continued growth.

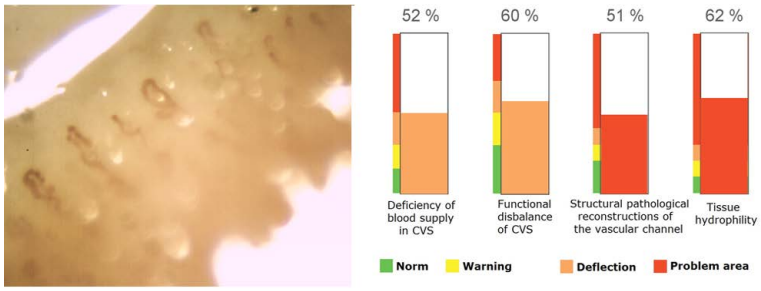


Figure and histogram 7.1. Patient A. Condition of microcirculation at the beginning of angiotherapy (04/2012). (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

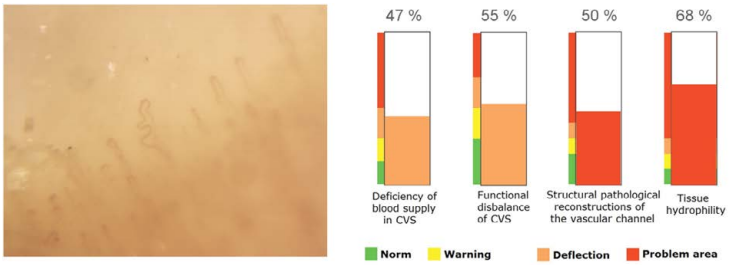


Figure and histogram 7.2. Patient A. Results of vascular screening after the completion of a 3-month course of treatment (2012) (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

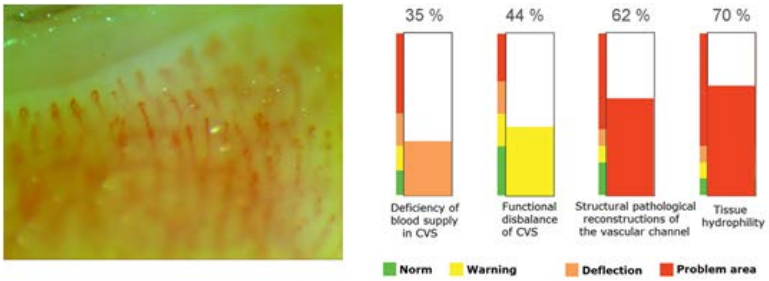


Figure and histogram 7.3. Patient A. Control test after 5 years without repeated courses of angiotherapy (2017). Available microcirculatory changes are alarming with regard to the phenomenon of hypervascularization and require angiocorrection of hemodynamic parameters. (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

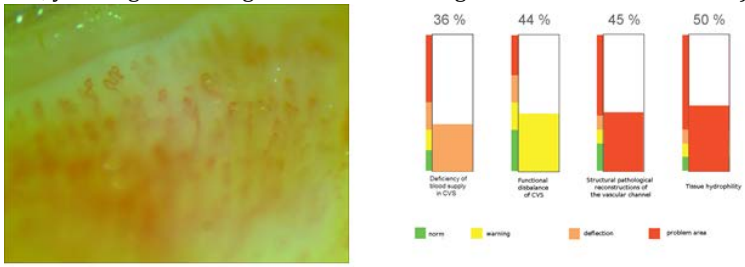


Figure and histogram 7.4. Control check-up in 2017 (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

Resuming the following catamnesis for the last 9 years, the patient is alive and able to work so far (2021), feels satisfactory. She does not feel the need for treatment and angiocorrection.

This example indicates the need to form a travel card for cancer patients with key stages of control of pathological NeoAngioOncogenesis, monitoring the dynamics of the process before and after specific treatment of the tumor (chemotherapy, radiotherapy, hormone therapy, etc.), involvement of vascular program to correct existing disorders of NeoAngiogenesis by evidence-based medicine - vascular screening data at the microvascular level and angiomarkers at the macrovascular level.

It is the process-management controlled at key points that can achieve quality management in the end result and ensure the extension of life expectancy (in this case it is 9 years of full life) and adequate quality of life of cancer patients (still able to work at age 69). As angiotransformations are earlier and more sensitive at the microvascular level the vascular screening technology with VIAT AngioSmart enables to monitor even the early preclinical stages of NeoAngioOncogenesis.

1.3. Patient V. 57y. Diagnosis: Cr. Mammae sinistra, T2 N2a M1(2010). Multi mts cerebri. Mastectomia totalis sin. 2010

Clinical history of 8 years from the diagnosis. 13 courses of chemotherapy for 2 years (2010-2012) and the next "stroke" (october-2012) with verification of 10 brain metastases and the appearance of epileptic seazures. She applied to our clinic with brain symptoms to maintain and ensure the highest possible quality of life.

The patient received our treatment and rehabilitation almost daily for 2 years.

The example of the "forced" curator of a patient after mastectomy, 13 courses of chemotherapy, resulting from clinical picture of stroke and MRI-identification of 10 metastases in the brain. We emphasize the correlation of macro- and microvascular status with a clinical picture of general cerebral symptoms, epi-seizures and dynamics of the microcirculatory picture.

The patient was on a day care hospital in the Clinic of Vascular Innovations since 2012 for 3 years until spring 2015, received the course of angiotherapy and angiocorrection practically continuously, passed the phase of epi-seizures and successfully came out it (7 - months of absence of attacks before death), body weight renewal, attempts of social and professional rehabilitation.

During the angiocorrecting treatment, she took 2 courses of radioactive metastatic foci of the brain (local targeted radiotherapy for brain metastases). After the 1st irradiation, the loci did not change, the patient's condition deteriorated slightly due to disorientation, impaired vision and instable walking. After the 2nd course of irradiation, the patient's condition significantly deteriorated, the previous complaints were accompanied by weakness, a constant feeling of fatigue, signs of mental retardation and headache in the back of the head.

Dynamics of metastases for 2 years.

For 2-3 weeks before death, there were symptoms of vomiting on food intake, which was accompanied by rapid weight loss.

The control and last MRI revealed destruction of brain tissue at the metastases area, an increase of perifocal edema with exceeding the first size in several times and impaired liquor dynamics. Later, the dynamics became sharply negative and the patient soon died against the background of the growth of cerebral signs with the transition from inhibition to sopor-stupor for 2-3 days, a coma up to 5 days and a lethal end.

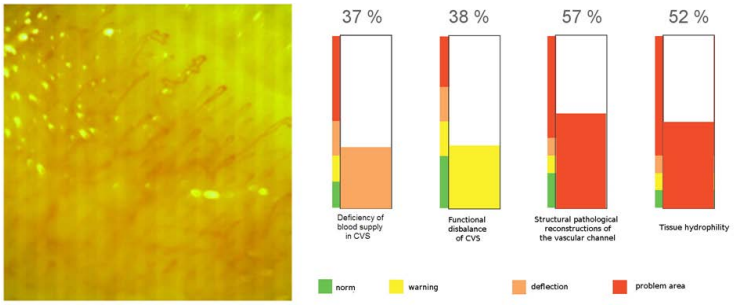


Figure and histogram 8.1. Patient V. Results of vascular screening at the time of treatment after a stroke (2012) before the start of angiocorrective treatment. (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

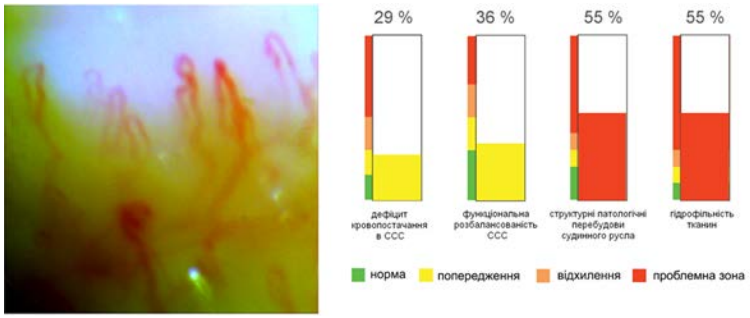


Figure and histogram 8.2. Patient V. Vascular screening after the first session of angiocorrection and angiotherapy. (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

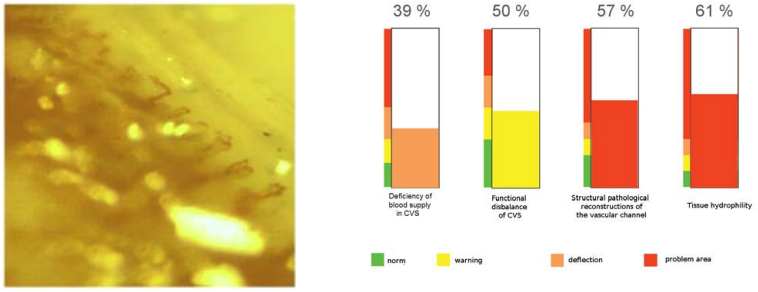


Figure and histogram 8.3. Patient V. Prior to 3-rd course of angiocorrecting treatment (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

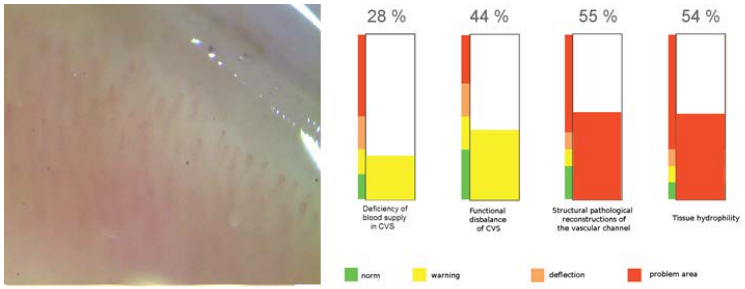


Figure and histogram 8.4. Patient V. Completed 2nd angiocorrection course (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

