Review

https://doi.org/10.23934/2223-9022-2022-11-1-86-95

Quantitative and Qualitative Analysis of CSF Flow Dynamics

A.S. Tokarev, D.A. Talypova[⊠], I.A. Terekhin, A.A. Grin

Radiosurgery Centre, Department of Emergency Neurosurgery N.V. Sklifosovsky Research Institute for Emergency Medicine 3 Bolshaya Sukharevskaya Sq., Moscow 129090, Russian Federation

🖂 Contacts: Daria A. Talypova, Resident, Department of Rentgenology, N.V. Sklifosovsky Research Institute for Emergency Medicine. Email: talypova_daria@mail.ru

ABSTRACT Disorders of cerebrospinal fluid (CSF) secretion, dynamics and absorption are common in different illnesses and injuries of the central nervous system (CNS). Nowadays magnetic-resonance tomography (MRI) is the leading research method of CSF dynamics. There are some MRI techniques for both qualitative and quantitative evaluation of CSF dynamic. The assessment of CSF movement is needed to define treatment strategy for patients with different types of hydrocephalus. In this review we have summarized the information about physic basement, area of application of modern MRI techniques. The main attention was paid to modern views on hydrocephalus pathogenesis, pathological CSF flow dynamics in CNS disorders and traumatic brain injury.

Keywords: cerebrospinal fluid, phase-contrast MRI, cerebrospinal fluid dynamics

For citation Tokarev AS, Talypova DA, Terekhin IA, Grin AA. Quantitative and Qualitative Analysis of CSF Flow Dynamics. Russian Sklifosovsky Journal of Emergency Medical Care. 2022;11(1):86–95. https://doi.org/10.23934/2223-9022-2022-11-1-86-95 (in Russ.)

Conflict of interest Authors declare lack of the conflicts of interests

Acknowledgments, sponsorship The study has no sponsorship

Affiliations

Aleksey S. Tokarev	Candidate of Medical Sciences, Researcher, Department of Emergency Neurosurgery, N.V. Sklifosovsky Research Institute for Emergency Medicine; https://orcid.org/0000-0002-8415-5602, tokarev@neurosklif.ru; 40%, study concept and design, article editing
Daria A. Talypova	Resident, Department of Rentgenology, N.V. Sklifosovsky Research Institute for Emergency Medicine; https://orcid.org/0000-0001-7188-450X, talypova_daria@mail.ru; 30%, collection and processing of material, text writing, analyzing data, correspondence with the publisher
Ivan A. Terekhin	Rentgenologist, «Gamma-knife» Department, N.V. Sklifosovsky Research Institute for Emergency Medicine; https://orcid.org/0000-0002-8502-7792, ivan79206260182@mail.ru; 20%, collection and processing of material
Andrey A. Grin	Doctor of Medical Sciences, Head of the Department of Emergency Neurosurgery, N.V. Sklifosovsky Research Institute for Emergency Medicine; https://orcid.org/0000-0003-3515-8329, aagreen@yandex.ru; 10%, research concept and design, article editing

ICP — intracranial pressure	FOV — rectangular-field-of-view
DPCC — diastolic phase of the cardiac cycle	IR — inversion recovery
MR signal — magnetic resonance signal	PC-MRI — phase – contrast MRI
MRI — magnetic resonance imaging	ROI — region of interest
RF pulse —– radiofrequency pulse	SNR — signal to noise ratio
CSF — cerebrospinal fluid	SSFP — Steady-state free precession
SPCC — systolic phase of the cardiac cycle	TI — time inversion
CNS — central nervous system	Time SLIP — Time Spatial Inversion Pulse
TBI — traumatic brain injury	TR — repetition time
ASL — arterial spin labeling	VENC — velocity encoding
ASSET — Array coil Spatial Sensitivity Encoding	VPS — views per segment
CFD — computational fluid dynamics	

PHYSIOLOGY OF CEREBROSPINAL FLUID DYNAMICS

Cerebrospinal fluid (CSF) is the main intrathecal biological medium circulating through the ventricular system of the brain, along the CSF pathways, subarachnoid space of the brain and spinal cord. CSF is a blood plasma filtrate and has a weak alkaline reaction. The main function of the CSF, which forms a water "cushion", is to protect the brain and spinal cord from external mechanical impact. Also, cerebrospinal fluid is an additional way of transporting various ions, molecules, proteins from the brain matter [1], [2].

The concept of CSF dynamics includes the following processes: CSF production, CSF circulation along the CSF pathways, and CSF reabsorption [3].

CSF FORMATION

According to the latest data, 80% of CSF is produced by the choroid plexuses of the cerebral ventricles which are a highly vascularized structure of epithelial cells. The process of CSF formation includes passive filtration of plasma from the capillaries of the plexus into the interstitial space of the plexus due to the pressure gradient; and then the filtrate is transported from the interstitial space to the ventricular cavity due to the activation of carbonic anhydrase and membrane transport proteins [3], [4]. Carbonic anhydrase catalyzes the formation of hydrogen ions (H+) and bicarbonate (HCO3-) from water and carbon dioxide. The transport proteins of the basement membrane of the plexus change H+, HCO3- for sodium (Na+) and chloride (Cl-) ions [5], [6]. Through the ion pump in the apical membrane, Na+, potassium ions (K+) and Cl- enter the ventricular cavity [4]. Transport of water provided by aquaporin-1 of the apical membrane occurs due to the osmotic gradient provided by the ion pump [7], [8]. The Na-K-2Cl cotransporter of the apical membrane transports ions in both directions and is involved in the regulation of CSF secretion and composition [9].

The choroid plexuses also produce a number of other substances, such as vitamins B1, B12, C and folates. Some researchers suggest that they can affect the subventricular zone and participate in the restoration of tissues damaged by hydrocephalus [5].

