Review

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The Role of Stereotactic Radiosurgery in the Treatment of Large Brain Metastases

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ABSTRACT Stereotactic radiosurgery is a modern treatment modality for patients with intracranial metastases. However, it has long been acknowledged that radiosurgery of large tumors results in limited efficacy and increased rate of complications. There have been still debates on the need of combination of radiosurgery and open surgery for intracranial metastases and the sequence of these modalities. The next question is about the proper treatment for metastases that could not be resected. There is a paucity of data describing the relationship between radiosurgical options and radiobiological effect, in particular how prescribed dose, type of fractionation, volume of irradiated tumor and morphology of cancer are related. The information presented in this review highlights opportunities of stereotactic radiosurgery for treatment of patients with large intracranial metastases in combination with open surgery as well as a stand-alone method when using hypofractionation regimen.

Keywords: stereotactic radiosurgery, brain metastases

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BM – brain metastases
CRC – colorectal cancer
HFSTRS – hypofractionated stereotactic radiosurgery
LC – local control
LMD – leptomeningeal dissemination
MRI – magnetic resonance imaging
NSCLC – non-small cell lung cancer
OS – overall survival
PD – prescribed dose (dose delivered to the edge of the tumor)

PTV – planning target volume
RN – radiation necrosis
RT – radiation therapy
SR – surgical resection
SRN – symptomatic radiation necrosis
STRS – stereotactic radiosurgery
WBRT – whole brain radiotherapy

INTRODUCTION

Brain metastases (BMs) are the most common intracranial malignancies in the adult population [1, 2]. The incidence of BM in cancer patients ranges from 10–30% and depends on the type of primary cancer and the stage of the disease [3–5]. In most cases, BMs are detected in non-small cell lung cancer (NSCLC), breast cancer, skin melanoma, and colorectal cancer (CRC) [4] and are diagnosed simultaneously with the primary tumor in 12–20% of patients [1, 6]. Improving systemic therapy increases the life expectancy of cancer patients [7-9], but only some chemotherapy drugs effectively penetrate the blood-brain barrier. This requires further study of the possibilities of methods of local treatment of BMs. Currently, for this purpose, they resort to the use of surgical treatment and external beam radiation therapy (RT):

1. Surgical treatment can be carried out in the following scope:

— microsurgical resection of brain metastases;
— stereotactic biopsy;
— application of fractional drainage system.

2. Remote RT is carried out using gamma-ray devices, linear electron accelerators, accelerators of heavy charged particles and may be performed as:

— whole brain radiotherapy;
— stereotaxic RT;
— stereotactic radiosurgery;
— proton therapy.

3. Combined treatment.

The modern approach to local treatment of BM has minimized the use of surgical methods in an independent variant due to the need to improve local control over the tumor, while radical and cytoreductive operations can be a key factor in the implementation of combined methods for the treatment of patients with BM, including preoperative or postoperative remote RT.

MICROSURGICAL RESECTION OF BRAIN METASTASES

Surgical resection (SR) has firmly established itself as the main method of treating patients with solitary and oligometastatic brain lesions [10]. The goal of surgery for intracranial metastases is to prevent further tumor growth, identify molecular characteristics, and relieve neurological symptoms.

The generally accepted indications for surgical treatment of BMs [11–13] are the presence of a supratentorial solitary metastasis more than 3 cm in diameter or a smaller metastasis located in the posterior cranial fossa or a functionally significant area in the presence of neurological symptoms due to cerebral edema.

The surgery may help confirm the diagnosis in patients with BM from an unknown primary tumor. The detection of BM is the first sign of the disease in about 10% of cancer patients. In the event that a systemic lesion and BM were found at the same time, SR may be the first step in the treatment plan. In addition, a patient with a known primary cancer may have a brain lesion with radiographic features of an alternative pathological diagnosis. In 11% of cases, focal brain changes are not single BMs, but primary tumors, abscesses, or inflammatory reactions [14], which gives SR a decisive diagnostic value.

Three factors should be taken into account when selecting patients for chemotherapy: the characteristics of intracranial metastases, the clinical and functional state of the patient, and the state of systemic disease.

