Progress of Science: Theory and Practice
Volume 1, Issue 1, December, 2024

MAGNETIC RESONANCE IMAGING IN THE DIAGNOSTICS OF GLIAL TUMORS OF THE BRAIN IN LIGHT OF THE NEW CLASSIFICATION OF CNS TUMORS

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ABSTRACT Glial brain tumors continue to be a pressing issue in oncology. They are typically characterized by rapid growth rates, invasiveness, frequent recurrence, and an unfavorable prognosis. This literature review aims to familiarize with the diagnostic capabilities of MRI in recognizing glial tumors. It includes 44 sources published between 2005 and 2023.

Key words: glioblastoma, glioma, radiological diagnostics, magnetic resonance imaging, neuroimaging, brain tumors.

INTRODUCTION

Gliomas (neuroectodermal, neuroepithelial tumors) are primary tumors of the central nervous system that arise from glial cells. Currently, the problem of glial tumors of the brain is due to the steady increase in the number of patients with gliomas in the overall structure of oncological morbidity. Moreover, these tumors account for 40-50% of all intracranial blastomas [1, 2, 3]. About 70% of primary brain tumors are represented by various gliomas, of which more than half are already high-grade gliomas (WHO grade III-IV according to the World Health Organization (WHO) classification) at the time of diagnosis [4, 5]. The concept of the degree of malignancy, or grade, has come a long way from a visual assessment of mitotic activity, cell density, cellular and nuclear polymorphism, necrotic component, microvascular proliferation to a combination of the above approach with molecular genetic diagnostic methods [5]. One of the first classifications of brain tumors related to gliomas was proposed by Bailey and Cushing in 1926 [6, 7] and was based on the histogenesis of brain tissue. Later, the classification of Zulch K. was proposed, it used a 5-step gradation from 0 to IV, then, in 1952, Kernohan J. presented a classification, where 0 is a neuroma, meningioma, craniopharyngioma, pituitary adenoma, and IV is a medulloblastoma, glioblastoma [8, 9]. In the 5th version of 2021, changes were made to the classification of CNS tumors, of which it is important to highlight 2 main points: 1. The Arabic numbering of the degrees of tumor malignancy (grading) was introduced (1, 2, 3, 4); 2. They are graded within each type [9, 10]. The main types of gliomas are: astrocytic tumors — develop from astrocytes; oligodendroglial

tumors — from oligodendrocytes; mixed gliomas, such as oligoastrocytoma, contain cells of different types of glia [10, 11, 12,]. Based on epidemiological studies, gliomas are localized [13, 14, 15]: in the cerebral hemispheres — 70%; ventricles — 7%; basal ganglia — 6%; brainstem — 6%; corpus callosum — 5%; cerebellum — 4–4.5%. The main markers in the diagnosis of primary CNS tumors remain mutations in the IDH1/IDH2 genes and codeletion 1p/19q. Mutation in one of them leads to epigenetic change due to accumulation of 2-hydroxygluturate (2HG), which causes uncontrolled methylation of histones and genes, thereby determining tumorigenesis. Mutations in the IDH1/IDH2 genes are rare in tumors outside the CNS, although currently clinical developments are underway worldwide to study the effectiveness of an inhibitor of the metabolite of the mutant IDH1 gene (2-hydroxyglutarate) in patients with acute myeloid leukemia, cholangiocarcinoma, myelodysplastic syndrome, solid tumors, including gliomas.

The WHO classification (2021) distinguishes 4 degrees of malignancy:

Grade 1 - no criteria for malignancy;

Grade 2 - one criterion of malignancy is determined (nuclear atypia);

Grade 3 - two criteria of malignancy are determined (nuclear atypia and mitoses);

Grade 4 – three or four criteria of malignancy (nuclear atypia, mitoses, endothelial proliferation, necrosis).

MRI CAPABILITIES IN THE DIAGNOSTICS OF GLIAL TUMORS

Currently, in modern neuroimaging, MRI is the gold standard for diagnosing brain tumors [16, 17]. At this stage of development, the standard for examining patients with malignant CNS tumors is performing MRI of the brain in T1 without contrast, T2, T2 FLAIR, T1 with contrast modes - either in three planes or thin slices of 1 mm thickness in the axial plane [18, 19]. Using these techniques, it is possible to obtain diagnostically significant information about the localization, structure, size of the tumor, its relationship to the anatomical regions of the brain, main vessels, etc. [18]. Based on the results of standard MR imaging, it is possible to differentiate low- and high-grade gliomas [19] and grades 3 and 4 [20, 21]. Also included in the standard MR examination protocol are diffusion-weighted images (DWI), which help to differentiate between high- and low-grade gliomas based on the measured diffusion coefficient (DC) [22, 23]. However, these pulse sequences have limited capabilities in differentiating between high-grade glioma and single brain metastases. The necessary additional information can be provided by MR perfusion (including non-contrast), MR spectroscopy [24, 25], MR relaxometry, diffusion tensor MRI (DT-MRI), and diffusion kurtosis MRI. The term "perfusion" refers to the level of blood delivery to tissues, which is measured using capillary blood flow. MR

