

# Intraoperative Chemotherapy for Leptomeningeal Metastases After Ommaya Placement

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## Research Article

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# Abstract

## Introduction

There is a wide variety in the timing of the first intraventricular chemotherapy dose after Ommaya reservoir placement. Given the rapid nature of leptomeningeal metastasis, it is important to avoid any delays in treatment in order to have the optimal therapeutic benefit. We present the first series of immediate intraoperative intraventricular infusion of chemotherapy after Ommaya placement.

## Methods

A single-institution, retrospective review of twenty patients who underwent surgical placement of an Ommaya reservoir from 2012 to 2020 and had intraoperative infusion of chemotherapy was conducted. Inclusion criteria consisted of patients 18 years and older with a diagnosis of leptomeningeal metastases, central nervous system lymphoma or leukemia. Outcomes such as leukoencephalopathy, wound healing, intracranial hemorrhage, catheter malfunction, Ommaya days, mortality, and other complications were reviewed.

## Results

The mean patient age was 55.1 years and the most common diagnosis was breast cancer (40%). All catheters were placed into the ventricular system, and there were no wound healing complications, infections or symptomatic leukoencephalopathy. Intraventricular chemotherapy was administered for a total of 201 cycles and a mean of 10 times per patient. The number of Ommaya days ranged from 7 to 2177, with a mean of 326.5 days, and 30-day mortality was 10%.

## Conclusions

Ommaya reservoirs are effective intraventricular delivery mechanism for chemotherapy in patients with leptomeningeal metastases. Endoscopy-assisted placement of Ommaya catheters provides a real-time, visual confirmation of adequate placement. Immediate intraoperative intraventricular infusion of chemotherapy after Ommaya placement is safe, effective, and may increase efficiency in time to treatment for patients.

## Introduction

Patients with metastatic cancer are living longer due to multifactorial improvement in overall medical management. Benign tumors and metastatic cancer are increasingly diagnosed at earlier stages secondary to the ease of access and sensitivity of imaging modalities such as magnetic resonance imaging (MRI). The discovery of targeted molecular and genetically based treatments has also improved survival of cancer patients. Longevity resulting from these factors has translated into a significant number of patients with leptomeningeal metastases and carcinomatous meningitis [1-3]. Melanoma, lung and breast cancer have the highest incidence of leptomeningeal metastasis with rates at 23%, 9-25%, and 5% respectively, but intraventricular metastases can also be seen in less common pathologies such as colorectal cancer [1, 4-6].

The mainstay of treating of leptomeningeal metastases and central nervous system (CNS) leukemia and lymphoma has been the addition of intra-cerebrospinal fluid (CSF) chemotherapy to a combination of radiotherapy and systemic chemo- or immunotherapy [7]. Historically, this has been performed with repeated lumbar punctures which are uncomfortable and have risks such as epidural hematoma and meningitis in patients who are typically thrombocytopenic and immunosuppressed. In addition, the drug distribution of lumbar intrathecal injections is fraught with potential delivery risks such as epidural injections, inadequate CSF penetration which can occur in up to 10% of intralumbar injections [8,9], and variable or low drug concentration in the intracranial compartment which directly impacts therapeutic efficacy [10]. Given these drawbacks, Ommaya reservoirs have become the standard of care for intra-CSF delivery of drugs in patients with CNS leukemias, lymphomas and leptomeningeal metastases.