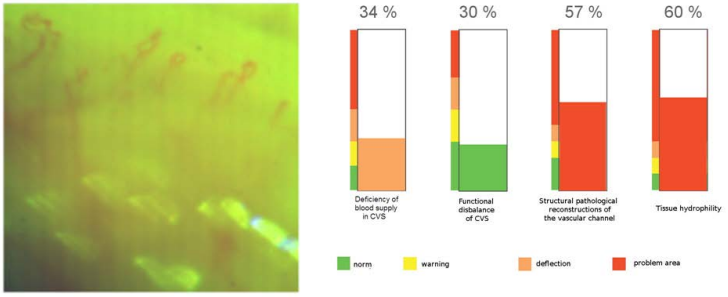


Figure and histogram 8.5. Patient V. Results of vascular screening after the first 3 months of angiocorrective treatment (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

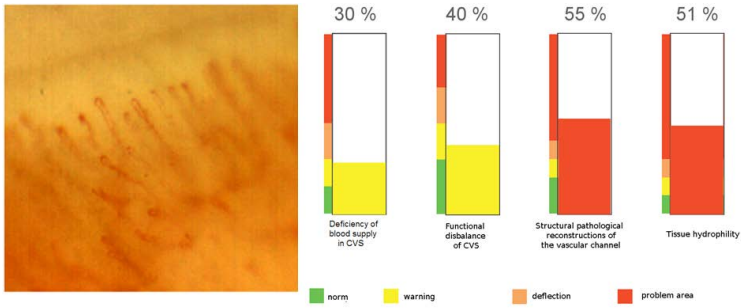


Figure and histogram 8.6. Patient V. Periodic control by vascular screening reflects positive dynamics, but requires further long-term treatment to correct and stabilize all hemodynamic parameters. (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

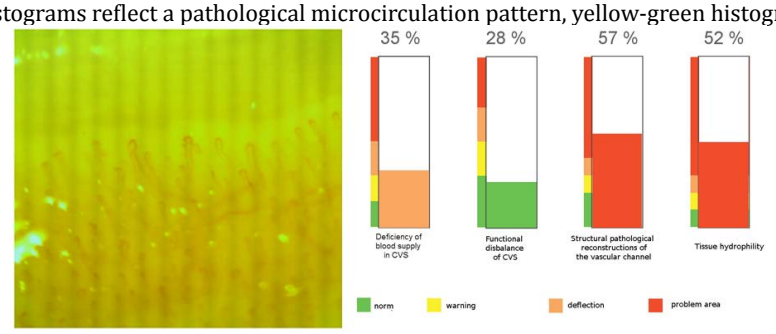


Figure and histogram 8.7. Patient V. Vascular screening after 1 year of angiocorrection and angiotherapy. (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

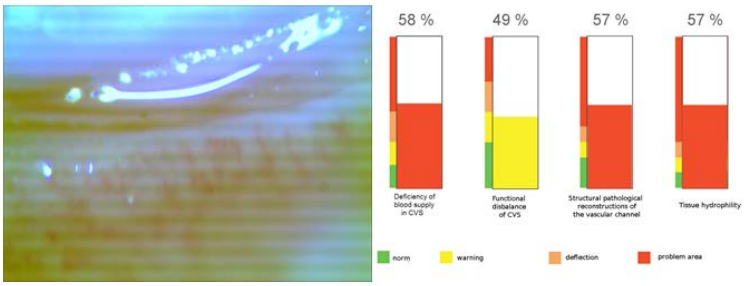


Figure and histogram 8.8. Patient V. After the 2nd course of targeted radiotherapy of brain metastases (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

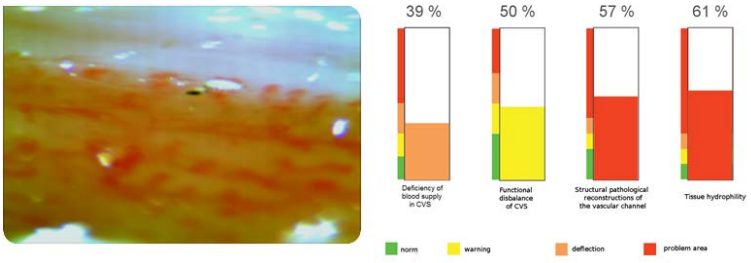


Figure 8.9. Patient V. Negative dynamics of edema increasing and venular stasis with expressed imbalance of microcirculation in 1 month after targeted radiotherapy of metastases. (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

Discussion of Results

The ideology and algorithms of the use of evidence-based medicine as instrumental monitoring in the process of angio-correction of

oncological patients

Despite numerous studies, a long period of study of oncogenesis and angiogenesis on the latest basis of the latest technology, the pathogenesis of AngioOncogenesis remains unexplored, treatment is partially effective, but the prognosis of life and quality of life is not predictable.

Therefore, let's start with the discussion of terminology because various literature calls the same processes differently.

We tried to introduce the unification of these terms in the terminology section in order to minimize the different versions of the perception of such terms.

In this situation, we consider the result discussed is appropriate and it is important to discuss the fact and the terminology sequence of the names of AngioOncogenesis.

We deliberately use the term PathoNeoAngioOncogenesis, but not OncoAngiogenesis, because we are convinced that the vascular bed and the uncontrolled process of vascularization are the basis for tumor development and the background for the risk of tumor developing [28,40,63].

Transformation of the microcirculatory channel creates such hemodynamic preconditions with a pattern of venous stasis, where pathological infectious elements can successfully multiply, mutate and form uncontrolled growth of flora and tissues without the participation of control systems of the body (immune, humoral, hemodynamic, mechanical turbulence). We called this place as an infectious marsh.

The launch of an infectious marsh in the body is a local place where a quiet plant (venous stasis, ischemia and hypoxia + anaerobic metabolism, in some cases amplified by hyperglycemia) is created for the reproduction of pathological elements (fungi, viruses, bacteria), their mutations and the formation of the primary foggy foci [40,58,93,97-100].

We believe that all hemodynamic pathological processes in the body are aimed at reducing the rate of arterial blood flow and reducing oxygenation at the level of microcirculation in the tissues. The primary link of distal deficiency of the arterial link is manifested as a sign of ischemia and hypoxia of a specific organ in cardiovascular failure. At the same time, we observe clinical signs of organ deficiency in cardiovascular or cerebrovascular insufficiency. In contrast to vascular dyshemia, NeoAngioOncogenesis results in a much deeper vascular lesion than in cardiovascular disease, as we have seen when comparing this study with 3 patient groups.

At the same time, expressed changes in the microcirculatory level in cancer patients appear clinically much later, unlike vascular patients.

These results of our study (Figures 9-12) in the form of the domination of structural changes in the microcirculatory bed in oncopathology compared with vascular patients, we try to explain from several sides.

The PathoNeoAngioOncogenesis leads to the structural rearrangement of the capillaries, a decrease in the longitudinal intravascular pressure of the blood, and the loss of hemodynamic turbulence in blood flows, which in their essence have a sanogenic mission of destroying atypical cells. Reperfusion syndrome, microembolization with tumor elements contribute to hematogenous spreading, and the general hemodynamic picture of system venous stasis, PathoNeoAngioOncogenesis locally at the area of an infectious marsh and ischemic-hypoxic changes contribute to anaerobic metabolism and the formation of metastases.

We came to these assumptions through the use of analytical and visualizing life-time vascular innovative technologies that enable us to observe in vivo hemodynamic changes in the bloodstream, to simulate various situations for the study of pathological and sanogeneous changes in the circulatory system.

Transcranial dopplerography [40] is the optimal method for the objectification of hemodynamic reconstructions as well as blood flow turbulence at the macrocirculatory ArterioVenous level. The most complete picture of hemodynamic disorders at the regional and systemic levels is presented by the technology of angiomarkers with an estimation of about 50 hemodynamic parameters of the arterial and venous link and displacement of the ArterioVenous balance [93].

At the microcirculatory level, the technology for vascular screening is the most informative and evidentiary with the possibility of visualization and quantitative and qualitative analytical assessment of microcirculation disorders in 4 parameters: blood supply deficiency, structural changes in capillaries, functional disorders of microcirculation, perivascular hydrodynamic conflict [87,88].

It should be emphasized that microcirculatory changes are primary at the time of diagnosis, and macrocirculatory in the form of a vascular leg can be detected in the later stages of the cancer process, when oncopathology has "grown" to the level of the regional vascular reservoir.

Therefore, further we will try to formulate certain algorithms of macro- and microcirculation, which, in our opinion, reflect the hemodynamic signs of PathoNeoAngioOncoVascularization.

Hemodynamic levels of living activity of a living organism and the possibility of their research by modern methods of instrumental diagnostics in PathoNeoAngiogenesis and PathoNeoAngioOncogenesis:

Considering the human body as a living system capable for autoidentification and autoregulation, self-management, and decision-making [102,103] we use this algorithm for mathematical modeling of all pathological conditions in the body before angiocorrection and angiotherapy of detected imbalances.

Therefore, consideration of the hierarchical levels of inter-system balance and mutual subordination between different systems and subsystems is extremely important in terms of O**ncoNeogenesis**. Speaking about the vascular bed and its **angiotransformations** at micro- and macrolevels, it is advisable to highlight key points that have a significant effect on pathological transformation within the vascular blood flow:

1. Hydrodynamic level of system functioning:

- A phenomenon of hydrodynamic conflict in closed cavities - the skull, small pelvis, chest cavity.
- A phenomenon of intracellular hypertension.
- A phenomenon of perivascular edema.
- A phenomenon of pathological wetting of the vascular wall and tissue hydrophilicity.

2. Hemodynamic level of life support of organs and systems:

Intravascular pressure is longitudinal in the arterial link.

- The intravascular pressure is transverse in the arterial and venous links.
- ArterioVenous balance at the regional and systemic levels.
- Dependence of intravascular pressure of the cardiovascular system from intravascular influences.
- Dependence of intravascular pressure of cardiovascular system from extravasal influences.

