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NEW RESEARCHES
ON MATHEMATICAL MODELS AND NUMERICAL SIMULATIONS OF BLOOD FLOW IN HUMAN VESSELS WITH DIFFERENT PATHOLOGIES.
IS THE STROKE PREDICTABLE?

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Foreword

The current work offered for publishing is the result of in-depth interdisciplinary investigations performed by neuroscientists and cardiologists in cooperation with specialists in applied mathematics, fluid dynamics and numerical analysis.

The authors Vitalie Vacaras, M.D., specialized in neurosciences and the physicist Balazs Albert, Ph.D. in applied mathematics/fluid dynamics sought to construct mathematical models of the blood flow through various vessel types that would allow numerical simulations of the effective flow. Throughout the content organized in fourteen chapters the authors analyze large (arteries) as well as small (arterioles and capillaries) blood vessels in pathological circumstances often encountered in medical practice. The numerical simulations performed using the package COMSOL Multiphysics (versions 3.3 and 4.4) yield supplementary information about the pathologies in question. Special emphasis is put on the numerical determination of the wall shear stress (WSS), one of the main pathogenic factors in the development of cerebrovascular accidents (strokes).

The first four chapters cover the necessary fundamental concepts of blood and blood vessels physics, dynamics of blood flow through the circulatory system and mechanics of the blood vessel walls. The rest of the work is devoted to the concrete implementation of the blood flow mathematical models using the COMSOL Multiphysics software. The step by step instructions allow users with no special mathematical or information science training to analyze specific medical cases

involving blood vessel pathologies. That makes this work a valuable instrument for obtaining additional significant information that can be used to prescribe the appropriate course of patient treatment.

A major topic throughout the work is WSS, a main determinant of strokes – currently a major medical problem. The reader will be able to learn how to pinpoint the time and location of major risk events prior to the actual occurrence of a cerebrovascular accident as well as in a post-surgical environment.

The methodology presented in this work, which is addressed to cardiologists and neurologists, can be of real help in the treatment of patients. The work is an example of a truly interdisciplinary project. Besides the elegance of the mathematical models on which it is based, this approach can make a real contribution to the healing of gravely ill patients.

As far as we know there are no similar works in the literature that could serve as a useful instrument in dealing with pathologies of the type mentioned above.

Significant progress in understanding how the cardiovascular system functions in both normal and pathological physiological circumstances was achieved recently by using mathematical models combined with the appropriate numerical algorithms.

The resulting numerical simulations can aid physicians – neurologists, hematologists, surgeons – to choose the most appropriate treatments for patients with circulatory problems.

This new perspective gave birth to a new discipline – computational hemodynamics. It is based on the mathematical models of fluid dynamics, particularly

of blood flow, and the appropriate computational methods. Much progress has been made in both the modeling and computational aspects of hemodynamics. However, many difficulties related to the study of the cardiovascular system remain unresolved. Undoubtedly, they will be the subject of future research.

This book provides a practical instrument to neurologists, hematologists and surgeons for selecting the optimal treatment modalities of blood circulation pathologies. Identification of the maximum risk regions and assignation of specific values to the risk parameters at the earliest stages of treatment are crucial for a positive outcome. The techniques presented in this work are designed to achieve those objectives.

Using medical imaging information such as the geometry of the affected vessel, the shape of the stenosis or aneurysm, etc., the algorithm presented here makes possible the quantification of the immediate risk of potential, sometime lethal, complications.

Most of the models used in this work focus on the calculation of the wall shear stress (WSS) which plays a major role in the breaking off of atheromatous plaques. Besides wide vessels (arteries), we take into consideration narrow vessels (arterioles) and capillary vessels.

Throughout the work blood is treated as a non-Newtonian fluid (following a viscosity law of type Cross) flowing through vessels with viscoelastic, elastic or poroelastic walls, i.e., arteries, arterioles or capillaries, respectively.