The remaining 20% of CSF is produced through the system of interaction between CSF and the interstitial fluid of the brain [10]. Interstitial fluid fills the extracellular space between neurons and glia, cerebrospinal fluid fills the subarachnoid space and the ventricles of the brain. Communication between the two media occurs in the perivascular spaces surrounding the cerebral vessels that supply blood to the brain parenchyma [9].

The approximate CSF production rate is 0.4 ml/min, thus, approximately 500-600 ml of CSF is produced per day [11].

CSF secretion is regulated in several ways.

1. Due to the autonomous cholinergic, adrenergic, serotonergic and peptidergic innervation of the choroid plexuses of the ventricles. The sympathetic nervous system reduces the level of CSF secretion, while the parasympathetic nervous system increases CSF secretion. The autonomic nervous system is responsible for daily fluctuations in the level of CSF production [12].

2. By changes in the activity of carbonic anhydrase, aquaporins, and a membrane carrier protein (such as co-transporter Na-K-2Cl) in case of acid-base imbalance [12], [13].

3. Because of influence of some neuropeptide factors. The vascular plexus epithelium has receptors for dopamine, serotonin, melatonin, atrial natriuretic hormone, and vasopressin. Thus, the atrial natriuretic hormone, vasopressin, reduces the level of CSF secretion by affecting aquaporin 1 [12].

FEATURES OF CSF CIRCULATION

Transport from the ventricles of the brain, where the main part of the CSF is formed, to the subarachnoid space passes through the cavities and holes that form the CSF pathways. From the lateral ventricles, through the interventricular foramen (the foramen of Monro), the cerebrospinal fluid enters the third ventricle, through the cerebral aqueduct - into the fourth ventricle. From there, through the lateral foramen (of Luschka) and median foramen (of Magendie), CSF enters the basal cisterns of the brain and through the cisterna magna of the brain into the spinal space [14].

Before the advent of non-invasive neuroimaging techniques, it was assumed that the CSF flow was laminar, and the circulation was supported by the pressure differences between the cavities, the vertical position of our body in space, and the movement of the villi of the ependyma that lines the ventricles of the brain [14].

With the development of various imaging methods, a more detailed study of the CSF flow through the ventricular system of the brain became possible [3]. Thus, the unidirectional theory of the fluid flow was refuted with the development of phase-contrast magnetic resonance imaging (MRI) technology. In the first studies, the area of interest was the aqueduct of Sylvius, due to its central position in the ventricular system. Gated MRI made it possible to detect the bidirectional movement of cerebrospinal fluid through the aqueduct of Sylvius. In cardiac systole, the movement was noted in the caudal direction, in diastole - in the cranial

direction. With the further development of technology, a more detailed assessment of the CSF flow was made, and as a result the turbulent nature of the fluid flow towards the third ventricle was revealed. The same trend in CSF dynamics was soon found in the area of the foramen of Monro [14].

Another quantitative characteristic of CSF dynamics is the velocity of fluid motion. Already in1943, O'Connell suggested that the flow of cerebrospinal fluid is enhanced by the pulsation of the right and left thalamus, expanding during blood filling in systole, between which the third ventricle is located. Thus, the fluid flow velocity in the third and fourth ventricles is greater than in the lateral ventricles [15]. Further studies have shown that the pulsation of the epidural venous plexus in the cervical spine, which occurs due to changes in intrathoracic pressure during respiratory movements of the chest, also contributes to the acceleration of CSF flow in the subarachnoid space [16].

REABSORPTION OF CEREBROSPINAL FLUID

CSF reabsorption is understood as its reverse return to the venous bed. The main site of CSF reabsorption is the arachnoid granulations (pacchionian granulations) which are located convexitally along the superior sagittal sinus [17].

A large number of experiments have been carried out on the introduction of marker substances into the cerebrospinal fluid system to study the absorption process. As a result, it was suggested that there are alternative routes of CSF reabsorption, namely through the lymphatic system. This theory is currently controversial. During the experiments, it was found that a certain part of CSF can be absorbed into the CSF system through the perineural spaces of the cranial nerves. The significance of this path is not completely clear [17]. According to various sources, the proportion of reabsorption through the perineural spaces can be 5–40%.

The glymphatic system plays a significant role in the formation and absorption of CSF [5]. The major cerebral arteries are located in cisterns, channels containing CSF. At these levels, the arteries are covered by a pial sheath formed by leptomeningeal cells. Approaching the cerebral cortex, the arteries branch into the vessels of the pia mater. In the parenchyma, the arteries form penetrating arterioles which are surrounded by the perivascular space (Virchow–Robin space) [18]. This space is surrounded internally by the pial sheath and externally by the basement membrane of the astrocytic end-foot (glial limiting membrane). This system is called the glymphatic system, and in its function and structure it resembles the lymphatic system [19]. The glymphatic system is involved in the formation of the interstitial fluid of the brain, the sources of which are blood and CSF [1].

In most tissues, the transport of interstitial fluid occurs due to the difference in hydrostatic pressure which is created in the systole phase of the cardiac cycle [19]. In the brain, the transport of fluids and solutes is provided by the glymphatic system which includes a special system of aquaporin-4 channels [1].

CAUSES AND TYPES OF HYDROCEPHALUS

Hydrocephalus is a disease that is accompanied by an excessive accumulation of CSF in the ventricles of the brain and subarachnoid space. Clinical signs of hydrocephalus are rather nonspecific. These may include cerebral symptoms (headache, nausea, vomiting), diplopia, impaired concentration, gait disturbance, bladder dysfunction, and so on [20].

Hydrocephalus is caused by an imbalance between the production, transport and reabsorption of CSF [21]. Excessive accumulation of CSF leads to a breakdown of dynamic equilibrium of intracranial contents (blood, cerebrospinal fluid, brain matter) and an increase in intracranial pressure (ICP).

The first classification of hydrocephalus was proposed by W. Dandy in 1931. He divided hydrocephalus into two types - obstructive and communicating ones.

The cause for the development of obstructive hydrocephalus is impairment of CSF flow [22].