3. Variants of angioarchitectonics at macro- and microlevels.

4. Reactivity of the vascular system.

5. Hemodynamic reserve.

The potential of evidence-based medicine in the screening risk of PathoNeoAngioOncogenesis

Speaking about early diagnosis of angiotransformations in oncopathology, we tried to analyze non-invasive and rapidly accessible diagnostic methods that could identify vascular reconstructions in the future in screening regimens.

As a result of the study, it was found that in 76% of cases USDG was the most sensitive method of diagnosis of the vascular pedicle when studying the regional reservoir in the onco-process area.

The capillaroscopic picture in 94% of cases reflected disorders in the microcirculatory channel and was accompanied by various deviations in the structure of **MicroAngioArchitectonics** with a specific gravity of pathology more than 50% in sight - in 83% of cancer patients, dominant manifestations of venular stasis in 97% of cases, atypical forms of capillaries in 65% of cases, the dominance of hemostasis and microaggregation in 98% of cases in the group of cancer patients.

Therefore, taking into account the above facts, we concentrated on two levels of angiogenesis – neovascularization - **MicroPathoNeoAngiogenesis** at the level of microcirculation and **MacroPathoNeoAngiogenesis** at the level of major and peripheral vessels in the regional vascular reservoir of one or another organ.

MicroPathoNeoAngioOncogenesis: disorders of microcirculation in cancer patients

Since capillary circulation carries the main function of the microcirculatory system - transcapillary metabolism, i.e. metabolism between blood and tissues, the condition of microcirculation serves as an arbiter for the well-being of systemic hemodynamics and reflects the preserved ArterioVenous balance in regional vascular reservoirs [28,88].

Therefore, the attention of scientists and practitioners are once again turned to the microcirculatory link. At the present stage of the development of visualization technologies in vivo, a logical renaissance of the long-forgotten technique of life-time visualization of the smallest vessels - capillaroscopy. And words of AS Zalmanoff of more than 100-year-old are again actual, *Disorder of the capillary physiology are so widespread and so often observed that they should be considered not a minor phenomenon, but, on the contrary, one of the main elements of organic disorders in the patient, whatever the disease* [104].

The development of capillaroscopy as a method of obtaining the microcirculation image in life and the formation of vascular screening technology have several essential steps:

1. The capillaroscopy started as a method of individual visualization of microcirculation in a microscope lens and did not receive proper support and recognition in the 1960's, as there were no possibilities for fixing images for archiving and display, no interpretation techniques.

2. The capillaroscopy renaissance at the end of the 20th century. Digital technologies gave a new opportunity for the renaissance of capillaroscopy, namely: getting an image on the monitor allowed both the doctor and the patient to watch the same image that could be discussed by physicians and developed algorithms for logical solutions for the treatment of a particular pathology.

Compared to other methods of microcirculation research, the advantage of the method of smart capillaroscopy is the visualization of the process of blood flow in real-time, which greatly simplifies the perception of capillary pictures for the physician, makes it possible to study and analyze more deeply obtained images with the software of vascular screening technology.

3. Clinical interpretation of capillaroscopic images and analysis of microcirculation in dynamics. At the beginning of the 21st century, the technique of smart optical capillaroscopy gradually received:

- software for the primary and analytical clinical data processing,
- mathematical models for the optical system of the capillaroscopy were developed;
- algorithms for non-invasive obtaining of a static and dynamic image of microcirculation in vivo,
- mathematical models of microcirculation and hemodynamics in small vessels,
- mathematical models for screening algorithms for norm and pathology at the microcirculatory level.

4. Transfer quantity to quality: the creation of **VIAT AngioSmart** vascular screening technology. Due to the above-mentioned additions and innovations, this methodology of native optical capillaroscopy has developed into vascular screening technology and received a new stage of development within the framework of technology and sub-technologies in accordance with specific nosological forms by sections of medical branches - psychoneurology, endocrinology, oncology, insurance medicine, neonatology, pediatrics, dentistry, cardiology, etc.

Previously, the method of obtaining and analyzing microcirculation data was not used in oncopathology studies.

Therefore, our developments and the observation of patients in the dynamics have led us to the need for the development of new technological products - sub-technologies [105]. Among the sub-technologies of the oncological direction, we chose the name "Oncocapillaries". This sub-technology is the most demanded by both developers and its potential consumers - the population all over the world.

Comparative characteristics of changes in microcirculation and signs of MicroPathoNeoAngioOncogenesis in different groups of patients

At first glance, this idea is somewhat unexpected. Because few researchers investigate the vascular system in oncopathology. However, our long-term experience (over 20 years, daily we are investigating microcirculatory changes in different groups of patients) allowed us to visually distinguish between specific and non-specific patterns of microcirculation changes. Therefore, there was such an unexpected decision to find common and distinctive features in 2 groups of patients with different nosological units and the 1st control group of healthy people of the same age.

Speaking about the specificity of angiooncotransformations, qualitative and quantitative comparison of images in 3 groups was appropriate: 1 - control group of practically healthy (n=170), 2 – CVD patients (n=780), 3 – a group of verified oncologic patients(n=58). All patients were in the same age range (26-82 years), the avwrage age was 52 ± 18 years.

The control group was practically healthy and patients with cerebrovascular pathology were without cancer. Therefore, we can talk about certain specific features in the picture of microcirculation in cancer patients.

Figures and histograms 9.1-9.4 of the 1st group of virtually healthy:

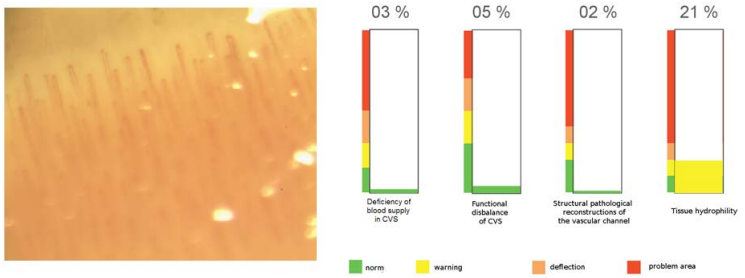


Figure and histogram 9.1. (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

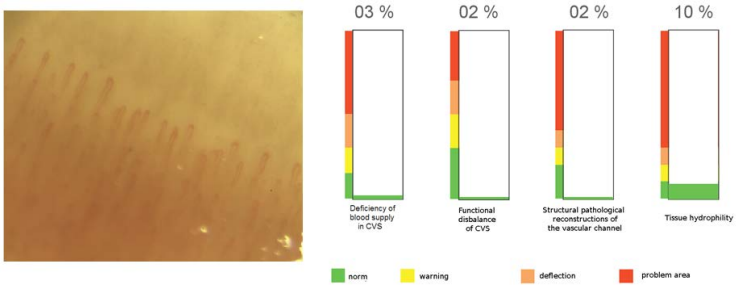


Figure and histogram 9.2. (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

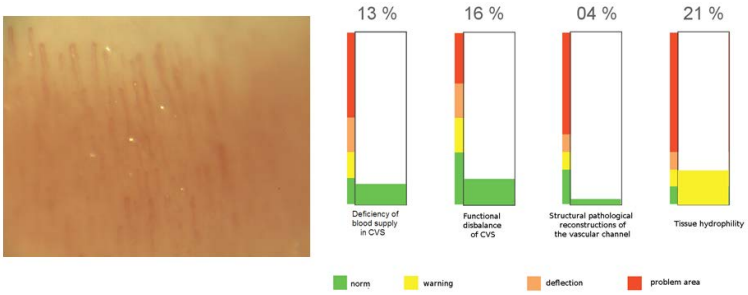


Figure and histogram 9.3. (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

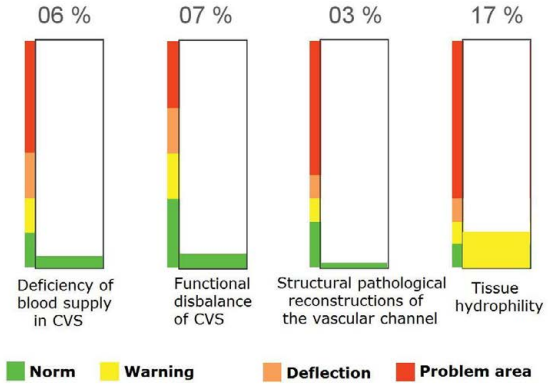


Figure 9.4. Generalized histogram for the 1st group

Figures and histograms 10.1-10.10.1 - the 2nd group of CVD patients

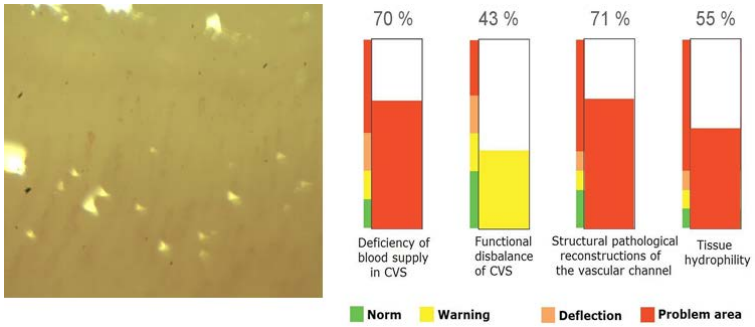


Figure and histogram 10.1. CVD without treatment (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

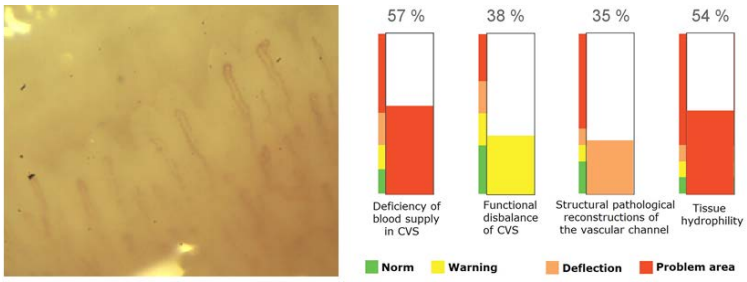


Figure and histogram 10.2. CVD without treatment (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