The numerical simulations were performed running the Comsol Multiphysics 3.3 simulation software on a personal computer with an Intel Core 2 2.13 GHz processor, 3GB RAM memory and a 600 GB hard disk drive. There was no need for any specialized hardware.

The book presents succinctly basic relevant medical concepts, e.g., blood, blood vessels, stenosis, aneurysm. The reader is introduced also to fluid dynamics concepts such as the mathematical model for the study of fluid motions in wide, narrow and capillary vessels with initial conditions and at the adequate boundaries, and the analysis of the mechanical properties of the three types of vessel walls, i.e., viscoelastic, elastic or poroelastic, respectively.

All the mathematical and mechanical concepts are presented briefly and without proofs. No prior specialty training is necessary unless new approaches or different generalizations are attempted in response to new medical challenges.

Because of the interdisciplinary character of the work in-depth knowledge of the concepts mentioned above is not required unless potential extensions of the algorithm are attempted in face of significantly more complex medical circumstances.

The models effectively built in this study pertain to frequently encountered specific medical cases. The technique and steps to follow are the same in other similar or even more complex circumstances.

The following medical problems were analyzed and modeled successively: internal carotid artery (ICA) with stenosis; abdominal artery presenting a double aneurysm (AAA); pseudoaneurysm related to a prosthetic device; Fahraeus-Lindqvist

effect in arterioles; blood flow in capillaries; an artery with stenosis in a post-stenting situation; obturation of arterioles; basilar artery with stenosis.

The majority of calculations were performed assuming a particular geometry, namely axial symmetry. This was done for logistical reasons but also because the objective was to allow anybody who wishes to simulate a problem related to the pathology of blood movement in vessels to do so even with limited computer resources. The same exact steps may be followed for any three-dimensional geometry but a faster computer with more memory should be used to allow the use of the Comsol 4.3, instead of the Comsol 3.3 package.

Special emphasis was put on cases related to pathologies in brain blood vessels implicated directly in cerebrovascular accidents (strokes). The research subjects were provided by the Neurology Clinic of the Iuliu Haţieganu University of Medicine and Pharmacy, Cluj-Napoca. The results of numerical simulations had a decisive influence during the treatment.

This works is addressed especially to physicians interested in the pathology of blood vessels: neurologists, hematologists, surgeons, etc. By following the prescribed steps, it allows them to pinpoint the regions of maximum risk, to assign the respective risk parameters and, implicitly, decide on intervention methods. This can be done without specialized knowledge in mathematics or fluid mechanics.

The book is also meant for specialists in computational fluid dynamics. They may be interested in developing the existing mathematical-mechanical models beyond the

current pathologies covered by computational hemodynamics in order to meet new medical challenges.

This research was conducted under the auspices of the Academy of Romanian Scientists over a period of six years.

The authors are Vitalie Vacaras, M.D. specialized in neurology who provided the research subjects and the physicist Balazs Albert, Ph.D. (mathematics, specialized in fluid dynamics).

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coordinator of research related to mathematical modeling of blood flow.

CHAPTER 1
The Cardio-Cerebro-Vascular System
Methods of Investigation

The cardio-vascular system has, as a main role, the transport of nutrients and oxygen towards every cell of the human body. The cardio-vascular system is made up of the heart and blood vessels (arteries, transporting blood from the heart to the tissues, and veins, transporting blood to the heart). The blood vessels' system looks like a tree, in which the main artery, the aorta, branches out into blood vessels with smaller and smaller diameters, leading finally to the formation of the capillary network ([26], [140].

The cardio-vascular system is, actually, made up of two circulatory networks – the systemic circulation, whose role is to insure the nutrition of the human tissues, in such a manner that they receive the needed nutrients and oxygen, and the pulmonary circulation, which insures the blood oxygenation and the elimination of carbon dioxide [39].

