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INTRAOPERATIVE FLUORESCENT CONTRASTING FOR PRIMARY AND SECONDARY BRAIN TUMORS: A LITERATURE REVIEW

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ABSTRACT

Relevance: *Surgical resection of a brain tumor that is as radical and safe as possible remains an important step in the treatment of patients with primary and secondary brain tumors. It is difficult to distinguish tumor tissue from normal brain tissue during surgery using traditional white light microscopy. Intraoperative fluorescent contrast enhancement methods for brain tumors are used in real-time during the operation to overcome this limitation without disrupting the workflow. Several fluorescent drugs have been studied in recent decades, including 5-aminolevulinic acid (5-ALA), sodium fluorescein, and indocyanine green.*

The study aimed to *evaluate the experience of using intraoperative fluorescent contrast at the present and diagnostic capabilities, significance, application, and development prospects for primary and secondary brain tumors based on an analysis of literature data.*

Methods: *A systematic search of publications in the MEDLINE/PubMed database was performed using keywords related to the results of fluorescence contrasting in brain tumors with potential clinical significance.*

Results: *According to the literature review, 5-ALA has been the most studied drug among the listed fluorescent drugs. It is approved for use in different countries for intraoperative fluorescent contrast of grade III and IV malignancy glial tumors. Package Inserts do not indicate using 5-ALA to treat primary and secondary brain tumors of other histological structures or using sodium fluorescein and indocyanine green to treat brain tumors. However, the literature analysis demonstrates a large experience of their successful use.*

Conclusion: *Fluorescent contrast of primary and secondary brain tumors is a new, promising, and insufficiently studied method of visualizing brain tumor tissue during surgery in real time. Studying the possibilities and features of fluorescent contrasting primary and secondary brain tumors is a relevant and promising area of study, and its implementation in practice will improve treatment results.*

Keywords: *fluorescence-guided surgery, brain tumor; brain metastases, aminolaevulinic acid (5-ALA), sodium fluorescein, indocyanine green, fluorescence.*

Introduction: Treatment of malignant primary and secondary central nervous system (CNS) tumors is an urgent problem. According to the Register of Cancer Patients of Kazakh Institute of Oncology and Radiology (KazIOR, Almaty, Kazakhstan) for 2020-2023, the incidence of central nervous system malignant neoplasms (CNS MNs) in the Republic of Kazakhstan (RK) is about 800 new cases annually with an upward trend (815 cases in 2022) and reaches 4.0-4.2 cases per 100 thousand population. Mortality from CNS MNs in dynamics decreased from 2.1 per 100 thousand population (388 cases) in 2020 to 1.6 per 100 thousand population (320 cases) in 2023. Surgical treatment was performed on patients as monotherapy and as part of complex and combined treatment. In dynamics, there is an increase in the number of cases of surgical treatment performed from 69% in 2020 to 83.5% in 2023 [1, 2] (Figures 1-3).

A decrease in mortality from CNS MNs with increasing morbidity rates indicates an improvement in the quality of neuro-oncologic care in the Republic of Kazakhstan. The graphs show that the growth of neurosurgical care in combination with chemotherapy and radiation therapy plays an important role in achieving this. Improving the quality of neurosurgical care is a significant component of further improving the treatment outcomes in patients with primary and secondary brain tumors.

One of the main goals of neurosurgical intervention in brain neoplasms is the most possible radical and safe tumor resection. At the same time, the effectiveness of surgical intervention is limited by infiltrative tumor growth and the impossibility of total resection without damaging healthy brain tissue. As a result of damage to functionally significant areas of the brain, neurological deficits and disability of patients may develop, and in case of damage to vital areas - death. It is paramount to determine the extent of resection during surgery, especially at the border of the tumor and healthy tissue. The absence of a clear border characterizes infiltrative tumor growth. Differentiating tumor tissue from normal brain tissue during surgery using conventional white light microscopy is challenging. Intraoperative fluorescence contrast (IFC) techniques for tumors have been developed and used [3-28] to overcome this limitation.

The study aimed to evaluate the experience of using intraoperative fluorescence contrasting at the present stage, diagnostic capabilities, significance, application and development prospects in primary and secondary brain tumors based on the analysis of literature data.