Most of the publications on Ommaya reservoirs over the past two decades have focused on ways to improve intraoperative placement and complication rates. Adjuncts of surgical placement such as pneumoencephalography [11], neuronavigation [12] and endoscopy [13] have been evaluated. These studies have also focused on the analysis of frame-based versus frameless image navigation [14]. Most of these publications have not addressed the timing of their first intraventricular chemotherapy dose. The few papers that do mention the timing of their earliest dose have ranged from five days to four hours post-placement [15-17]. In most cases, patients are discharged on the first postoperative day, and the infusion and timing of intraventricular chemotherapy is left to the patients' oncologist. Given the rapidly progressive nature of leptomeningeal metastasis and the dismal prognosis of this disease, it is important for patients to avoid any delays in treatment in order to have the optimal therapeutic benefit. Concerns of leukoencephalopathy, wound healing and adequate ventricular placement confirmation have been previously cited reasons why the infusion of chemotherapeutic agents should be delayed after Ommaya placement. We present the first series of immediate intraoperative intraventricular infusion of chemotherapy after Ommaya placement, and we review the risks, complications and outcomes in twenty patients.

## Methods

### Search Strategy and Selection Criteria

A single-institution, retrospective review of patients who underwent surgical placement of an Ommaya reservoir from 2012 to 2020 and had intraoperative infusion of chemotherapy was conducted. The inclusion criteria consisted of patients 18 years of age and older with a diagnosis of leptomeningeal metastases, CNS lymphoma or leukemia, and who underwent first-time Ommaya reservoir placement with intraoperative infusion of chemotherapy. The medical records over the 8-year period were reviewed to record variables such as patient age at diagnosis, sex, pathological diagnosis, intraventricular drug type, number of infusions, perioperative antibiotic use, systemic treatment, final ventricular catheter tip location, catheter depth, and surgical adjuncts. Outcomes such as leukoencephalopathy, wound healing, postoperative [computed tomography](#) (CT) findings, intracranial hemorrhage, catheter malfunction, Ommaya days, 30-day mortality and overall mortality were reviewed. Informed consent was obtained for all patients. All surgeries were performed by the last author (R.M.C.) except one patient which was performed by the second author (J.S.Y.).

They are both experienced attending neurosurgeons who are very familiar with neuroendoscopy and neuronavigation.

### Statistical Analysis

Statistical analysis was completed using Microsoft Excel, Microsoft Office 365 (Microsoft Corporation, Redmond, WA). Continuous variables were expressed as mean  $\pm$  standard deviation, and categorical variables as percentages (%).

### Operative Technique

All patients had a previous preoperative MRI of the brain as part of their oncological workup. A preoperative stereotactic CT head was not obtained since endoscopy was the primary surgical adjunct in all cases. After patient identification and smooth induction of general endotracheal anesthesia, the head was positioned supine in gel head-holder with the nose directly up. Two grams of cefazolin was given. The entry point was measured as 11 cm posterior to the nasion and 3 cm laterally to the right (Kocher's point) with a curvilinear incision planned there. This area was shaved, prepped and draped in the usual sterile fashion. A proper time-out was performed. The incision was marked, infiltrated with bupivacaine and opened with a #10 blade. Dissection was continued to the level of the skull and the pericranium was spared. A generous pocket for the reservoir was created and the pericranium was mobilized at the bur hole site. A bur hole was created with a Midas Rex drill and an M8 attachment (Medtronic, Minneapolis, Minnesota, USA). The dura and pia were coagulated and fenestrated sequentially. Using the Medtronic NeuroPen and InnerVision ventricular catheter (Medtronic, Minneapolis, Minnesota, USA), the frontal horn of the right lateral ventricle was accessed. The catheter was advanced until the third ventricle was entered, and then trimmed to the appropriate length and attached to the reservoir with a suture. The reservoir was pulled in the pocket. The proximal catheter was placed in the catheter holder and anchored with 4-0 Nurolon sutures. The field is then irrigated with antibiotic containing solution, and a small gelfoam is placed in the bur hole. The wound is closed with Vicryl sutures for the galea and 4-0 Monocryl for the skin.

The Ommaya reservoir is then accessed, CSF is withdrawn, followed by injection of the recommended drug(s) previously ordered by the oncologist. Bacitracin and sterile dressings are applied. A letter 'X' is placed over the dome of the reservoir. The patient is then extubated and taken to the recovery room.

