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Features Of Venous Hemodynamics and Perfusion of The Brain in Chronic Cerebral Ischemia

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ABSTRACT

The article presents data on the state of hemodynamics and perfusion of the brain at different stages of chronic cerebral ischemia. A correlation was made between the data on the state of perfusion and hemodynamic changes in the brain.

Keywords: *chronic cerebral ischemia, cerebral hemodynamics, perfusion computed tomography*

INTRODUCTION

Perfusion computed tomography (CT perfusion) has a number of undeniable advantages over other methods for assessing the microvasculature of the brain, the main of which are wide availability, speed of implementation and the minimum number of contraindications [4,5,12,14]. This also determines the main area of its application - the examination of patients, if necessary, a quick and reliable diagnosis of the presence of cerebrovascular accident.

Chronic cerebral ischemia of varying severity in most cases precedes the development of stroke, and in the event of a progressive neurological and cognitive deficit, it is necessary not only to assess the degree of damage to the main vessels of the neck, but also the functional state of brain tissues, to identify risk groups for possible intra and postoperative complications. It is worth emphasizing that there are still no clear indications for the use of CT perfusion outside of acute conditions.

Despite the existence of works describing the application of the method in the examination of different groups of patients with chronic lesions of the arteries of the neck [6,8,9,13], there are no exact criteria for selecting patients who need a mandatory comprehensive examination, including an assessment of the microcirculatory bed of the brain.

Purpose of the study

Show the features of CT-perfusion of the brain at various stages of chronic cerebral ischemia CCI.

MATERIAL AND RESEARCH METHODS

The study included 90 patients aged 56 to 84 years with chronic cerebral ischemia (mean age 64.7±8.1 years). The diagnosis and stages of CCI were established using the criteria accepted in our country [1] based on the results of clinical neurological, neuropsychological and instrumental

(duplex scanning, magnetic resonance angiography of the brain) examinations of patients. The duration of the disease by the beginning of the examination of patients according to the anamnesis and analysis of medical records varied from 4 to 12 years, averaging 5.7 ± 0.8 years.

In all patients, the neurological status was studied according to the generally accepted method, neuropsychological testing was carried out to determine the cognitive and psycho-emotional status.

All examined patients were divided into 3 clinical groups: group 1 - 30 patients with CCI stage 1 (compensation stage), group 2 - 30 patients with CCI stage 2 (subcompensation stage), group 3 - 30 patients with CCI stage 3 (decompensation stage).).

Doppler ultrasound (General Electric Healthcare) was performed on a GE Vivid 7 machine. Extracranial (4 MHz transducer) and intracranial (2 MHz transducer) arteries were examined with registration of the main Doppler parameters (qualitative and quantitative).

To assess brain perfusion, single-photon emission computed tomography (SPECT) was performed on a SOMATOM Definition AS dual-detector gamma camera. To visualize cerebral perfusion, Iohexol was used, which was administered intravenously by bolus at a dose of 740 mBq. Scanning was carried out in static mode for 35 minutes with a post-injection delay of at least 15 minutes. Data processing included selection of a reference region in the cerebellar region. The difference in the inclusion of iohexol in the symmetrical contralateral zones of the brain was more than 10-12% was considered reliable. The blood supply to the brain was studied by angioscanning of the brachiocephalic arteries (AS BCA) using Sonoline Elegra (Siemens, Germany) HDI 5000 (Philips, Belgium) and "GE" (USA) devices.

Mathematical processing of the obtained data was carried out by the method of analysis of variations. The average values (M) and their average error (± m) were determined, the differences between the average values 0), the correspondence criterion (x2), the probability value (p).

The relationship between the studied parameters was determined using the linear correlation coefficient (±r). The results were considered statistically significant at $p<0.05$. The assessment of direct correlation was considered: up to ±0.3 - small; from ±0.3 to ±0.7 - medium; ±0.7 to 1.0 large.

Research results

Duplex sanitation (DS) and magnetic resonance angiography (MRA) revealed in patients the presence of stenosing processes in the form of tortuosity and narrowing. In group I, tortuosity occurred in 23.3%. In group II. - in 36.6% of patients, in group III - in 30.0% of patients No statistically significant difference between the parties was obtained ($p > 0.5$).

The study of the Doppler characteristics of cerebral blood flow made it possible to establish certain patterns of changes in blood flow in the main arteries and veins of the brain at the stages of development of chronic cerebral ischemia.