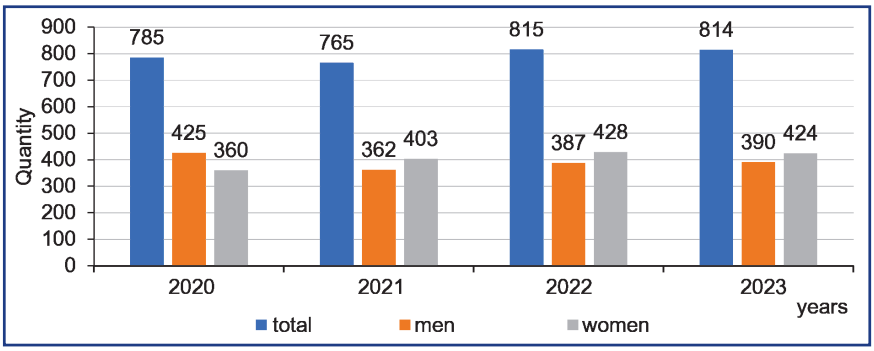

Figure 1 – Incidence of central nervous system malignant neoplasms in the Republic of Kazakhstan, 2020-2023 (4.0-4.2 cases per 100 thousand population), according to KazIOR Register

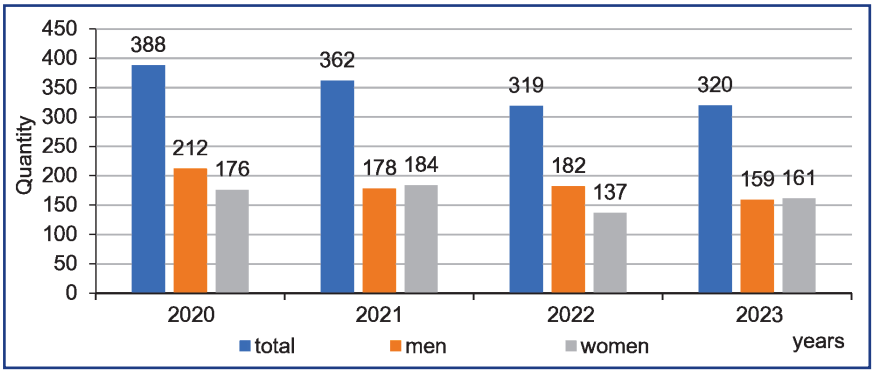

Figure 2 – Mortality from central nervous system malignant neoplasms in the Republic of Kazakhstan (1.6-2.1 cases per 100 thousand population), according to KazIOR Register

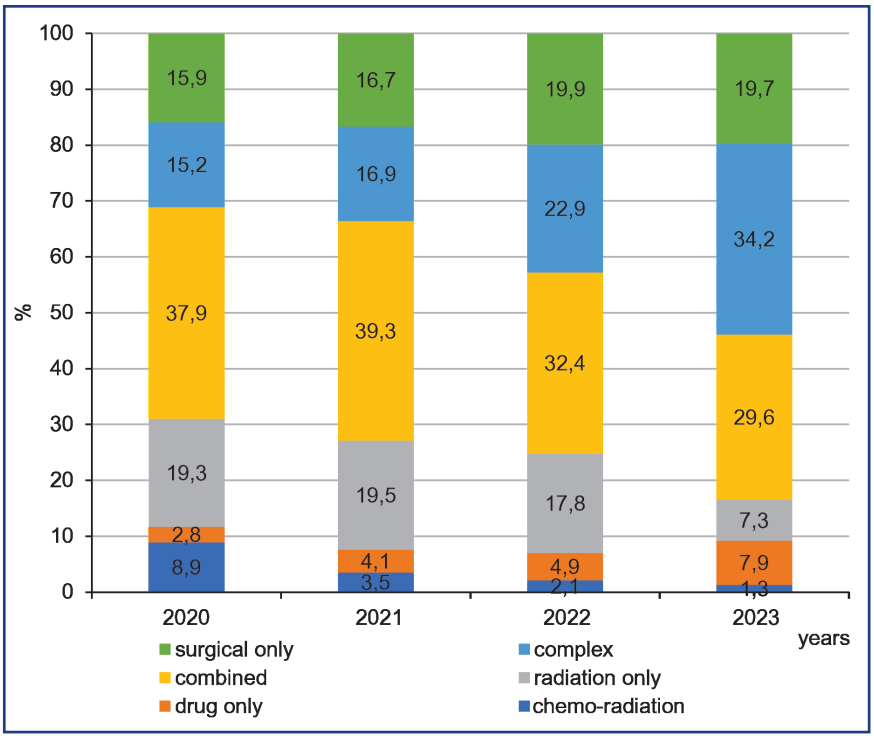

Figure 3 – Types of treatment for central nervous system malignant neoplasms in the Republic of Kazakhstan, 2020-2023, according to KazIOR Register

Materials and methods: We systematically searched publications from the MEDLINE/PubMed database using keywords related to fluorescence contrasting in brain tumors with potential clinical significance. Thirty-three publications were selected and analyzed for the study.

Results: The method of IFC of primary and secondary brain tumors is based on the ability of the fluores-

cent drug to accumulate in places of permeability violation of the blood-brain barrier (BBB) and tumor cells of the brain, as well as its ability to fluoresce when exposed to light of a certain wavelength. After a certain time, the drug is injected into the body, accumulating in the tumor tissue and on the border of the tumor in places of damaged BBB. Then, during surgery, the light of a certain wavelength causes luminescence (fluorescence) with the light of a different wavelength (a different color), contrasting tumor tissue against the background of healthy brain tissue.

