CSF leak in transsphenoidal surgery

TO THE EDITOR: We read with great interest the article by Mehta and Oldfield (Mehta GU, Oldfield EH: Prevention of intraoperative cerebrospinal fluid leaks by lumbar cerebrospinal fluid drainage during surgery for pituitary macroadenomas. J Neurosurg 116:1299–1303, June 2012). The authors investigated the role of lumbar drainage in transsphenoidal surgery, comparing the results of 114 operations without an intraoperative CSF drain to 44 cases in which a lumbar subarachnoid catheter was placed before surgery to drain CSF at the time of tumor removal. The intraoperative CSF leak rate was significantly lower when the spinal drain was used; the postoperative CSF leak rate was the same (5%) in both groups. The authors’ conclusion is that intraoperative CSF drainage is useful, low risk, and obviates the need for sellar repair by lowering the intraoperative incidence of CSF leakage.

The article is of great interest because it provides new data to add to the ongoing discussion on the use of CSF drainage in transsphenoidal surgery. Most advocates stress the usefulness of lowering intracranial pressure (ICP) to allow a definitive sealing of the subarachnoid space; opponents underline the possible risks of lumbar drainage and the lack of clear indications for it. The authors support its use because it lowers the incidence of intraoperative CSF leaks and therefore diminishes the need of sellar reconstruction. Examining the article’s data, though, this conclusion does not seem to be supported; furthermore, some data, which would add even more value to the paper, are missing.

The most important clinical outcome reported by Mehta and Oldfield is that the rate of postoperative CSF leak does not decrease in the group with intraoperative drainage compared to the group without it; the rate was 5% in both groups. This might have two possible explanations: 1) the evidence of intraoperative CSF leaks in patients with lumbar drain is underestimated because of CSF diversion during surgery; 2) although the incidence of intraoperative CSF leaks is really lower, some other factors lead to postoperative leakage. The authors do not dwell on sellar packing, but they report that sellar reconstruction was performed less frequently when CSF diversion was used intraoperatively. Could this be the reason for the postoperative CSF leak? In Fig. 1 of their paper, the authors depict the physiopathogenesis of low-flow CSF leaks in transsphenoidal surgery: the removal of a macroadenoma leads to the descent of the suprasellar arachnoid, which then “weeps.” If sellar reconstruction is not performed in these cases, one could assume that a Valsalva maneuver (e.g., during extubation, coughing, or sneezing) might breach the arachnoid that is not supported. We could then interpret the reported data as support for sellar reconstruction rather than for CSF diversion (Fig. 1). This was indeed the case in our clinical practice: When we were not systematically using sellar packing with the endoscopic approach, we observed a postoperative CSF leak in a patient in whom no intraoperative CSF leakage occurred; postoperatively, the patient developed pneumonia, with persistent coughing, and subsequent evidence of a CSF leak.

In other words, if the incidence of postoperative CSF leakage is the same regardless of whether we use an intraoperatively placed lumbar catheter, then the major benefit of lumbar drainage lies in lowering the incidence of intraoperative CSF leaks, which is what the authors report. However, the lack of data on sellar packing makes it difficult to draw firm conclusions. Further studies are needed to clarify the role of lumbar drainage in transsphenoidal surgery.

Fig. 1. Artist’s renderings of macroadenoma removal. Once the macroadenoma has been removed, normal ICP causes a descent of the suprasellar arachnoid in the sella (A and B). If no packing is used (C), there is an increased risk of postoperative CSF leakage, especially if the ICP is increased. If sellar packing is used (D), the breach of the suprasellar arachnoid might be less likely because the ICP is counterbalanced by the packing itself. Copyright Francesco Doglietto. Published with permission. Figure is available in color online only.
operative CSF drain or not, could we hypothesize that the advantage of CSF diversion was lost due to decreased sellar reconstruction? This would be a noteworthy conclusion, as many authors do not perform any sellar reconstruction when no CSF leak is evident."