The efficacy and safety of SR depend on the location of BMs. When comparing the results of total SR of tumors with the removal of infiltratively affected brain tissue located outside functionally significant areas, and SR within the tumor tissue without removal of the brain parenchyma adjacent to the metastasis, the recurrence rate within two years in the group of patients with more aggressive surgical tactics was 29.1%, and in the 2nd group it was 63.2% [15]. For patients with metastases located in functionally significant areas, the risk of an increase in neurological symptoms after SR is 21% [16].

The metastasis size is also one of the risk factors for continued tumor growth after SR. For example, a study by *Patel et al.* (2010) showed that the risk of continued growth increases with a metastasis volume of more than 9.7 cm^3 [17]. The possibility of recurrence increases when the metastasis is removed in parts compared to en block resection [18].

The histological type of the tumor is an important indicator affecting survival: two-year survival after SR BM was higher in patients with breast cancer (87.5%) compared with other tumors (67%) and separately with NSCLC (0%) [19].

STEREOTACTIC BIOPSY

Stereotactic biopsy is a minimally invasive intervention in neurosurgical practice that allows obtaining pathological tissue samples for in vivo pathological examination. Carrying out a stereotactic biopsy is relevant in case of solitary or multiple focal lesions of the brain and the absence of information about the patient's primary cancer, ambiguous radiological characteristics of the intracranial lesion.

FRACTIONAL DRAINAGE SYSTEM (OMMAYA RESERVOIR)

Most BMs have a solid structure with foci of necrosis and surrounding swelling of the brain tissue, however, there are also large cystic metastases that require a special neurosurgical approach. The loose walls of such neoplasms are poorly separated from the adjacent medulla and are often torn when removed. There is a risk of saving a section of the cyst wall in the wound, which leads to a rapid recurrence of metastasis. In such cases, with large metastases of the cystic and solid cystic structure, it is advisable to use drainage systems to evacuate the contents of the cystic component of the tumor. The use of the Ommaya reservoir has an advantage over the SR of metastases with a signigicant cystic component, as it allows drainage of the contents of the metastasis even if it is located in functionally significant areas. In the early postoperative period, drainage leads to a complete or partial regression of neurological symptoms and creates conditions for the continuation of combined treatment, increasing the susceptibility of the tumor to radiation. The implantation can be carried out as a second stage after performing a stereotactic biopsy with the collection of the cystic component of the tumor for cytological examination and/or with the collection of the solid component for histological examination.

MULTIPLE METASTATIC BRAIN INJURY

The question of whether there are indications for SR in multiple metastatic brain lesions remains open. Surgical intervention is performed in cases where there are dominant lesions that cause neurological symptoms, which removal would provide clinical improvement. Currently, there are no prospective randomized trials to evaluate the efficacy of chemotherapy in patients with multiple BMs. A study by *Schackert et al*. (2013) showed that the survival rate of patients with 4 or more BMs after SR was 3.3 months, which is significantly less than in the group of patients with 1–3 BMs (7.8 months) [20]. For comparison, in a study *by Pessina et al*. (2016) in patients with solitary metastases, overall survival after open surgery is 24 months, while the authors note 100% achievement of local control over 2 years. Clinical improvement after surgery was achieved in 90.5% of patients; no serious complications, including liquorrhea, were noted [19]. In *Stark et al*. (2005) the best survival rate was achieved in patients with 1 to 3 BMs [21].

As we already mentioned, in addition to the characteristics of cerebral metastases, when considering the feasibility of surgical intervention, the oncological status and functional state of the patient himself should be taken into account. To solve this problem, various classification tools are used to combine patients with BM into groups that differ in severity and overall survival. The most commonly used prognostic scale for assessing overall survival (*Graded Prognostic Assessment*), which includes four prognostic factors: age, functional status, extracranial metastases and the number of BMs. Each factor is assigned values equal to 0; 0.5 or 1 point. Based on the total score obtained, four prognostic groups were formed: 0-1 point (median survival 2.6 months), 1.5-2.5 points (3.8 months), 3 points (6.9 months) and 3. 5–4.0 (11 months).

As a rule, the best candidates for SR of metastasis are patients with solitary or oligometastatic brain lesions, as well as controlled or absent systemic spread of the primary disease [22].