TABLE 1: Characteristics of changes in the main and intracranial arteries depending on the stage of CCI

Characteristic	group I (1)			group II (2)			group III (3)		
	abc	%	r-1-2 <	abc	%	r-2-3<	abc	%	r-1-3<
Norm variant	2	6,7%		2	6,7%		0	0,0%	
Thickening, thickening of the intima-media complex	3	10,0%	0,05	10	33,3%	0,05	8	26,7%	0,005
MRA deformations	11	36,7%		21	70,0%		21	70,0%	0,005
congenital anomalies	2	6,7%		5	16,7%		3	10,0%	

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Hemodynamically insignificant stenoses of the MRA	5	16,7%	0,05	13	43,3%	0,05	17	56,7%	0,005
Hemodynamically significant stenoses of the MRA	3	10,0%	0,05	12	40,0%	0,05	11	36,7%	0,005
Hemodynamically significant stenoses of the ICA	0	0,0%		4	13,3%	0,05	7	23,3%	0,005
Hemodynamically significant VA stenoses	2	6,7%	0,056	8	26,7%		9	30,0%	0,005
Hemodynamically significant stenoses - combined, multiple	1	3,3%	0,05	11	36,7%	0,05	12	40,0%	0,005
Changes in the intracranial arteries	1	3,3%	0,05	6	20,0%	0,05	8	26,7%	0,005

Atherosclerotic changes in the ICA were detected in 45.6% (n=41) of all examined patients (n=90). At the same time, thickening of the carotid artery wall was noted, atherosclerotic plaques, loosening and thickening of the intima of the vessels were detected. Data when measuring the size of the intima-media complex were recorded with significant deviations and ranged from 0.6 to 2.7 mm (mean 1.4 + 0.4). There were no patients with occlusion of the internal carotid artery in our studies.

Analysis of LBF in the CCA in group II showed a slight decrease in the left CCA (26.5 cm/s; a 3.14) compared with the control group (30.9 cm/s; a 3.44; $p<0.05$) . Here and below, the data are presented as the arithmetic mean (M) and standard deviation (a).

In group III, in the left CCA, the average (25.2 cm/s; a 4.43; in the comparison group - 30.9 cm/s; a 3.44), maximum (84.0 cm/s; a 15 .1; in the control group - 105.1 cm/s; a 13.8) and minimal (26.0 cm/s; a 4.4; in the control group - 32.2 cm/s; a 5.2) linear blood flow velocities ($p < 0.01$), in the right CCA these changes were less pronounced (Table 1).

Assessing the linear velocity of blood flow, it can be stated that as the disease progresses, a decrease in LBF occurs. Attention is drawn to the fact that for patients of groups II and III a significant decrease in LBF is more characteristic of the left CCA.

In order to assess hemodynamic changes during CCI, the volumetric blood flow rate Q (in ml/min) in the CA and VA, as well as the total volumetric velocity Qsumm (Table 2).

The study of the volumetric blood flow velocity in the main arteries of the head revealed a significant decrease in the volumetric blood flow velocity in almost all extracranial vessels (CCA, ICA, VA), as well as the total volumetric velocity Qsumm, depending on the stage of CCI.

TABLE 2: Data on volumetric blood flow velocity (Q, ml/min) of intracranial arteries depending on the stage of CCI

Q	group I	group II	group III	CT
CCA	545,2 ± 71,5	495,8 ± 96,1 *	468,2 ± 91,4 *	523,6 ± 89,3
ICA	274,1 ± 48,4	246,2 ± 39,4 *	213,6 ± 48,0 * ^	292,6 ± 68,5
VA	92,5 ± 26,1	81,6 ± 29,3	54,9 ± 240,4 *	96,3 ± 35,5
Qsumm	754,7 ± 15,1	634,4 ± 106,1 *	578,9 ± 78,2 *^	798,4 ± 84,7

Note:

*-significance of differences with group I ($p<0.005$);

^-significance of differences with group II ($p<0.005$)

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Deceleration of blood flow through the main veins of the brain in patients with atherosclerosis and a sufficiently low cardiac output by 25-50% slightly changes the hemodynamic reserve of the brain, while its increase changes the critical levels of the hemodynamic reserve of the brain towards pronounced stages of CCI. That is, with a low fractional ejection and with preserved mechanisms for controlling vascular tone, an increase in the rate of blood flow in the cerebral veins creates a model of a "vascular shunt", and this leads to a disruption in the release of oxygen and glucose from the capillary network of the brain.

