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## ЖУРНАЛ БИОМЕДИЦИНЫ И ПРАКТИКИ
## JOURNAL OF BIOMEDICINE AND PRACTICE


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ISSN 2181-9300

DOI Journal 10.26739/2181-9300

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10 ЖИЛД, 2 СОН

# ЖУРНАЛ БИОМЕДИЦИНЫ И ПРАКТИКИ

ТОМ 10, НОМЕР 2

# JOURNAL OF BIOMEDICINE AND PRACTICE

VOLUME 10, ISSUE 2

ТОШКЕНТ-2025

# БИОМЕДИЦИНА ВА АМАЛИЁТ ЖУРНАЛИ

№2 (2025) DOI http://dx.doi.org/10.26739/2181-9300-2025-2





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ЖУРНАЛ БИОМЕДИЦИНЫ И ПРАКТИКИ | JOURNAL OF BIOMEDICINE AND PRACTICE

УДК 616.831-006.6:615.849.1

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# MR SPECTROSCOPY OF BRAIN TUMORS AND CORRELATION OF METABOLIC CHANGES WITH HISTOLOGICAL CHARACTERISTICS

**For citation:** Bakhritdinov Bekzod Rustamovich, Aliev Mansur Abduholikovich. MR spectroscopy of brain tumors and correlation of metabolic changes with histological characteristics. // Journal of Biomedicine and Practice. 2025, vol. 10, issue 2.

**http://dx.doi.org/10.5281/zenodo.15198886**

**ABSTRACT**

**Introduction:** Brain tumors remain one of the most challenging problems in neuro-oncology. Conventional MRI often fails to determine tumor grade accurately. Magnetic resonance spectroscopy (MRS) offers a promising non-invasive method for evaluating the metabolic profile of brain neoplasms.

**Methods:** Forty-eight patients with brain tumors were examined using proton MRS ($^1$H-MRS). Tumors included gliomas (n=33), meningiomas (n=10), and metastases (n=5). Metabolites analyzed included choline (Cho), creatine (Cr), N-acetylaspartate (NAA), lactate (Lac), and lipids (Lip). Correlation and comparative analysis were used to assess the relationship between metabolite levels and tumor histology.

**Results:** Increased Cho, Lac, and Lip and decreased NAA strongly correlated with higher anaplasia grades ($p<0.001$). Cho/Cr and Lip/Cr were the most significant markers. NAA/Cr distinguished glioblastomas from metastases ($p=0.04$). MRS demonstrated high diagnostic value in evaluating metabolic features and malignancy.

**Discussion:** MRS allows non-invasive grading, differential diagnosis of recurrence vs. radiation necrosis, and monitoring of treatment response. It can reduce the need for biopsy in complex cases and support clinical decision-making in neuro-oncology.

**Keywords:** magnetic resonance spectroscopy, brain tumors, metabolites, anaplasia, glioblastoma, metastasis.

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# МР-СПЕКТРОСКОПИЯ ОПУХОЛЕЙ МОЗГА И КОРРЕЛЯЦИЯ МЕТАБОЛИЧЕСКИХ ИЗМЕНЕНИЙ С ГИСТОЛОГИЧЕСКИМИ ХАРАКТЕРИСТИКАМИ


## АННОТАЦИЯ

**Введение:** Опухоли головного мозга представляют собой одну из наиболее сложных задач нейроонкологии. Стандартные методы МРТ не всегда позволяют точно определить степень злокачественности опухоли. В этой связи актуальным становится использование магнитно-резонансной спектроскопии (МРС), позволяющей оценить метаболический профиль опухоли.
**Методы:** Проведено исследование 48 пациентов с различными типами опухолей мозга, включая глиомы, менингиомы и метастазы. Использовалась протонная МРС ($^1$H-МРС), с анализом метаболитов (Cho, Cr, NAA, Lac, Lip). Установлены соотношения метаболитов и их связь с гистологической степенью анаплазии. Данные обработаны методами корреляционного и сравнительного анализа.
**Результаты:** Повышение уровней Cho, Lac и Lip и снижение NAA достоверно коррелируют с ростом степени анаплазии ($p<0,001$). Особенно значимыми оказались показатели Cho/Cr и Lip/Cr. Отличия между глиобластомами и метастазами выявлены по уровню NAA/Cr. МРС продемонстрировала высокую чувствительность и специфичность в оценке биохимических характеристик опухоли.
**Обсуждение:** МРС позволяет неинвазивно оценить степень злокачественности, дифференцировать рецидив от постлучевого некроза, а также контролировать эффективность терапии. Спектроскопия может служить альтернативой биопсии в сложных клинических случаях и расширяет возможности диагностики в нейроонкологии.