STEREOTACTIC RADIOSURGERY FOR LARGE INTRACRANIAL METASTASES

Stereotactic radiosurgery (STRS) is one of the most effective methods for treating BMs [23–26]. Researchers have presented evidence of the effective treatment of 10 or more BMs [27, 28], but the question of the dependence of the result of STRS on the volume of irradiated metastasis has long been a subject of controversy. *Wiggenraad R. et al.* (2011) analyzed 123 studies mentioning actuarial local control (LC) in order to establish the relationship between the magnitude of the prescribed dose (PD) and the duration of the effect. The authors concluded that when irradiating BMs less than 3 cm in diameter, LC for 12 months at doses above 20 Gy is 80% or more, above 60% at doses of 18 Gy, and less than 50% corresponds to doses of 15 Gy [29]. *Han J.H. et al.* (2012) [30] reviewed the results of treatment of 80 patients who used PD 15-16 Gy for tumors of 14-25 cm^3 , 12-14 Gy for tumors 26-35 cm^3 and 10-11 Gy for tumors larger than 36 cm^3 and recognized the need to change the STRS dosing regimen for large BMs, given the high level of negative radiation effects.

Numerous studies have demonstrated the deterioration of LC control parameters when prescribing PD below 18 Gy or increasing the BM diameter more than 1–2 cm [30–33], and a correlation between PD and target volume with the development of radiation necrosis (RN) [34–38] .

As a result, a definition of "large" metastasis appeared, which referred to tumors larger than 2 cm in diameter and marked the border of the best efficiency of STRS [7, 30, 39–44]. To date, it has been established that patients with a large volume of the pathological focus have the worst LC, since in order to reduce the risk of radiation complications, it is necessary to reduce PD [34-38]. The reason for the high frequency of radiation damage is considered to be an increase in the volume of normal tissue surrounding the target, which is also exposed to radiation: an increase in the target diameter by 50% leads to an increase in the volume of brain tissue surrounding the target by 150% [45].

POSTOPERATIVE STEREOTACTIC RADIOSURGERY

New operating techniques, technological innovations, and an improved understanding of patient selection have helped neurosurgeons develop safer procedures, while the LC rate within a year after surgery is estimated at 40–50% [46–48]. The most likely reason for these results is the high proportion of cases of invasive BM growth, which were previously considered as neoplasms, clearly separated from the brain parenchyma. Recently, such forms of metastasis growth as vascular cooptation (migration along adjacent vessels) and diffuse infiltration with signs of invasion at a distance of 12.5–450 μm (56.2 μm on average) and up to 5 mm have been identified [49, 50]. Based on the available data, postoperative radiation therapy is of great importance for increasing the effectiveness of antiblastic measures and improving local control indicators.

Several large clinical studies have resulted in the conclusion that a combination of surgery and whole brain radiation therapy (WBRT) has a positive effect on LC parameters [14, 51, 52]. Over time, a negative effect of WBRT on neurocognitive function was revealed, as well as the quality of life of patients without an increase in its duration [48, 53–57], and conformal radiation of the postoperative area by STRS in most cases replaced WBRT [58, 59].

The advantage of combined treatment in patients with large BMs was confirmed by *Prabhu R.S. et al*. (2017) in a retrospective analysis of LC and overall survival (OS) in 213 patients with 223 BMs larger than 2 cm in diameter [60]. There were 66 BMs, treated by the STRS method, combined treatment was carried out for 157 BMs. OS and LC were significantly better in the combination treatment group. In the STRS group, the median OS was 10 months compared with 15.2 months in the SR+STRS group ($p = 0.01$). Local recurrence rates at both 1 year and 2 years were significantly lower in the combined group (1 year: 20.5% vs 36.7%; 2 years: 25.6% vs 43.1%; $p = 0.007$).

The technique for performing postoperative STRS has evolved over time.

Soltys S.G. et al. (2008) studied the outcome of 72 patients who underwent postoperative STRS between 1998 and 2006 [61]. The treatment plan for the majority of patients was formed by contouring the immediate postoperative cavity without additional indentation. The authors found that LC was significantly higher in patients with less conformal STRS plans. It has been suggested that the causes of unsuccessful outcomes are related to the difficulty of delineating the postoperative cavity; a decision was made to expand the volume of the target due to the indentation from the edge of the cavity by 2 mm. This approach significantly improved LC without increasing the number of radiation complications. The cumulative incidence of continued growth at 12 months was 3% and 16% for treatment plans with and without target volume expansion, respectively ($p = 0.04$, statistically significant), while rates of radiation complications were not statistically significantly different (p =0.27) and amounted to 3–8% [62].