Scanning of the vertebral veins (VV) in patients was performed in the supine position. Blood flow according to VV was determined in patients of group II - in 26.4% of cases, in group III - in 42.7%. When moving to a sitting position - in 100.0% of cases in both study groups. Artifact of vertebral vein imaging was associated with overall scan quality. Thus, more often VV were inconsistent in patients of groups II and III ($p < 0.05$).

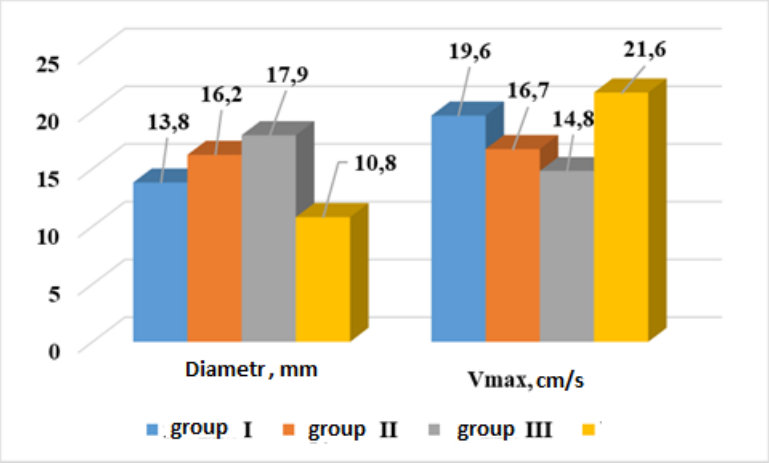

FIGURE 1: Diameter and flow velocity in the internal jugular vein depending on the stage of CCI.

In the control group, the blood flow in the direct sinus and in the basal vein of Rosenthal was monophasic on both sides. The blood flow parameters are presented in table 3.

TABLE 3: Parameters of blood flow in intracranial veins depending on the stage of VSD

Options	group I		group II		group III	
	Vmax, sm/s	PI	Vmax, sm/s	PI	Vmax, sm/s	PI
Vienna Rosenthal	12,8 ± 5,4	0,41 ± 0,08	21,8 ± 7,2	0,28 ± 0,08	23,4 ± 7,2 *	0,21 ± 0,07*
Direct sine	20,1 ± 6,2	0,48 ± 0,07	29,6 ± 7,8	0,32 ± 0,07	31,2 ± 6,2 *	0,24 ± 0,08*

In the study of the quantitative parameters of the venous cerebral circulation of the brain in patients of group II, obstruction of blood flow was revealed during normal insonation of the intracranial veins. At the same time, a significant increase in LBF was noted in the deep venous system against the background of a pronounced decrease in PI.

In patients of group III, the parameters of LBF in the blood flow along the direct sinus and basal veins of Rosenthal did not differ significantly from patients in group II, however, a tendency to a progressive decrease in PI was observed. A significant difference in all four parameters was observed in patients of group II compared with patients in group I.

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TABLE 4: Comparative analysis of linear blood flow velocity in some venous collectors in CCI

Patient groups	group I	group II	group III	CT
Number of observations	29	51	56	25
Linear blood flow velocity, cm/s in the right basal vein	21,2 ±0,83*	14,4 ±1,78**	22,1 ±1,57*	16,1 ±0,68**
Linear blood flow velocity, cm/s, in the left basal vein	21,1 ±0,90*	14,3 ± 1,83**	23,5 ±1,66*	18,2 ±0,72**
Linear blood flow velocity, cm/s, in the direct sinus in patients	27,3±1,24	29,5 ±1,73 #	32,3±1,01 *#	26,3 ± 1,12

Note: * - significant compared with CG ($p < 0.05$);

- significant compared with group I ($p < 0.05$).

The analysis of LVBF parameters in the direct sinus and basal veins from both sides was carried out at different stages of chronic cerebral dyscirculation and in the CG. The study of LBF values in the right basal vein in the groups of patients with CCI and in the CG is presented in Table 4.

From Table. 4 it follows that the LVBF values in the basal vein on the right in groups I and II did not differ much. There were no significant differences in this indicator in group I and in the CG. Differences were revealed when comparing the parameters of LVBF in patients of groups I and III, that is, the linear blood flow velocity in the right basal vein in group I was significantly higher than in patients of group III, and in patients of groups II and III in comparison with patients with CG ($p<0.05$).