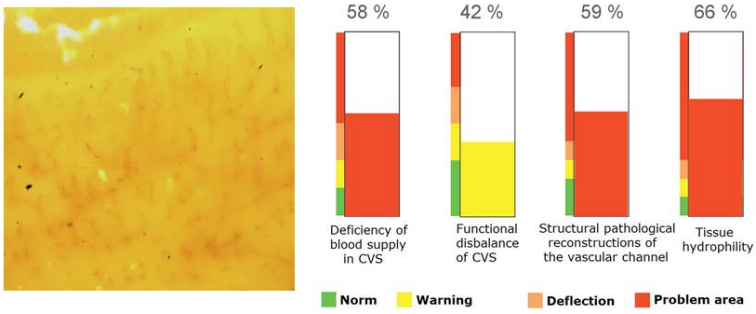


Figure and histogram 10.3. CVD without treatment (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

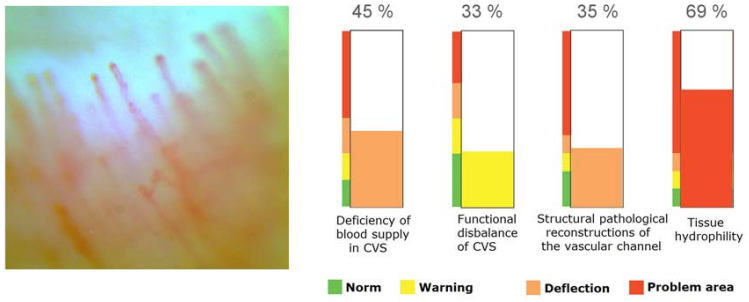


Figure and histogram 10.4.1. CVD before treatment (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

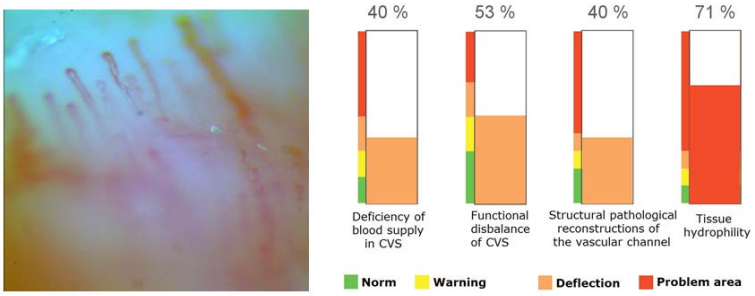


Figure and histogram 10.4.2. CVD after treatment. This case indicates the low informativeness of the quantitative parameters of vascular screening at the beginning of angiocorrection, because all the main parameters are almost in the pathological area. The index of blood supply deficit has positive dynamics, which indicates the correctness of the chosen treatment tactics. (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

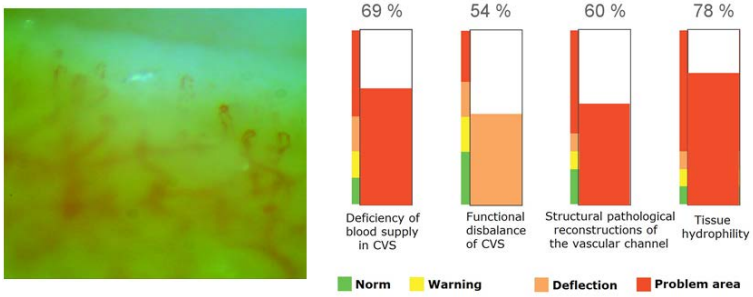


Figure and histogram 10.5.1. CVD before treatment (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

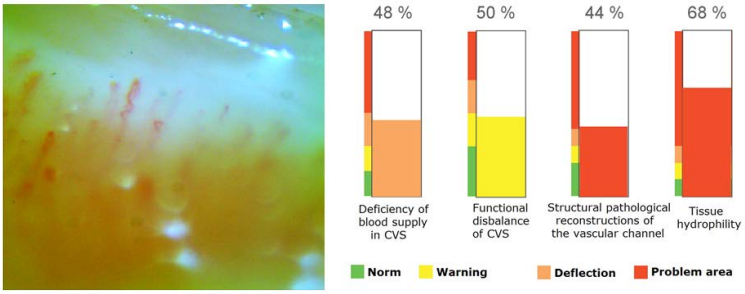


Figure and histogram 10.5.2. CVD after treatment (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

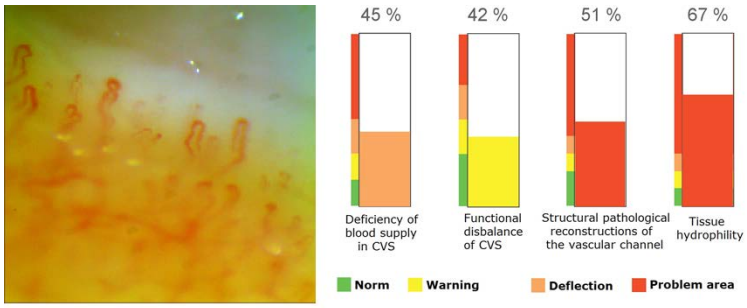


Figure and histogram 10.6.1. CVD before treatment (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

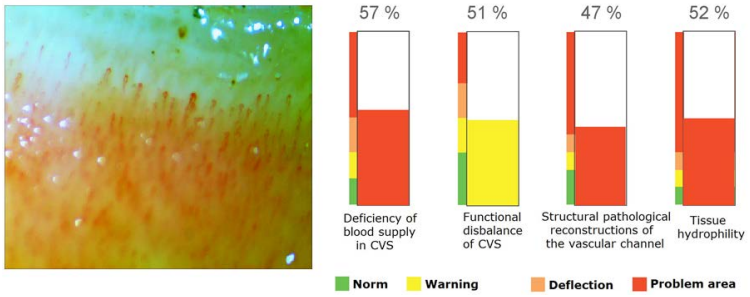


Figure and histogram 10.6.2. CVD after treatment. Negative dynamics of increasing blood supply deficit against the background of stimulation of unproductive angiogenesis. Treatment tactics are not chosen correctly. (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

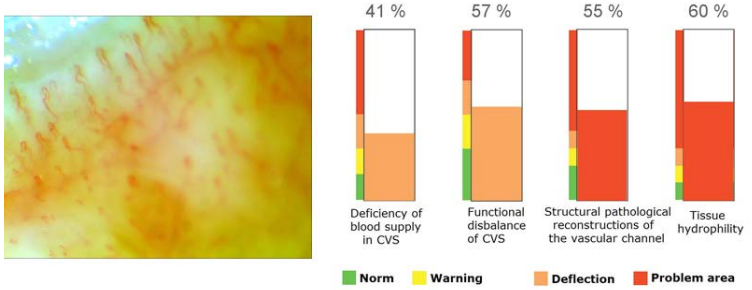


Figure and histogram 10.7.1. CVD before treatment (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

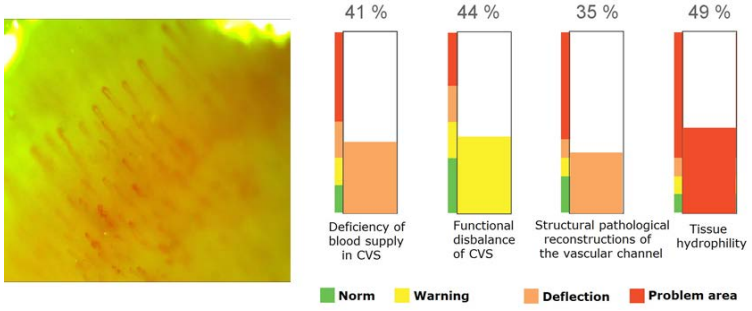


Figure and histogram 10.7.2. CVD after treatment (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

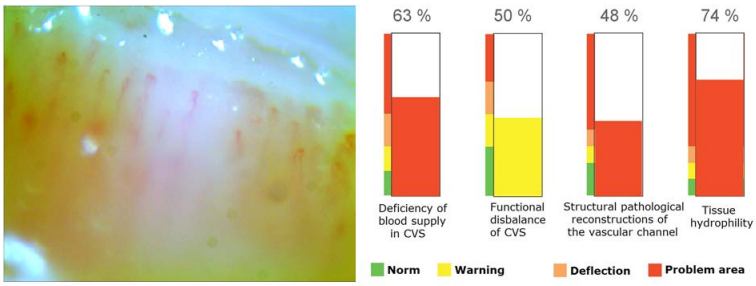


Figure and histogram 10.8.1. CVD before treatment. The presence of 3 of 4 indices of vascular screening in the red range indicates an expressed imbalance of hemodynamic parameters and a high risk of vascular accidents. Therefore, long-term treatment is required to achieve normalization of all parameters. (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

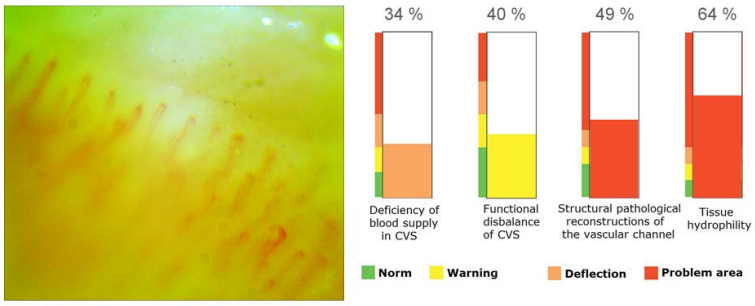


Figure and histogram 10.8.2. CVD after treatment. Significant reduction of blood supply deficit as the first signs of positive dynamics during the first month of intensive angiocorrection and angiotherapy. (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

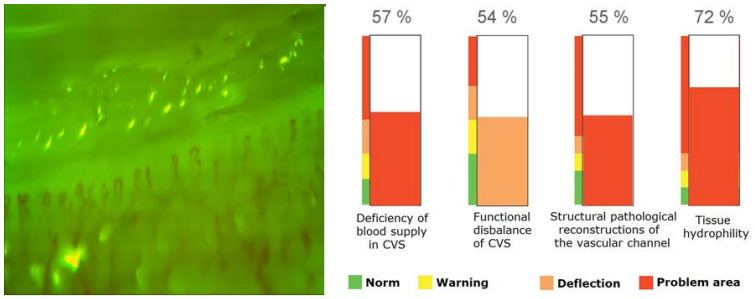


Figure and histogram 10.9.1. CVD before treatment (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