This strategy inherently intentionally increased the volume of irradiated brain tissue in order to overcome the uncertainty of the boundaries of the postoperative cavity. Probably precisely because of concern about the increased risk of radiation necrosis in patients with large post-resection cavities, 2 mm expansion has not been uniformly accepted in clinical practice. *Jhaveri J. et al.* (2018) analyzed the results of postoperative STRS with an expansion of the planning target volume (PTV) by 1 mm and an expansion of more than 1 mm (median 1.9 mm, mean value - 2.0 mm) in 133 patients with 139 postoperative cavities (1 mm group: 36 patients with 35 cavities; over 1 mm group: 97 patients with 104 cavities) [63]. The study found that 1 mm dilatation had a similar rate of local recurrences within a year (15.2% vs 14.3%) with a significantly lower risk of symptomatic radiation necrosis (SRN) compared to more than 1 mm dilatation (1 year: 6% vs 20.9%; 2 years: 9.1% vs 26.6%; p = 0.028). The only factor associated with an increased risk of local recurrence was the volume of the resection cavity more than 15 cm^3.

Several studies have been undertaken to investigate the relationship between pre-resection tumor size and postoperative cavity size in order to determine the optimal timing for adjuvant radiosurgery [64, 65]. Only in 2014 *Ahmed S. et al*. showed a significant relationship between the severity of edema, which was visualized on magnetic resonance imaging (MRI) in the immediate postoperative period, and the likelihood of a significant decrease in the volume of the cavity. Vasogenic edema greater than 1.5 cm^3 was a predictor of 10% or more cavity size reduction [66]. This potential for cavity involution should be taken into account when choosing the tactics of combined treatment of large BMs. It is also necessary to take into account the high probability of developing leptomeningeal dissemination (LMD) in the case of postoperative STRS for large post-resection cavities. Risk factors for LMD are secondary brain damage in breast cancer [67–70], infratentorial location of lesions [68], and the presence of multiple BMs [70, 71]. Another circumstance that potentially contributes to LMD in postoperative STRS is the presence of a area of extended encephalotomy or damaged structures of the dura mater, not included in PTV. This problem has been addressed in the manual for contouring postoperative cavities [72]. The authors recommended to cover the entire post-resection cavity and encephalotomy area, to include in the irradiation field an area equal to 5–10 mm along the bone flap, if the dura mater was affected by a metastatic process before surgery (1–5 mm, if it was not involved), to capture 1-5 mm along the venous sinus if the tumor was adjacent to the sinus.

Given the possible disadvantages of the combination of SR and postoperative STRS, such as the presence of postoperative complications that can delay the start of irradiation, especially with more extensive resections required for large BMs; the risk of LMD after neurosurgical intervention; the need to expand the radiation area for optimal LC due to the uncertainty of the boundaries of the postoperative area, as an alternative, researchers began to study preoperative or neoadjuvant STRS.

PREOPERATIVE STEREOTACTIC RADIOSURGERY

In neoadjuvant STRS, the volume of intact metastasis is exposed to radiation, which is well identified by neuroimaging and does not require any expansion of the boundaries during treatment [73–75]. The absence of the need to expand the irradiation area and the possibility of dose reduction during planned preoperative STRS reduce the volume of healthy brain tissue receiving 10–12 Gy, which is a prognostic parameter for the development of radiation complications [73, 76]. In a study by *Prabhu R.S. et al.* (2017, 2019) report a 5% risk of developing RN within a year and 8.1–9% within two years during preoperative STRS [60, 74]. *Prabhu R.S. et al.* confirmed that the incidence of CRN was 4.9% at two years for preoperative STRS, which was significantly less than 16.4% for postoperative radiosurgery (p = 0.01) [60]. Regarding the potential reduction in the risk of developing LMD, a multicentre retrospective study by *Patel K.R. et al.* (2016) in a study of 180 patients with 189 BMs who underwent chemotherapy and either preoperative or postoperative radiation, demonstrates the following fact: postoperative STRS is associated with a significantly higher incidence of LMD compared to preoperative STRS (16.6% vs. 3.2% within 2 years, p = 0.010) [71]. The same group of authors compared preoperative STRS with postoperative WBRT [77]. There was no difference in life expectancy or cumulative incidence of continued growth at the surgical site between groups (24.5% vs. 25.1%, p = 0.81). Importantly, there were also no statistically significant differences in the incidence of LMD between groups over two years: 3.5% vs. 9%, respectively (p = 0.66). This finding suggests that neoadjuvant STRS can exert antiblastic effects in radically resected tumor beds without increasing the risk of LMD.

