Life expectancy in glioblastoma patients who had undergone stereotactic biopsy: a retrospective single-center study

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Objective. The best results in glioblastoma (GBM) are obtained through aggressive treatment comprising maximally radical but safe resection followed by chemoradiotherapy. However, certain patients will undergo only stereotactic biopsy. This paper aims to evaluate life expectancy in GBM patients who underwent only stereotactic biopsy, including the effect of subsequent oncological treatment.
Patients and Methods. Patients with confirmed GBM histology who had undergone stereotactic biopsy between June 2006 and December 2016 were retrospectively selected. Each patient had received a CT scan, followed by an MRI scan with a contrast agent. None of the patients were amenable to microsurgical resection.
Results. Of the 60 patients, 41 (69%) received no subsequent oncological treatment, while 14 (23%) underwent isolated radiotherapy. Mean survival time of all patients was 2.8 months. Those who received no additional treatment had an average survival time of 2.3 months; patients who received any type of oncological treatment was 3.7 months. Of these, those receiving radiotherapy alone had a mean survival of 3.1 months. Patients who received oncological treatment with the Stupp protocol had a survival time of 6.6 months.
Conclusion. Diagnostic and surgical advances related to GBM treatment mean that radical resections can be performed even in eloquent brain areas. However, patients not indicated for resection will experience a major reduction in life expectancy. Patients who underwent stereotactic biopsy and received some form of oncological treatment experienced slightly increased overall survival relative to patients with a natural disease course. Patients with favorable clinical factors reacted better to treatment.

Key words: glioblastoma, needle biopsy, palliative care

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BACKGROUND

Glioblastoma (GBM) is both the most frequent and most malignant primary brain tumor in adults, and is associated with an overall survival (OS) of 16–24 months[1,2]. The best results are obtained through aggressive treatment as maximally radical, but safe, resection[3] – and even potentially supraradical resection – followed by adjuvant chemoradiotherapy (CH + RT) (ref.[4]). However, not all patients meet the criteria for radical surgery. Moreover, since histological tumor confirmation is required for the initiation of oncological treatment, certain patients are indicated for stereotactic biopsy[5-7].

The objective of this paper is to evaluate life expectancy among patients who have had GBM confirmed by needle biopsy, as well as determine whether follow-up oncological treatment has a noticeable effect on life expectancy.

PATIENTS AND METHODS

Patients with confirmed GBM histology who underwent stereotactic frame-based or frameless image-guided brain lesion biopsy were retrospectively selected from a time period spanning 1 June 2006 to 31 December 2016.

If a brain tumor was suspected, each patient had a CT scan followed by an MRI scan in T2 and T1-weighted sequences with and without a contrast agent. Several MRI non-enhanced tumors were additionally scanned by PET/CT to help define the metabolic hotspots for subsequent biopsy[8]. All of the patients were not amenable to microsurgical resection due to either tumor location or unfavorable clinical condition, e.g., Karnofsky score below 60 and Performance status higher than 2. Patient age was used as an additional factor, taking into account the patient's general condition and comorbidities. Image-guided biopsy was ordered either by a consultant neurosurgeon or during a regular institutional neuro-oncology board discussion.

Both the site of sample collection for histology and the entry point for the biopsy needle were identified based on postcontrast images prior to the biopsy procedure. It is of no less importance to plan the sampling trajectory in order for it to avoid vascular structures.

Initially the stereotactic biopsies were carried out under local anesthesia using a Leksell stereotactic frame, with the planning based on the results of an intraoperative CT scan. It should be noted that the stereotactic procedure, including mounting of the reference frame under local anesthesia and subsequent imaging for stereotactic localization, is time-consuming and can be an unpleasant experience for the patient[9]. For this reason, the center which handled the patients switched to image-guided biopsy via the Stealth S7/S8 navigation system (Medtronic, Minneapolis, MO, USA) under short general anesthesia. Compared to the stereotactic biopsy procedure, image-guided biopsy requires less time, is more comfortable for both the patient and operator, and provides comparable accuracy[10]. After induction of general anesthesia and with the head secured in a three-point Mayfield clamp, the patient is registered into the Stealth S7/S8 navigation system, and the entry point, biopsy target, and needle trajectory are determined.

A pre-calibrated needle with two reflective markers is inserted through the lockable stereotactic arm with three rotational joints, which serves as a trajectory guide. The navigation system provides real-time visual feedback about the position of the sampling window. Moreover, the system is a non-rigid device that allows any changes to the trajectory that may be required during the procedure. The system can then be used for serial sampling of successive portions of the tumor mass along the trajectory of the biopsy needle.