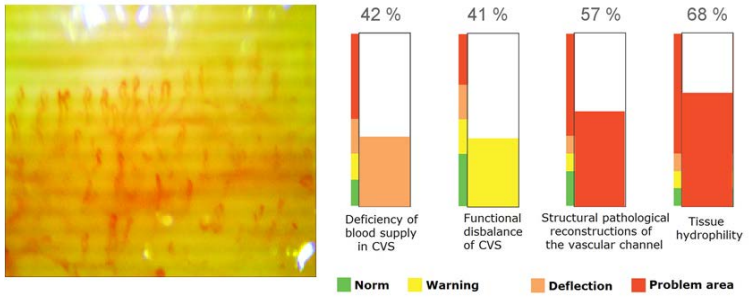


Figure and histogram 10.9.2. CVD after 2-month treatment. Blood supply deficit has decreased, structural changes in microvessels and tissue hydrophilicity require long-term angiocorrection. (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

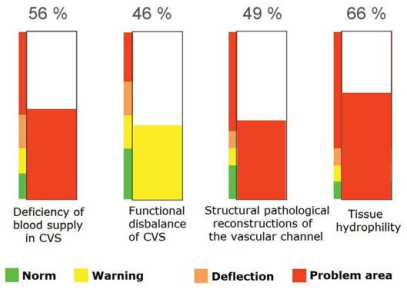


Figure 10.10.1. Generalized histogram for 2nd group - CVD, before treatment (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

For comparison, we place the general histragram of the 1st group of virtually healthy.

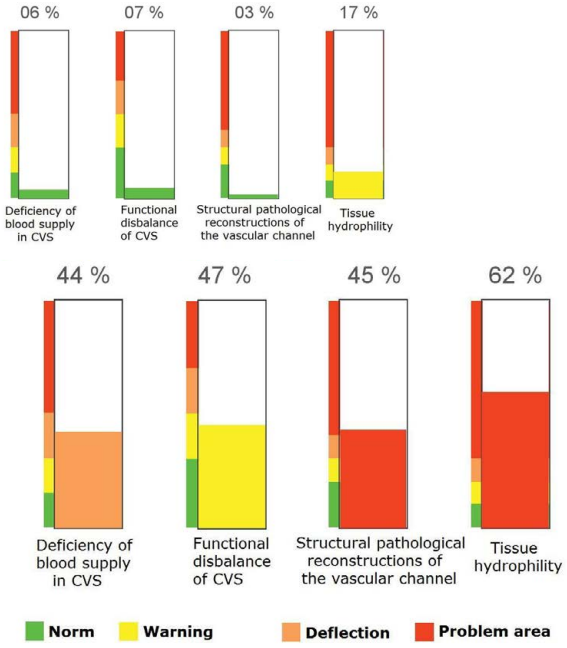


Figure 10.10.2. Generalized histogram for the 2nd group, after treatment.

Figures and histograms 11.1-11.5 show the results of Vascular screening of the 3rd group - verified oncopatients.

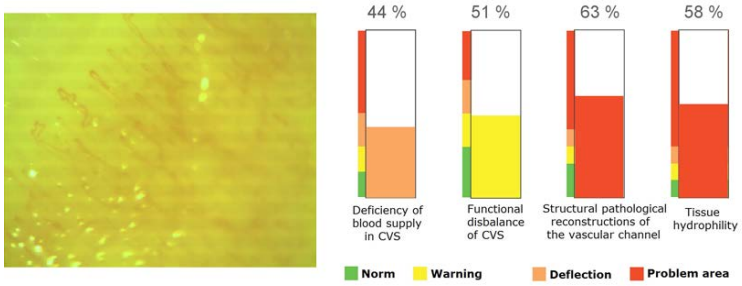


Figure and histogram 11.1. Verified oncopatients (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

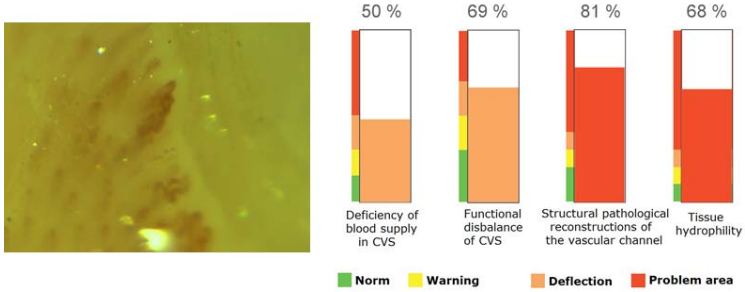


Figure and histogram 11.2. Verified oncopatients (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

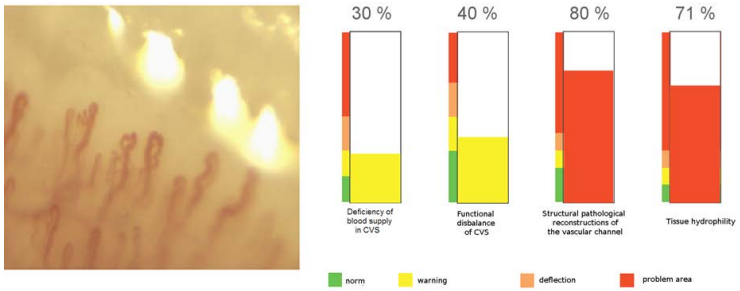


Figure and histogram 11.3. Verified oncopatients (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

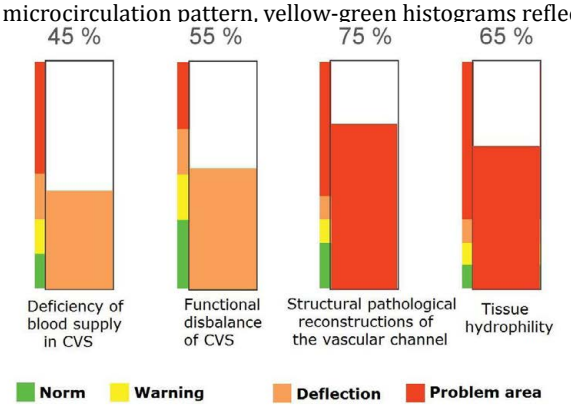


Figure 11.4. Generalized histogram for the 3rd group, before treatment (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

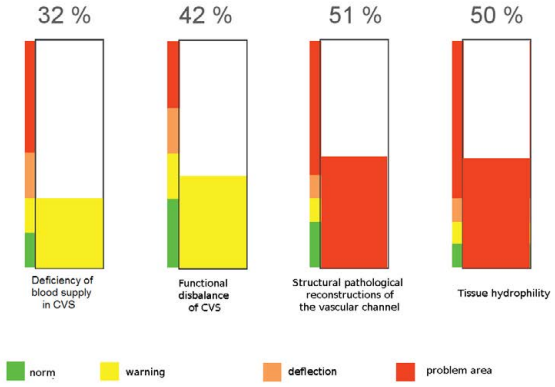


Figure 11.5. Generalized histogram for the 3rd group, after angiocorrection (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

This histogram shows that the parameters of blood supply deficit and functional disorders have decreased, but the parameters of structural changes and edema of perivascular tissues remain in the red zone of critical pathological changes.

Below we present Figures 12.1, 12.2, 12.3 for comparison of hemodynamic parameters of microcirculatory changes in the group of virtually healthy patients, with CVD, and in the group of cancer patients according to the vascular screening technology.

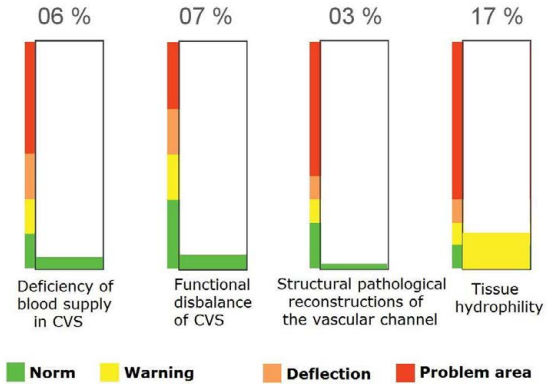


Figure 12.1. Generalized histogram for the 1st group – virtually healthy (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

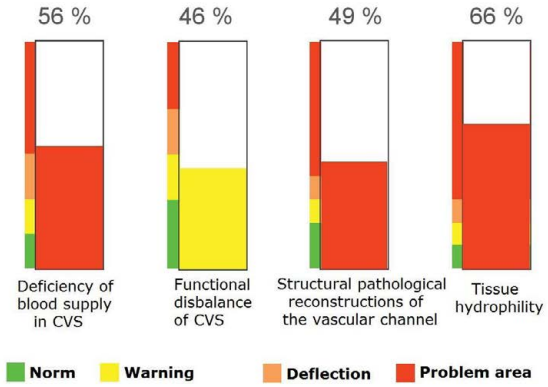


Figure 12.2. Generalized histogram for the 2nd group – CVD patients (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

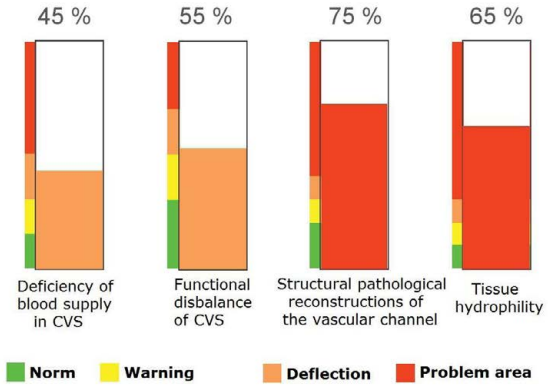


Figure 12.3. Generalized histogram for the 3rd group – oncopatients (from the VIAT AngioSmart database: orange and red in histograms reflect a pathological microcirculation pattern, yellow-green histograms reflect the range of microcirculation norm).