It would also be interesting to provide other data for this population, which are possibly taken for granted, but would add support to the authors’ conclusions. Was the tumor removal rate the same for both groups? One might question the maneuver of intraoperatively lowering the CSF leak pressure because it might decrease the chance of tumor removal.

Finally, we would like to thank the authors for their contribution: the paper has the merit of providing significant data to the ongoing debate about the role of intra- and postoperative CSF diversion in transphenoidal surgery from a study that would be difficult to perform in most centers.

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References

Response
Intraoperative CSF leaks are encountered frequently during surgery for pituitary macroadenomas, often require additional surgery of various types for repair, and can lead to postoperative CSF leakage. In 2012, we reported the results of a study using lumbar CSF drain placement after general anesthesia, just before beginning surgery, and CSF drainage during surgery to prevent CSF leaks during resection of pituitary macroadenomas. When compared with similar patients who had surgery before this protocol was instituted, we found that intraoperative CSF drainage reduced the rate of CSF leaks during surgery for macroadenomas with suprasellar extension, from 57% to 5% (p < 0.001). This, in turn, diminished the need to perform a fat graft harvest to repair an intraoperative CSF leak or postoperative lumbar drainage to prevent a postoperative leak. This reduction in the need to perform additional surgery or subject the patients to prolonged CSF drainage and bed rest was the principal benefit of this protocol, as we did not find a difference in the rates of postoperative CSF leaks between groups (5% in each).

We appreciate the interest of Doglietto and colleagues in our report. In their letter, they emphasize this last finding that no change in the rate of postoperative CSF leak occurred. We respectfully disagree with their, not our, interpretation that this was “the most important clinical outcome.” Rather, our study was specifically designed to test the effect of CSF drainage on intraoperative CSF leaks. Moreover, in our study it was not appropriate to reach a conclusion based on only the two instances of postoperative CSF leak in patients with intraoperative CSF drainage because, even had there been no postoperative CSF leaks in this group, our study was not powered to prove a difference (p = 0.32, Fisher’s exact test).

Doglietto and colleagues state that we indicate that the use of intraoperative CSF drainage “obviates the need for sellar repair by lowering the intraoperative incidence of CSF leakage,” that we “report that sellar reconstruction was performed less frequently when CSF diversion was used intraoperatively,” and suggest that a lack of sellar floor repair in the group with CSF drainage may explain the two postoperative CSF leaks. We did not make those statements, and do not now. As we stated in the Methods section of that report, “The surgical technique, including methods of sellar floor repair and observations during surgery leading to sellar floor repair, was uniform throughout all stages of the study.” We agree that after surgery for macroadenomas downward relaxation of the diaphragma sella could result in a persistent CSF fistula, and in cases with a large defect of the anterior face and floor of the sella, reconstruction of the sella face and floor may be necessary. Most patients in both groups, with or without intraoperative CSF drainage, underwent reconstruction of the sella. In most cases a small portion of gelatin sponge was placed within the sella to prevent extreme downward prolapse of the remaining sella contents and the diaphragm sella, and bone harvested during the approach, or a porous polyethylene implant, was used to reconstruct the anterior face and floor of the sella. In most cases a synthetic hydrogel was used to keep this reconstruction in place.

Finally, preoperative CSF drainage did not affect the rate of gross-total resection. With the operating microscope we typically visualize the suprasellar contents and the diaphragm with a Valsalva maneuver and do so despite intraoperative CSF drainage. As reported by Dalla-Piazza et al., by using the techniques that we describe, the rate of gross-total resection (83% documented by MRI at 1 year) of nonfunctioning adenomas (Knosp Grade 2 or less) was similar to that of the purely endoscopic approach performed by an experienced and skilled endoscopic pituitary surgeon.