The biopsy procedure was followed by a final histopathological assessment of the sample of the tumor mass. In this way, patients with a confirmed GBM were obtained, without considering IDH mutation. Each patient was advised to undergo adjuvant concomitant CH + RT (Stupp protocol) (ref.[11]). Patients, who were not able to undergo oncotherapy for complications of a needle biopsy, were excluded. The present study evaluated each patient's condition prior to surgery, further treatment(s), and overall survival.

RESULTS

The research included a total of 60 patients (27 women and 33 men) between the ages of 58 to 78 years, and a median age of 67 years.

Due to unfavorable clinical condition, 41 patients (69%) (22 women and 19 men) received no follow-up oncological treatment and were indicated to undergo symptomatic treatment (Fig. 1 and 2).

Of the studied group, 14 patients (23%) underwent isolated radiotherapy (RT) of the tumor. Only five patients received complete concomitant CHT + RT with adjuvant CH. It should be noted that patients who were clinical-

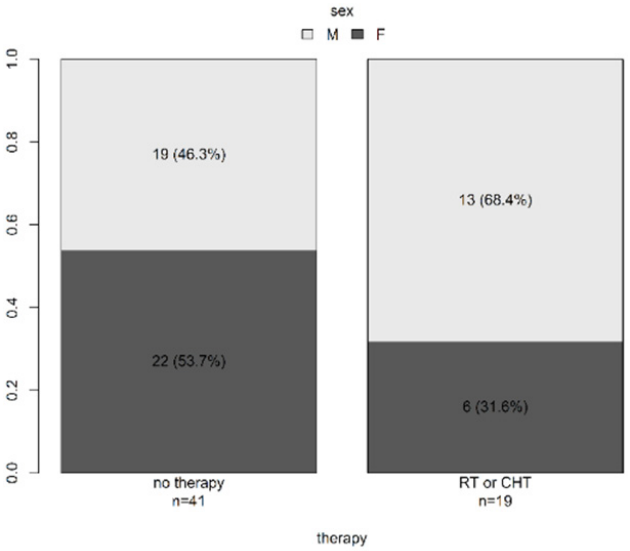

Fig. 1. Sex ratio in groups with and without oncotherapy.

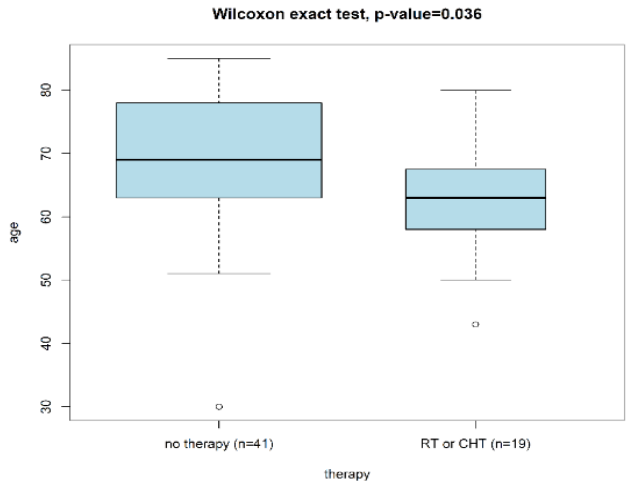

Fig. 2. Age-related characterization of groups with no therapy a with oncotherapy (RT or CHT).

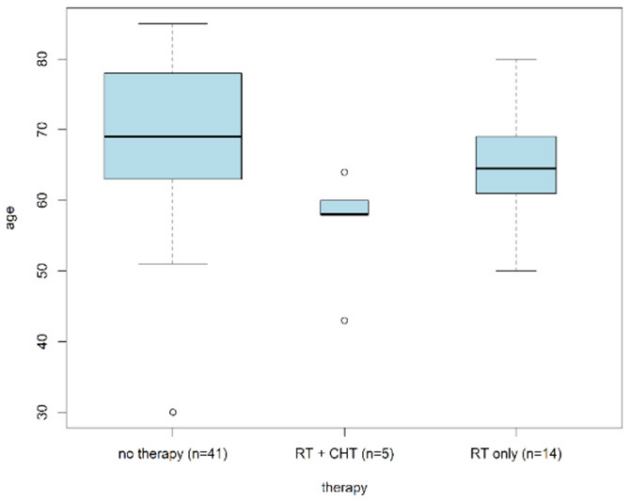

Fig. 3. Age-related characterization of groups with no therapy, with chemoradiotherapy (RT+CHT) and radiotherapy (RT) only.

ly able to receive complete oncological treatment were younger and in better clinical condition than patients who did not received complete oncological treatment (Fig. 3).