In the last two cases where image guidance was used in addition to endoscopy, the patients' preoperative stereotactic MRI or [CT scan](#) were registered with the patients' anatomy at the beginning of the case using the Medtronic StealthStation Navigation. A preoperative MRI of the brain without contrast was used in one, and a preoperative CT without contrast was used in the other. Both imaging were stereotactic sequences with skin fiducial markers. A stereotactic electromagnetic stylet placed through the InnerVision ventricular catheter was used to navigate the catheter insertion into the right lateral ventricle.

### Postoperative Management

The patients were admitted to the hospital for observation overnight and a routine postoperative Head CT was obtained within a few hours after surgery (Figure 1). Patients were typically discharged on the first postoperative day unless other inpatient needs are warranted. However, one patient was discharged on the same day. The patients' subsequent Ommaya injection schedules were determined by their oncologist.

## Results

### Patient Characteristics

Twenty patients met the selection criteria and their age at surgery range from 30 years to 79. The mean age was 55.1 years with a standard deviation of 13.1. Five patients (25%) were male and fifteen (75%) were female. The most common diagnosis was carcinomatous meningitis from breast cancer, occurring in 8 patients (40%), followed by non-small cell lung cancer in 4 patients (20%) and acute lymphocytic leukemia (ALL) in 3 patients (15%). The other five cases involved diagnoses of rhabdomyosarcoma, ovarian cancer, small cell lung cancer, Hodgkin lymphoma and diffuse large B-cell lymphoma.

### Treatment

The most common intraventricular treatment regimen was a single chemotherapeutic agent, which was employed in 60 percent of the cases (12 patients). Thirty-five percent (7) underwent the use of two different agents, and five percent (1) were treated with 3 different agents. Of the 12 patients who were treated with a single intraventricular agent, methotrexate was the most commonly used drug, employed in 5 cases. Thiotepa, cytarabine and trastuzumab alone were used in two patients each, and Rituximab alone was used to treat one patient. Of the seven patients who were treated with two agents over the course of their therapy, methotrexate was the most commonly used drug. The other drugs included in the combination were cytarabine, thiotepa, topotecan, trastuzumab and rituximab. The single patient treated with three different drugs received cytarabine, methotrexate and hydrocortisone. Based on available records, the number of times intraventricular chemotherapy was administered ranged from 1 to 23 times per patient for a total of 201 cycles. (Table 1) The mean number of administrations was 10 per patient with a standard deviation of 8.24. Ten patients received intravenous chemotherapy in addition to their intra-CSF treatment while one patient received additional oral chemotherapy. The other nine patients were treated with only intra-CSF medications.

### Outcomes

The 30-day mortality was 10% (2 patients), and two patients were lost to follow-up after initial treatment. Patient #20 relocated 32 days postoperatively after receiving 13 doses of intraventricular therapy while patient #3's last clinic visit was 77 days postoperatively and after 5 doses. Long-term all-cause mortality was 72.2% (13/18). There were no wound healing complications or documented infections. Based on postoperative imaging, all catheters were accurately placed in the third ventricle through the right frontal horn except in one patient with a catheter trajectory through the septum and distal tip in the left lateral ventricle. The catheter depth ranged from 7cm to 8.5cm from the outer table of the skull intraoperatively, and the mean depth was 7.9cm  $\pm$ 0.38. There were no patients with a previously placed ventriculoperitoneal

shunt, and only one patient had a postoperative shunt placement which was secondary to hydrocephalus. That patient underwent a right occipital shunt placement 1 week after her Ommaya reservoir was implanted. She developed headaches post-Ommaya placement and symptoms of speech, gait and cognition difficulties. The patient's symptoms improved after high volume CSF tap and a shunt was recommended. The number of Ommaya days ranged from 7 to 2177, and the mean was 326.5 days with a standard deviation of 524 days indicating a widely spread dataset. Ommaya days were calculated from the date of surgery until death or the date of data analysis for the 4 patients who were still alive with their catheters in place at the time of analysis. There were no patients with an external ventricular drain in place prior to surgery.