LVBF of blood flow in the direct sinus of the brain, as can be seen from Table 3.8, increased depending on the stage of CCI. Moreover, there were significant differences between group I and group III - 27.3 vs. 32.3 cm/s. And the indicators in the groups of patients of the II and III groups significantly differed compared to the CG.

In all groups of patients there were changes in brain perfusion, but there were distinctive features. So, when analyzing the obtained data on the state of brain perfusion (according to SPECT data), it is noteworthy that that almost every second patient of group I (46.7%) has normal brain perfusion, which is due to the fact that stage I CCI is a pathology at the initial stage of its development, as a rule, functional, "pre-morphological".

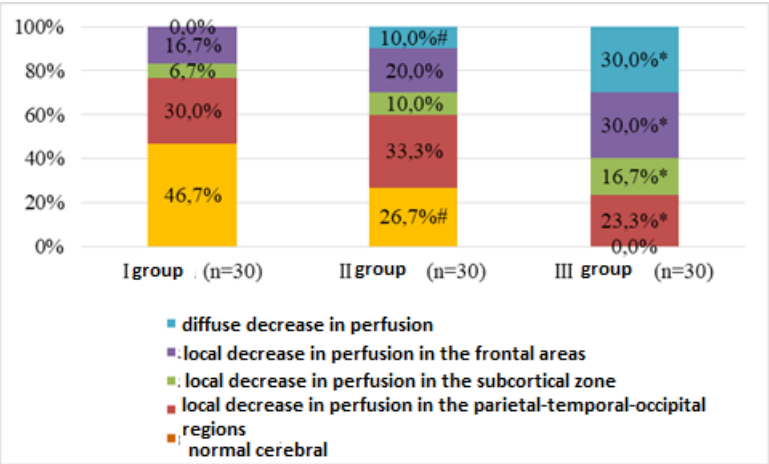

FIGURE 2: State of brain perfusion in different clinical groups

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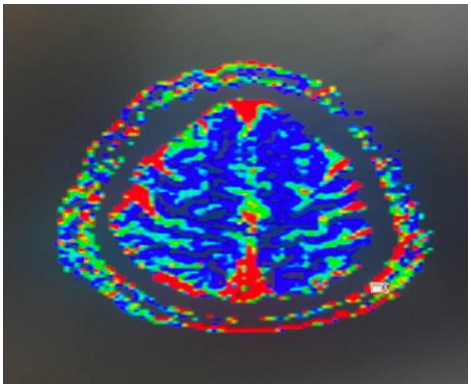
Note: *- significance of differences p<0.05 between groups II and III; # - significance of differences p<0.05 between groups I and II.

In this group, there was also a large percentage (30.0%) of patients with a local decrease in perfusion in the parietal-temporal-occipital regions (Fig. 2). In group II, normal parameters of brain perfusion were already significantly lower compared to group I in 26.7% of patients. The proportion of patients with decreased perfusion in the parietal-temporal-occipital areas increased (33.3%) and the percentage of patients with local changes in perfusion (decrease) in the frontal areas became more significant (20.0%). In 10.0% of patients, a diffuse decrease in cerebral perfusion is already diagnosed. In group II, small-focal zones of reduced perfusion in the frontal, parietal-occipital and temporal regions became more common due to multiple cortical infarcts in lesions of large and medium-sized arteries.



CLINICAL EXAMPLE 1: Patient D., 63 years old. Local decrease in perfusion of the cerebral cortex in stage I CCI against the background of a combined course of hypertension and cerebral atherosclerosis.

A diffuse decrease in perfusion may be a manifestation of small vessel damage, leading to damage to the white matter of the brain. In group III, the percentage of patients with a diffuse decrease in perfusion increases (30.0%) and the proportion of local areas with a decrease in brain perfusion increases - 30.0% in the frontal regions, 23.3% in the parietal-temporal-occipital regions. What is distinctive is that in the subcortical zone there was a low percentage of 6.7%, 10.0% and 16.7%, respectively, of a decrease in cerebral perfusion in all groups, at the same time, there was a tendency for the process to progress (Fig. 2, clinical example 1).