IFC enables the surgeon to visualize the tumor tissue in real-time during surgery and perform the safest and most effective tumor resection possible. The amount of accumulated drug determines the fluorescence intensity and indicates the peculiarities of the histological structure and metabolism of the tumor [3, 5-18].

One of the side effects of using fluorescent drugs is photosensitization and phototoxicity, which can be used for therapeutic purposes, and intraoperative photodynamic therapy (PDT) can be performed. The concept of PDT is that the fluorescent agent accumulates in malignant cells, which become sensitized to exposure to visible light, and upon light exposure (during PDT), the tumor cells remaining in the infiltration zone after surgical resection die. In contrast, healthy and functionally important brain cells remain intact [7].

According to selected literature sources, fluorescent agents such as 5-aminolevulinic acid (5-ALA), Sodium Fluorescein (SF), and Indocyanine green (ICG) are used for IFC and visualization of primary and secondary brain tumors. The diagnostic capabilities, methodology, and features of using IFC to treat primary and secondary brain tumors are described.

5-ALA, SF, and ICG are considered safe and approved for use in many countries worldwide. However, according to the instructions for use, only 5-ALA is indicated for visualization of malignant glioma tissue (WHO grade III and IV). 5-ALA is registered in the Republic of Kazakhstan under the "Gliolan" trade name, reg. No. РК-ЛС-5 No. 024769 [19]. According to the user instructions, SF and ICG are used to study and assess blood flow in various organs, including the choroid of the eye and cerebral vessels, whereas their use for IFC of brain tumor tissue is not listed among the indications [20, 21]. SF and ICG are not registered in the Republic of Kazakhstan.

The conducted analysis of the literature revealed a sufficient number of publications on the effective use of IFC with 5-ALA, SF, and ICG in the treatment of primary and secondary brain tumors of various histological types, which show development potential and require further study and expansion of indications for use.

The available data on the use of 5-ALA in the treatment of primary and secondary brain tumors is based on biosynthesis and tumor selectivity: 5-ALA is a precursor of the fluorescent and phototoxic protoporphyrin IX (PpIX) in the heme biosynthesis pathway and is a natural metabolite of hemoglobin in the human body. When administered orally, 5-ALA crosses the blood-brain barrier (BBB) and the tumor-brain interface, is absorbed by malignant tumor cells, and is metabolized in the mitochondria into the fluorescent metabolite PpIX. Increased production and accumulation of PpIX in tumor cells allows for visualization of violet-red fluorescence of tumor tissue after excitation with blue light at a wavelength of 405 nm. [5, 6, 22].

Procedure: three to four hours before anesthesia, 5-ALA is dissolved in 50 ml of drinking water and administered orally at 20 mg/kg of body weight.

During surgery, at the tumor removal stage, a microscope with a light emission of 440 - 460 nm at 1% intensity is used for the IFC of the tumor. At the same time, tissues with areas of fluorescence of different intensities and colors can be visualized in real-time. In the presence of PpIX, red fluorescence will be observed with peaks at 635 and 705 nm. In the surgical field, one can observe with the naked eye the blue light with a wavelength of about 450 nm emitted by the excitation light source, green fluorescence from endogenous fluorophores, and red fluorescence caused by PpIX [3, 5-11, 14, 15, 22-29].

Based on the intraoperative real-time data of tumor fluorescence contrast, the surgeon visually identifies, by fluorescence intensity, areas with the highest density of tumor cells, healthy brain tissue, and the infiltration zone. This enables optimal decision-making regarding the extent of maximal possible tumor resection with minimal damage to functionally important brain tissue.

In cases of insufficient fluorescence intensity, the sensitivity of IFC of brain tumors using 5-ALA can be improved by reducing the intensity of the excitation blue light. For "non-fluorescent" tumors, more sensitive methods of PpIX detection, such as fluorescence spectroscopy, may be helpful [6].

Interpretation of IFC data for brain tumors using 5-ALA depends on fluorescence intensity. The amount of PpIX accumulation and the fluorescence intensity depends on the nature and type of tumor growth. Thus, "strong" fluorescence is most characteristic of solidly proliferating tumors with a high density of tumor cells, while "weak" fluorescence is typical of infiltrative tumors with moderate tumor cell density. The current IFC method can only characterize the fluorescence intensity but cannot make a quantitative assessment. Neurosurgeons usually distinguish three levels of fluorescence intensity: strong, uncertain (or weak), and no fluorescence, corresponding to solid tumor, infiltration zone, and normal brain, respectively [6, 7].