The blood circulation starts with the blood passing from the left atrium to the left ventricle, during the diastole, followed by the blood being pumped out from the left ventricle to the aorta during the systole. Blood flows from the aorta to the large arteries, arterioles and capillary network. Here, at the capillary level, takes place the

exchange of substances between tissues and blood ([26], [39]). The blood, filled with carbon dioxide and toxic waste from the tissues comes back to the heart through the venous system, up until the right atrium. Here is where the pulmonary circulation starts, transporting poorly oxygenated blood from the heart to the lungs, through the pulmonary artery, where it will be oxygenated and the it comes back to the left atrium through the pulmonary veins ([26], [39])

The circulatory system is made up of blood vessels of different sizes and structures, well-adjusted to their roles [39].

Arteries

Arteries transport blood from the heart to the tissues. All arteries, except the pulmonary artery, transport oxygenated blood.

The arterial wall is made out of three layers:

1. Adventicea: the external layer of the arterial wall, made up of collagen fibers disposed in an irregular manner, fibroblasts, a few elastic fibers and blood vessels (vasa vasorum) [6].

2. Media: middle layer of the arterial wall, made up of concentrical layers of smooth muscle fibers mixed with elastic fibers, arranged between two layers of elastic fibers (internal elastic membrane and external elastic membrane). These are arranged in a substance rich in proteoglycans, which is the “cement” of interstitial spaces [6].

3. Intima: the internal layer of the arterial wall, made up of a layer of endothelial cells and conjunctive tissues [6].

The structure of the aorta and of the large vessels is in agreement with the roles they play in transporting blood and adjusting to the heart's pumping effect, through the elastic fibers in its structure ([6], [39]).

The wall of the arterioles has fewer elastic fibers and more muscular fibers. These produce resistance to the blood flow, even minimal alterations of the arteriolar diameter cause important effects on the peripheral blood pressure ([26], [39]). The muscular fibers are innervated by vasoconstrictor noradrenal fibers, and rare vasodilator collinergic fibers [39].

Capillaries are the blood vessels with the smallest diameter, through which the exchange of substances between blood and tissue is realised. The capillary wall is made up of a single layer of endothelial cells, facilitating in this way the passing of substances to and from the tissues. The main characteristic of the capillary wall is the selective permeability – it only allows certain substances to pass [39].

There are three types of capillaries:

- Fenestrated capillaries – have numerous pores of different sizes. They are found mainly in the small intestines and allow large sized molecules to pass ([6], [39]).
- Continuous capillaries – the endothelial wall has tight junctions, making them impervious to everything but very small molecules. This type of capillaries is found mainly in the brain tissue, and it allows only the passing of water and ions ([6], [39])
- Discontinuous capillaries – the endothelial wall has large sized pores and increased spaces between the cells, allowing large sized molecules to pass. This type of capillaries is found in the liver ([6], [39]).

The exchanges that happen at a capillary level are facilitated by a “game” of pressures. The blood passed to and from the capillaries through diffusions, the molecular movement going from the low-pressure compartment to the high pressure one.

This movement is influenced, on one side, by the hydrostatic pressure in the capillaries – basically, the arterial pressure or the pressure created by the blood flow through the vessels – and on the other side the osmotic pressure – constant pressure [39]. These two pressures interact at the capillary level and cause the exchange of nutrients at a tissulary level [39].

The veins transport blood filled with carbon dioxide and leftovers of the cellular process to the heart [39].

The venous wall is made up of three layers:

1. Adventice: the external venous layer, made up of collagen fibers and conjunctive tissue.
2. Media: made up of smooth muscle fibers and elastic fibers.
3. Intima: made up of endothelial cells.

Medium and large veins have valves, which prevent backwards blood flow and facilitate the flow of blood towards the heart [6].

Cerebral circulation

The brain is the most irrigated organ of the human body, the arterial flow at this level coming from two pairs of large sized arteries: the right and left internal carotid

arteries and right and left vertebral arteries (which come together as the basilar artery) [39], [48].