**Ключевые слова:** магнитно-резонансная спектроскопия, опухоли мозга, метаболиты, анаплазия, глиобластома, метастазы.


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# MIYA O‘SMALARINING MR-SPEKTROSKOPIYASI VA METABOLIK O‘ZGARISHLARNING GISTOLOGIK XUSUSIYATLAR BILAN KORRELYASIYASI


## ANNOTATSIYA

**Kirish:** Bosh miyaning o‘smalari neyroonkologiyada eng murakkab tashxislardan biri hisoblanadi. Oddiy MRT yordamida o‘smalarning malignlik darajasini aniqlash har doim ham imkoni bo‘lavermaydi. Shu sababli, metabolik profilingni baholashda MR-spektroskopiyaning (MRS) ahamiyati ortib bormoqda.
**Usullar:** 48 nafar bemor ishtirokida protonli MRS ($^1$H-MRS) o‘tkazildi. Ular orasida gliomalar (n=33), meningiomalar (n=10) va metastazlar (n=5) mavjud edi. Asosiy metabolitlar (Cho, Cr, NAA, Lac, Lip) tahlil qilinib, ularning histologik darajasi bilan bog‘liqligi baholandi. Tahlil statistik va korrelyatsion usullar bilan amalga oshirildi.
**Natijalar:** Cho, Lac va Lip ko‘rsatkichlarining oshishi, NAA darajasining pasayishi o‘sma malignlik darajasi bilan kuchli bog‘liqlikda ekanligi aniqlandi ($p<0,001$). Ayniqsa, Cho/Cr va Lip/Cr indekslari eng muhim markerlar sifatida ajralib turdi. NAA/Cr darajasi glioblastoma va metastazlarni farqlashda foydali bo‘ldi ($p=0.04$). MRS usuli o‘sma metabolizmini baholashda yuqori diagnostik imkoniyatlarga ega ekanligi tasdiqlandi.
**Muhokama:** MRS usuli yordamida o‘smaning malignlik darajasini invaziv bo‘lmagan usulda aniqlash, radsiyatsion nekrozdan rецидивni farqlash, davolash samaradorligini monitoring qilish mumkin. Bu usul biopsiyani almashtirishi va neyroonkologiyada tashxisni soddalashtirishi mumkin.

**Kalit so‘zlar:** magnit-rezonans spektroskopiya, miya o‘smalari, metabolitlar, анаплазия, glioblastoma, metastazlar.

**Relevance.** Brain tumors are one of the most complex and significant problems of modern neurooncology. Despite the development of diagnostic methods and improvement of therapeutic approaches, the prognosis for malignant neoplasms remains unfavorable. According to the World Health Organization (WHO), about 300,000 new cases of primary tumors of the central nervous system are registered annually, while the mortality rate from malignant gliomas remains high [5]. Glial tumors, which account for up to 70% of all primary brain neoplasms, are of the greatest clinical significance [6]. Among them, the most aggressive is glioblastoma (Grade IV according to WHO), characterized by infiltrative growth, rapid progression and high resistance to treatment. The average life expectancy of patients with glioblastoma is 12–18 months, and the five-year survival rate does not exceed 5% [1].

Modern neuroimaging methods, such as magnetic resonance imaging (MRI), are the main diagnostic tool for brain tumors, allowing us to determine their location, size, and structural features. However, standard MRI methods do not always allow us to reliably distinguish between benign and malignant tumors, as well as accurately differentiate between tumors of different degrees of anaplasia (Grade) [2].

Diagnosis of brain tumors is associated with a number of difficulties due to the similarity of their morphological and radiological characteristics. One of the key problems is the similarity of MRI images of tumors of different degrees of malignancy. For example, anaplastic astrocytoma (Grade III) and glioblastoma (Grade IV) can demonstrate similar signal characteristics on T1- and T2-weighted images, which makes it difficult to distinguish them [4].