Despite the high diagnostic value of IFC, the possibility of false-positive and false-negative fluorescence must be considered. False-positive fluorescence may occur close to tumor cells; reactive astrocytes (e.g., radiation necrosis tissue) may produce false-positive fluorescence. In rare cases, autofluorescence of normal healthy

tissue may be observed. False-negative fluorescence may occur:

– in tumors with diffuse-infiltrative growth patterns in areas with low tumor cell infiltration density. In such cases, spectroscopy may be used to improve diagnostic accuracy. This is also observed in low-grade gliomas, which are usually not visualized using standard violet-blue light.

– in the presence of structural barriers interfering with visualization, such as blood, overhanging parts of healthy brain tissue, etc.;

– due to a bleaching effect — where fluorescence diminishes under exposure to blue light at 400 nm or standard white light. Bleaching up to 36% may occur after exposure to blue light for more than 25 minutes and over 87 minutes under standard white light;

– if surgery begins too early (less than 2 hours) or too late, false-negative fluorescence may occur since 5-ALA reaches its peak plasma concentration 4 hours after ingestion; however, sufficient fluorescence may still be observed even after 12 hours [6].

Features of surgery with 5-ALA:

– the patient receives not a fluorochrome but its non-fluorescent precursor, which ensures higher contrast between tumor cells and healthy brain tissue due to the absence of nonspecific background fluorescence associated with fluorescent agents in the blood and interstitial space;

– there is selective accumulation of PpIX in tumor tissue at the cellular level;

– to prevent functional neurological deficits after surgery, functionally important brain areas potentially infiltrated by malignant cells must be considered, and once functioning brain areas are detected, tumor resection must be discontinued, even in the presence of fluorescence;

– it is necessary to dim the lights to avoid reflections that could be mistaken for PpIX fluorescence [6, 7].

Experience with the use of 5-ALA for IFC of primary and secondary brain tumors according to literature data: According to its instructions for use, 5-ALA is indicated for IFC of WHO grade III or IV gliomas; however, literature analysis shows that 5-ALA is also successfully used for IFC of primary and secondary brain tumors of other histological types [6 - 9].

R. Díez Valle *et al.* (2019) analyzed more than 300 articles on 5-ALA use and concluded that IFC of high-grade gliomas is a reliable and reproducible method that can influence the extent of tumor resection and patient outcomes. At the same time, IFC with 5-ALA for other tumor types requires further development [24].

H.A. Shah *et al.* (2022) conducted a systematic review on using 5-ALA for fluorescence-guided resection of brain metastases. Based on the analysis of 10 selected studies involving 631 patients, they noted that 5-ALA fluorescence rates for brain metastases ranged from 27.6% to 86.9%, depending on tumor type variability. None of the studies concluded that using 5-ALA improved surgical outcomes or survival. It has been concluded that current studies on using 5-ALA for brain metastases are limited and do not confirm the effectiveness in improving the extent of resection or postoperative survival and that fluorescence intensity varies depending on the tumor type. They highlight the need for further investigation into the benefits of IFC using 5-ALA for specific histological tumor types and the study of the diagnostic value of quantitative fluorescence assessment [23].

Based on data from 19 publications covering 175 surgeries performed under 5-ALA fluorescence guidance in pediatric tumors, M. Schwake *et al.* (2019) noted that this technique facilitates tumor identification during surgery and was useful in 78% of glioblastomas, 71% of WHO grade III anaplastic ependymomas, while its usefulness in pilocytic astrocytomas and medulloblastomas was lower - 12% and 22%, respectively [9].

F. Marhold *et al.* (2022) studied 29 cases of 5-ALA fluorescence contrast in brain melanoma metastases. Visible fluorescence was observed in only 28% of cases, while in 72%, it was absent. Analysis showed that the presence or absence of fluorescence was not associated with the degree of pigmentation, intratumoral hemosiderin, or hemorrhage [25].

Despite the low diagnostic value of 5-ALA fluorescence contrast in brain melanoma metastases, in the study by J. Takahashi *et al.* (2019), the therapeutic effectiveness of 5-ALA in PDT for brain melanoma metastases was demonstrated in an experimental setting [26].

M.A. Kamp *et al.* (2016) analyzed 84 cases of 5-ALA fluorescence contrast in brain metastases. Strong or weak fluorescence was noted in 40.5% of cases, while in 59.5%, no fluorescence was observed. The primary site and histological type of metastasis did not correlate with fluorescence behavior. A significant correlation was found between 5-ALA fluorescence and the local tumor progression rate in the brain. Patients with 5-ALA-negative metastases had a higher risk of local recurrence compared to 5-ALA-positive metastases [28].

In 2019, A. Boschi and A. Della Puppa conducted a literature review on using 5-ALA for IFC of brain tumors and concluded that this agent may be beneficial not only for WHO grade III and IV gliomas but also for tumors of other histological types. High efficacy was noted in low-grade gliomas with areas of anaplasia, meningiomas with parenchymal infiltration or skull bone invasion, ependymomas, lymphomas, and pediatric tumors [30].