The cerebral hemispheres are irrigated mainly by branches of the carotid arteries, and the cerebellum and brainstem by branches of the vertebral and basilar arteries.

The basilar artery together with the two carotid arteries and the communicating arteries come together in the brain in an anastomotic circle, known as the circle of Willis [48].

From the circle of Willis take form three pairs of arteries – the anterior, medium and posterior cerebral arteries – which irrigate through their branches the cerebral cortex.

Brain vessels architecture

Leptomeningeal blood vessels are intracranial blood vessels at the surface of brain hemispheres, are surrounded by cerebro-spinal fluid and branch out into smaller arteries who penetrate into the brain tissue. Penetrating arteries are situated in the Wirchow-Robin space (continuing the subarachnoid space) [48]. Once they reach the brain tissues, they become intraparenchymal arterioles [77].

There are a few differences, both structural and functional, between the surface and the parenchymal arteries.

The surface arteries are innervated by extrinsecal nervous fibers, belonging to the peripheral nervous system, and the parenchymal ones by intrinsic fibres, from the brain.

The parenchymal arteries have a single layer of smooth muscle fibers with a circumferential orientation, but with and increased base tonus, and don't respond to some neurotransmitters with important effects on the leptomeningeal arteries (ex. serotonin, norepinephrine) [20].

The surface vessels have a vast collateral network, so that the stenosis or occlusion of one of them does not cause an important decrease in the cerebral blood flow at that level. On the other hand, the parenchymal arteries are long, thin, branchless arteries, and the occlusion of one of those arteries causes the infarction of the tissue irrigated by it [65].

Despite the differences between the two types of arteries in the brain, they all have a high specialized endothelium with barrier properties different from the ones in the peripheral circulation. Because of these properties and of the extremely rigorous control of the nutrient, ions and water exchange between brain tissue and blood, the endothelium of the cerebral arteries has earned its name of "blood brain barrier" [1], [79].

The cerebral venous system is an interconnected system made up of dural sinuses and cerebral veins. The venous drain is made through two groups of valveless veins: cortical superficial veins and deep veins (central). The cortical superficial veins are located in the pia mater and insure the venous drainage of the cerebral cortex and the subcortical white matter. The deep veins are subependymal, internal cerebral, basal veins and the great vein of Galen. These veins insure the venous drainage of deep white matter and periventricular grey matter. Together with the superficial cerebral

veins they flow into the superior sagittal sinus, then sigmoid sinus and finally jugular veins. The venous drainage of the cerebellum is made mainly through the inferior cerebellar veins and occipital sinuses, and the brainstem's drainage is made into the transvers sinuses [50], [82].

Cerebral blood vessel structure

The cerebral artery wall is made out of three concentric layers: internal layer or intima is made up of a single layer of endothelial cells and internal elastic membrane; next layer is media, made up of smooth muscle fibers, collagen fibers and elastane; external layer or adventice is made up of collagen fibers, fibroblasts, perivascular nervous endings and rare astrocytes [55].

Unlike systemic arteries, cerebral arteries don not have an external elastic membrane in their structure, but they have a very well developed internal elastic membrane. Also, the elastic fibers are in a much lower number, and the adventice is much thinner [39], [55].

The number of smooth muscle fibers varies according to the size of the vessel, large vessels such as the internal carotid artery having up to 20 layers of muscle fibers; the superficial cerebral arteries have up to 3-4 layers of muscle fibers, and parenchimal arterioles have a single layer of muscle fibers. The muscle fibers in the media of the cerebral arteries are circular, with a perpendicular orientation on the direction of the blood flow. Cerebral veins have very thin walls, and unlike the peripheral veins, they don't have valves [50], [55].

Cerebral microcirculation

The capillary network is made up of a dense network of small sized vessels, interconnected, with highly specialized endothelial cells, without smooth muscle fibers [13].

Total length of the human brain capillaries is approximately 640 km [13].

