Nuclear magnetic resonance imaging in ischemic stroke

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Abstract

An ischemic stroke is a complex of sudden symptoms of focal or generalized brain disorder. It is the second most common cause of death and the most common cause of permanent disability in the world, which makes it necessary to use highly sensitive diagnostic techniques. The gold standard in ischemic stroke imaging is magnetic resonance imaging, which enables determination of the location, extent, and size of ischemia.

This article describes the etiology and social importance of ischemic stroke, as well as discusses the significance of contemporarily applied diagnostic modalities, with particular reference to diffusion-weighted imaging, magnetic resonance angiography, and perfusion-weighted imaging.

Keywords: ischemic stroke, nuclear magnetic resonance, diffusion-weighted imaging, magnetic resonance angiography, perfusion-weighted imaging, time-of-flight

Introduction

Stroke is the second most common cause of death and the most common cause of permanent disability in the world. It is estimated that about 90% of stroke incidents are ischemic strokes. According to data from the National Health Fund, in 2022, ischemia was found in as many as 73,900 patients, whose median age was 73 years. In recent years, however, an increase in the number of strokes in increasingly younger age groups has been observed [1].

The constantly growing number of ischemic strokes requires the use of diagnostic techniques with sufficiently high sensitivity, which will allow for precise diagnosis and enable the implementation of treatment in a period corresponding to the therapeutic window. One of these methods is magnetic resonance imaging (MRI), which allows to determine the localization of ischemic focus, the phase of a stroke, and the occurrence of microcalcifications. Comparing to computed tomography, in the case of ischemia, it is characterized by greater sensitivity and greater accuracy in determining the etiology. MRI ensures short image acquisition time, and the variety of sequences enables precise assessment of the ischemic focus, which influences the precision of the selected treatment [2].

Ischemic stroke

Ischemic stroke is a sudden, local or generalized loss of brain function lasting more than 24 hours, caused by insufficient blood supply due to hemodynamic, embolic, or thrombotic causes resulting from vascular, myocardial, or blood diseases. Reduction of blood flow below 10-12 ml/100 g of brain tissue/minute results in neuronal death and the formation of an area of necrosis, i.e., irreversible ischemia. It is surrounded by the penumbra, described as an area of the brain susceptible to thrombolytic treatment. Development of a compensatory circulation and a vascular bed, and the increased uptake of oxygen and glucose in this area maintain the membrane potential and the sodium-potassium pump, while preventing irreversible brain damage [3, 4]. Due to the area of ischemia, we distinguish complete ischemia, which involves the entire brain and may be a consequence of sudden circulatory arrest, and local ischemia occurring in the event of occlusion of one of the cerebral

Medicine Physicist & Engineer 1/2025 vol. 1

received: 27.01.2025; corrected: 29.01.2025; accepted: 01.02.2025

arteries. The effect of the first of these is the selective destruction of cells characterized by the greatest sensitivity to oxygen deficit. These include pyramidal cells of the hippocampus, Purkinje cells, pyramidal cells of the neocortex layer, and spiny neurons. Destruction of all brain cells with accompanying necrosis is, in turn, focal ischemia, which is surrounded by the aforementioned area of the penumbra. It is characterized by the co-occurrence of disruption of cell function and the lack of morphological damage. In this area, destruction of neurons occurs due to disruption of cerebral blood flow and energy processes [5].

Symptoms of ischemic stroke are differentiated according to the area affected by ischemia. The cerebral arterial system is divided into anterior vascularization supplied by the internal carotid arteries, posterior vascularization supplied by the vertebrobasilar arteries, and vascularization of the whole brain. Ischemia located in the anterior circulation may manifest as hemiparesis or hemiplegia, aphasia, agnosia, hemihypesthesia, pseudobulbar dysphagia, and visual disturbances in amblyopia or disturbances involving one eye. Circulatory disturbances from the posterior vascularization area are characterized by the occurrence of dizziness, nausea and vomiting, hearing problems, gait and balance disturbances, diplopia, and bulbar dysphagia. Ischemia involving the entire brain area concentrates the symptoms of ischemia from both of the above-mentioned areas [6].