A more complex clinical scenario develops in the case of subtotal resection of BMs [78, 79]. Postoperative STRS provides an opportunity to irradiate the residual tumor fragment adequately with the dose, whereas the choice of preoperative STRS, which is accompanied by a dose reduction of 20% due to theoretically better oxygenation of intact metastases, will require observation and consideration of repeated irradiation in case of progression [73]. Finally, it is not uncommon for patients with large BMs to present with marked perifocal edema and mass effect, requiring SR to be performed as soon as possible, and postoperative radiation therapy will be the most suitable combination for surgical intervention.

STEREOTACTIC RADIOSURGERY OF LARGE METASTASES IN HYPOFRACTIONATION MODE

In the treatment of large BMs, surgical intervention may be limited due to the size of the tumor and its location in the eloquent zone of the brain [16, 80–83]. BMs are a manifestation of stage IV cancer and SR is not always possible due to the prevalence of the extracranial tumor process. Some patients are not subject to surgical intervention due to the severity of concomitant diseases and low functional indicators of the cardiovascular and respiratory systems. If there is a high probability of immediate postoperative complications or contraindications to SR, STRS becomes an alternative method of treatment and is used as an independent option in patients with large BMs.

Schlienger M. et al. (2010), in order to improve local control for tumors larger than 2 cm in maximum diameter and reduce the risk of RN, suggest performing STRS in the hypofractionation mode [84].

Hypofractionated stereotactic radiosurgery (HFSTRS), namely, STRS with the number of irradiation stages from 2 to 5 [85], provides an opportunity to control the biological effects of ionizing radiation by changing the PD per fraction and interfractional interval, while maintaining the degree of radiogenic damage for the tumor and reducing it for surrounding brain tissue. The theoretical advantages of using large fractions over single-fraction STRS are considered to be more effective for tumors in a state of hypoxia, as well as activation of the patient's immune mechanisms [86, 87]. Unfortunately, the theoretical substantiation of this approach lags behind practical application due to the shortcomings of the available radiobiological models, and clinical results remain the main criterion for the application of this method [88]. Currently, a significant amount of clinical data has been accumulated describing the effect of HFSTRS in the treatment of large BMs.

In 2009, *Higuchi Y. et al*. presented a HFSTRS protocol consisting of three stages with a single dose of 10 Gy, each of which was carried out with an interval of 2 weeks [89]. They examined the results of treatment of 43 patients with 46 large BMs (10–35.5 cm^3). The authors noted a decrease in the volume of tumors during a two-week interval in 90.7% of cases, LC indicators after 6 and 12 months were 90% and 76%, respectively. There were 3 cases of continued tumor growth. The appearance of symptomatic perifocal edema was noted on average 6 months after treatment (3.8–6.6 months) in 4 patients.

In 2012, *Yomo S. et al*. conducted a prospective study including 27 patients with 28 large BMs [90]. Before the HFSTRS, six patients had already undergone SR, two patients had had WBRTs, and three patients had had Ommaya reservoirs installed. Radiation was performed according to the protocol with PD 10–16 Gy (median 13.3 Gy) per fraction, in total 2 fractions with an interval of 3 to 4 weeks. The average tumor volume was 17.8 cm^3 (10–53.3 cm^3), by the second stage of irradiation, a decrease in volume indicators by an average of 46% was noted. The incidence of LC at 6 and 12 months was 85% and 61% with a few cases of RN. Signs of continued tumor growth were seen in 6 patients (21%) with a median progression time of 6.2 months (between 1 and 13 months after the second HFSTRS fraction). *Yomo S.* and *Hayashi Y.* (2014) continued their study and later published the results of treatment of 58 patients with 61 large BMs [91], who underwent HHSTRS using the same protocol (2 fractions with PD 10–16 Gy). The results were similar to the first study: the LC rate at 6 and 12 months was 85% and 64%, respectively; for 14 large BMs, LC impairment was registered at an average of 6.2 months (range 1–14.5) after the first exposure. The authors found that more than half of the BM volume between fractions was the only predictor of longer LC. *Ito D. et al.* (2020) evaluated the results of two-stage STRS of 182 large BMs in 178 patients with three main types of cancer: breast cancer, NSCLC, CRC [92]. Their protocol included a mean PD of 13 Gy for both fractions, which were separated by an interval of 7 to 38 days. The mean reduction in tumor volume by the second session in patients with breast cancer, NSCLC, and CRC was 46.1%, 26.6%, and 18.2%, respectively. The authors hypothesized that the difference in tumor shrinkage could be due to differences in fractional interval, dose administered, and patient characteristics. In contrast to previous studies, they did not reveal a correlation between the rate of BM volume reduction and the duration of LC.