Comparative analysis of the obtained histograms has shown a clear difference in the change in the value of the main microcirculatory parameters; in the group of almost healthy the microcirculation indices are in the green-yellow range of the norm.

The groups of patients with CVD and verified cancer the most indices of vascular screening were in the orange-red range of pathology and had their specific features: the index of blood supply deficit was higher in the group of CVD and naturally reflected the critical condition of blood supply with psychoneurological deficit.

At the same time, the indices of structural changes and pathological hydrophilicity were high in both the CVD group and in the group of verified cancer patients, but their quantitative indicators differed: in the CVD group these indices were approximately 20% lower than in the cancer group, which confirms the similarity of the pathogenesis of blood supply deficiency developmen regardless of the etiogenesis of the disease.

As for the index of functional disorders, the parameters of these two groups differed slightly - within 10%, although they were more expressed in oncopathology. According to our experience functional disorders of arterial and / or venous tonus of the wall, instability of hemodynamic parameters, etc., appear the first, which leads to forced pathological transformation of microangioarchitectonics, regardless of the provoking etiopathogenetic factor.

Such pathological transformations on the background of neoangiogenesis can provoke uncontrolled processes of NeoAngioOncogenesis, which is difficult to eliminate at the organ and systemic vascular levels.

In our opinion, the increase in blood supply deficit at the level of the regional vascular reservoir leads to the clinical debut of oncopathology, often imitating critical vascular conditions (stroke, thromboembolism, necrosis - depending on the location of the tumor foci or metastases, and weakness of the vascular regional link - pain without pathology in some months, six months before the visualization of oncopathology).

The changes in the vascular mirror according to the patterns of vascular screening of rheumatological or oncoprofile patterns present in postCovid-19 vascular syndrome are already alarming in terms of long-term consequences, as vascular changes occur rapidly - up to 3 months after Covid-19, are hidden under the clinical picture like “reconvalescentia” however, a significant reduction in quality of life, general exhaustion and cerebral symptoms.

Figures 13.1-13.3 show post-Covid-19 syndrome in different age groups and pathological angiotransformation with microthromboangiopathy.

Figure 13.1. Pathological angiotransformation in patient Vi (20 years) with Covid-19 verified asymptomatic course of the disease. Negative dynamics of pathological angiotransformation for six months without angiocorrection.

Figure 13.2. Late post-Covid-19 vascular syndrome with rheumatological patterns.

Figure 13.3. Post-Covid-19 syndrome in the dynamics of the formation of pathological angiotransformation and microangiothrombopathy in patient V. (70 years) 2 weeks after suffering from moderate Covid-19.

Thus, pathological NeoAngioOncogenesis today can not only be visualized but also evaluated by quantitative and qualitative analysis of vascular screening, differentiate the main indices of vascular mirror disorders and form a plan of individual angiocorrection and angiotherapy to restore regional blood parameters and physiological parameters of the sick organism.

The above-mentioned images of pathological NeoAngiotransformation in cancer patients on the microcirculatory level evidently indicate specific changes in the capillary structure and microcirculatory channels, which we observed in nearly all cancer patients.

The above data represent that the capillary form did not change in the control group in the norm. In the group of CVD patients there was a varying degree of deviation of microcirculatory parameters from the norm, but mainly of the functional nature with severe deficiency of blood supply.

In the group of cancer patients, the microcirculatory picture sharply differed even visually. However, speaking of microcirculatory changes, one should rely on a quantitative-analytical analysis, since the probability of a macromistake when manually calculating microimages is quite high. Therefore, we preferred digital processing of images with the automatic formation of analytical histograms due to the application of vascular screening technology. As a result, we received sharply expressed structural changes that reached 49-75% in the 2 and 3-groups of patients. These changes were mainly observed in the venular segment of the capillaries and spread to the venules.

It should be noted that in cancer patients who received angiocorrection, the profile of microcirculatory images varied, and the form

of pathologically altered capillaries gradually underwent a phase of inverse involution.

The above data indicate the need to monitor pathological angiotransformations using dynamic technologies of objectification of vascular pathology - vascular screening, angiomarkers, which enable to monitor the dynamics of sanogenic changes in hemodynamic parameters during treatment to obtain a quality end result - improved quality of life, life duration.

It is the dynamic control over the condition of NeoAngioOncogenesis that allows both a doctor and a patient to believe in recovery, periodically monitoring the condition of the vascular system, relieving the patient's psychological stress on the incurability of cancer. This study can be performed at all stages: family physicians and primary link o health care, in laboratories, medical centers and pharmacies.

We believe that the role of family physicians and primary link of health care in vascular screening of NeoAngioOncogenesis is crucial for early detection of risk groups, pre-cancer and early preclinical signs. Such mass population control will allow to form risk groups of preclinical forms and to lead the process of medical management of angiotransformation, to form a travel card and to accompany such patients with control of key stages from the position of evidence-based medicine.

The above-mentioned images clearly show the difference in the capillary form, which dynamically successfully undergone a reverse, sanogenic transformation and approached the normal capillary form of a hairpin.

According to the correlation analysis of histograms of these images, it is evident that hemodynamic parameters tended to shift from the red-orange pathological zone to the yellow-green zone close to the norm.

Since the study of microcirculatory disorders with vascular screening technology in the treatment dynamics of single cancer patients was sensitive to angiooncotransformations, this suggests that such objectification of PathoNeoAngioOncogenesis is probable, and vascular screening technology needs further development in the aspect of the creation of subtechnology "PathoNeoAngioOncogenesis". The described phenomena require a further multicenter study of verified oncologic patients to detect correlation and specific pathological features in cancer patients compared with the control group.

Thus, vascular screening is a unique visual non-invasive technology for the study of microcirculation using the method of in vivo non-invasive smart optical capillaroscopy, since it is based on new approaches - combinations of technical components, new scientific knowledge and mathematical models of changes of angioarchitectonics on the microcirculatory level with pathological reorganization of hemodynamics locally in the ontogenesis area and the formation of the vascular pedicle.

The technical device, software, methodology for obtaining an image and clinical interpretation, combined in a single technological complex for vascular screening, allow modeling various hemodynamic situations both at the level of mathematical calculations and confirm experimentally the correctness of theoretical approaches.

We have developed an algorithm for research to obtain and analyze microcirculation data.

The vascular screening technology for microcirculation visualization and analysis of hemodynamic parameters reconstructions enables to consider in a new way the OncoAngiogenesis as AngioOncogenesis precisely PathoNeoAngioOncogenesis, to reveal specific features of microcirculation disorders and to enter the subtechnology for screening of neovascular disorders of microcirculation in cancer patients.

We consider this technology for detecting oncopatterns to be useful not only for the early diagnosis of oncoangiotransformations, but also in the treatment process as an evidence base of sanogenic vascular transformations in conducting various types of therapies in cancer patients and will increase the effectiveness of the treatment and objectivize the situation for the patient and to predict the course of AngioOncogenesis in the process of specific treatment. The latter option is very essential for the visualization of the treatment process in a cancer patient as they lose faith and psychologically do not withstand long-term treatment without objectification and positive prediction of the treatment process outcome.

This technology is a unique innovative technology that makes a breakthrough in changing strategic approaches to the diagnosis and treatment of vascular disorders in cancer patients since it enables to monitor the pathogenesis and dynamics of sanogenic changes in the vascular system at the microcirculation level and timely interfere with the threatening patterns of microaggregation, stasis, perifocal edema, which often causes the death of such patients.

The next stage of this study may be the development of an algorithm for conducting a screening study of microcirculation in cancer patients in order to detect disturbances in the microcirculation, possible changes in parameters that characterize the capillarys condition, and to identify the tendency for the formation of specific or nonspecific patterns of microcirculatory channel rearrangement.

MacroPathoNeoAngioOncogenesis: frequency of vascular abnormalities in onco-processes at the macroangiological level

In the process of studying the condition of the vascular bed in focal oncoprocesses we have found that vascular disorders in the

form of angioarchitectonic changes of regional vessels locally at the tumor area occurred in 46% of cases, according to MRA, in 78% of cases it was observed in the study of angioarchitectonics and vascular changes in blood flow during combined ultrasound examination - scanning and dopplerography (USDG) locally in situ. Today, some authors [61] note the affinity of oncology and vascular pathology.

It should be emphasized that disorder of the ArterioVenous balance (according to USDG) was observed in the area of the oncoprocess localization at the early stages of the disease (stage 1-2) and significantly progressed by the formation of pathological arterial hyperemia and venous hypertension on the background of the venous stasis in stages 3-4 of the oncopathology.

This research was aimed at examination of 34 patients with established and pathomorphologically confirmed diagnosis of oncopathology of different localization.

The research methods for all patients were performed using CT, MRI, MRI in angiomode (MRA), Vascular Hydro-Hemo ArterioVenous mutual USD scanning + doppler (MacroAngioMarker technology) [40, 86, 89] and capillaroscopy (Vascular Screening technology) [28, 89, 95].

MRI in angiography (as a static image of the angioarchitectonics of the vascular bed of the tumor and conducting vessels) and the dynamic objectivization of hemodynamic transformations by ultrasound diagnosis of peripheral arteries and veins were the most informative for the diagnosis of vascular bed reconstruction among the diagnostic methods of vascular transformations.

USDG-patterns at acute cerebrovascular failure on the background of brain tumors

USDG-patterns of brain tumors are characterized by an unpredictable increase of linear circulation rate in diastole in the common and internal carotid arteries at the tumor side, indicating the arterial peduncle of the tumor (several arterial tumor peduncles can be detected, even in different cerebral hemispheres, as well as in the basilar artery). This phenomenon indicates unjustified high-speed blood flow with reduced distal resistance as a phenomenon of hyperperfusion.