Thus, despite mixed results in the use of 5-ALA in the treatment of low-grade gliomas and brain metastases, authors agree that this issue requires further investigation into the diagnostic value of the method for tumors of different histological types [5, 7, 9, 22, 25, 27, 29-31]. They point to the potential for expanding the application in cases of negative fluorescence by using more sensitive fluorescence detection methods [6, 7, 10]. The potential for the therapeutic use of 5-ALA in photodynamic therapy is also emphasized separately [7, 26].

The literature analysis showed that 5-ALA, SF, and ICG are also used for fluorescence contrast of brain tumors [12 - 18, 27, 30, 31].

Currently, it is believed that SF and ICG penetrate and accumulate in the intercellular space in areas of the brain where the BBB is disrupted, which allows visualization of tumor margins during fluorescence imaging, similar to the contrast enhancement observed with gadolinium-enhanced MRI [12, 14, 15, 17]. Lower cost compared to 5-ALA, non-toxicity, ease of use (intravenous administration during surgery), and a wide range of diagnostic capabilities covering all contrast-enhancing brain lesions with BBB disruption are reasons for the growing interest in using these fluorochromes for IFC in the treatment of primary and secondary brain tumors [12 - 18].

SF is excited by light at 460 - 500 nm wavelength and fluoresces green at 540 - 690 nm. A visual representation of glioblastoma under fluorescence contrast using 5-ALA and SF is shown in Figure 4 [14].

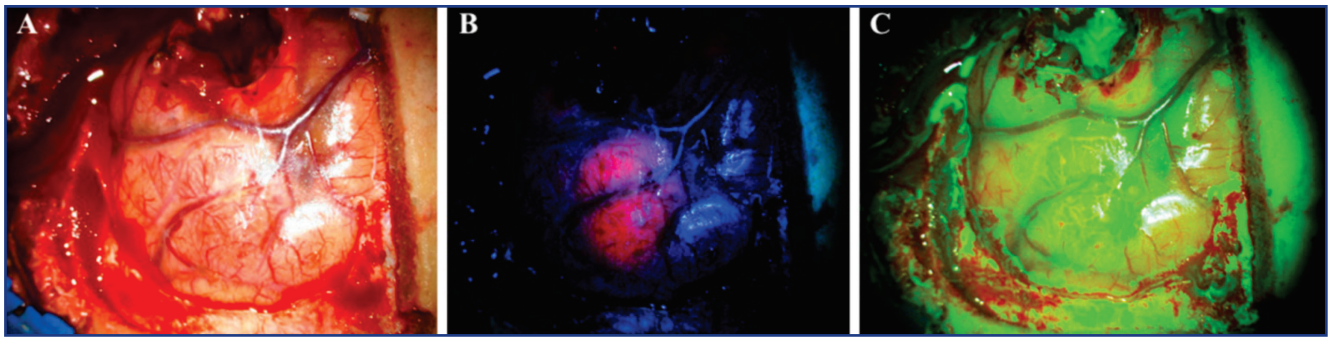

Figure 4 – View of tumor and healthy tissue during intraoperative fluorescence contrast of glioblastoma: A – under white light; B – under blue light with 5-ALA, red glow on a blue background is observed; C – under yellow light with Sodium Fluorescein, the tumor glows green on a yellow background [14].

SF is administered intravenously during anesthesia before surgery, after which the agent accumulates in areas of BBB disruption, and fluorescence can be visualized within 4 hours after injection [14, 18]. Previously, SF was used for fluorescence at high doses (20 mg/kg) and visualized under an operating microscope using white light. Using a special yellow filter with excitation light at a wavelength of 560 nm allowed for increased sensitivity and reduction of the dose to 3 - 5 mg/kg, administered before surgery [14, 18].

L.C. Ahrens *et al.* (2022) presented an analysis of data on the use of fluorescence with 5-ALA and SF, concluding that SF can be a viable alternative to 5-ALA for surgical removal of high-grade gliomas. Moreover, SF is useful for fluorescence-guided visualization of many primary and secondary brain tumors, including metastases, and has several advantages over 5-ALA, such as a broader application spectrum, lower cost, and easier administration. The authors emphasize the need for further research [14].

B. Musca *et al.* (2023) revealed in their study that SF not only accumulates in areas of BBB disruption in the intercellular space but is also absorbed intracellularly by tumor and immune cells [12].

A. Narducci *et al.* (2023), based on a study of 48 patients with suspected high-grade glioma who underwent stereotactic biopsy with SF fluorescence contrast, demonstrated the utility of this method, which increased the accuracy of tissue sampling by 13.8% compared to the non-fluorescence method while reducing the average number of biopsy samples from 4.4 to 3.3 [31].