Obstruction at the level of the foramen of Monro causes unilateral ventriculomegaly. The most common causes of obstruction are glial tumors; ependymal, epidermoid, dermoid cysts; intraventricular hematomas.

The main causes of aqueductal stenosis are pineal tumors, gliomas, tentorial meningiomas, and vein of Galen–related aneurysms.

The cause of obstructed Luschka or Magendie is intraventricular hemorrhage, meningitis [23].

Narrowing of the CSF pathways in the area of the foramen magnum can occur due to osteochondrodysplasia, metabolic disorders, Arnold-Chiari malformation, syringomyelia and syringobulbia.

Acute hydrocephalus is possible after traumatic injuries of the posterior cranial fossa, intraventricular hemorrhages of traumatic and non-traumatic origin [24].

Obstructive hydrocephalus leads to increased ICP, which is an emergency situation requiring immediate action.

Another reason for the development of hydrocephalus is blocked or reduced CSF reabsorption. Traumatic subarachnoid hemorrhage causes damage to the ventricular cilia involved in CSF reabsorption [25]. Gradual restoration of cilia occurs after 30 days, which in turn in some cases leads to the restoration of CSF reabsorption. A history of subarachnoid hemorrhage increases the risk of developing hydrocephalus by 3 times during the first 2 years after injury [20]. Normal-pressure hydrocephalus is characterized by a progressive enlargement of the ventricular system against the background of normal ICP and the gradual development of clinical symptoms — the Hakim–Adams triad: gait disturbance, dementia, urinary incontinence [26]. Normal-pressure hydrocephalus can develop after intracranial hemorrhage, traumatic brain injury (TBI), and inflammatory diseases [1]. The main mechanism for the development of the disease is the occlusion of CSF reabsorption sites, the difficulty of transporting it into the blood.

ASSESSMENT OF CSF FLOW DYNAMICS USING MRI

MRI is the method of choice for the assessment of the CSF system of the brain and spinal cord, since it has a high diagnostic ability to detect both structural and functional disorders of the CSF flow [15].

The earliest MRI visualization of CSF flow was based on the detection of flow artifacts caused by high velocity characteristics and manifested by the loss of the MR signal on standard T2-weighted spin-echo images [27]. A quantitative assessment of the CSF flow was carried out based on the calculation of CSF relaxation times T1 and T2 and the determination of the degree of saturation between static tissues and moving CSF. Later, modified gradient sequences began to be used, in which the phase shift was induced by bipolar gradients built into the pulse sequence, which significantly improved the visualization of the CSF flow. For qualitative and quantitative assessment of CSF flow dynamics, cardiac-gated phase-contrast MRI is currently widely used [27].

PHYSICAL PRINCIPLES OF PHASE-CONTRAST MRI

Phase-contrast MRI is based on the use of a bipolar magnetic field gradient, that is, a gradient with the same positive and negative magnitude and the same time of its application. Using one part of the gradient allows imaging of the fluid flow in one direction, so it is necessary to use both parts of the gradient in three planes to obtain a complete study. Phase-contrast MRI allows for both qualitative and quantitative assessment of the fluid movement. Thus, one of the main areas of its application in medicine has become the study of CSF flow [28].

The changing magnetic field creates a bipolar gradient that causes a phase shift to the moving spins. Spins moving in the direction of the bipolar gradient receive a positive phase shift, while spins moving in the opposite direction receive a negative phase shift. The number of phase shifts obtained is directly proportional to the fluid flow velocity and the time of application of the bipolar gradient.

Spins in a stable structure receive the same amount of negative and positive phase shift when a bipolar gradient is applied. Thus, the lack of movement, staying in the same position, obtaining the same gradient strength leads to zero phase shift. In every study using phase-contrast MRI, an image with zero phase shift is used as a reference image, which will subsequently be subtracted from the high-speed image. As a result, an image will be obtained only from moving spins [28].

The key parameter of phase-contrast MRI is VENC (velocity encoding), which is the encoding parameter for the velocities of spins moving in the flow [22]. From the point of view of physics, this parameter is understood as the speed at which a phase shift of 1 radian (180°) will occur. Incorrect selection of this parameter on the console of the MRI scanner significantly degrades the quality of the image obtained from the fluid due to an increase in the signal-to-noise ratio (SNR). The value of this parameter should be close to the actual values of the fluid flow, but not exceed it. Thus, for cerebrospinal fluid, this parameter is 5–20 cm/s (for example, in the region of the foramen magnum, the CSF flow velocity is 10 cm/s, in the area of the aqueduct it is 8 cm/s). However, in case of some pathological conditions, for example, stenosis of the CSF pathways, the VENC value should be chosen larger. Choosing an overestimated value of the VENC parameter can simulate the fluid flow in the opposite direction, which will lead to incorrect research results [29].

The lower the VENC value, the stronger the bipolar gradient must be applied for a longer time, which will increase the TR (repetition time) value. However, TR cannot increase indefinitely.

With phase-contrast MRI, magnitude and phase images are obtained. On the magnitude image, the CSF flow has a hyperintense signal, the signal from the "immobile" tissues is hypointense. The phase shift of the spins is encoded in the phase image. Accordingly, in case of the anterograde fluid flow, there will be a hyperintense signal, and a hypointense signal with the retrograde flow. Thus, the phase image carries information about the fluid flow velocity, which can be quantified.

Cardiac-gated phase-contrast MRI also allows evaluation of pulsatile fluid flow. This technique consists in receiving a signal from the fluid for several minutes, which is then averaged and synchronized with the heart rate [30].

To synchronize MRI data with the cardiac cycle, it is possible to use electrocardiography or digital plethysmography. Fluid flow information for each cardiac cycle is averaged at the end. This is why the phase-contrast MRI technique is insensitive to dynamic changes in the fluid flow [31].

The use of phase-contrast MRI has a number of limitations. First, the evaluation of such quantitative parameters as mean peak velocity, peak systolic velocity and stroke volume can only be measured in one plane perpendicular to the fluid flow. Accordingly, this technique will be ineffective in the study of the fluid flow inside arachnoid (subarachnoid) cysts, in the study of turbulent movement.