An additional difficulty is the need to differentiate tumor recurrence and post-radiation necrosis. After radiation therapy, both processes may be accompanied by the accumulation of contrast agent, which makes it difficult to choose further treatment tactics [7].

Another problem is the similarity between metastases and primary glial tumors. They can look the same on standard MRI studies, which requires the use of additional diagnostic methods to accurately determine the nature of the neoplasm [3].

Despite the proven effectiveness of MRS in diagnosing brain tumors, its use in clinical practice is still limited due to insufficient standardization of the method and the complexity of interpreting spectral data. In this regard, there is a need for a detailed study of the correlation between biochemical changes in tumor tissue and its histological structure, which will improve diagnostic accuracy and expand the use of the method in neurooncology.

**The aim of the study** is to analyze spectroscopic data of patients with various brain tumors and identify a correlation between metabolic changes and the degree of tumor anaplasia.

**Materials and methods.** The study using the proton magnetic resonance spectroscopy (MRS) method ($^1$H-MRS) included 48 patients with the most common brain tumors: glial tumors – 33 patients (68.8%), meningiomas – 10 patients (20.8%), brain metastases – 5 patients (10.4%).

The group of patients with glial tumors was divided into three subgroups by the degree of anaplasia (Grade):

• Grade II (8 patients) – fibrillary-protoplasmic astrocytoma, oligodendroglioma
• Grade III (14 patients) – anaplastic astrocytoma
• Grade IV (11 patients) – glioblastoma

MRS was performed with the analysis of the ratios of the following metabolites:

Cho / Cr – an indicator of cellular proliferation;
NAA / Cr – a marker of neuronal degradation;
Lac / Cr – an indicator of hypoxia;
Lip / Cr – a marker of necrotic changes.

Comparison of the mean values in the groups was performed using the Student's t-test (for normal distribution) and the Mann-Whitney test (for abnormal distribution). The correlation between metabolic parameters and the degree of anaplasia was estimated using the Pearson coefficient (r). The significance of differences was assessed at a level of $p < 0.05$

Research results. Unlike standard MRI, MRS allows not only to visualize the tumor process, but also to evaluate changes in metabolites characteristic of malignant growth. Proton MRS ($^1$H-MRS), the most widely used method, analyzes the biochemical composition of tumor tissues, including:

• N-acetylaspartate (NAA) is a marker of neuronal integrity, a decrease in which indicates neuronal damage.

• Choline (Cho) is an indicator of cellular proliferation, an increased level of which indicates malignant growth.

• Creatine (Cr) is an indicator of energy metabolism, used as an internal normalizing standard.

• Lactate (Lac) is evidence of hypoxia and anaerobic metabolism, characteristic of aggressive tumors.

• Lipids (Lip) is a marker of necrosis, reflecting the destruction of tumor cells.

Changes in the ratios of these metabolites make it possible to differentiate tumors of varying degrees of malignancy, identify metastases, and distinguish tumor relapse from post-radiation necrosis.

**Table 1.**

**Average values of metabolites in subgroups of glial tumors**

| **Group** | **Cho / Cr (M ± m)** | **NAA / Cr (M ± m)** | **Lac / Cr (M ± m)** | **Lip / Cr (M ± m)** |
|---|---|---|---|---|
| **Grade II (n=8)** | 1.8 ± 0.4 | 0.8 ± 0.2 | 1.2 ± 0.3 | 0.9 ± 0.2 |
| **Grade III (n=14)** | 2.7 ± 0.6 | 0.6 ± 0.1 | 1.8 ± 0.4 | 1.5 ± 0.3 |
| **Grade IV (n=11)** | 3.9 ± 0.8 | 0.4 ± 0.1 | 2.9 ± 0.5 | 3.8 ± 0.6 |

Table 1 presents the mean metabolite values in the subgroups of glial tumors. Statistical analysis of differences between tumor groups shows significant changes in metabolite levels with increasing grade of anaplasia. The Cho/Cr ratio shows statistically significant differences between Grade II and III tumors ($p = 0.012$), as well as between Grade III and IV ($p = 0.009$), indicating a progressive increase in choline content with increasing malignancy.