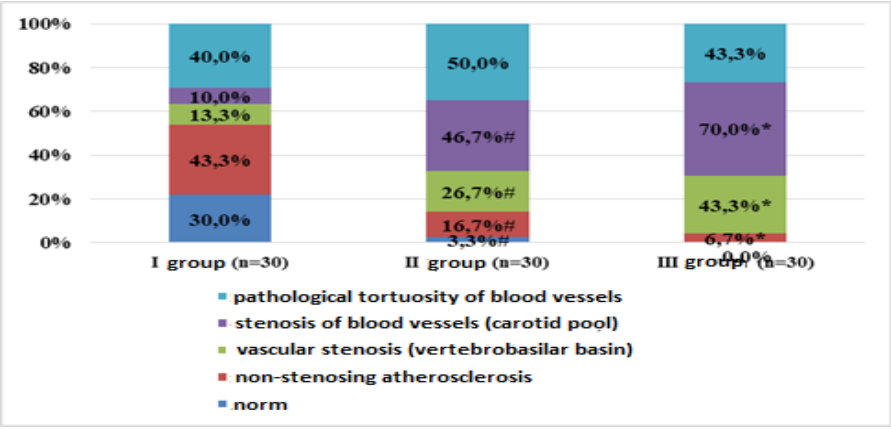


FIGURE 3: Pathology of the vascular system of the brain in CCI depending on the stage.

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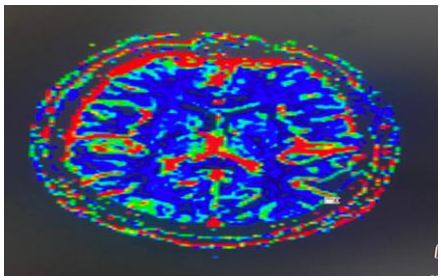
Note: *- significance of differences $p<0.05$ between groups II and III; # - significance of differences $p<0.05$ between groups I and II.

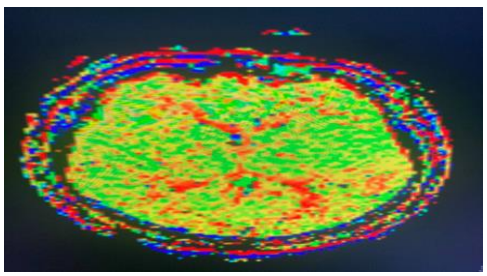
When correlating TCDS data and CT perfusion parameters in patients of groups I and II, it was found that stenoses of the brachiocephalic arteries (BCA), pathological tortuosity of the vessels, do not have a significant correlation with a decrease in brain perfusion ($p>0.05$). With the existing BCA pathology in Group I - non-stenosing atherosclerosis - 43.3%, pathological tortuosity - 40.0%, stenosis in the vertebrobasilar (VBB) vascular system up to 13.3% of patients - there is normal perfusion in 46.7% of patients (Fig. .2 and fig.3). This is explained by the fact that the state of regional perfusion of the brain depends on many factors, and not only on the state of the main vascular system of the brain. Perfusion depends on the functional needs of the brain, the state of metabolism in a particular area, on the abilities and state of autoregulation of the suprasegmental divisions of the autonomic nervous system in ensuring life and maintaining homeostasis. In group II, it can be seen that changes in BCA and a decrease in perfusion "regionally" coincide (clinical example 2).



CLINICAL EXAMPLE 2: Patient H., 69 years old. Local more pronounced decrease in perfusion of the cortex and subcortical region of the brain in stage II CCI against the background of a combined course of HA and cerebral atherosclerosis.

Diffuse perfusion disorders are the result of damage not only to large, but also to small penetrating vessels. It is the defeat of small vessels that underlies the pathogenesis of the formation of chronic cerebrovascular insufficiency and vascular cognitive insufficiency. In patients of group II, stenosis of the vessels of the carotid basin (CB) was detected in 46.7% of cases, and in 26.7% of cases, stenosis of the vessels in the VBI (Fig. 3).

When analyzing the state of blood supply dynamics in different clinical groups, the decrease in perfusion and changes in BCA in the corresponding pools were most often determined in group III. It can be concluded that if the zone of blood supply deficiency and reduced perfusion coincide, it is the cause of decompensation of the functioning of the brain (clinical example 3).



CLINICAL EXAMPLE 3: Patient M., 81 years old. Diffuse pronounced decrease in perfusion of the cortex and subcortical region of the brain in stage III CCI against the background of a long-term combined course of hypertension and cerebral atherosclerosis.