This capillary network is the main place where nutrient and oxygen exchange takes place. In the brain, practically all the capillaries are permanently perfused, and it was estimated that nearly every neuron in the brain has its own capillary, proving once more the interdependence between the neuronal and the vascular compartments [102].

The intravascular pressure gradient between the precapillary arteriole and postcapillary vein is the main regulating element of the capillary blood flow. The arteriolar dilatation increases the microvascular pressure gradient and, this way, the capillary blood flow. So, the flow alterations at capillary level are obtained through flow alterations and microvascular pressure alterations at the arteriolar level [102].

The movement speed of the red blood cells in the capillary microcirculation is incredibly high (about 1mm/sec) and heterogenous (from 0,3 to 3,2mm/sec). This heterogeneity ensures an efficiency of the oxygen transportation to the neuronal tissue, tissue that has increased metabolic necessities with important fluctuations [96].

In physiological conditions, the capillary density in the brain varies according to the area in the brain and its metabolic necessities (the capillary density is higher in the grey matter than in the white matter). Certain pathological, physiological or environmental circumstances can influence a change in the capillary density. For

example, chronic hypoxia leads to an increase in the capillary density through some angiogenesis mechanisms activated by a decrease in the oxygen pressure (ex. HIGF1 and VEGF) – the capillary density is doubled in 1 to 3 weeks of chronic exposure to hypoxia. This adaptive growth of capillary density in chronic hypoxia leads to an increase in the cerebral blood flow and balance to oxygen pressure at tissue level [14], [100].

Hypertension can affect the capillary density in the brain. In a similar matter to the effects it has on the peripheral circulation, hypertension can cause a decrease in the number of capillaries and the inhibition of angiogenesis [83].

The structure of the cerebral capillaries is also unique, compared to that of the systemic capillaries. The endothelial cells and the pericytes are incorporated in the basal lamina (with a thickness of approximately 30-40nm), which has type IV collagen, proteoglycans, laminin, fibronectin and other extracellular proteins. The cerebral capillary endothelium's basal lamina is continuous and has astrocytic terminations surrounding the capillaries. The astrocytes have a significant influence over the capillary function – the regulation of cerebral blood flow, maintaining the ionic and water balance and is a direct interface with the neurons ([9], [40], [57]).

Although the blood brain barrier properties are given by the tight junctions of the endothelial capillary cells, an important role in it efficient functioning is taken by its other components – basal membrane, pericytes, astrocytes and neurons ([9], [40], [57]).

There are multiple connections between all these cells and elements of the blood-brain barrier, known as a neurovascular unit. Treating these elements as a unit is important for understanding the processes that cause bleeding, vasogenic edema, infections and inflammation. The neurovascular unit can represent the main element of dysfunction; in other cases, such as atherosclerosis, large arteries are mainly affected, and hypertension affects all vascular segments ([9], [40], [57]).

Arterial pathology

Taking into account the vital role of circulation, it is obvious that every alteration of the vessel's diameter will cause an alteration of the tissues it feeds.

To what concerns the cardio-cerebro-vascular system, any change in the carotids, vertebral of basilar arteries will cause a cerebrovascular disease.

Carotid stenosis

Carotid stenosis represents a progressive narrowing of the vessels' lumen following a process called atherosclerosis. This process consists of the formation of atheromatous plaques on the vascular wall, plaques made up of cholesterol, other lipids, fibers and calcium. These plaques, as they increase in dimension, they cause the narrowing of the vascular lumen and a decrease of blood flow at this level [26], [39].

The arterial wall will have an irregular surface, which will facilitate the formation of thrombi which can completely occupy the vessel's lumen or they can break and migrate into the blood flow, causing the occlusion of smaller sized vessels [39].

The presence of an atheromatous plaque on the carotid can cause a cerebrovascular event not just by its prothrombotic effect, but by the plaque's instability. The blood will flow turbulently, at a high speed, which will determine the break of small pieces of the plaque, which will migrate into the blood flow and cause the occlusion of small vessels [39].