perfusion can be non-contrast and with intravenous contrast [24]. The advantage of non-contrast perfusion is its non-invasiveness and, accordingly, safety. Non-contrast MR perfusion, or the arterial spin labeling (ASL) technique, allows assessing cerebral blood flow without the introduction of a contrast agent, since the natural contrast is arterial blood, which becomes a kind of "labeled bolus" when special impulses are applied. This technique allows performing studies as many times as necessary, since there is no exogenous contrast agent [26, 27], and has broad prospects for clinical use, especially for the purpose of differentiating glial tumors. There is magnetic susceptibility-weighted MR perfusion with dynamic contrast enhancement (MSW-MRI) and dynamic contrast-enhanced MR perfusion (DC-MRI). The essence of the techniques is that in MCAP-MRI the movement of the contrast agent bolus through the brain is tracked using a series of T2 or T2*-weighted images, while in MR perfusion with dynamic contrast enhancement changes in a series of T1-weighted images occur before, during and after the introduction of gadolinium-containing drugs. The use of these techniques in examining patients with suspected brain tumors allows visualizing the tumor itself, as well as quantitatively assessing the change in MR signal intensity after dynamic contrast enhancement. Their use also makes it possible to study in detail the quantitative indicators of the permeability of the BBB and microvascular system, which provides a more complete assessment of brain tumor angiogenesis (DCE MRI) [28, 29]. MR spectroscopy is a special technique that allows determining the composition of metabolites in the area under study and in the contralateral hemisphere using the so-called chemical shift principle [30, 31]. MR spectroscopy is used in primary brain tumors for differential diagnostics with non-neoplastic lesions [32, 33], as well as between radiation necrosis and continued tumor growth [34, 35], and for assessing the degree of malignancy. Thanks to the development of computing technology and electronics, it has become possible to transform conventional spectroscopic data into metabolic maps. The method is based on the use of mapping a large area of the brain with a multi-voxel volume, which allows localizing 16 to 64 voxels in the brain simultaneously. Based on the data obtained from each volume (voxel), metabolic maps and color mapping maps are created, reflecting the spatial concentration of certain metabolites in accordance with the anatomical structure of organs. This technique significantly simplifies the analysis of the obtained data array, and also makes this procedure much more visual. N-acetylaspartate is a derivative of amino acids synthesized in neurons and then transported along axons. In glial tumors of the brain, axons, neurons and dendrites are destroyed with the development of a deficiency of the enzyme system involved in the acetylation of aspartate, which leads to a decrease in its

content. Substituted choline phosphates are the structural basis of phospholipids, the most important building material of basal membranes. In glial tumors of the brain, cell membranes are destroyed with the release of choline, as a result of which its content increases. The amount of ATP formed is insufficient to cover the energy needs during active cellular proliferation of tumors. Therefore, in addition to oxidative phosphorylation (Krebs cycle), additional pathways for obtaining ATP are formed - anaerobic glycolysis and serinelysis (serine first turns into 3-phosphoglycerate, and then into pyruvate and lactate with the formation of ATP). Thus, the most significant changes in patients with glial brain tumors compared to patients with unchanged brain matter on the contralateral side are: a decrease in the proportion of NAA, an increase in Cho and Lac. The results of modern studies also indicate the ability of perfusion MR images and MR spectroscopy to distinguish between IDH1-mutant gliomas and wild-type gliomas [36, 37]. Based on molecular biological data, astrocytic and oligodendroglial tumors are subdivided depending on the presence or absence of IDH1 or IDH2 mutation in the genome of their cells [38, 39]. Wang et al. (2019) point to the differentiating role of only relative cerebral blood flow, but not absolute values. In their opinion, MR spectroscopy data for 2-hydroxyglutarate give a false positive result in 21% of cases of wild-type glial tumors for IDH1 [40, 41]. As a result, the question arises about additional research methods that can increase the efficiency of non-invasive differentiation of gliomas by malignancy grades and molecular genetic status. In 2022, Chenochina IV was published, in which the authors discuss the advantages of MR relaxometry. This work conducted a study that included 72 patients with glial brain tumors aged 27 to 74 years (median 46 years). The MR study included obtaining standard structural images, MR relaxometric study using MAGiC (Magnetic Resonance Image Compilation) technology. DWI (Diffusion Weighted Imaging), also associated with the study of tissue hydration, was chosen as a reference technique. As a result of the work, the authors proved that mapping of relaxation parameters, proton density and ADC helps in differentiating grade 3 and 4 gliomas, as well as IDH1-mutant gliomas and wild-type gliomas; proton density - in differentiating grade 2 and 4 gliomas based on the tumor zone [42]. Byrnes TJ, Jensen JH and Steven AJ agreed that diffusion tensor MRI (DTMRI) shows good results in differentiating high-grade gliomas and solitary metastases in the brain [43, 44]. High-grade gliomas are similar to low-grade astrocytomas, but are more variable, and the tumor can demonstrate high heterogeneity due to the presence of cystic degeneration or foci of hemorrhage. On T1-WI, glial tumors are usually characterized by a hypointense MR signal relative to the white matter. On T2-WI, they are hyperintense, but may be heterogeneous in the presence of