## Complications

One patient underwent removal of the Ommaya catheter and reservoir six days after placement due to a concern for infection. The patient presented with headaches, nausea, vomiting, a fever that started on her second post-operative day and incisional pain. She was readmitted and despite CSF showing no bacteria, the infectious disease and oncology team favored removal of the Ommaya reservoir and catheter. The device was then removed, and the final CSF, blood and intraoperative cultures were negative for any bacterial growth. There was no catheter malfunction, pseudomeningocele, CSF leak, infection or hemorrhage noted on postoperative imaging. One patient developed asymptomatic leukoencephalopathy on imaging about 4 months after Ommaya placement. A brain MRI 1 month after placement (Figure 2) compared with 10 months post-placement (Figure 3) revealed white matter changes along the catheter tract on FLAIR and T1 sequences and delayed loss of white matter and leukomalacia surrounding the catheter.

## Discussion

Since the invention of the Ommaya reservoir in 1963 [18], its use has evolved from the intra-CSF delivery of antifungal medications for which it was originally designed [19], to become the primary method of administering chemotherapeutic agents intraventricularly. Over the past two decades, as neuronavigation has gained prominence and become the standard of care for many neurosurgical procedures, its use in Ommaya placement has been frequently evaluated along with other surgical adjuncts such as endoscopy [11-14,16]. A meta-analysis by Lau et al. reviewed the operative complications of 43 pooled Ommaya studies, and reported an improvement in total surgical complication rate from 13.6% with conventional freehand placement to 6% with image navigation [14]. However, that study which is reportedly the largest observational analysis of operative Ommaya outcomes noted a higher risk of hemorrhage in image-guided surgical placements (3.4%) versus non image-guided placements (2.4%). Other complications such as catheter malfunction, malposition, early infection and mortality were shown to have a slight benefit with image guidance at rates of 2%, 2.3%, 0.7% and 0.6% respectively. Our results compare favorably with those of the meta-analysis as we had a 0% rate of catheter malfunction, infection, hemorrhage, CSF leak or pseudomeningocele. Of the 5 patients still alive at the time of data analysis, 3 (60%) were patients with carcinomatous meningitis from breast cancer, one had ALL and the other had Hodgkin lymphoma. Our longest surviving patient (2177 days post-placement) was the only one with a diagnosis of Hodgkin lymphoma which speaks to the curative nature of aggressive treatment in patients with this disease. Even

though our long-term mortality rate for leptomeningeal breast cancer was 62.5% (5/8), the second longest surviving patient (1421 days post-placement) was a breast cancer patient. However, she had a favorable molecular profile; estrogen, progesterone and Her2 positive, thereby highlighting the heterogeneity of breast cancer and the importance of molecular and genetic factors as prognostic indicators.

### Endoscopic placement

All the cases in our series utilized endoscopy assisted catheter placement and 90% of the cases used endoscopy alone without image navigation. We believe that direct visualization of the catheter tip within the ventricle using the endoscope provides a real-time visual confirmation of adequate placement which is not possible with other surgical adjuncts. There have only been a few publications that have mentioned the endoscopic-assisted Ommaya placement, and most of them have focused on placement into cystic craniopharyngiomas [11, 20-22]. Although a direct outcome-based comparison between image-guided placement and endoscopically placed Ommaya catheters have not been published, Wang et al. performed a retrospective cost-benefit analysis of placing Ommaya reservoirs with image guidance alone versus a combination of image guidance and neuroendoscopy [13]. This comparison revealed a cost benefit of \$4784 savings per patient with the endoscope group due to the high complication-associated costs of two mispositioned catheters and one catheter-related hemorrhage in the image-guidance only group.