The NAA/Cr ratio significantly decreases between Grade II and IV ($p = 0.003$), reflecting neuronal death and loss of functional tissue. The Lac/Cr level differs significantly between all groups ($p < 0.01$), indicating increased anaerobic metabolism. The greatest increase is shown by Lip/Cr, which increases significantly from Grade II to Grade IV ($p < 0.001$), confirming active destruction of cell membranes. As the degree of anaplasia increases, there is a marked increase in the concentration of choline (Cho), lactate (Lac) and lipids (Lip), accompanied by a significant decrease in the level of NAA, indicating the progression of the tumor process.

Table 2.

Correlation analysis between metabolites and the degree of anaplasia

| **Parameter** | **r** | **p** | **Significance of the relationship** |
|---|---|---|---|
| Cho / Cr ↔ Grade | 0.82 | <0.001 | Strong positive |
| NAA / Cr ↔ Grade | -0.76 | <0.001 | Strong negative |
| Lac / Cr ↔ Grade | 0.68 | 0.002 | Moderate positive |
| Lip / Cr ↔ Grade | 0.88 | <0.001 | Strong positive |

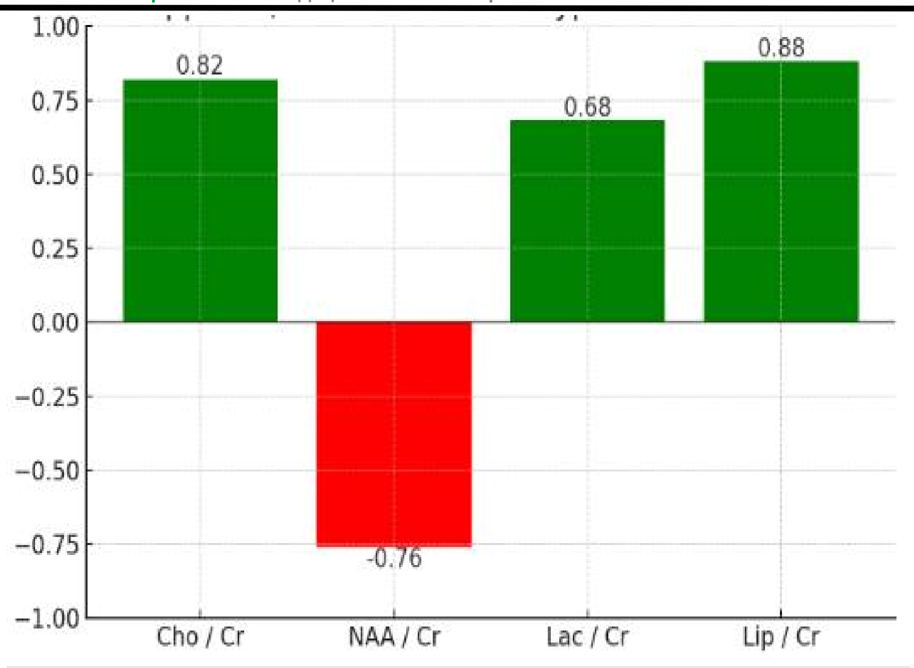


Figure 1. Correlation of metabolites with the level of anaplasia.

In the diagram (Fig. 1) showing the correlation of metabolites with the level of anaplasia, positive correlations (Cho / Cr, Lac / Cr, Lip / Cr) are highlighted in green, and negative (NAA / Cr) in red. The higher the r value, the stronger the correlation. The calculation of the Pearson correlation coefficient (r) shows that choline (Cho) and lipids (Lip) demonstrate the most pronounced correlation with tumor aggressiveness ($p < 0.001$), which confirms their role in reflecting the intensity of cell proliferation and membrane destruction. The higher the degree of anaplasia, the higher the levels of these metabolites, which makes them reliable markers of malignancy.

N-acetylaspartate (NAA) is inversely correlated with the degree of anaplasia: as the malignancy of the tumor increases, its level decreases ($p < 0.001$). This is due to the destruction of normal neuronal tissue and the loss of functional cells in the affected area.

The Lac/Cr ratio shows a moderate but statistically significant correlation with anaplasia ($p=0.002$), which is explained by hypoxia in the tumor. The accumulation of lactate indicates the predominance of anaerobic glycolysis, which is typical for aggressive neoplasms with impaired blood supply.