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Low dose rate brachytherapy for the treatment of brain metastases

TO THE EDITOR: With high interest we follow the work of Wernicke et al. and appreciated their article (Wernicke AG, Yondorf MZ, Peng L, et al: Phase I/II study of resection and intraoperative cesium-131 radioisotope brachytherapy in patients with newly diagnosed brain metastases. J Neurosurg 121:338–348, August 2014) suggesting a combination of resection followed by the intraoperative placement of cesium-131 (131Cs) seeds into the resection cavity for interstitial low dose rate brachytherapy to treat selected patients with brain metastases.16 Applying this technique in 24 patients in the setting of a prospective Phase I/II study, the authors demonstrate not only the feasibility and a relatively low procedural complication rate of 12.5% (3 patients: infection, dural fistula, and seizures) but also show a reasonable efficacy regarding local tumor control (freedom from progression after 1 year of 93.8% (95% CI 63.2%–99.1%) as a valuable local treatment concept.7

This report supports in general the feasibility, oncological efficacy, and safety of (stereotactically guided) brachytherapy for the treatment of well-circumscribed brain tumors with a diameter less than 4 cm. It goes well in line with recent reports using this minimally invasive technique in selected patients with low- and high-grade gliomas as well as metastases that are not eligible for resection due to localization in eloquent structures such as the thalamus, pontine, and central sulcus.2,3,5–11,13,14

Wernicke et al.16 suggest the use of 131Cs due to the high initial dose rate (0.342 Gy/hr), which, in their opinion, is superior to the dose rate of iodine-125 (I251). This statement is correct for the method described in their study when leaving the seeds in place (permanent implantation). However, I251 can deliver equal dose rates when applied temporarily. This approach requires the removal of the seeds after a defined time.7

Treating over 1200 brain tumor patients with brachytherapy at the University of Cologne, we use a different method from that described by Wernicke et al.16 We place high-activity seeds into catheters that are then implanted and stereotactically guided into the target volume. After delivery of the prescribed surface dose, the seed catheters can easily be removed after local anesthesia is administered. This allows a temporary exposure with comparable dose rates also adapting the presumed reproduction cycle of fast proliferating tumor cells (e.g., metastases and malignant gliomas). Furthermore, we use special planning software that enables for each patient the individual calculation of surface dose, dose conformity, and number and activity of seeds prior to surgery. In addition, we combine stereotactic placement of the catheters containing the seeds with intraoperative radiography (or CT imaging) allowing the detection and correction of potentially displaced seeds within one surgical procedure.11,15 Finally, this method also allows the later comparison of the brachytherapy irradiation plan and follow-up imaging to differentiate radiation-induced tissue changes from local or loco-regional recurrences.2,5–11,14,15

As primary and stand-alone treatment we applied stereotactic implantation of 125I seeds (temporary implantation for 35–42 days; surface dose 50 Gy; initial dose rate 150–175 cGy/day) in 90 patients with singular cerebral metastases. Actuarial local tumor control was 94.6%. The median overall survival was 8.5 months and 18.1 months for the subgroup of patients with recursive partitioning analysis Class I characteristics. Procedure-related mortality was zero, morbidity was transient and low (3.3%), and there was no radiation-induced necrosis requiring surgical intervention.11 This also holds true for local recurrences after previous irradiation (whole-brain radiation therapy [WBRT], stereotactic radiosurgery [SRS]).6

The concept of using low dose rate implantation schemes applied by Wernicke et al.16 and routinely used by our and other German groups avoids substantial radiation-induced toxicity compared with formerly reported and frequently criticized high-dose and high dose rate brachytherapy schemes for malignant gliomas and metastases6,4,12 but still enables a remarkable oncological (local) outcome in select patients. Being restricted to one surgical procedure within a very short hospital stay, patients can immediately receive parallel treatment for their systemic disease. Furthermore, due to the very localized nature of the brachytherapy treatment, later percutaneous irradiation (WBRT, SRS) for distant local cerebral disease may be administered. Overall, (stereotactic) low dose rate brachytherapy should—as one of the oldest neurosurgical techniques—maintain its legitimation as safe and effective treatment option for select patients.