Secondly, in a phase-contrast study, a manual selection of a region of interest (ROI) is implied. The volume of the selected zone will affect such parameters as stroke volume, flow velocity, average peak velocity [32].

The phase-contrast study technique is associated with the patient's cardiac cycle and represents, as a result, averaged data obtained over a certain period of time.

EVALUATION OF THE FLUID FLOW GRAPH IN PHASE-CONTRAST MRI

The graph contains both positive and negative values of the fluid flow velocity. Positive values correspond to the cranio-caudal direction of the fluid movement and the systolic phase of the cardiac cycle (SPCC), while negative values correspond to the caudocranial direction and diastolic phase (DPCC) [33]. The maximum flow velocity in systole and diastole on the graph is indicated as "a" and "b", respectively. The space of the graph below peak "a" corresponds to the systolic volume of CSF, and the diastolic volume of CSF is above the peak "b" (Fig. 1) [34].



Fig. 1. Graph of cerebrospinal fluid flow associated with the cardiac cycle. Notes: $\Box O - diastolic volume$; $\Box \Phi C \amalg - diastolic phase of the cardiac cycle$; $C \Phi C \amalg - systolic phase of the cardiac cycle$; C O - systolic volume. a - peak systolic velocity (cranio-caudal CSF flow); B - caudo-cranial CSF peak velocity during diastole

Japanese researchers proposed an improved method of phase-contrast study. Acceleration of the MRI technique was achieved by combining the methods of parallel imaging, rectangular field of view (FOV) and segmented k-space [31]. Parallel imaging using array spatial sensitivity encoding technique (ASSET) is based on the sensitivity encoding technique. This method allows data acquisition to be accelerated due to a so-called acceleration reduction factor by reducing the number of discrete phase encoding lines, although the

signal-to-noise ratio is somewhat reduced. Similar to parallel imaging, the rectangular FOV method can also reduce scan time by reducing the FOV phase encoding, i.e. reducing the number of selective phase encoding lines, although this also reduces the signal-to-noise ratio [35].

In the segmented k-space technique, the R–R interval of a cardiac cycle is divided into phases corresponding to k-space segments, and multiple k-space lines are built up during each cardiac cycle by reducing temporal resolution. Each phase of the cardiac cycle occupies one line (views per segment – VPS) of k-space. In the case of 2 VPS, the two k-space lines are filled sequentially during the cardiac cycle of k-space. As a result, the number of cardiac cycles required to complete k-space is halved, allowing information to be received twice as fast. In addition, this method makes it possible to reduce the scanning time without reducing the spatial resolution [31].

Most often, the phase-contrast technique is used to assess CSF flow dynamics in patients with arachnoid cysts and Arnold-Chiari malformation. Accurate knowledge of the anatomical structure of the arachnoid cyst and the type of its communication with the subarachnoid space allows planning the course of surgical intervention [36].

When planning a surgical intervention in patients with Arnold-Chiari malformation, it is necessary to study the CSF flow in the region of the craniovertebral junction. The phase-contrast method made it possible to evaluate the effect of multiple sclerosis on CSF dynamics [24]. In patients with multiple sclerosis, the volume of cranio-caudal and caudocranial CSF flow, as well as stroke volume, was higher [34].

PHASE-CONTRAST MRI IN THE EVALUATION OF CSF SHUNT OPERATIONS

The use of various MRI techniques makes it possible to evaluate the effectiveness of CSF shunt surgeries in patients with normal pressure hydrocephalus. A study by W. Bradley et al. (1996) showed that the significantly better effect after CSF shunt operations was in patients with a greater CSF stroke volume (more than 42 µl) [37]. In turn, M. Mase et al. (1998) found a larger amplitude of CSF flow in the cerebral aqueduct in patients with normal pressure hydrocephalus than with asymptomatic ventricular dilatation or brain atrophy. The amplitude of the flow is significantly reduced in the convexity subarachnoid spaces. The authors also revealed the relationship between the CSF flow velocity in the cerebral aqueduct and intracranial pressure. In patients with normal pressure hydrocephalus, CSF dynamics at the level of the cervical subarachnoid spaces remains within the normal range. With age, the elastic properties of the brain tissue decrease, and venous outflow decreases, but this does not lead to changes in the intracranial ratio. In patients with hydrocephalus, a slowdown in venous outflow, a decrease in pulsation in the convexital subarachnoid spaces, leads to CSF hyperpulsation in the ventricles [38].

Other researchers, when analyzing the surgical treatment of a large number of patients with hydrocephalus, did not reveal a relationship between CSF pressure and its peak flow velocity. The study also showed the relationship between CSF pressure and its average flow velocity. The authors conclude that the correctness of the ICP determination is largely affected by the magnetic field strength of the magnet used in the MRI machine. In 3T MRI machines and with a higher field strength, the noise level is significantly lower and a greater deviation of the VENC value is allowed than in scanners with a lower field strength, especially in case of a slow CSF flow rate [39].

In Russia, studies have also been conducted on the features of CSF flow dynamics in various diseases of the CNS. N.V. Arutyunov et al. (2016) examined a large group of patients who had disc herniations of various localizations, traumatic brachial plexus lesions and root avulsions, cysts filled with cerebrospinal fluid, empty sella syndrome, basal liquorrhea, congenital malformations of the brain, Arnold-Chiari pathology, obstructive hydrocephalus, open form of hydrocephalus and colloid cysts of the third ventricle. Some of the patients underwent triventriculostomy. The authors believe that phase-contrast MRI makes it possible to determine the qualitative and quantitative characteristics of CSF flow in various parts of the brain, which is necessary when determining the nature of hydrocephalus and pathology of the cerebral aqueduct (stenosis, occlusion, dilatation) [40].