Table 3.

**The difference between metastases and glial tumors**

| Parameter | Glioblastoma (n=11) | Metastases (n=5) | p |
|---|---|---|---|
| **Cho / Cr** | 3.9 ± 0.8 | 4.2 ± 0.7 | 0.18 (insignificant) |
| **NAA / Cr** | 0.4 ± 0.1 | 0.3 ± 0.1 | 0.04 (significant) |
| **Lac / Cr** | 2.9 ± 0.5 | 3.5 ± 0.6 | 0.09 (tendency towards significance) |
| **Lip / Cr** | 3.8 ± 0.6 | 4.5 ± 0.8 | 0.07 (tendency towards significance) |

The difference in parameters between metastases and glial tumors is presented in Table 3. In the table, p-value shows the level of statistical significance of differences between metastases and glioblastoma. A value less than 0.05 indicates a significant difference between the groups. The range from 0.05 to 0.1 indicates a tendency to significance requiring additional data. Values above 0.1 mean no statistically significant differences. In the presented data, the difference is significant for NAA/Cr, and Lac/Cr and Lip/Cr show a tendency to significance. Cho/Cr does not show significant differences.

Metastases and glioblastomas demonstrate similar Cho/Cr and Lac/Cr values, which makes it difficult to differentiate them solely by these metabolites. However, the difference in NAA/Cr levels ($p = 0.04$) indicates that metastatic tumors destroy neuronal tissue more aggressively than glioblastomas. In addition, the Lip/Cr ratio is higher in metastases, which is explained by the pronounced necrotic process. This indicates significant destruction of cell membranes and a high degree of tissue damage, characteristic of metastatic lesions.

**Discussion of results.** Magnetic resonance spectroscopy (MRS) allows differentiating glial tumors of varying degrees of malignancy by analyzing metabolites in brain tissue. With increasing anaplasia, there is an increase in the choline to creatine (Cho / Cr) and lipid to creatine (Lip / Cr) ratios, which is associated with increased cellular proliferation and membrane destruction. At the same time, the N-acetylaspartate to creatine (NAA / Cr) ratio decreases, reflecting neuronal death and loss of functional tissue.

The correlation between the degree of anaplasia and the level of metabolites is statistically confirmed. Lip / Cr and Cho / Cr demonstrate the greatest relationship with the gradation of malignancy, while the correlation coefficient exceeds 0.8 ($p < 0.001$).

Metastases and glioblastomas have a similar spectral profile, but differ in the level of NAA / Cr. This difference is statistically significant ($p = 0.04$), which makes this indicator an important criterion in differential diagnosis.

Thus, the use of MRS helps improve preoperative diagnostics of tumors, allowing more accurate determination of their nature and degree of malignancy. This method makes it possible to detect relapses at early stages, which significantly increases the chances of timely intervention and effective treatment. In addition, MRS helps differentiate gliomas and metastatic lesions, which is important for choosing the optimal treatment tactics.

The use of this method reduces the need for invasive procedures, such as biopsy, in patients with suspected high-grade tumors, thereby reducing the risk of possible complications. Identification of specific metabolic markers of relapse allows for dynamic monitoring of the patient's condition, assessment of the effectiveness of the treatment and timely adjustment of the therapeutic strategy.

**Conclusions**. MR spectroscopy is a valuable diagnostic method for brain tumors, allowing to assess the degree of tumor malignancy without invasive intervention. The metabolic profile, including increased Cho/Cr, decreased NAA/Cr and accumulation of Lac/Cr and Lip/Cr, can be used for differential diagnostics of tumors of various nature. The obtained data confirm that MRS can be a useful tool for predicting tumor aggressiveness and monitoring the effectiveness of treatment.

MR spectroscopy allows not only to see the tumor, but also to understand its nature. High choline indicates aggressive proliferation, low NAA - brain destruction, lactate indicates hypoxia, and lipids - necrosis.

How does it help doctors? Determines tumor malignancy without biopsy. Helps to distinguish between tumor relapse and radiation necrosis. Assess the effectiveness of treatment. Each tumor leaves its own biochemical trace, and MRS is a tool that helps to decipher it.

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ISSN 2181-9300

DOI Journal 10.26739/2181-9300

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VOLUME 10, ISSUE 2

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