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References


Response

In response to the Letter to the Editor by Ruge, Rueß, Hellerbach, and Treuer, we would like to express our appre- ciation of the support the authors expressed for our recent article and encouragement for the appropriate application of the long-standing tradition of radioisotope brachytherapy. In our publication, we demonstrate that intraoperative brachytherapy at the time of neurosurgical resection has tremendous clinical advantages to patients not only in terms of convenience but also with respect to radiobiology of the tumor and achieving local control. In essence, a patient with a newly diagnosed metastasis is rendered 2 procedures at the same time: a maximally safe neurosurgical resection and an adjuvant radiation therapy —all achieved in one setting. Such one-time combination therapy obviates the need for fractionated radiotherapy, which requires a number of visits to radiation facilities, planning sessions, additional imaging, financial expenditure, and time commitment. But more than convenience, from the prospective of radiation biology, immediate application of radiotherapy in a form of brachytherapy addresses and minimizes the concerns of tumor cell repopulation and repair, which are associated with delaying the start of radiation due to the healing of the surgical wound and fractionation of standard external beam radiation schedule.

We present 131Cs as a novel permanent FDA-cleared stranded radioisotope that has physical advantages over many older radioactive seeds. Historically, brachytherapy in brain tumors has seen its light many decades ago with 125I with various rates of success and side effects, in particular, a high risk of radiation necrosis of up to 26%,1,2,3,5,6,8,9 Permanent placement of a radioisotope spares a patient the second surgery associated with the removal of temporarily placed seeds. The dose distribution of 131Cs is rather compact and its half-life is quite short, compared with 125I, which may explain the low incidence and the general risk of radiation necrosis. Unlike the external technique of SRS, which produces the best results of local control in tumors smaller than 3 cm,4 implantation with 131Cs produces excellent results irrespective of the size of the resected tumor and produces a high dose homogeneity and conformality indexes.

We applaud our colleagues from the University of Cologne for their tireless efforts in treating patients with brain tumors with intraoperative brachytherapy. Their center has been employing 125I with initial dose rate of 150–175 cGy/day and with great success: excellent rates of local control of 94.6% in patients with recursive partitioning analysis Class 1 and low incidence of side effects of 3.3% and no radiation necrosis.7 The methodology of using high-activity seeds placed into the stereotactically guided target volume allows for a temporary exposure to patients with brain metastases. It involves pre-planning, real-time intraoperative CT imaging or radiography for rendering accuracy of detection and correction of potentially displaced seeds and potentially avoids seed migration.10 However, we would argue that the methodology used by our group is much more patient friendly as well as just as effective. Based on the dimensions of the metastasis on the preoperative MRI, we are able to predict the number of seeds that will be utilized in the operating room, relying on the calculations carried out as dictated by nomogram developed by our physics group. We use 131Cs stranded seeds, which do not have the tendency of migrating as easily as the loose seeds.
by virtue of being stranded on a suture. Further advantage with our technique is that it does not require any additional time under anesthesia for image verification with a CT scan or radiograph, thus decreasing the overall time under anesthesia and in the operating room. Our quality assurance process takes place 24–48 hours after the surgery in the dedicated CT simulator in our department with the subsequent generation of the full plan reflecting the dose distribution. Lastly, we feel that a tremendous advantage to brachytherapy with the $^{131}$Cs technique is its quick delivery (90% of the dose is delivered in 1 month), thus allowing the patients to commence systemic therapy.

We are completing the expanded analysis of all of our patients accrued to the trial and will be publishing our updated results with mature follow-up in the near future. But our freedom from progression at 1 year of 93.8% and a minimal rate of complications, including 0% of radiation necrosis, reflect that the application of $^{131}$Cs in the newly resected brain metastases holds a very promising future. Additionally, we have gained promising results by implanting patients with recurrent but previously irradiated metastases, whether with WBRT, SRS, or a combination thereof (WBRT+SRS). In conclusion, we are convinced that there is a clear role for the permanent low dose rate $^{131}$Cs brachytherapy in patients with resected metastases as a patient-friendly, safe, and effective option that achieves excellent and durable local control, minimal radiation necrosis, and allows quick recovery and initiation of systemic therapy.

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