Mean survival time among the group of patients who received a biopsy was 2.8 months regardless of the treatment provided. Patients who did not receive treatment and, thus, had a worse general prognosis, showed an average survival time of 2.3 months (Fig. 4).

Patients who received oncological treatment experienced an increase in OS relative to the other patients. Mean survival time among the group of patients who had received any form of oncological treatment (RT or CH + RT) was 3.7 months (Fig. 4). Of these patients, those who had only received radiotherapy had a mean survival time of 3.1 months (6 women and 8 men). Patients with RT only received radiation in hypofractioned schedule (36Gy/6 fractions – 44Gy/10 fractions). According to literature these schemes offer the resembling efficacy as a standard fractioned RT (ref.[12,13]). Patients who received complete oncological treatment (Stupp protocol) had a survival time of 6.6 months. This group comprised five men of younger age who were primarily in good clinical condition (Fig. 5).

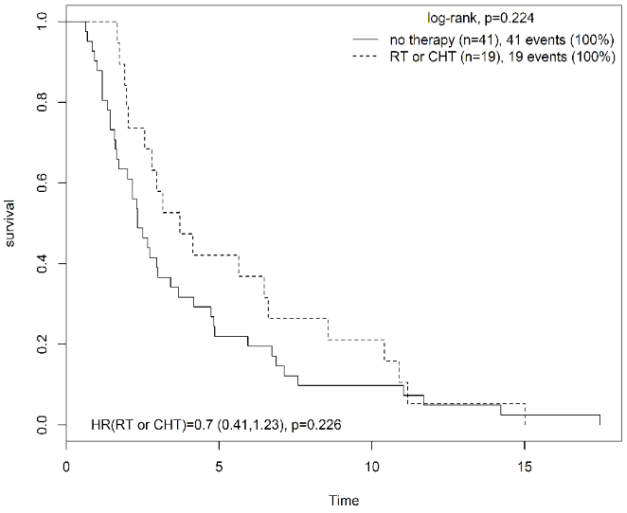

Fig. 4. Survival of patients in groups with no therapy a with oncotherapy (RT or CHT).

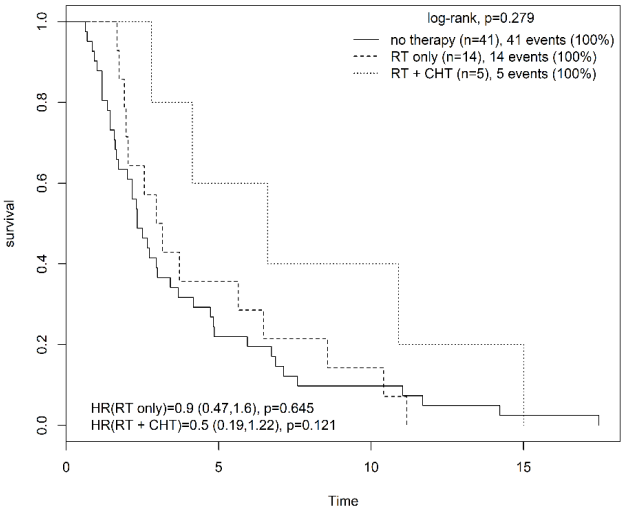

Fig. 5. Survival of patients in groups with no therapy a with no therapy, with chemoradiotherapy (RT+CHT) and radiotherapy (RT) only.

DISCUSSION

The 2021 EANO guidelines highlight that resection or tumor biopsy followed by oncotherapy in accordance with the Stupp protocol is the standard treatment strategy in GBM patients who are under 70 years of age and have a Karnofsky performance status above 70 (ref.[14]). Prognostic factors in GBM patients include age, preoperative neurological findings, tumor location, and the possibility for successful radical resection[15]. Thus, tumor resection is both therapeutic and diagnostic in nature. Advances in diagnostic and surgical techniques related to the treatment of GBM in recent decades now enable professionals to safely perform radical resections even in eloquent brain areas[16]. A patient who, for whichever reason, is not suitable for resection will experience a major reduction in their life expectancy.