FUNDAMENTALS OF THE TIME SLIP TECHNIQUE

Time-spatial Labeling Inversion Pulse (Time-SLIP) is a type of the ASL technique, the method of arterial spin labeling, which allows visualizing the dynamics of fluid movement by combining the selective and non-selective inversion recovery (IR) effects [41]. The non-selective IR effect is used to invert (flip) all proton spins

in the area under study, which become "tagged". In the time SLIP technique, the fluid itself is an endogenous marker; therefore, it is possible to obtain data from the fluid flow only until the radio frequency (RF) pulse is attenuated [42]. The spatially selective IR effect is used to invert all spins in the fluid under study repeatedly. As a result, after labeling the outflow of spins, an image is formed. The longitudinal magnetization of the spins outside the labeled region is restored, depending on the recovery time TI (TI - time inversion) of this tissue. Therefore, spins outside the labeled region are displayed as a low signal zone. The time to data acquisition, referred to as TI, performs two important roles: 1 - suppression of the signal from the background, 2 - marking the spins passing through the labeled region. This technique is recommended for visualization of several specific seconds of fluid flow, which makes it possible to visualize, for example, turbulent reflux flow between the aqueduct and the third ventricle (Fig. 2) [43]. The processes of obtaining an image using phase-contrast MRI and time SLIP techniques differ significantly and the resulting data cannot be directly compared.



The use of the time SLIP technique allowed us to expand our knowledge of the pathogenesis of syringomyelia. With its help, several types of cerebrospinal fluid flow were recorded in the syringomyelia cavities: fast, "bubble", "spasmodic". Thus, the researchers suggested that the fast flow is formed due to a narrow obstacle, bubbles are created in the place of turbulent CSF flow, and the spasmodic flow is formed when passing through the arachnoid membrane and the septum of the syringomyelia cavity [44].

4D PHASE-CONTRAST MRI

Unlike 2D phase-contrast MRI, 4D phase-contrast imaging uses four-point scanning by measuring threedirectional velocity encodings and one flow compensation encoding [45], [46].

Assuming that the background phase shift is the same in four different scans, the velocities in the 3 vector projection can be obtained by replacing the phase shifts in the 3 vector projection with the phase in the reference image [47], [48]. In a 4D phase-contrast study, three-vector volumetric phase images are usually used to reconstruct the flow velocity, one volumetric image of magnitude and 4 volumetric vector difference images (three-vector images and one summation image) to display the anatomy of the object of study (blood vessel, CSF pathways) (Fig. 3) [49], [50].



Despite the fact that obtaining a 3D image with the 4D phase-contrast study takes a lot of time compared to the conventional 2D phase-contrast study (PC-MRI), it has significant advantages, allowing you to examine the cerebrospinal fluid in any plane. In addition, 4D phase-contrast MRI, in parallel with obtaining a 3D image with high accuracy (comparable to a conventional 2D phase-contrast study), can determine the quantitative parameters of CSF flow dynamics. Quantification of CSF flow dynamics using 2D phase-contrast MRI may be inaccurate due to movements of the area under study (movement of the arachnoid membrane during the valve mechanism of hygroma formation), and 4D phase-contrast MRI can take into account the movement of areas of interest [42].

One of the promising methods for studying CSF flow dynamics is 4D phase-contrast MRI using computational fluid dynamics (CFD) techniques. The technique is based on mathematical modeling of the anatomy of the cervical spine based on 3D turbo spin-echo sequences with high T2 resolution. The 3D model was adapted to the actual anatomical dimensions. Reconstruction was performed separately for each level from the foramen magnum to the C7 vertebra. The CSF flow in the mathematical model was calculated using the Navier-Stokes equation. A comparative study of CSF flow dynamics in patients with Arnold–Chiari malformation showed the need to refine the method, in particular, taking into account fine anatomical structures, such as nerve roots and ligaments [51].

As a result, the obtained data of the two methods differed significantly. It is suggested that the deviation of CFD results from 4D phase contrast MRI measurements is likely due to the neglect of small anatomical structures in the cervical canal and tissue movement.

SSFP SEQUENCE

To diagnose the pathology of the CSF system, the SSFP sequence (Steady-state free precession) is also used, in which a nonzero steady state develops between pulse repetitions for transverse and longitudinal relaxation of the tissues under study. This requires a small angle of rotation and a short relaxation time. A feature of this technique is the ability to generate a strong signal in tissues that have a significant T2/T1 contrast, for example, CSF and adipose tissue [52]. Another advantage of SSFP sequences is a shorter scan time compared to other MRI sequences, which helps to eliminate CSF pulsation artifacts. Areas with turbulent CSF flow have a reduced signal (or even its absence). The disadvantage of this type of sequences is the low contrast resolution of soft tissues, the high sensitivity of the gradient echo pulse sequences to magnetic field inhomogeneity and the occurrence of various artifacts (for example, in the presence of metal, pronounced CSF hyperpulsation, tissue-liquid boundary zones, etc.). As for T2-weighted SSFP sequence, it may be difficult to differentiate between inflamed sinus mucosa and CSF accumulations, both of which have high signal

intensity. In addition, the image of major anatomical landmarks may be distorted due to submillimeter slice thickness. Thus, despite the static nature, this technique can be most effectively used in the diagnosis of skull base CSF fistulas, the assessment of the functioning of the ventriculostomy, however, in 8–10% of cases, this technique does not allow the detection of cerebrospinal fluid fistulas [53].

CHANGE IN FLUID FLOW DEPENDING ON THE TYPE OF HYDROCEPHALUS

When determining the CSF flow parameters among different age groups and between sexes, it was found that the velocity values of the CSF flow do not depend on gender, vary widely and differ significantly at different levels of the CSF system. It has been noted that peak linear velocities can be significantly increased in young people up to 14 years of age as a result of the high elasticity of the vascular wall. However, the mean linear and volumetric flow rates remained comparable to those in the middle age groups [54].