In their review of 23 cases of brain tumor lesions that showed gadolinium enhancement on MRI and stereotactic biopsies with SF contrast (93 samples), D.K. Singh *et al.* (2021) proposed SF fluorescence as a convenient tool for stereotactic brain tumor biopsies that can improve diagnostic accuracy [32].

ICG is a water-soluble dye approved by the FDA for biomedical purposes. Due to its fluorescence in the near-infrared (NIR) spectrum, it is widely used in medical applications. Its maximum light absorption occurs in the infrared range at 800 nm (778 - 806 nm), with peak emission measured by fluorescence at 830 nm and peak radiation at 835 nm in biological tissues. ICG fluorescence emission in the NIR range has a greater tissue penetration depth of up to 15 mm, whereas visible-light fluorophores penetrate up to 3 mm. In addition, NIR fluorescence with ICG is less affected by autofluorescence since biological tissue generally does not emit fluorescence in the NIR spectrum. In the early 2000s, ICG was officially introduced into neurosurgical practice as an intraoperative cerebrovascular contrast agent for brain vessel imaging (video angiography). In 2016, a group of authors developed a new technique called "Second Window Indocyanine Green" (SWIG), which involves the infusion of a high dose of ICG (5.0 mg/kg) 24 hours before surgery. ICG acts as a passive targeting agent and accumulates in areas with BBB disruption and in tumor tissue. Unlike 5-ALA and SF, ICG is a NIR fluorophore, which provides higher resolution with deeper tissue penetration [15 - 18, 33]. An example of ICG fluorescence visualization is shown in Figure 5 [16].

As an infrared fluorochrome, ICG has advantages over other fluorochromes currently operating in the visible spectrum due to the increased tissue penetration of

NIR fluorescence and reduced autofluorescence. According to reviewed sources, SWIG has been used in patients with high-grade gliomas, meningiomas, brain metastases, pituitary adenomas, craniopharyngiomas, chordomas, and pineal region tumors [15 - 18, 33]. This indicates the promising potential for further study and broader application of ICG in treating primary and secondary brain tumors.