Stereotactic biopsy is a robust and minimally invasive procedure to characterize lesions of the central nervous system[5-7]. Currently, frameless biopsy techniques – which are better accepted and tolerated by patients – are the preferred option. With regard to trajectory accuracy, complication rates, and diagnostic results, a recent prospective and randomized trial failed to confirm a difference between frame-based and frame-less procedures[10].

In case resection cannot be safely performed, biopsy is clearly the method of choice. Based on our experience, image-guided or stereotactic biopsy is the last option in the diagnostic-therapeutic process. The goal of the procedure is merely to diagnose an intracranial lesion; this approach cannot influence the mass effect of the tumor or its perifocal edema. Needle biopsy is reserved for multimorbid patients and/or those with an unfavorable clinical condition, and for patients with tumors situated deep in the brain, e.g., lesions which infiltrate the midline structures (corpus callosum, thalamus, basal ganglia), or for multilocular expansions.

The purpose of performing a biopsy in inoperable lesions is to first prevent misdiagnosis, as well as collect biomarkers which enable professionals to choose the optimal treatment strategy. In this study, patients who were able to undergo oncological treatment experienced a slight increase in their overall survival. Patients who received no additional treatment had an average survival time of 2.3 months. An average survival time of patients with any type of oncological treatment was 3.7 months. In the group with RT alone was a mean survival of 3.1 months. The effect of this treatment was enhanced in patients with favorable clinical factors such as age and Karnofsky score. So, patients who received oncological treatment with the Stupp protocol were younger (Fig. 3 and 5), in good clinical condition (Karnofsky score > 70) and had a survival time of 6.6 months.

However, the biopsy procedure only collects small amounts of tumor tissue, which limits the possibility for a comprehensive range of cytogenetic investigations[17]. On the other hand, obtaining a histological diagnosis allows professionals to stop active treatment and start symptomatic, palliative therapy.

As we have already mentioned, aggressive chemoradiotherapy in Stupp regime emerges the best results. Based on the poor clinical conditions of patients with GBM verified by the stereotactic biopsy alone, the oncotherapy usually have to be modified. GBM retrospective studies have demonstrated the same effectiveness of hypofractionated radiotherapy in elderly patients or in the patients with unfavorable clinic status. To preserve acceptable quality-of-life, the crucial issue is concerned on the control of the tumor progression and elimination of adverse RT effects[12].

Generally, a decision to initiate palliative care without histological diagnosis should be avoided. The reasons for omitting biopsy are a high risk of complications associated with the decision to perform a needle biopsy, patients with a very bulky tumor, or patients with a very poor, or rapidly deteriorating, clinical condition despite conservative therapy. Advanced MRI technics such as dynamic contrast-enhanced, and dynamic susceptibility contrast imaging, arterial spin labeling and diffusion MRI, vessel imaging, relaxometry and MR fingerprinting, magnetic resonance spectroscopy, chemical exchange saturation transfer, susceptibility-weighted imaging, MRI-PET, MR elastography are very helpful to identify border or infiltration zone of tumor, to distinguish tumor and nontumor lesions, to define biologic behavior of tumor. If the brain tumors do not even eligible for a stereotactic biopsy, some of these tools (diffusion MRI, magnetic resonance spectroscopy, MRI-PET) can improve the diagnostic discrimination accuracy of the intracranial lesion imaging. But, due to the brain tumor structural and metabolic heterogeneity, no all results are absolutely unambigious[18,19]. PET imaging with amino acid tracers, particularly, is useful to reveal recurrent Glioblastoma, or hot-spot, upgraded tumor region in former low grade gliomas. Also, these PET imaging facilitates GBM border delineation before surgery, or before RT. FDG PET plays a more limited role than amino acid PET in the imaging of gliomas due to the high physiological uptake of FDG in normal brain grey matter[19].

CONCLUSION

Patients with a GBM diagnosis by needle biopsy represent a minority group with a dismal prognosis. For this reason, we would not recommend these patients to be included in comprehensive studies of GBM treatment options. We confirmed the literature on the slightly greater efficacy of RT only on survival, in comparison with a supportive, palliative therapy, in patients with stereotactic biopsy. This group usually comprises elderly patients, in unfavorable clinical conditions. On the other hand, we continue to consider the needle biopsy a standard beneficial, diagnostic tool, particularly for younger patients in a good clinical condition, with the unresectable glioblastoma and who are able to undergo following oncotherapy in Stupp regime. Although the present gold standard for the diagnosis in GBM is histologic investigation, in a very specific case, we can allow diagnosis per advanced MR imaging technics.