Magnetic resonance imaging is the gold standard in ischemic stroke imaging, enabling localization of the ischemic focus, determining the stroke phase, and the occurrence of microcalcifications. Compared to CT in the case of ischemia, it is characterized by greater sensitivity and greater accuracy in determining the etiology. Due to the almost immediate reaction of neurons to ischemia, which amounts to a loss of 1.9 million cells per minute, the most important factor in the diagnosis of ischemia is time. It should be remembered that the therapeutic window for thrombolytic treatment is only 4.5 hours from the onset of symptoms, while for mechanical thrombectomy it is 6 hours. MRI ensures a short image acquisition time, and the variety of sequences used allows for a precise assessment of the ischemic focus, influencing the precision of the selected treatment [2].

Basic diagnostic methods used in ischemic stroke imaging

Diffusion magnetic resonance imaging (DWI)

The diffusion magnetic resonance sequence is based on water molecules' migration in the extracellular space. DWI reflects the difference in the spontaneous penetration of water molecules in brain tissue and provides information about its size, type, and the space in which it occurs. This penetration is Brownian motion, described as the uncoordinated movement of liquid molecules resulting from their collisions. Diffusion magnetic resonance imaging is one of the gradient sequences. Activation of the gradient in a uniform magnetic field stops the movement of hydrogen nuclei, which results in a change in the signal. To increase the precision of imaging, the bipolar Stejskal-Tanner sequence is used, i.e., two bilaterally located gradient pulses around a pulse of 180°. The sequence is described by the b-value according to the following formula:

$$b = \gamma^2 G^2 \delta^2 \left(\Delta - \frac{\delta}{3} \right)$$

The value includes the gyromagnetic coefficient γ, the amplitude gradient G, the gradient length δ, and the periodic distance separating both pulses Δ. The limitation of water diffusion is presented on T2-weighted images as a hyperintense area.

Diffusion disturbance is also assessed based on the apparent diffusion coefficient (ADC) and ADC maps, where ischemia appears as a hypointense signal. ADC for a given voxel is calculated by the linear regression method of the b value, according to the following equation:

$$ADC = \frac{\ln\left(\frac{SI}{SI_0} \right)}{b}$$

SI is the signal intensity in DWI, while SI_0 is the signal intensity in the T2-weighted image in the absence of magnetic field gradients [7].

Vascular obstruction caused by ischemic stroke contributes to the disturbance of sodium-potassium pump function and increased calcium concentration in the intracellular space. This results in cytotoxic edema and reduced Brownian motion, and ultimately also in reduced diffusion [2].

The high sensitivity and specificity of diffusion-weighted magnetic resonance imaging in the first minutes after the onset of symptoms make this method the gold standard in detecting and differentiating ischemic stroke. For accurate diagnostic evaluation, DWI images should be viewed together with diffusion-weighted ADC maps that do not contain a T2 component. Ischemic stroke is indicated by hyperintense restricted diffusion signals in the DWI sequence and corresponding hypointense restricted areas on ADC maps. This method of interpretation provides information on the severity and reversibility of ischemia [7]. Diffusion-weighted magnetic resonance imaging detects ischemic changes as early as 11 minutes after the onset of the first symptoms, while a decrease in ADC values is observed as early as 30 minutes after the onset of ischemia. ADC stabilization occurs 2 to 4 weeks after the onset of ischemia, which is due to the increasing predominance of the vascular component of edema over the cytotoxic component [2]. The location of ischemic changes on DWI images varies depending on the pathogenesis of the stroke, as well as the size, site of thrombus formation, and structure [8].

The further course of the disease and the response to the treatment are closely related to the volume of the ischemic area, which can be estimated based on images obtained in the DWI sequence.

Diffusion magnetic resonance imaging is a highly precise method for diagnosing lacunar strokes and ischemic strokes from the posterior cerebral vascularization area. A lesion suggesting ischemia in the DWI/ADC image combination should be differentiated from an abscess, some neoplasms (lymphomas), encephalitis, postictal states, and transient global amnesia [2].