Also, using the phase-contrast MRI technique, the influence of body position on physiological processes in the cranial cavity was studied through the relationship between the dynamics of blood flow and CSF flow and their age-related changes [33]. With age, CSF pulsation weakens in proportion to the decrease in cerebral blood flow.

The advent of modern functional techniques has significantly expanded the diagnostic capabilities of MRI. Currently, the largest number of publications is devoted to the diagnosis of normal pressure hydrocephalus and its differential diagnosis with other types of senile dementia [22]. Much less research is devoted to the use of functional flow-sensitive MRI techniques (including the time-SLIP technique) in the diagnosis of various forms of obstructive hydrocephalus. Insufficient attention is paid to the pathogenesis of post-traumatic subdural hygromas, malabsorptive hydrocephalus after intracranial hemorrhages. Therefore, it is necessary to further study the possibilities of functional MRI techniques in the diagnosis of various types of hydrocephalus, as well as after surgical treatment.

REFERENCES

- 1. Osborn AG. Essentials of Osborn's Brain: A Fundamental Guide for Residents and Fellows. Elsevier; 2016.
- Johanson C, Stopa E Barid A, Sharma H. Traumatic brain injury and recovery mechanisms: peptide modulation of periventricular neurogenic regions by the choroid plexus–CSF nexus. J Neural Transm (Vienna). 2011;118(1):115–133. PMID: 20936524 https://doi.org/10.1007/s00702-010-0498-0
- Johanson CE, Duncan JA 3rd, Klinge PM, Brinker T, Stopa EG, Silverberg GD. Multiplicity of cerebrospinal fluid functions: New challenges in health and disease. *Cerebrospinal Fluid Res.* 2008;5:10. PMID: 18479516 https://doi.org/10.1186/1743-8454-5-10
- Bulat M, Klarica M. Fluid filtration and reabsorption across microvascular walls: control by oncotic or osmotic pressure? (secondary publication). Croat Med J. 2014;55(4):291–298. PMID: 25300098
- Hladky SB, Barrand MA. Mechanisms of fluid movement into, through and out of the brain: evaluation of the evidence. *Fluids Barriers* CNS. 2014;11(1):26. PMID: 25678956 https://doi.org/10.1186/2045-8118-11-26 eCollection 2014.
- Kant S, Stopa EG, Johanson CE, Baird A, Silverberg GD. Choroid plexus genes for CSF production and brain homeostasis are altered in Alzheimer's disease. *Fluids Barriers CNS*. 2018;15(1):34. PMID: 30541599 https://doi.org/10.1186/s12987-018-0120-7
- Stiebel-Kalish H, Eyal S, Steiner I. The role of aquaporin-1 in idiopathic and drug-induced intracranial hypertension. *Med Hypotheses*. 2013;81(6):1059–1062. PMID: 24169407 https://doi.org/10.1016/j.mehy.2013.10.002
- Nagelhus EA, Ottersen OP. Physiological roles of aquaporin-4 in brain. Physiol Rev. 2013;93(4):1543–1562. PMID: 24137016 https://doi.org/10.1152/physrev.00011.2013.
- Brinker T, Stopa E, Morrison J, Klinge P. A new look at cerebrospinal fluid circulation. *Fluids Barriers CNS*. 2014;11:10. PMID: 24817998 https://doi.org/10.1186/2045-8118-11-10 eCollection 2014.
- Redzic ZB, Preston JE, Duncan JA, Chodobski A, Szmydynger-Chodobska J. The choroid plexus-cerebrospinal fluid system: from development to aging. *Curr Top Dev Biol*. 2005;71:1–52. PMID: 16344101 https://doi.org/10.1016/S0070-2153(05)71001-2
- 11. Sakka L, Coll G, Chazal J. Anatomy and physiology of cerebrospinal fluid. *Eur Ann Otorhinolaryngol Head Neck Dis.* 2011;128(6):309–316. PMID: 22100360 https://doi.org/10.1016/j.anorl.2011.03.002
- 12. Johanson C, Stopa E, McMillan P, Roth D, Funk J, Krinke G. The distributional nexus of choroid plexus to cerebrospinal fluid, ependyma and brain: toxicologic/pathologic phenomena, periventricular destabilization, and lesion spread. *Toxicol Pathol.* 2011;39(1):186–212. PMID: 21189316 https://doi.org/10.1177/0192623310394214
- 13. Bairamian D, Johanson CE, Parmelee JT, Epstein MH. Potassium cotransport with sodium and chloride in the choroid plexus. *J Neurochem*. 1991;56(5):1623–1629. PMID: 2013757 https://doi.org/10.1111/j.1471-4159.1991.tb02060.x
- 14. Matsumae M, Kuroda K, Yatsushiro S, Hirayama A, Hayashi N, Takizawaet K, et al. Changing the Currently Held Concept of Cerebrospinal Fluid Dynamics Based on Shared Findings of Cerebrospinal Fluid Motion in the Cranial Cavity Using Various Types of Magnetic Resonance Imaging Techniques. *Neurol Med Chir (Tokyo)*. 2019;59(4):133–146. PMID: 30814424 https://doi.org/10.2176/nmc.ra.2018-0272
- 15. Takizawa K, Matsumae M, Hayashi N, Hirayama A, Sano F, Yatsushiro S, et al. The Choroid Plexus of the Lateral Ventricle as the Origin of CSF Pulsation Is Questionable. *Neurol Med Chir (Tokyo)*. 2018;58(1):23–31. PMID: 29142154 https://doi.org/10.2176/nmc.oa.2017-0117
- 16. O'Connell JE. The vascular factor in intracranial pressure and the maintenace of the cerebrospinal fluid circulation. *Brain*. 1943;66(3):204–228. https://doi.org/10.1093/brain/66.3.204
- 17. Korshunov AYe. Physiology of CSF System and Pathophysiology of Hydrocephalus. *Zhurnal Voprosy Neirokhirurgii Imeni N.N. Burdenko*. 2010;(4):45–50. (in Russ.)