The atheromatous plaques will form mostly at the carotid bifurcation, but they can form at any level.

Besides this narrowing of the lumen caused by the formation of atheromatous plaques, the atherosclerotic process causes a decrease in the elasticity of the arterial wall, which become more rigid [26], [39].

Risk factors for carotid atherosclerosis are high blood pressure, diabetes, high cholesterol, smoking, obesity [26].

From a clinical point of view, carotid stenosis can be asymptomatic or symptomatic. The clinical signs of a corotis stenosis can be transient ischaemic attacks or even ischaemic strokes [26].

The evaluation of carotid stenosis can be done by various invasive and non-invasive methods:

- CTA: non-invasive method using X rays and offering detailed images of anatomical brain structures. This method implies injecting an intra-venous contrast agent to facilitate the visualisation of carotid and cerebral arteries. This type of investigation offers the best overall image of both brain tissue and blood vessels.

- MRA: non-invasive method, similar to CTA, without the side effect of irradiation. The visualisation of blood vessels is possible by using an intra-venous contrast agent. MRA offers a higher quality of the images of the brain tissue.
- Angiography: minimal invasive investigation, allowing the visualisation of blood vessels by injecting an intravenous contrast agent into the femoral artery and the use of X rays.
- Doppler ultrasonography: noninvasive, quick and accessible investigation, without any contraindications, which evaluates arterial blood flow by the use of ultrasounds. This type of investigation allows, besides evaluating the degree of stenosis, the evaluation of the atheromatose plaque itself (stable/unstable), and of the blood flow type.

Ultrasonographic investigation of the carotid and vertebral arteries

Accessibility, low costs, non-invasiveness and the absence of contraindications for the use of ultrasonography in the evaluation of the carotid and vertebral arteries, together with perfecting the methods and the devices used in the last decades makes this investigation very useful in the evaluation of patients with cerebrovascular disease.

Besides its use in establishing an etiology for ischaemic strokes, ultrasonography can be used as a screening and monitoring method for the patients with risk factors for developing atherosclerosis.

Blood flow respects the laws of fluid mechanics. Applying a mathematical model in this case is difficult, because of the geometric complexity and the non-linear behaviour of the blood vessels. Even so, we can use certain algorithms for determining values of blood flow speed at vascular level and the type of blood flow [45].

In the evaluation of carotid and vertebral arteries the following medium values are used: medium diameter of the common carotid artery is 6,5mm, medium speed at the center of the vessel is 0,75m/sec during the systole and 0,25m/sec in the diastole. The blood can have a laminary flow (regular flux) or a turbulent one (the fluid is led by its own weight and presents variations in speed) [45], [23].

For the ultrasonographic evaluation of the circulatory system we use two physical principles: the Doppler effect – for the study of circulatory speeds and the reflection of pulsing echoes for visualising the vascular structures. By combining these two principles we have been able to perfect the Doppler ultrasonography. By coding the Doppler signal into different colors, we have made it possible to receive a visual information of the blood flow at the same time as visualising the vascular structures. The measurement of the stenosis degree can be done by using spectral and speed information [45].

The investigation is conducted with the patient on its back. Examining the carotid territory means examining the common, internal and external carotid arteries and the ophthalmic artery, and examining the vertebra-basilar territory means examining the vertebral and subclavicular arteries. The recognition of blood vessels during the

exploration is possible based on the topography and the acoustical characteristics of the ultrasonographic signal [45], [23].

The semiology of the Doppler investigation has a topographical component (signals will be analised compared to the lesions) and an analytical component (describing speed and flow alterations).

The topographical semiology takes into account the obstacle signals – it evaluates the obstacle standing in the way of blood flow, direct signals – alterations of speed correlated with the lesion and amortization signs – speed alterations after the lesion. Speed alterations will always be compared to the values of the opposing carotid artery [45].