But in 12% of cases, we observed a sudden decrease of the linear circulation rate in the cerebral artery and at the same time a high venous blood flow in the brain tumor projection, which gave us a reason to suspect extravasal compression of the arterial pedicle of the tumor and/or ArterioVenous shunting in the tumor. Patients with brain tumor were observed a gradual exhaustion of the reserve capacity of the cerebral and systemic blood supply on the background of progressive uncontrolled growth of the brain tumor, which was clinically revealed only at the later stages.

The hemodynamic picture of blood supply to the brain tumor in adults resembled USDG physiological pattern of pathological hyperemia, which indicates norm in children as increased arterial blood flow to the brain, which structurally and functionally develop till the age of 20 years [84].

According to our and other research data, we have made a detailed analysis of the features of hemodynamic reorganization of cerebral hemodynamics, and we assume that a physiologically unjustified age-related pathological hyperemia of the brain tissue locally in one cranial fossa is the cock zone for the tumor growing.

Since almost all patients with cerebral tumors had the expressed venous cerebral discirculation that was not compensated through either vertebral venous plexus, or through supratrochlear veins, and at the same time unjustified enhanced arterial blood supply for the brain, we concluded that the brain tumor is formed only in the presence of venous blood stasis [40].

Congestive hyperemia is a favorable background for “enticing” capillaries saturated with blood on the “service” of a non-cancerous tumor.

According to references, the wall of the arterial pedicle of the tumor mass is an immature arterial structure, which pathomorphologists explain by dysembriogenesis.

We believe that the smallest vessels (arterioles, venules and capillaries) can gradually expand to receive large amounts of blood as tumor grow. They do not have a complete structure of the vascular wall (no elastic membrane, muscle layer) [28,34,40].

At the same time, the lack of elastic fibers results in the inability of the vascular wall to withstand hemodynamic strain of the vascular bed of the tumor, which can lead to a rupture of the vascular pedicle and is accompanied by a hemorrhagic stroke [61].

Consequently, by their nature the tumor is programmed to break off the autoregulation due to extravasal compression of the vascular pedicle by the mass of tumor formation or rupture of the vessel in the stage of critical blood filling [40].

In turn, critical hyperemia was caused by progressive increasing of arterial inflow to the mass of the tumor, partial shunting and simultaneous absence or impossibility of the compensatory involvement of the venous collateral outflow from the brain. On the other hand, if we look at the vascular network of the tumor as a tangle of arteriolar-venular shunts, it can be assumed that this blood circulates in the vascular tumorous tangle constantly and only a part of it returns to the venous bed. Therefore, there is no visual data on the overload of the venous bed or the opening of the compensatory and collateral blood flow. Such a local, uncontrolled organism is the microvascular system with pseudo-blasting flows.

The congestive hyperemia of the brain and the forced increased hydrophilicity of the brain tissue provokes cerebral symptoms and subjective discomfort in these patients. If to detail the complaints of patients with brain tumors, all these complaints belong to the group of venous dyshemias - scattering of attention, morning headaches, venous stagnation on the fundus, reduction of operational memory and dulling of cognitive processes, reaction rates, memorization of current information, reduction of visual acuity, etc.

Considering features of the hemodynamic picture we believe that vegeto-vascular dystonia in the form of severe venous cerebral dystonia with local congestive hyperemia may be the background for blood supply to the mutant group of cells.

The sad outcome of the twenty-five-year history of the dynamics of morbidity after the Chernobyl disaster confirmed the dominance and progression of severe forms of vegetative-vascular dystonia in the first years after the Chernobyl disaster (which were veiled by radiophobia, psychosomatic disorders) and parallel progressive increase of oncopathology rate [10-13].

This hypothesis was first published in 2005 and had further development and confirmation in our studies of angiooncogenesis. This hypothesis of hemodynamic transformation at tumors was first published by Lushchyk U.B. in 2005 [40] and during this time found further development and confirmation in our studies PathoNeoAngioOncogenesis.

The discussed result of the visualization of PathoNeoAngioOncogenesis at the microcirculatory level due to vascular screening technology.

Today's view of the PathoNeoAngioOncogenesis has become even more interesting in the light of the last comparison of microcirculatory changes in the groups of CVD patients and with oncopathology. Covid-19 and post-Covid-19 patients during the Covid-19 pandemic need real mechanisms in the aspect of lifelong diagnosis of vascular disorders to prevent complications and critical conditions. Such patients require medical care on the background of general exhaustion, weakness and almost asymptomatic convalescent period, as the post-Covid-19 vascular syndrome progresses clinically asymptomatically.

Vascular screening technology enables to visualize vascular disorders of microcirculation and is the evidence base in the process of angiocorrection to restore normal functioning of the body after a strong infectious and mutagenic agent.

The use of primary vascular screening technology by physicians will reveal the sudden development of angiotransformations and microangiothrombopathies on an evidence basis. Therefore, we have introduced a term of post-Covid-19 vascular syndrome, travel card for post-Covid-19 patients in the process of forming the evidence base.

In our opinion, the presence of anaerobic metabolism is an important factor in PathoNeoAngioOncogenesis, which is a much deeper pathogen than ischemic disorders. Taking into account the long course of oncopathology without a clinical picture, in contrast to the clinical picture of ischemic-hypoxic changes in cardiovascular pathology, we assume a variant of PathoNeoAngioOncogenesis with the launch locally due to capillary and venous hypoxia up to the anaerobic type of metabolism in the venular segments that are the primary focus - called infectious marsh, which creates favorable conditions for infectious mutations and carcinogenesis.

If we compare the clinical picture of hypoxia, then it is clear that it is much deeper than in cardiovascular diseases (ischemia-hypoxia of the arteriolar bed) and, at the same time, is not accompanied by clinical symptoms of deficiency or loss of function for a long time, there is also no phase of irritation of the nervous structures, preceding the phase of loss of functions. Only with the hypoxia location in the venous channel it is possible such a long asymptomatic course of the disease, the gradual extinction of the speed of neurodynamic processes.

We assume that tumor requires hyperperfusion because it is powered by hypoxic blood from the venule, therefore, on the one hand, the beneficial effect of vascularization is low, but a numerical vascular network is required for maximum possible contact with the surface of the tumor. Also, we do not rule out that the discovery of arteriolar-venular shunts can quickly increase the volume of the vascular net of the tumor, where the blood circulates according to the rules of ArterioVenous shunting. Thus, the shunts and venules receive diluted arterial blood, but without sanogenic turbulence.

It is important to emphasize that during mechanical injuries there is a protective mechanism for the opening embryonic ArterioVenous shunts as a result of hydraulic shock and forced prevention of possible hemorrhage. However, nature is created in such a way that at the intranatal stage of development embryonic shunts are closed and a major type of blood flow is formed. In the postnatal period, the body itself cannot cover these shunts, and with their long functioning, they become a good environment for uncontrolled use of large blood volumes, which merges into the venous system, passing capillaries.

The **infectious mutagent** (fungi, viruses, bacteria) that enter foci of venular stagnation may form the primary foci of inflammation and carcinogenesis, which we conventionally called an infectious marsh.

Thus, it is possible to form a fundamentally new theory of PathoNeoAngioOncogenesis as an isolated MicroAngiogenesis with the development of its venular network at the area of an infectious marsh, the creation of conditions for anaerobic metabolism and uncontrolled reproduction of infectious carcinogenic mutagens and hemato- and lymphogenous spread of onco-embolisms.

Our assumptions are confirmed by scientific findings of other authors from other fields of medicine, who claim the viral and

bacterial nature of tumors, combining them into generalized concepts - oncovirus, oncobacteria [97-101].

The algorithm for the study of the vascular system at the up-to-date clinical-instrumental level of biomarkers, which can identify angiotransformations in PathoNeoAngioOncogenesis at the level of MacroVascularization in the vascular tract

The theory of the vascular blood flow (blood duct) [39] is the basis of our mathematical models for vascular dyshemias, which enables to simulate vascular transformations within a single closed system of diverse tubes on the arterial, venous and microcirculatory levels.

Therefore, we try to present some of these developments in the algorithms of **NeoAngioOncogenesis**.

At the level of the study of major and peripheral vessels, intra-organ vessels (level of macroangiology) the following hemodynamic indices may be important in indicating angiomarkers of angiooncogenesis:

1. Unjustified high blood supply (probability 50-60%)

Linear blood flow velocity - maximum systolic frequency (LCR-MSF) of distal segment of arteries exceeds LCR-MSF of proximal segment more than in 1.5 times.

2. Unjustified high blood supply for one of the major arteries (subclavian, carotid, femoral) - LCR-MSF in these arteries is almost identical. Therefore, deviation of LCR in one of them, or in paired arteries, in comparison with others more than in 1.5 times can also be alerted as the formation of NeoAngioOncogenesis (probability 70%).

3. At the presence of 1 and 2 of the above-mentioned phenomena in the same artery, there is 80-85% probability of PathoNeoAngioOncogenesis in the distal segment of this regional reservoir.

4. The proportion of end-diastolic frequency EDF to MSF in major arteries also changes, however, it has number of specific features that should be differentiated from other patterns of ArterioVenous shunting, compensatory-collateral blood flow, stole syndromes etc. Therefore, the study of major and peripheral arteries should be conducted by qualitative and quantitative analysis and analysis of all hemodynamic parameters and indices in general.

5. Arterio-venous balance is mostly displaced in the direction of arterial hyperemia, but there are many variants of displacement at oncopathology, which should be profoundly considered realizing the essence of the process.

6. The study of the regional venous reservoir is also extremely important since it helps to identify certain situations regarding the compensatory capacity of the organism and at certain stages allows making angiocorrection of hemodynamic parameters of the ArterioVenous bed.

7. The study of the severity of the deficit of blood pressure and blood supply on the microcirculatory level as the most distant segment of CVS is required since it is the most remote blood supply segment from the heart pump in the circulatory system, which is the most sensitive to early angiotransformations, often with signs of capillary stasis and microtrombing, a sludge-phenomenon in the microcirculatory channel. The revealed signs of disturbance in the microcirculation require an expanded study of the vascular system of the organism at the macrolevel. In such cases, it is necessary to examine at least one of the links in the single closed CVS.