The largest retrospective multicentre study comparing 3-stage versus 2-stage HFSTRS was conducted *by Serizawa T. et al.* (2018) involving 212 patients who were irradiated according to protocols with PD 9–11 Gy per fraction for 3 fractions or with PD 11.8–14.2 Gy per fraction for 2 fractions [93]. BM progression rates were 21.6% and 16.7% in the three and two fraction groups, respectively, but this difference was not statistically significant. No significant difference was found between mean survival time, cumulative rate of tumor progression, or rate of serious radiation-related adverse events.

DISCUSSION

The treatment of large BMs is a unique clinical problem, for which for a long time only one option was available, craniotomy and microsurgical removal of pathological tissue. However, even with the observance of the principles of ablastics, there is a possibility of recurrence in SR of BM, including LMD. The use of such a method as WBRT after BM removal was until recently the generally accepted standard in the combined treatment of large solitary BMs, which significantly increased the likelihood of achieving local control. At the same time, WBRT, although it is a fairly simple method, has a low selectivity of exposure. Along with an increase in the effectiveness of systemic therapy for malignant tumors, adverse long-term effects of WBRT began to appear more often, and the problem of the impossibility of repeating the course of irradiation with the progression of the intracranial process arose. In the last 30 years, thanks to the improvement of both equipment for radiation treatment and diagnostic methods, a method of local impact on tumors has been actively developed based on other radiobiological principles than classical fractionation, STRS. The work *of Prabhu R.S. et al.*, *Mahajan A. et al.*, *Brown P.D. et al.* and other researchers suggest that STRS can be used as part of the combined treatment of BM both in adjuvant and neoadjuvant options, is not inferior to WBRT in terms of efficiency, and is safer in assessing the radiation toxicity [48, 53, 73].

Unfortunately, a significant part of patients have features of the course of the disease that worsen the prognosis during open surgery: multiple BMs, uncontrolled extracranial oncological process, impaired liver and kidney function, respiratory and cardiovascular insufficiency. Although the STRS method does not have the inherent radicalness of surgical treatment, it nevertheless has fewer limitations and factors that negatively affect the outcome of treatment. However, back in 2006, *Vogelbaum M.A. et al.* described the limited possibilities of a single radiosurgical treatment of large BMs: with a PD of 15 Gy, the probability of local control over 12 months was only 45%, while an increase in PD led to an unacceptably high level of side effects and a decrease in the quality of life of patients [33] . The solution to this problem was the use of the hypofractional approach: going beyond the limits of classical radiobiology, the HFSTRS method made it possible to overcome the radioresistance (in relation to classical fractionation) of most tumors and maintain a low risk of radiation toxicity [94–96].

Nevertheless, many issues of the HFSTRS remain unresolved - a general radiobiological model of the HFSTRS has not been developed, the optimal size of the BM and the preferred mode of fractionation in each case have not been determined. Despite the large amount of literature data, there is no possibility of a direct comparison of the results of the HFSTRS, carried out using different devices (gamma knife, linear accelerators). PTV formation tactics, off-target dose reduction characteristics can differ significantly between radiosurgical techniques, as well as the impact of these characteristics on fractionation schemes in terms of dose reduction to normal tissues. There are also few studies with a high level of evidence that would more clearly define the place of STRS in the treatment of large BMs.

CONCLUSION

Literature data indicate that stereotactic radiosurgery as part of a combined approach and hypofractionated stereotactic radiosurgery are promising methods for providing local control in patients with large brain metastases [96]. It is the combined treatment in the form of an open neurosurgery and stereotactic radiosurgery that seems to be the most effective, however, when choosing an approach to the treatment of such patients, the potential benefits and consequences of surgery and radiation exposure should be balanced.

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