Pathological alterations are the following:

- Upstream signals: decrease in diastolic speed – decrease of downstream resistance (arterio-venous fistula, vasodilation), and its increase – increase of downstream resistance (tight stenosis, occlusion) ([23], [45], [64]).
- Direct signals – acceleration (localised speed increase), turbulence (low frequencies spectrum), lack of signal [23], [45].
- Downstream signals – are present in situations of reversal of blood flow direction, in the arterial segments which are not perfused in a physiological direction [23], [45].

The speed alterations turn up only if the internal carotid stenosis is higher than 65%.

If the stenosis is between 65% and 75%, the increase in the blood flow speed is the only sign of stenosis. Before establishing the diagnosis of carotid stenosis, we have to rule out other causes of increased blood flow speed (fibromuscular dysplasia, aneurisms, other side carotid occlusion) and we will take into account the diameter of the other side carotid artery and the speed at that level ([23], [45], [64]).

Carotid stenosis higher than 75% associate with increased speed and downstream turbulence. Tight stenosis will always associate increased speed, turbulence and flow alterations in the ophthalmic artery ([23], [45], [64]).

In the case of a very tight stenosis, pseudo-occlusive, the resistance index in the carotid arteries on the same side as the stenosis will be increased ([23], [45], [64]).

The internal carotid artery occlusion is set in case there is no Doppler signal at that level and we find indirect obstacle signals on the carotids. This diagnosis needs confirmation by and angiographic investigation.

The common carotid artery stenosis is recognised by a local increase in speed. If the stenosis is tight, it will associate a decrease in speed in the internal and external carotid arteries on the same side [45].

External carotid artery stenosis is recognised by the existence of an increase in speed at its origin, associated with an increase in amplitude in the ophthalmic artery.

Ultrasonographic investigation of the vertebra-basilar

system is more difficult, especially because of the deep location of the subclavian and vertebral arteries, near bone structures which absorb the ultrasounds [45].

Vertebral arterial will be visualized generally at the ostium and in their V3 retromastoidian segment [45].

Ostium stenosis is recognized by an increased speed associated with a protosistolic crease in V3 [45].

The occlusion of the vertebral artery must be differentiated from hypoplasia or agenesy, and for its recognition the entire cervical region will be analyzed for indirect signs (collateral circulation) [45].

The evaluation of the arterial wall will be done by the orientation of the ultrasound beam in a perpendicular position on the arterial surface of the wall and deep on the common carotid artery, calculating the distance between the lumen on the inside and an inecogenous line on the outside. The medium value of the internal carotid artery wall has to be under 0,6mm for a patient under 50. An increase in the wall thickness can be observed in patients over 50, with high blood pressure, diabetics, smokers and with increased cholesterol ([39], [45], [64]).

The diameter is measured in a transverse section of the common carotid artery, of the carotid bifurcation, of the internal carotid artery bulb.

Atheromatous plaques show up in the ultrasonographic investigation as a discontinuity between the parallelism of the arterial walls and the internal side of the lesion. The measurement of the plaque thickness is made in both longitudinal and transverse sections. The ecostructure of the plaques will be homogenous, heterogenous, hipoecogenous or hyperecogenous (calcified) [64].

A plaque may become complicated with the following:

- Hemorrhage under the plaque – inecogenous area between the wall and the plaque [64]
- Hemorrhage inside the plaque – hypoecogenous area with clear margins, inside the plaque [64].
- Ulceration – difficult to identify and evaluate [64]

The stenosis degree will be evaluated in a transverse section, where the stenosis is most significant. It is difficult to appreciate if the stenosis is tight or calcified. The hypo and isoecogenous stenosis will be evaluated by calculating the report between the residual section and the entire surface of the vessel.

Ultrasonographic investigation of the intracranial vessels

The evaluation of the patient with cerebrovascular implies not only the evaluation of the carotid and vertebral arteries, but also the evaluation of the intracranial vessels.