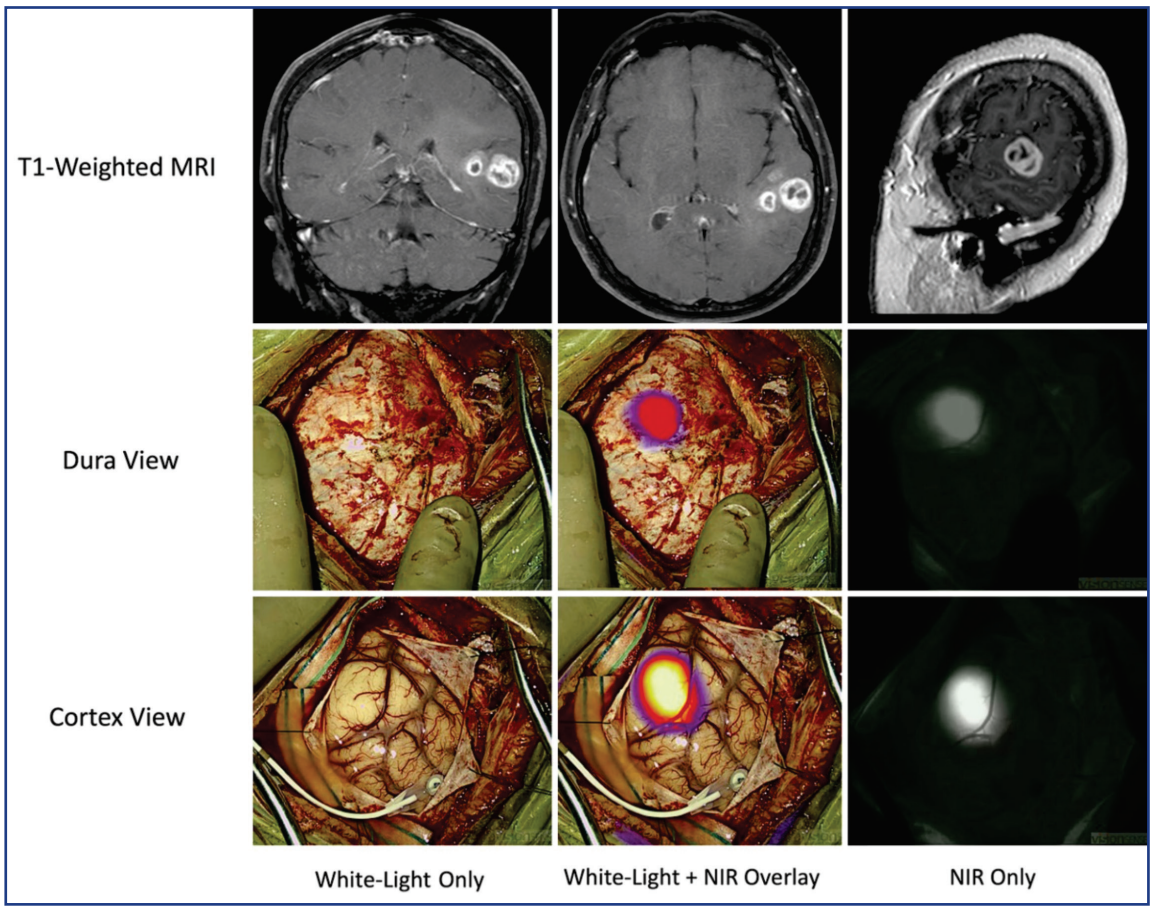

Figure 5 – The top row shows MRI scans of a patient with glioblastoma multiforme in T1-weighted contrast-enhanced mode (T1-Weighted MRI). The second and third rows show images under white light only and during fluoroscopy using the Second Window ICG under white light combined with infrared imaging (White-Light + NIR Overlay) and under infrared only (NIR Only). The second and third rows present images before (Dura View) and after durotomy (Cortex View) [16].

Discussion: Maximally radical and safe surgical resection of brain tumors remains a crucial stage in the treatment of patients with primary and secondary brain tumors. Differentiating tumor tissue from normal brain tissue during surgery using conventional white light microscopy is challenging. Real-time implementation of IFC methods without interrupting the surgical process allows us to overcome this limitation. Over the past decades, several fluorescent agents have been studied, including 5-ALA, SF, and ICG [11].

According to the literature review, among these agents, 5-ALA is the most extensively studied and approved for use in IFC of WHO grade III and IV gliomas, as reflected in the instructions for use. The instructions do not indicate the use of 5-ALA for treating primary and secondary brain tumors of other histological types. Similarly, SF and ICG are not indicated for the treatment of brain tumors according to their respective instructions for use. However, the literature review revealed substantial clinical experience demonstrating their successful application [3, 5 - 33].

Takeaways:

– IFC of primary and secondary brain tumors is an effective tool for real-time visualization of tumor tissue, which expands the surgeon's capabilities during the procedure, enables the selection of the most optimal resection volume, and thereby improves the quality of surgeries and treatment outcomes;

– The data from the literature review demonstrate the high diagnostic value of IFC for high-grade gliomas using 5-ALA, which is recommended for implementation and use in clinical practice, as reflected in the instructions for use. Expanding the indications for the use of 5-ALA for intraoperative contrast of primary and secondary brain tumors of other histological types is promising and insufficiently studied;

– The extension of current indications of SF and ICG for fluorescence-guided contrast imaging of primary

and secondary brain tumors is promising and necessary for improving the quality of treatment of CNS neoplasms;

– Intraoperative use of fluorescent agents expands not only the diagnostic capabilities of the surgeon but also the therapeutic potential for treating primary and secondary brain tumors through photodynamic therapy, although this method requires further study before clinical implementation.

Conclusion: According to the literature review, fluorescence-guided contrast imaging of primary and secondary brain tumors is a novel, promising, and insufficiently studied method of visualizing tumor tissue and the brain during real-time surgery. In addition to its diagnostic value, the use of fluorescent agents also has a therapeutic effect when performing intraoperative PDT.

Thus, the study of the potential and specific features of fluorescence-guided contrast imaging for primary and secondary brain tumors is a relevant and promising area of research, and its implementation into practice could improve treatment outcomes.

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АҢДАТПА

АЛҒАШҚЫ ЖӘНЕ ЕКІНШІЛІК МИ ІСІКТЕРІН ИНТРАОПЕРАЦИЯЛЫҚ ФЛУОРЕСЦЕНТТІК КОНТРАСТТАУ: ӘДЕБИ ШОЛУ

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Өзектілігі: *Ми ісігінің ең радикалды және қауіпсіз хирургиялық резекциясы бас миының бастапқы және қайталама ісіктері бар науқастарды емдеудегі маңызды қадам болып қала береді. Дәстүрлі ақ жарық микроскопиясын қолданып операция кезінде ісік тінін қалыпты ми тінінен ажырату қиын. Бұл шектеуді еңсеру үшін операция кезінде нақты уақыт режимінде және жұмыс процесін бұзбай, ми ісіктерін интраоперациялық флуоресцентті контрастты күшейту әдістері қолданылады. Соңғы онжылдықтарда бірнеше флуоресцентті препараттар зерттелді, соның ішінде 5-аминолевулин қышқылы (5-ALA), натрий флуоресцеин және жасыл индоцианин.*

Мақсат: *Әдебиет деректерін талдау негізінде қазіргі кезеңде интраоперациялық флуоресцентті контрастты қолдану тәжірибесін, диагностикалық мүмкіндіктерін, маңызын, біріншілік және қайталама ми ісіктерін қолдану және даму перспективаларын бағалау.*