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REFERENCES

1. Louis DN, Perry A, Reifenberger G, von Deimling A, Figarella-Branger D, Cavenee WK, Ohgaki H, Wiestler OD, Kleihues P, Ellison DW. The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary. Acta Neuropathol 2016;131(6):803-20. doi: 10.1007/s00401-016-1545-1
2. Louis DN, Perry A, Wesseling P, Brat DJ, Cree IA, Figarella-Branger D, Hawkins C, Ng HK, Pfister SM, Reifenberger G, Soffietti R, von Deimling A, Ellison DW. The 2021 WHO Classification of Tumors of the Central Nervous System: a summary. Neuro Oncol 2021;23(8):1231-51. doi: 10.1093/neuonc/noab106
3. Di L, Heath RN, Shah AH, Sanjurjo AD, Eichberg DG, Luther EM, de la Fuente MI, Komotar RJ, Ivan ME. Resection versus biopsy in the treatment of multifocal glioblastoma: a weighted survival analysis. J Neurooncol 2020;148(1):155-64. doi: 10.1007/s11060-020-03508-6
4. Shah AH, Mahavadi A, Di L, Sanjurjo A, Eichberg DG, Borowy V, Figueroa J, Luther E, de la Fuente MI, Semonche A, Ivan ME, Komotar RJ. Survival benefit of lobectomy for glioblastoma: moving towards radical supramaximal resection. J Neurooncol 2020;148(3):501-8. doi: 10.1007/s11060-020-03541-5
5. Hamisch CA, Minartz J, Blau T, Hafkemeyer V, Rueß D, Hellerbach A, Grau SJ, Ruge MI. Frame-based stereotactic biopsy of deep-seated and midline structures in 511 procedures: feasibility, risk profile, and diagnostic yield. Acta Neurochir 2019;161(10):2065-71. doi: 10.1007/s00701-019-04020-1
6. Callovini GM, Telera S, Sherkat S, Sperduti I, Callovini T, Carapella CM. How is stereotactic brain biopsy evolving? A multicentric analysis of a series of 421 cases treated in Rome over the last sixteen years. Clin Neurol Neurosurg 2018;174:101-7. doi: 10.1016/j.clineuro.2018.09.020
7. Sciortino T, Fernandes B, Conti Nibali M, Gay LG, Rossi M, Lopci E, Colombo AE, Elefante MG, Pessina F, Bello L, Riva M. Frameless stereotactic biopsy for precision neurosurgery: diagnostic value, safety, and accuracy. Acta Neurochir 2019;161(5):967-74. doi: 10.1007/s00701-019-03873-w
8. Albert NL, Weller M, Suchorska B, Galldiks N, Soffietti R, Kim MM, la Fougère C, Pope W, Law I, Arbizu J, Chamberlain MC, Vogelbaum M, Ellingson BM, Tonn JC. Response Assessment in Neuro-Oncology working group and European Association for Neuro-Oncology recommendations for the clinical use of PET imaging in gliomas. Neuro Oncol 2016;18(9):1199-208. doi: 10.1093/neuonc/now058
9. Lobão CA, Nogueira J, Souto AA, Oliveira JA. Cerebral biopsy: comparison between frame-based stereotaxy and neuronavigation in

an oncology center. Arq Neuropsiquiatr 2009;67(3B):876-81. doi: 10.1590/s0004-282x2009000500018