Transcranial Doppler represents a quick, accessible and non-invasive method of evaluating intracranial vessels. It is currently used not only for the study of vasospasm in the subarachnoid bleeding, but also in the evaluation of intracranial arterial stenosis, hemodynamic blocks, arterio-venous malformations.

It evaluated the main intracranial vessels by placing the probe over the bone areas of the skull (windows).

The temporal approach, above the zygomatic arcade and behind the orbital rebord offers access to the examination of the proximal segments of the medial, anterior and posterior cerebral arteries (M1, A1, P1) and anterior and posterior communicating arteries [45].

The suboccipital approach, between the occipital bone and the posterior processus of the first cervical vertebrae offers access to the examination of the intracranial vertebral arteries (V4) and of the basilar artery [45].

The transorbitary and transocular approach, by placing the probe above the closed eyelid allow access to the carotid and the ophthalmic artery at its origin [45].

No matter the approach, the identification of the artery is made by its depth compared to the probe, with the direction of the ultrasound beam and the direction of the flow.

The diagnosis of intracranial stenosis and/or occlusions is made by associating multiple signs – accelerated flow compared to the other side, turbulent flow (with a decrease in systolic frequencies), the luminosity increases phenomena in low frequencies [23], [45].

Transcranial Doppler is the only non-invasive method that allows the continuous monitoring of intracranial circulation.

During the carotid endarterectomy procedure, we can evaluate the tolerance of the carotid clamping and we can take a decision of passing to a shunt, when the circle of Willis does not allow a proper conservation of the sylvian territory perfusion. The

monitoring of the sylvian flow can prevent the installation of a cerebral ischaemia by hypoperfusion (if a residual flow of 0,3m/sec is maintained) [23], [45].

The high incidence of the cardiocerebrovascular pathology has determined a perfection of the evaluation methods, in order to determine the etiology of the vascular event and a prognosis after such an event.

At the same time, the evolution of modern medicine towards prophylactic medicine has led to the development of non-invasive and accessible methods of screening for patients at risk of developing a vascular event.

The ultrasonographic investigation of the carotids and vertebral arteries is now part of the evaluation of a patient who has suffered a cardiocerebrovascular event such as a stroke. This type of investigation allows the detection of intra and extracranial lesions of the cervical and cerebral vessels and a proper evaluation of the impact they have on the cerebral circulation, as well as an evaluation of the carotid atherosclerosis.

For patients with a symptomatic internal carotid artery stenosis the ultrasonographic investigation sets the lesion type and its degree, evaluates the impact on the cerebral hemodynamics and can be used as a starting point in monitoring its evolution [23].

For the symptomatic patient with a transient ischaemic attack, the ultrasonographic investigation will be an emergency investigation and can show multiple situations that allow a clinical and therapeutic approach with the lowest risk for the patient. For example, if it shows an occlusion of the internal carotid artery, it will lead to the avoidance of the angiographical risk for a patient who will benefit

from an exclusive medical treatment. In the case of an internal carotid artery stenosis higher than 70% without intracranial implications, we will perform an angiography and an endarterectomy [64].

The evaluation through transcranial Doppler of the intracranial circulation will give us precise data about downstream blocks and about the collaterals at that level.

The ultrasonographic approach can be useful in the quick and non-invasive identification of a carotid of vertebral artery dissection for patient with a clinical setting raising such a suspicion. This type of investigation is also useful in monitoring the healing process after such an event and allows the correct appreciation of the moment when the anticoagulants should be interrupted.

For transient ischaemic attacks, the ultrasonographic investigation offers vital information for the etiological diagnosis and the specific treatment. By using the ultrasounds, we can identify tight stenosis, carotid or vertebral occlusions or even intracranial occlusions.

The ultrasonographic investigation allows obtaining in a quick and non-invasive way, vital information about blood flow in the arteries irrigating the brain and about alterations in their walls.

The limits of current methods of exploring the cardio-cerebro-vascular system

As new technical discoveries were made, the methods of investigating the circulatory system have improves as well. Nowadays the doctors have at their disposal