

## Carmustine Wafer Implantation at the Era of Standardized Chemoradiation Protocol

Sir,

We read with great interest the recent paper by Salle *et al.*, entitled (adverse event with the use of carmustine wafers and postoperative radiochemotherapy for the treatment of high-grade glioma).<sup>[1]</sup> The authors report a single-case experience about carmustine wafer implantation (CWI) in a newly diagnosed glioblastoma.

First, we have concerns about how the efficacy and indications of CWI have been presented as well as discussed. Here, the authors mix together different subtypes of high-grade gliomas under the generic name “high-grade gliomas,” but the current standard of care, they refer to actually differ between high-grade glioma subtypes. This should be detailed as is directly impacts the indication for CWI in high-grade gliomas, as recently proposed in French Neurosurgical Guidelines.<sup>[2]</sup>

Second, the case presentation lacks the information as whether corticosteroids were administered or not following surgical resection and at the beginning of chemoradiotherapy? This is of paramount importance since their administration in the early postoperative period is highly recommended to reduce CWI-related edema.<sup>[2]</sup> In addition, since the upper limb monoplegia occurred 4 weeks after surgery and 1 week after starting the chemoradiotherapy, this edema-related event can be hypothetically attributed equally to chemoradiotherapy and/or to CWI and no follow-up imaging, except the early postoperative computed tomography-scan, is available to document the timing of edema extension. As a consequence, the conclusions of this case report cannot be drawn at the light of the presented clinical data.

Third, the literature review of CWI-related adverse events is incomplete and the statement that “only small retrospective studies assess the risks of multimodal treatment strategies combining local and systemic chemotherapy with radiotherapy,” if possibly thoughtful in 2010 at the time of the Bock *et al.* study, is no longer true.<sup>[3]</sup> The current literature<sup>[4-7]</sup> and the experience of the neuro-oncology club of the French Society of Neurosurgery<sup>[2,8-10]</sup> adds significant data from large and prospective cohort studies. Recent systematic reviews, including studies performed at the standard radiochemotherapy era, did not show a significant increase of adverse effects related to CWI.<sup>[4-7]</sup> In addition, a French, prospective, observational, cohort study including 92 high-grade gliomas patients treated with surgical resection plus CWI followed by the standard radiochemotherapy protocol showed interesting survival results without increased adverse events.<sup>[8]</sup> Last, a recent

systematic review of the neuro-oncology club of the French Society of Neurosurgery analyzed the safety of CWI in 23 studies and suggested that the observed varying results about postoperative complications could be related to the experience of the surgeon who practices neurosurgical oncology procedures.<sup>[2]</sup> Last, in our own experience, the number of implanted wafers was not correlated with a higher risk of postoperative morbidity.<sup>[11]</sup> These results require a prospective evaluation, and no formal conclusion can be made.

As the authors stated that they choose a multimodal treatment, including CWI, whenever total resection of the tumor is possible, it will be of practical interest to the neuro-oncological community to report their whole experience rather than a single case.

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### Conflicts of interest

There are no conflicts of interest.

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### References

1. Salle F, Lahiani W, Spagnuolo E, Palfi S. Adverse event with the use of carmustine wafers and postoperative radiochemotherapy for the treatment of high-grade glioma. *Asian J Neurosurg* 2018;13:1171-4.
2. Roux A, Caire F, Guyotat J, Menei P, Metellus P, Pallud J, *et al.* Carmustine wafer implantation for high-grade gliomas: Evidence-based safety efficacy and practical recommendations from the neuro-oncology club of the French society of neurosurgery. *Neurochirurgie* 2017;63:433-43.
3. Bock HC, Puchner MJ, Lohmann F, Schütze M, Koll S, Ketter R, *et al.* First-line treatment of malignant glioma with carmustine implants followed by concomitant radiochemotherapy: A multicenter experience. *Neurosurg Rev* 2010;33:441-9.
4. Hart MG, Grant R, Garside R, Rogers G, Somerville M, Stein K, *et al.* Chemotherapeutic wafers for high grade glioma. *Cochrane Database Syst Rev* 2008;CD007294.
5. Hart MG, Grant R, Garside R, Rogers G, Somerville M, Stein K, *et al.* Chemotherapy wafers for high grade glioma. *Cochrane Database Syst Rev* 2011;CD007294.

6. Chowdhary SA, Ryken T, Newton HB. Survival outcomes and safety of carmustine wafers in the treatment of high-grade gliomas: A meta-analysis. *J Neurooncol* 2015;122:367-82.
7. Ashby LS, Smith KA, Stea B. Gliadel wafer implantation combined with standard radiotherapy and concurrent followed by adjuvant temozolomide for treatment of newly diagnosed high-grade glioma: A systematic literature review. *World J Surg Oncol* 2016;14:225.
8. Duntze J, Litré CF, Eap C, Théret E, Debreuve A, Jovenin N, *et al.* Implanted carmustine wafers followed by concomitant radiochemotherapy to treat newly diagnosed malignant gliomas: Prospective, observational, multicenter study on 92 cases. *Ann Surg Oncol* 2013;20:2065-72.
9. Menei P, Metellus P, Parot-Schinkel E, Loiseau H, Capelle L, Jacquet G, *et al.* Biodegradable carmustine wafers (Gliadel) alone or in combination with chemoradiotherapy: The French experience. *Ann Surg Oncol* 2010;17:1740-6.
10. Pallud J, Audureau E, Noel G, Corns R, Lechapt-Zalcman E, Duntze J, *et al.* Long-term results of carmustine wafer implantation for newly diagnosed glioblastomas: A controlled propensity-matched analysis of a French multicenter cohort. *Neuro Oncol* 2015;17:1609-19.
11. Pavlov V, Page P, Abi-Lahoud G, Nataf F, Dezamis E,

Robin A, *et al.* Combining intraoperative carmustine wafers and stupp regimen in multimodal first-line treatment of primary glioblastomas. *Br J Neurosurg* 2015;29:524-31.

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