- Abbott NJ. Evidence for bulk flow of brain interstitial fluid: significance for physiology and pathology. Neurochem Int. 2004;45(4):545–552. PMID: 15186921 https://doi.org/10.1016/j.neuint.2003.11.006
- 19. Mestre H, Mori Y, Nedergaard M. The Brain's Glymphatic System: Current Controversies. Trends Neurosci. 2020;43(7):458-466. PMID: 32423764 https://doi.org/10.1016/j.tins.2020.04.003
- 20. Chen K-H, Lee C-P, Yang Y-H, Yang Y-H, Chen C-M, Lu M-L et al. Incidence of hydrocephalus in traumatic brain injury: A nationwide population-based cohort study. *Medicine (Baltimore)*. 2019;98(42):e17568. PMID: 31626123 https://doi.org/10.1097/MD.000000000017568
- 21. Damkier HH, Brown PD, Praetorius J. Cerebrospinal fluid secretion by the choroid plexus. *Physiol Rev.* 2013;93(4):1847–1892. PMID: 24137023 https://doi.org/10.1152/physrev.00004.2013
- 22. Long J, Lin H, Cao G, Wang M-Z, Huang X-J, Xia J, et al. Relationship between intracranial pressure and phase-contrast cine MRI-derived measures of cerebrospinal fluid parameters in communicating hydrocephalus. *Quant Imaging Med Surg.* 2019;9(8):1413–1420. PMID: 31559170 https://doi.org/10.21037/qims.2019.08.04
- 23. Forsting M, Jansen O. MR Neueroimaging: Brain, Spine, Peripheral Nerves. Stuttgart: New York: Thieme; 2017.
- 24. Kartal MG, Algin O. Evaluation of hydrocephalus and other cerebrospinal fluid disorders with MRI: An update. *Insights Imaging*. 2014;5(4):531–541. PMID: 24903254 https://doi.org/10.1007/s13244-014-0333-5
- 25. Tanaka N, Yamaguchi S, Ishikawa H, Ishii H, Meguro K. Prevalence of possible idiopathic normal-pressure hydrocephalus in Japan: the Osaki-Tajiri project. *Neuroepidemiology*. 2009;32(3):171–175. PMID: 19096225 https://doi.org/10.1159/000186501
- 26. Ooi LY, Walker BR, Bodkin PA, Whittle IR Idiopathic intracranial hypertension: can studies of obesity provide the key to understanding pathogenesis? Br J Neurosurg. 2008;22(2):187–194. PMID: 18348012 https://doi.org/10.1080/02688690701827340
- Odéen H, Uppman M, Markl M, Spottiswoode BS. Assessing cerebrospinal fluid flow connectivity using 3D gradient echo phase contrast velocity encoded MRI. *Physiol Meas*. 2011;32(4):407–421. PMID: 21343652 https://doi.org/10.1088/0967-3334/32/4/003
- 28. Korbecki A, Zimny A, Podgórski P, Sąsiadek M, Bladowska J. Imaging of cerebrospinal fluid flow: fundamentals, techniques, and clinical applications of phase-contrast magnetic resonance imaging. *Pol J Radiol.* 2019;84:e240–e250. PMID: 31481996 https://doi.org/10.5114/pjr.2019.86881
- 29. Saloner D. The AAPM/RSNA physics tutorial for residents. An introduction to MR angiography. *RadioGraphics*. 1995;15(2):453-465. https://doi.org/10.1148/radiographics.15.2.7761648
- 30. McDonnell CH 3rd, Herfkens RJ, Norbash AM, Rubin GD. Magnetic resonance imaging and measurement of blood flow. West J Med. 1994;160(3):237-242. PMID: 8191756
- 31. Ohno N, Miyati T, Noda T, Alperin N, Hamaguchi T, Ohno M, et al. Fast Phase-Contrast Cine MRI for Assessing Intracranial Hemodynamics and Cerebrospinal Fluid Dynamics. *Diagnostics (Basel)*. 2020;10(4):241. PMID: 32326291 https://doi.org/10.3390/diagnostics10040241
- 32. Unal O, Kartum A, Avcu S, Etlik O, Arslan H, Bora A. Cine phasecontrast MRI evaluation of normal aqueductal cerebrospinal fl uid fl ow according to sex and age. *Diagn Interv Radiol*. 2009;15(4):227–231. PMID: 19862673 https://doi.org/10.4261/1305-3825.DIR.2321-08.1
- 33. Xu Q, Yu S-B, Zheng N, Yuan X-Y, Chi Y-Y, Liu C, et al. Head movement, an important contributor to human cerebrospinal fluid circulation. *Sci Rep.* 2016;6:31787. PMID: 27538827 https://doi.org/10.1038/srep31787
- 34. Gorucu Y, Albayram S, Balci B, Hasiloglu ZI, Yenigul K, Yargic F, et al. Cerebrospinal fluid flow dynamics in patients with multiple sclerosis: a phase contrast magnetic resonance study. *Funct Neurol*. 2011;26(4):215–222. PMID: 22364942
- 35. Glockner J, Hu HH, Stanley DW, Angelos L, King K. Parallel MR imaging: a user's guide. *Radiographics*. 2005;25(5):1279–1297. PMID: 16160112 https://doi.org/10.1148/rg.255045202
- 36. Alperin N. MR–Intracranial Compliance and Pressure: A Method for Noninvasive Measurement of Important Neurophysiologic Parameters. *Methods Enzymol.* 2004;386:323–349. PMID: 15120260 https://doi.org/10.1016/S0076-6879(04)86016-6
- 37. Bradley WG Jr, Scalzo D, Queralt J, Nitz WN, Atkinson DJ, Wong P. Normal-pressure hydrocephalus: evaluation with cerebrospinal fluid flow measurements at MR imaging. *Radiology*. 1996;198(2):523–529. PMID: 8596861 https://doi.org/10.1148/radiology.198.2.8596861
- 38. Mase M, Yamada K, Banno T, Miyachi T, Ohara S, Matsumoto T. Quantitative analysis of CSF flow dynamics using MRI in normal pressure hydrocephalus. Acta Neurochir Suppl. 1998;71:350-353. PMID: 9779227 https://doi.org/10.1007/978-3-7091-6475-4_101
- 39. Pashkova AA. Magnitno-rezonansnaya tomografiya v kachestvennoy i kolichestvennoy otsenke likovorodinamiki i sostoyaniya veshchestva golovnogo mozga u bol'nykh s gidrotsefaliey: cand. med. sci. diss. synopsis. Saint Petersburg; 2014. (in Russ.)
- 40. Arutyunov NV, Kornienko VN, Melnikova-Pitshelauri TV, Fadeeva LN. Modern Methods of Studying CSF System Pathology. *Diagnostic radiology and radiotherapy*. 2012;3(3):117–126. (in Russ.)
- 41. Miyazaki M, Isoda H. Non-contrast-enhanced MR angiography of the abdomen. *Eur J Radiol.* 2011;80(1):9–23. PMID: 21330081 10.1016/j.ejrad.2011.01.093
- 42. Yamada S. Cerebrospinal fluid physiology: visualization of cerebrospinal fluid dynamics using the magnetic resonance imaging Time-Spatial Inversion Pulse method. *Croat Med J.* 2014;55(4):337–346. PMID: 25165048 https://doi.org/10.3325/cmj.2014.55.337
- 43. Shibukawa S, Miyati T, Niwa T, Matsumae M, Ogino T, Horie T, et al. Time-spatial Labeling Inversion Pulse (Time-SLIP) with Pencil Beam Pulse: A Selective Labeling Technique for Observing Cerebrospinal Fluid Flow Dynamics. *Magn Reson Med Sci.* 2018;17(3):259–264. PMID: 28835572 https://doi.org/10.2463/mrms.tn.2017-0032
- 44. Takeuchi K, Ono A, Hashiguchi Y, Misawa H, Takahata T, Teramoto A, et al. Visualization of cerebrospinal fluid flow in syringomyelia through noninvasive magnetic resonance imaging with a time-spatial labeling inversion pulse (Time-SLIP). *J Spinal Cord Med.* 2017;40(3):368–371. PMID: 26864698 https://doi.org/10.1080/10790268.2016.1140391
- 45. Matsumae M, Hirayama A, Atsumi H, Yatsushiro S, Kuroda K. Velocity and pressure gradients of cerebrospinal fluid assessed with magnetic resonance imaging. *J Neurosurg*. 2014;120(1):218–227. PMID: 23930855 https://doi.org/10.3171/2013.7.JNS121859
- 46. Hirayama A, Matsumae M, Yatsushiro S, Abdulla A, Atsumi H, Kuroda K. Visualization of pulsatile CSF motion around membrane-like structures with both 4D velocity mapping and time-slip technique. *Magn Reson Med Sci.* 2015;14(4):263–273. PMID: 25994034 https://doi.org/10.2463/mrms.2014-0089
- 47. Yatsushiro S, Hirayama A, Matsumae M, Kajiwara N, Abdullah A, Kuroda K Correlation mapping for visualizing propagation of pulsatile CSF motion in intracranial space based on magnetic resonance phase contrast velocity images: preliminary results. *Annu Int Conf IEEE Eng Med Biol Soc.* 2014;2014:3300–3303. PMID: 25570696 https://doi.org/10.1109/EMBC.2014.6944328