Perfusion- Weighted Imaging (PWI)

Perfusion-Weighted Imaging enables the assessment of tissue blood flow in the brain and provides information on the hemodynamic state of brain tissue. Ischemic stroke is associated with changes in cerebral perfusion pressure (CPP), described as the difference between mean arterial pressure and intracranial pressure. As a result of ischemia, arterioles dilate to reduce cerebrovascular resistance, which helps maintain normal cerebral blood flow (CBF). The consequence of the increased lumen of the vessels is also an increase in cerebral blood volume (CBV) and an increase in mean transit time (MTT), i.e., the time spent by erythrocytes in a given volume of blood. These values are related to each other by the following relationship:

$$MTT = \frac{CBV}{CBF}$$

The described vasodilatory mechanism does not occur in the case of a rapid decrease in CPP. Then, there is a significant decrease in CBF and a decrease in cerebral metabolic rate of oxygen consumption (CMRO2), which in turn leads to neurological deficits. The higher the $CMRO_2$ value, the greater the probability of restoring blood flow in the tissue. Death of brain tissue due to complete ischemia occurs within a few minutes of its occurrence, but if the ischemia is minor and the tissue structure has not been damaged, it is called the "penumbra", and there is a probability of stopping the ischemia process using thrombolytic treatment. The main role of PWI is therefore to detect potentially reversible areas of ischemia based on the assessment of perfusion maps and brain hemodynamic parameters [9].

PWI can be performed using arterial spin labeling (ASL) or the first-pass technique (dynamic susceptibility contrast, DSC). ASL involves marking water spins in arterial blood reaching a given cross-section with pulsed RF pulses and selectively inverting longitudinal magnetization in the area before the actual area. The magnetization map reflects local perfusion, hence the obtained CBF value is the ratio of magnetization values before and after inversion. The advantage of this method is regional assessment of perfusion and no need to use a contrast agent. Unfortunately, due to low SNR, long imaging time, and low sensitivity of the assessment of CBF and MTT decrease, ASL is currently rarely used [9].

The first-pass technique uses a T2*-weighted sequence. During the examination, the patient is intravenously injected with a paramagnetic contrast agent, which produces local susceptibility gradients in the bloodstream that reduce the T2* relaxation time. As a result, the flow of contrast through the vessels is accompanied by a momentary loss of signal intensity. The high speed of contrast flow through the vessels requires the use of a fast gradient echo sequence, EPI, which allows for measurements in 1.5 to 2 seconds. Tissue flow is assessed based on CBV, CBF, and MTT, which are obtained on perfusion maps, on the paramagnetic concentration versus time curves - they can be obtained for each voxel of brain tissue. The CBV value is indicated by the size of the area under the curve. Low CBV and CBF values indicate the occurrence of ischemia, while their increase indicates reperfusion of ischemic tissue and is described as "luxury perfusion" [10].

Precise imaging of early ischemic changes together with the estimation of the penumbra zone became possible thanks to the simultaneous assessment of ischemia in the PWI and DWI sequences. The area of reduced perfusion in PWI is larger than the area of restricted diffusion in DWI, and the difference between them is defined as the area of perfusion-diffusion mismatch and is identical to the area of permanent ischemia [10]

Magnetic resonance angiography (MRA)

Magnetic resonance angiography (MRA) is a non-invasive examination that allows for the assessment of the vascular system. There are contrast-enhanced MRA and phase-contrast (PC) sequences and the time-of-flight (TOF) technique, which do not require the administration of a contrast agent.

Contrast-enhanced magnetic resonance angiography (CE) requires the administration of a paramagnetic contrast agent in the form of gadolinium. The use of a paramagnet allows for obtaining a high SNR value of the vessel relative to the background and its good visualization due to the shortening of the T1 relaxation time of the blood. CE MRA is characterized by low TE and TR values and is performed based on a gradient echo sequence. The consequence of gadolinium application is the time limit of acquisition, reduced spatial resolution, and the risk of nephrogenic systemic fibrosis [11, 12].

MRA without the use of contrast can be performed using the time-of-flight technique or the phase contrast method. PC consists of the assessment of the protons of moving blood in a plane or space. The sequence consists of a bipolar gradient preceding phase encoding and readout gradients. The introduction of bipolar gradients begins with the application of an RF pulse, after which all protons from the examined area are in phase. The next step is the application of half of the bipolar gradient in the flow direction, which results in a phase shift caused by the position of the protons, which, as a result of continuous movement, experience phase shifts relative to the protons of the surrounding tissues. Then, the second part of the bipolar gradient is applied, which is in the flow direction and has the same magnitude but the opposite value. As a result, the phase shift of stationary tissues is corrected, and all protons are encoded with a phase shift. The elimination of the phase shift associated with stationary protons and the modification of the phase of protons moving