Әдістері: *MEDLINE/PubMed деректер базасын жүйелі іздеу ықтимал клиникалық маңызы бар ми ісіктері кезіндегі флуоресценциялық контраст нәтижелеріне қатысты түйінді сөздерді пайдалана отырып жүргізілді.*

Нәтижелері: *Әдебиеттік шолуға сәйкес, аталған препараттардың ішінде 5-аминолевулин қышқылы ең көп зерттелгені және әлемнің әртүрлі елдерінде III және IV дәрежелі қатерлі ісіктердің глиальды ісіктерінің интраоперациялық флуоресцентті*

контрастын қолдану үшін рұқсат етілгені анық. Басқа гистологиялық құрылымдардың бастапқы және қайталама ми ісіктерін емдеу үшін 5-ALA қолдану нұсқаулықта көрсетілмеген, сонымен қатар натрий флуоресцеинін және индоцианин жасылын қолдану жөніндегі нұсқаулықта емдеуде қолдануға көрсеткіштер жоқ; ми ісіктері, ал әдебиет деректерін талдау оларды сәтті қолданудың үлкен тәжірибесін көрсетті.

Қорытынды: *Бастапқы және қайталама ми ісіктерінің флуоресценциялық контрастты бейнелеуі операция кезінде мидың нақты уақыт режимінде бейнеленуінің жаңа перспективалы және аз зерттелген әдісі болып табылады. Бастапқы және қайталама ми ісіктерінің флуоресценттті контрастын қолдану мүмкіндіктері мен ерекшеліктерін зерттеу өзекті және перспективалық зерттеу бағыты болып табылады және оны тәжірибеге енгізу емдеу нәтижелерін жақсартады.*

Түйінді сөздер: *флуоресценциямен басқарылатын хирургия; ми ісігі; мидағы метастаздар; аминолевулин қышқылы (5-ALA); натрий флуоресцеин; индоцианин жасыл; флуоресценция.*

АННОТАЦИЯ

ИНТРАОПЕРАЦИОННОЕ ФЛУОРЕСЦЕНТНОЕ КОН-ТРАСТИРОВАНИЕ ПРИ ПЕРВИЧНЫХ И ВТОРИЧНЫХ ОПУХОЛЯХ ГОЛОВНОГО МОЗГА: ОБЗОР ЛИТЕРАТУРЫ

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Актуальность: *Максимально возможное удаление опухолевой ткани с сохранением функционально значимых участков головного мозга остается одной из основных целей хирургического удаления первичных и вторичных опухолей головного мозга. Отличить опухолевую ткань от нормальной ткани мозга во время операции с использованием традиционной микроскопии в белом свете затруднительно. Для преодоления этого ограничения используются методы интраоперационного флуоресцентного контрастирования опухолей головного мозга с использованием флуоресцентных препаратов. Наиболее изученными флуоресцентными препаратами являются 5-аминолевулиновая кислота, Флуоресцеин натрия и Индоцианин зеленый.*

Цель исследования *– оценить опыт использования интраоперационного флюоресцентного контрастирования на современном этапе, диагностические возможности, значение, применение и перспективы развития при первичных и вторичных опухолях головного мозга на основании анализа литературных данных.*

Методы: *Проведен системный поиск публикаций из базы данных MEDLINE/PubMed по ключевым словам, связанным с результатами применения флюоресцентного контрастирования при опухолях головного мозга, которые имеют потенциальное клиническое значение. Для исследования выбрано и проанализировано 33 публикации.*

Результаты: *По данным проведенного литературного обзора видно, что из перечисленных флуоресцентных препаратов 5-аминолевулиновая кислота наиболее изучена и одобрена к применению для интраоперационного флуоресцентного контрастирования глиальных опухолей III и IV степени злокачественности, что отражено в инструкции по применению препарата. Использование 5-аминолевулиновой кислоты для лечения первичных и вторичных опухолей головного мозга другой гистологической структуры в инструкции по применению не указаны, также в инструкции по применению Флуоресцеина натрия и Индоцианина зеленого нет показаний для применения при лечении опухолей головного мозга, тогда как проведенный анализ литературных данных показал большой опыт их успешного применения.*

Заключение: *Флуоресцентное контрастирование первичных и вторичных опухолей головного мозга является новым перспективным и недостаточно изученным методом визуализации опухолевой ткани и мозга во время операции в режиме реального времени. Изучение возможностей и особенностей применения флуоресцентного контрастирования первичных и вторичных опухолей головного мозга является актуальным и перспективным направлением в изучении, а его внедрение в практику позволит улучшить результаты лечения.*

Ключевые слова: *хирургия под флуоресцентным контролем, опухоль головного мозга, метастазы в головной мозг, аминолевулиновая кислота (5-ALA), Флуоресцеин натрия (FS), Индоцианин зеленый (ICG), флуоресценция.*

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