- 48. Hayashi N, Matsumae M, Yatsushiro S, Hirayama A, Abdullah A, Kuroda K. Quantitative analysis of cerebrospinal fluid pressure gradients in healthy volunteers and patients with normal pressure hydrocephalus. *Neurol Med Chir (Tokyo)*. 2015;55(8):657–662. PMID: 26226976 https://doi.org/10.2176/nmc.oa.2014-0339
- 49. Yavuz Ilik S, Otani T, Yamada S, Watanabe Y, Wada S. A subject-specific assessment of measurement errors and their correction in cerebrospinal fluid velocity maps using 4D flow MRI. *Magn Reson Med.* 2021 Dec 6. PMID: 34866235 https://doi.org/10.1002/mrm.29111 Online ahead of print.
- 50. Ha H, Kim GB, Kweon J, Lee SJ, Kim Y-H, Lee DH, et al. Hemodynamic Measurement Using Four-Dimensional Phase-Contrast MRI: Quantification of Hemodynamic Parameters and Clinical Applications. *Korean J Radiol*. 2016;17(4):445–462. PMID: 27390537 https://doi.org/10.3348/kjr.2016.17.4.445
- 51. Yiallourou TI, Kröger JR, Stergiopulos N, Maintz D, Martin BA, Bunck AC. Comparison of 4D phase-contrast MRI flow measurements to computational fluid dynamics simulations of cerebrospinal fluid motion in the cervical spine. *PLoS One.* 2012;7(12):e52284. PMID: 23284970 https://doi.org/10.1371/journal.pone.0052284
- 52. Foo TKF, Ho VB, Marcos HB, Hood MN, Choyke PL. MR angiography using steady-state free precession. *Magn Reson Med*. 2002;48(4):699–706. PMID: 12353288 https://doi.org/10.1002/mrm.10278
- 53. Potthast S, Maki JH. Non-Contrast-Enhanced MR Imaging of the Renal Arteries. *Magn Reson Imaging Clin N Am.* 2008;16(4):573–584. PMID: 18926423 https://doi.org/10.1016/j.mric.2008.07.007
- 54. Bogomyakova O.B., Stankevich Yu. A., Shraybman L.A., Tulupov A.A. Gender, Age and Topographical Features of Cerebrospinal Fluid Parameters in Patients with Benign Intracranial Hypertension. *Vestnik NSU. Series: Biology, Clinical medicine*. 2015;(4):57–63. (in Russ.)

Received on 02.04.2021 Review completed on 28.04.2021 Accepted on 27.12.2021