towards the gradient are achieved by applying the opposite gradient. The deconstruction of the signal phase causes the phase shift to be maintained only by blood protons. The phase shift of protons is directly proportional to their velocity in the gradient direction, which is subject to qualitative assessment based on the visual projection of the phase shift. Due to the limitations of modular arithmetic, angles exceeding 180° are characterized by signal distortion (aliasing). From the equation describing the phase shift:

$$\Delta\varnothing = \gamma\vec{v} \cdot M_1$$

where γ is the gyromagnetic coefficient, $\vec{v}$ is the proton velocity, and ΔM_1 is the change in the magnetic moment, it follows that the angle. The phase is also directly proportional to the gradient strength. In turn, the relationship between measurable velocity and gradient strength is inversely proportional, hence a specific gradient can be assigned a measurable maximum velocity before the aliasing phenomenon occurs. It is called the encoding velocity, and knowledge of its value allows the selection of parameters that allow obtaining the best diagnostic values of the examination [13].

Magnetic resonance imaging is a sensitive and specific method in the examination of intra- and extracranial vessels, detecting their stenoses and dissections, and also enabling the determination of the etiopathogenesis of stroke. Localization of the vessel lumen occlusion allows for the implementation of intravascular treatment within the first hours of the onset of symptoms and determines the prognosis after the procedure. CE MRA, on the other hand, allows for the detection of atherosclerosis, which is one of the causes of ischemic stroke. It has also been proven that CE MRA is an equivalent method to digital subtraction angiography in the diagnosis of carotid artery stenosis. Moreover, this method is characterized by higher sensitivity in detecting vascular occlusion compared to Doppler ultrasonography and computed tomography angiography [14].

Time-of-Flight (TOF) technique

The time-of-flight technique uses the blood inflow effect, described as the difference between the exposure to the RF pulse of the spins of the stationary tissue and the exposure of the spins of the inflowing blood [15].

Cyclically transmitted radiofrequency pulses saturate the stationary spins, and the value of the longitudinal component of magnetization reaches a value close to 0, which results in a low signal. In turn, the value of the longitudinal component of the spins of the blood flowing into the imaged volume is 1, which translates into hyperintensity of the signal. The inflow effect is related to the speed of blood inflow into the examined volume. Slow blood inflow is associated with the presence of blood spins from two successive inflows in the imaged layer, while in the case of high blood velocity, a complete exchange of fluid tissue occurs. The spins of the tissues surrounding the vessels do not move, so they are constantly saturated [15].

The blood volume renewed in a given cross-section is a function of the blood inflow velocity, TR, and the vessel's cross-sectional area. Complete blood exchange in the imaged volume occurs if its flow velocity is greater than the ratio of the layer thickness and the repetition time. The lower the flow velocity, the greater the probability of incomplete saturation when the impulse from the blood is affected by the excitation reversal angle and the tissue T1 time. To prevent signal loss due to the change in the spin phase due to flow, the time-of-flight technique is performed with flow compensation. It consists of reducing the zero gradient by using additional gradient flaps [15]. The combination of the time-of-flight technique and the maximum intensity projection allows for obtaining a three-dimensional image of hyperintense cerebral vessels on a hypointense background in the form of an angiogram.

The 3D time-of-flight technique allows for a precise assessment of the arteries and veins supplying the brain, and consequently for the diagnosis of stenosis or occlusion of the vessel and for the determination of the artery whose vascularization range includes ischemic changes. Overestimation of the degree of vascular stenosis in distal parts due to turbulent flow and poor visualization of vessels located parallel to the imaged layer means that TOF is not routinely used in the diagnosis of ischemic stroke.

Conclusion

Imaging of ischemic stroke using nuclear magnetic resonance imaging enables precise determination of the cause, location, and extent of ischemia. Moreover, the use of diffusion-weighted imaging as one of the elements of the treatment plan in patients with symptoms of acute ischemic stroke significantly shortens the diagnostic protocol and consequently increases the chance of implementing endovascular treatment. Magnetic resonance angiographic sequences, on the other hand, enable precise determination of the artery whose stenosis/occlusion caused ischemia, as well as assessment of other intracranial and precerebral arteries, the changes of which pose a potential risk of another stroke incident.

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