10. Bradac O, Steklacova A, Nebrenska K, Vrana J, de Lacy P, Benes V. Accuracy of VarioGuide frameless stereotactic system against frame-based stereotaxy: prospective, randomized, single-center study. World Neurosurg 2017;104:831-40. doi: 10.1016/j.wneu.2017.04.104
11. Stupp R, Hegi ME, Mason WP, van den Bent MJ, Taphoorn MJ, Janzer RC, Ludwin SK, Allgeier A, Fisher B, Belanger K, Hau P, Brandes AA, Gijtenbeek J, Marosi C, Vecht CJ, Mokhtari K, Wesseling P, Villa S, Eisenhauer E, Gorlia T, Weller M, Lacombe D, Cairncross JG, Mirimanoff RO, European Organisation for Research and Treatment of Cancer Brain Tumour and Radiation Oncology Groups, National Cancer Institute of Canada Clinical Trials Group. Effects of radiotherapy with concomitant and adjuvant temozolomide versus radiotherapy alone on survival in glioblastoma in a randomised phase III study: 5-year analysis of the EORTC-NCIC trial. Lancet Oncol 2009;10(5):459-66. doi: 10.1016/S1470-2045(09)70025-7
12. Matsui JK, Perlow HK, Facer BD, McCalla A, Marrazzo L, Detti B, Scorsetti M, Clerici E, Scoccianti S, Navarria P, Trifiletti DM, Gondi V, Bovi J, Huang J, Brown PD, Palmer JD. Radiotherapy for elderly patients with glioblastoma: an assessment of hypofractionation and modern treatment techniques. Chin Clin Oncol 2022 Oct;11(5):38. doi: 10.21037/cco-22-76
13. Asmaa A, Dixit S, Rowland-Hill C, Achawal S, Rajaraman C, O'Reilly G, Highley R, Hussain M, Baker L, Gill L, Morris H, Hingorani M. Management of elderly patients with glioblastoma-multiforme-a systematic review. Br J Radiol 2018;91(1088):20170271. doi: 10.1259/bjr.20170271
14. Weller M, van den Bent M, Preusser M, Le Rhun E, Tonn JC, Minniti G, Bendszus M, Balana C, Chinot O, Dirven L, French P, Hegi ME, Jakola AS, Platten M, Roth P, Rudà R, Short S, Smits M, Taphoorn MJB, von Deimling A, Westphal M, Soffietti R, Reifenberger G, Wick W. EANO guidelines on the diagnosis and treatment of diffuse gliomas of adulthood. Nat Rev Clin Oncol 2021;18(3):170-86. doi: 10.1038/s41571-020-00447-z. Erratum in: Nat Rev Clin Oncol 2022;19(5):357-8.
15. Chaichana KL, Garzon-Muvdi T, Parker S, Weingart JD, Olivi A, Bennett R, Brem H, Quiñones-Hinojosa A. Supratentorial glioblastoma multiforme: the role of surgical resection versus biopsy among older patients. Ann Surg Oncol 2011;18(1):239-45. doi: 10.1245/s10434-010-1242-6.
16. Gallet C, Clavreul A, Morandi X, Delion M, Madec N, Menei P, Lemée JM. What surgical approach for left-sided eloquent glioblastoma: biopsy, resection under general anesthesia or awake craniotomy? J Neurooncol 2022;160(2):445-54. doi: 10.1007/s11060-022-04163-9
17. Vuorinen V, Hinkka S, Färkkilä M, Jääskeläinen J. Debulking or biopsy of malignant glioma in elderly people - a randomised study. Acta Neurochir 2003;145(1):5-10. doi: 10.1007/s00701-002-1030-6
18. Hirschler L, Sollmann N, Schmitz-Abecassis B, Pinto J, Arzanforoosh F, Barkhof F, Booth T, Calvo-Imirizaldu M, Cassia G, Chmelik M, Clement P, Ercan E, Fernández-Seara MA, Furtner J, Fuster-Garcia E, Grech-Sollars M, Guven NT, Hatay GH, Karami G, Keil VC, Kim M, Koekkoek JAF, Kukran S, Mancini L, Nechifor RE, Özcan A, Ozturk-Isik E, Piskin S, Schmainda K, Svensson SF, Tseng CH, Unnikrishnan S, Vos F, Warnert E, Zhao MY, Jancalek R, Nunes T, Emblem KE, Smits M, Petr J, Hangel G. Advanced MR Techniques for Preoperative Glioma Characterization: Part 1. Magn Reson Imaging 2023;57(6):1655-75. doi: 10.1002/jmri.28662
19. Hangel G, Schmitz-Abecassis B, Sollmann N, Pinto J, Arzanforoosh F, Barkhof F, Booth T, Calvo-Imirizaldu M, Cassia G, Chmelik M, Clement P, Ercan E, Fernández-Seara MA, Furtner J, Fuster-Garcia E, Grech-Sollars M, Guven NT, Hatay GH, Karami G, Keil VC, Kim M, Koekkoek JAF, Kukran S, Mancini L, Nechifor RE, Özcan A, Ozturk-Isik E, Piskin S, Schmainda KM, Svensson SF, Tseng CH, Unnikrishnan S, Vos F, Warnert E, Zhao MY, Jancalek R, Nunes T, Hirschler L, Smits M, Petr J, Emblem KE. Advanced MR Techniques for Preoperative Glioma Characterization: Part 2. J Magn Reson Imaging 2023;57(6):1676-95. doi: 10.1002/jmri.28663