8. **AngioArchitectonics** as a marker for the structure of the vascular tree reflects the caliber, length, the nature of segmentation by the type of bi-, tri-, quadrifurcation and is a significant risk factor for pathological transformations. In the majority of cases, the large-caliber type of angioarchitectonics can become a background for pathological neovascularization and thrombotic formation. We have developed mathematical models of different-caliber type of angioarchitectonics with the calculation of the risk of hydraulic shocks with atypical tabs of angioarchitectonics of the arterial bed [28, 35]. The methodology for the study and evaluation of angioarchitectonics requires further development of software for ultrasound technology and MRI of the arteries of the body.

In general, we have developed mathematical models of a multivector approach to the structure of angioarchitectonics and functioning of the cardiovascular system in vascular dyshemia, which can be further adapted to the PathoNeoAngioOncogenesis indication since for this pathology it is important to use non-quantitative indices, analytical approaches to the systemic assessment of circulatory disorders in general and at the regional level of CVS [28].

Possibilities of application of applied analytical hemodynamics and mathematical modeling of sanogenic and pathogenic vascular transformations in angiocorrection of hemodynamic parameters and vascular disorders in cancer patients

Recently, mathematical models for estimation and interpretation of data of instrumental diagnostic methods became topical.

On the other hand, predicting and searching for correlations with systems of non-destructive in vivo systems is especially important in solving unexplored scientific problems, in particular, the study of the system of vascularization in normal tissues and tumors. Often it

is very difficult to find the boundary between healthy tissue and tumor for its resection, and therefore the methods of digital processing become extremely important in cases where the human eye is not able to distinguish a border of pathological and healthy tissues [63,106].

The practical diagnosis of hemodynamic factors of tumor development based on the principles of assessing the unreasonable and uncontrolled blood supply, the formation of vascular pedicles [40] for the growth of pathologically altered tissues may be the basis for such models.

Application of mathematical modeling in the image processing enables more closely to analyze the microcirculation picture, transfer it in numerical characteristics. A combination of quality image and quantitative calculations can be an addition to the analytical and clinical interpretations of existing pathology.

We have proposed hemodynamic patterns for diagnostics of blood supply disorders in tissues and organs that enables us to clarify the mathematical model and to use it effectively in the course of angiocorrection of vascular transformations and pathological changes in hemodynamics in cancer patients.

These parameters should be taken into account in the mathematical modeling of PathoNeoAngioOncogenesis, using analytical approaches in the study of the vascular system.

Due to new technologies (USD, MRI in angiomode, vascular screening) for the study of CVS, it is possible to model experimentally hemodynamic transformations in vascular systems in vivo under control of visualization methods of diagnosis. This can be a significant complement for theoretical calculations and hypotheses after mathematical modeling of the **NeoAngioOncogenesis**.

At the same time, the profound study and application of the laws of hydro- and hemodynamics, ultrasound physics, optics, the theory of vascular blood flow (hemoduct), the principles of the functioning of the arterial and venous link in various types of angioarchitectonics, may open new perspectives in NeoAngiogenesis research both on the physiological and pathological levels.

Thus, the existing changes in the vascular bed at the micro- and macrocirculatory level require changes in diagnostic and monitoring protocols in the treatment of cancer patients, increasing the mentality of oncologists to understand the crucial role of NeoAngioOncogenesis in the dynamics of cancer and improving the travel card for such patients.

Changes in NeoAngiogenesis in the microvascular bed can be quickly detected and monitored in dynamics thanks to vascular screening technology and quantitative-qualitative analysis from the AngioSmart software package with clinical interpretation of the detected pathology and expert-level conclusions.

The current dynamics of quantitative indicators in the change of indices of blood supply deficit, functional and structural changes of microvessels and hydrophilicity of perivascular tissues is a tool of evidence-based medicine and an arbiter of sanogenic or pathological changes of the vascular mirror and vascular transformations during treatment.

Pathological NeoAngioOncogenesis today can be visualized using non-invasive vascular screening technology, verified oncoprocess in the traditionally established way, and then angiotransformations require appropriate vascular treatment - angiocorrection to restore the ArterioVenous and ArterioVenular balance at the cardiovascular and organ level in a certain vascular rservoir.

Early timely diagnosis of the preclinical phase of NeoAngioOncogenesis may signal the beginning of the cancer process. Appropriate vascular correction of NeoAngioOncogenesis enables to normalize the hemodynamic parameters of CVS and restrain the development of the tumor process by normalizing the parameters of the microvascular mirror long before their appearance at the macrovascular organ level.

On the other hand, the travel card for cancer management should include vascular screening technology as evidence in the treatment of cancer patients, tracking the key stages of specific therapy and the place of angiotransformations in the regression of cancer and minimization of hematogenous metastasis.

VIAT AngioSmart vascular screening technology is a key stage of evidence-based medicine in the diagnosis, monitoring of treatment effectiveness and dynamics of pathological NeoAngioOncogenesis in the population, differentiation of rheumatological and oncological profile of patients as a complication of vascular syndrome.

Today non-invasive imaging of NeoAngioOncogenesis has become a reality of asymptomatic diagnosis of pathological angiotransformations using vascular screening technology.

Competent logistics of gastric endoscopy as an early diagnosis of gastric cancer in Japan has radically changed the sad statistics of incurable conditions and diagnosed gastric cancer at stage 1 in the 90s of last century.

Competent logistics of VIAT AngioSmart vascular screening technology enables to perform non-invasive oncoscreening of the world's population at the asymptomatic level only by non-invasive imaging of microvascular angiotransformations, to differentiate specific risk groups of oncogenesis at the preclinical level at the level of laboratories, primary care physicians and specialized medical centers, etc.

Conclusions

1. The personalized approach to the diagnosis of circulatory disorders can optimize the further treatment tactics of cancer patients - angiocorrection with an adequate selection of doses and treatment regimens under the control of modern equipment - VIAT AngioSmart vascular screening technology.
2. Angiogenesis is the basis for neovascularization. It is unknown mechanisms of pathological neovascularization as a sign of the loss of control of the organism over the sanogenic processes of apoptosis of old cells and uncontrolled neoangiogenesis. Pathological neoangiogenesis is the background for the development of NeoAngioOncogenesis. The presence of oncobacteria and oncoviruses accelerates the transition of pathological angiotransformations to the phase of NeoAngioOncogenesis.
3. The visual assessment of neovascularization as a general picture of an organism's loss of control over angiogenesis processes is possible and effective due to non-invasive **VIAT AngioSmart** vascular screening technology (VST).
4. Pathological neovascularization is ahead of the structural visualization of pathological tumors and can be considered as a significant factor in the early diagnosis and screening of tumors. Therefore, the term NeoAngioOncogenesis is more appropriate for everyday use than NeoOncoAngiogenesis.
5. The vascular screening technology allows visualization of in vivo native changes in the angioarchitectonics of the microcirculatory bed at the level of pathological transformation of capillaries, arterioles and venules, transformation into pathological forms of onco-capillaries.
6. The vascular screening technology (VST) can get a picture of microcirculation live, carry out a quantitative and qualitative analysis of the image and clinical analysis at the expert level. Due to the use of modern technology of VIAT AngioSmart for objective analysis and clinical interpretation, it is possible to minimize the subjective opinion of medical workers, who do not have profound knowledge of hemo-hydrodynamics, fluid motion, physics and mechanics of non-Newtonian fluids and suspensions, and at the same time to help clinicians quickly and in vivo non-invasively obtaining meaningful and reliable information on the status of vascular disorders in patients.
7. Vascular disorders in oncopathology are primary. We have developed the criteria for diagnosing vascular disorders at the local regional level of the major vessels (MacroAngioMarkers) and at the level of microcirculation (MicroAngioMarkers) that allow us to talk about the technology for vascular screening as a preventive for the entire population of the world. VIAT AngioSmart is considered as a technology of evidence-based medicine for early detection of risks of NeoAngioOncogenesis in the early preclinical stages of oncopathology. At the same time, the monthly dynamics of NeoAngioOncogenesis in the travelcard of the world's population can serve as an indicator of the progression of oncopathology or blockade of pathological NeoAngioOncogenesis, serve as a tool of visual evidence medicine to improve quality of life and life expectancy of cancer patients.
8. Since vascular and oncological diseases today are the dominant lethal pathology in the world, this vascular screening technology is capable not only for detecting early forms of vascular OncoTransformation and pathological NeoAngioOncogenesis, but also tracking the inverse transformation of onco-capillaries into normal forms during personalized angiocorrection and angiotherapy.
9. The logistics of cancer management should include key stages of control due to vascular screening technology before and after treatment as a quality non-invasive alternative to blood tests. Vascular screening technology can be an affordable means of patient self-monitoring with online access to the VIAT AngioSmart program.
10. Individual approach in the diagnosis of circulatory disorders enables to optimize the further tactics of treating cancer patients with adequate selection of doses and treatment regimens on the basis of evidence-based medicine under the control of modern diagnostic equipment and vascular innovative technologies with the ability to obtain analytical data and clinical interpretation of the changes made at the expert conclusion level.
11. Pathological angiogenesis requires effective tools for controlling the process of reverse sanogeneous angiotransformation on the micro- and macrocirculatory levels in both the arterial and venous links. The vascular screening technologies and angiomarkers enable to objectify and synchronize data on changes in practically all hemodynamic parameters.
12. Today, medical practice requires in-depth analytical technology with appropriate software to obtain a clinical interpretation of vascular pathology at the expert level. During Covid-19, every scientist and practitioner was challenged to find algorithms and evidence for rapid decision-making in the diagnosis and treatment of severe cancer patients and those who are virtually healthy.

Abbreviations

CVD – cardiovascular diseases

CVS – cardiovascular system

EDF – end diastolic frequency

LCR- linear circulation rate

MSF – maximum systolic frequency

VPF/VEGF - vascular permeability factor also known as vascular endothelial growth factor or VEGF

VST – vascular screening technology

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