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Thus, certain venous dysgemic disorders (increased LVBF in the basal veins and direct sinus) found in the examined patients with early manifestations of CCI confirm the opinion of a number of researchers about the early involvement of intracranial veins in the formation of vascular encephalopathy (CCI) even with minor changes in the arterial pools that feed brain [1,2,7].

The revealed relationship between venous cerebral dyscirculation and depression is consistent with the literature data: depression, which is based on dysfunction of a number of neurochemical systems of the brain [3,10], is one of the factors affecting the tone of cerebral vessels and venous outflow from the cranial cavity [2,3, eleven]. The study showed no correlation between the state of brain perfusion and the state of its blood supply in the early stages of CCI, which once again proves that oxygenation of the brain is more dependent on its functional needs, on the state of metabolism, as well as on the characteristics of autoregulation of blood circulation. Various types of changes in brain perfusion occur in stages II and III of CCI, in which a clear correlation between the state is already determined.

Thus, the state of regional perfusion in comparison with the arterial and venous hemodynamics of the brain are important pathogenetic components of the progression of chronic cerebral ischemia.

REFERENCES

1. Belova L.A. The role of arteriovenous relationships in the formation of clinical and pathogenetic variants of hypertensive encephalopathy.// Zhurn. nevrol. and a psychiatrist. them. S.S. Korsakov. – 2012. – №6. – C.8-12.
2. Vasiliev I.A., Stupak V.V., Chernykh V.A., Polovnikov E.V., Chernykh E.R., Shevela E.Ya., Dergilev A.P. Pathogenetic aspects of violations of the venous circulation of the brain // Internet magazine applied and fundamental research.– 2014. – № 9, h. 3. – P.23-26.
3. Gachechiladze D.G., Berulava D.V., Antiya T.A. Features of cerebral venous hemodynamics in chronic disorders of cerebral circulation // Med. visualization. – 2012, №4. – P.104-12.
4. Study of perfusion in disorders of cerebral circulation. Part I (history, basic postulates and methods of study). Review / S. E. Semenov et al. // Reviews and lectures.- 2016.- P. 95-102.
5. Study of tissue perfusion of the brain using computed tomography / V.N. Kornienko [et al.] // Medical visualization.-2007.- № 2.- P.70-81.
6. Lipovetsky B. M., Kataeva G. V. Differentiated assessment of regional brain perfusion in patients with cerebrovascular disease in comparison with the further course / B. M. Lipovetsky, G. V. Kataeva // Med. visualization.- 2012.- No 4.- P. 91–95.
7. Nazarova J.A. Indicators of cognitive functions in patients with chronic cerebral ischemia depending on the presence of venous cerebral dysfunction // Neurology. -Tashkent, 2019. - № 1.- P.7-8.
8. Nemirovskaya T.A. Perfusion computed tomography in the diagnosis of patients with chronic ischemic brain lesions: Ph.D. diss. ... cand. Sciences / T.A. Nemirovskaya: Kazan. – 2011.- P. 23.
9. CT brain perfusion: A phantom based study of image quality and dose / S Midgley et al. // Journal of Medical Imaging and Radiation Oncology.- 2014.- vol.58.- p.184–343
10. Henry-Feugeas M.C., Koskas P. Cerebral vascular aging: extending the concept of pulse wave encephalopathy through capillaries to the cerebral veins // Chinese Med. J. – 2012. – № 125 (7). – P. 1303-1309.
11. Li Q., Khatibi N., Zhang J.H. Vascular neural network: the importance of vein drainage in stroke // Transl Stroke Res. – 2014. – Vol.5, N2. – P.163-166.
12. Miles K.A., Eastwood J.D., Konig M. Multidetector computed tomography in cerebrovascular disease. CT perfusion imaging. Informa, UK. 2007; 175 p.
13. Optimization of Contrast Material Dose for Abdominal Multi-Detector Row CT: Predicting Patient LeanBody Weight by Using Preliminary Transverse CT Images / A.Guerri et al. // Advances in Computed Tomography.- 2014.- vol.3.- p.1-10.
14. Radiation exposure in perfusion CT of the brain / A. Ringelstein et al.// Journal of Computer Assisted Tomography (JCAT).- 2014.- Vol. 38 (Issue 1). – p. 1-152.

J Popul Ther Clin Pharmacol Vol 30(12):e348–e355; 24 May 2023.