blood breakdown products. On T2-WI, perifocal edema, characteristic of these forms of astrocytomas, is clearly visible, having a hyperintense signal and a characteristic shape in the form of diverging rays. It should be noted that the infiltrative growth of astrocytomas leads to the fact that tumor tissue can spread beyond the zone of signal change visible on T2-WI. The presence of a "mass effect" is also typical. The key to distinguishing anaplastic astrocytomas from low-grade tumors is the accumulation of a contrast agent, which should be absent in the latter (although it should be noted that some types of tumors, especially gemistocytic astrocytomas, can demonstrate contrast enhancement). Contrast enhancement patterns are very variable. Anaplastic astrocytomas are characterized by intense enhancement of the MR signal after the introduction of a paramagnetic contrast agent. This significantly improves visualization of the internal structure of the tumor, its boundaries and extent. The ratio of cystic and solid components is determined by the characteristics of contrast agent accumulation. Unlike glioblastomas, pronounced necrosis is not determined in anaplastic astrocytoma. Accordingly, centrally located areas that do not accumulate contrast agent, corresponding to fluids by their signal characteristics, should be absent. Post-contrast T1-WI: varies, but there is accumulation of contrast agent. The presence of annular accumulation of contrast enhancement is characteristic of glioblastoma, but not anaplastic astrocytoma. MR perfusion: increased CBV. MR spectroscopy: increased Cho/Cr ratio, N-acetylaspartate peak is preserved or slightly reduced, lactate is absent, intermediate myo-inositol level (lower than in low-grade tumors and higher than in glioblastoma). Glioblastoma usually consists of solid, cystic, and necrotic components. The tumor center is isointense or hyperintense relative to the surrounding brain tissue, depending on its cellular density. On T1-WI, they have iso- and hypointense signal. Tumor features on T2-WI are also varied: areas of hypo-, iso- and hyperintense signal from the tumor stroma, necrosis, cystic cavities, and hemorrhage foci. The necrotic zone appears brighter on T2-WI. Perifocal edema appears hypointense on T1-WI and hyperintense on T2-WI and FLAIR images. Edema may extend beyond the corpus callosum to the contralateral side; this is a sign of malignancy. Solid tumor components have a high signal intensity on DWI, whereas necrotic components are characterized by a low signal intensity. An increase in orCVC by two times compared to the norm is a sign of malignancy. Heterogeneous accumulation of the contrast agent is noted after intravenous enhancement. In this case, the tumor stroma intensively accumulates the contrast agent, and the areas of necrosis located in the center of the tumor do not change the MR signal. Pronounced ring-shaped contrast enhancement. As a rule, the tumor edge accumulating the contrast agent is adjacent to the ventricular system and/or ependyma. This is a sign of the

beginning of spread along the meninges. Hemorrhage foci have a characteristic MR signal intensity depending on the stage of the process. A sign of malignancy of glioblastomas is the detection of arteriovenous shunts on MR tomograms, which are visualized as uneven, tortuous arteries and veins along the periphery of the tumor. In 5% of cases, multiple glioblastomas are found, which are practically indistinguishable from metastases. Garanina NV (2023) compares diffusion tensor imaging (DTI) and diffusion kurtosis imaging (DKI), citing primary sources that state that DT-MRI is based on the fact that the diffusion of water molecules corresponds to a Gaussian distribution [45]. In turn, diffusion kurtosis imaging (DKI) is a more extended version of DT-MRI and characterizes non-Gaussian diffusion of water molecules, as a result of which it significantly increases the specificity of its determination. Diffusion of water molecules in normal and tumor tissues always follows a non-Gaussian distribution [46]. Therefore, it can be said that diffusion kurtosis imaging (DKI) can more accurately reflect the real direction of movement of water molecules in tumor tissue than diffusion tensor imaging (DTI) [47, 48]. DCI may be of particular interest in the differential diagnosis of high-grade gliomas from solitary metastases in the brain [49, 50]. CONCLUSION Thus, magnetic resonance imaging is of significant help in the differential diagnosis of glial tumors of the brain. The advantages of this method include obtaining high-contrast images of brain structures, non-invasiveness of the study, absence of radiation exposure, and obtaining data on structural and functional changes in the brain in various histological types of tumors.

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