### Timing of intraventricular administration

Very few published articles on Ommaya reservoirs have addressed the timing of intraventricular administration of chemotherapeutic agents after Ommaya placement. There is no consensus on the optimal or recommended time to start using Ommaya reservoirs after placement, and studies that have mentioned the time of use post-placement have varied from no earlier than 5 days postoperatively to as soon as 4 hours after implantation [15-17]. Classically, the recommendation to wait a few days prior to using an Ommaya reservoir post-placement was to allow for proper wound healing and to reduce the risk of backflow of the chemotherapeutic agent through the catheter tract [15]. However, there are no strong evidence for this stipulation although the rate of symptomatic leukoencephalopathy and neurotoxicity was reported to be 3% in a large series [17]. This compares to a 0% rate of neurotoxicity in our series and a 5% rate of asymptomatic leukoencephalopathy. With endoscopic placement of the catheter, the goal is to ensure that not only is the catheter within the ventricle, but all the holes of the catheter are intraventricular which would consequently limit the leakage of chemotherapy into the parenchyma.

Others have strongly recommended getting a postoperative head CT to confirm the location of the catheter tip prior to use [11]. In this review, we present the first report of intraoperative administration of chemotherapeutic agents immediately after Ommaya placement. Our 0% rate of wound dehiscence, infection, CSF leak, pseudomeningocele or symptomatic leukoencephalopathy provides evidence to counter the classic reasons and dogma to wait a few days prior to using Ommaya reservoirs post-placement. Patients with leptomeningeal disease and leukemic meningitis have a high risk of rapid disease progression and recent 12-month overall survival rates are as low as 10% with intra-CSF chemotherapy in patients with leptomeningeal breast cancer despite new molecular advances in therapeutic management [23]. It is therefore imperative to start intraventricular chemotherapy in these patients as soon as possible. In our

experience, we have also seen delays in patients receiving their intraventricular drugs post-discharge from the hospital due to unforeseen insurance, administrative and logistical difficulties. By administering the intraventricular therapy intraoperatively, patients at least start getting therapeutic benefit immediately even if unforeseen situation arises postoperatively. Additionally, intra-operative delivery is comfortable for the patient under anesthesia and is not subject to availability of the oncologist to deliver the medicine in the next few days postoperatively. There are also increasing issues with oncologists who may not have hospital privileges of administering intraventricular chemotherapy as it is rare. Intraoperative delivery limits the risk of patients waiting for an oncologist to deliver chemotherapy at a later date when their schedule permits and allows same day surgery for Ommaya reservoir placement and intraventricular chemotherapy treatment.

The risk of encephalopathy and neurotoxicity particularly from intraventricular methotrexate has been shown to be reducible by avoiding simultaneous combination of systemic and intraventricular chemotherapy [24]. This is because high dose systemic methotrexate will result in cytotoxic CSF concentrations within 24 to 72 hours after administration [25]. Although, we defer chemotherapeutic regimen to the patients' oncologist, it is advisable to avoid administering intraventricular methotrexate at the same time as systemic methotrexate.

### Catheter Malpositioning

Our data revealed that endoscopic placement of Ommaya reservoir can be associated with a 100% rate of ventricular placement or a 95% rate of accurate positioning within the third ventricle, and a postoperative head CT is not necessarily mandatory prior to using Ommaya reservoir due to the visual confirmation afforded by endoscopy. However, we still obtained a postoperative head CT after the intraoperative drug infusion in order to establish an imaging baseline. It is important to note that regardless of the surgical adjunct employed for Ommaya catheter placement, there is always a small risk of catheter malpositioning, albeit, smaller than that observed with free-hand placement. As demonstrated by our single case with the catheter tip in the contralateral ventricle, endoscopic guidance is not fool proof. Sandberg et al. reported that of 5 patients who required Ommaya catheter repositioning, one had been placed with an endoscope, two catheters were placed under fluoroscopic guidance, one with the use of stereotactic techniques, and one without any intraoperative aids [11].

## Limitations

This study is a single-institution retrospective review and is limited by its relatively small patient cohort. Leptomeningeal disease, leukemic meningitis and CNS lymphoma are rare diagnoses which inherently limited our cohort size. The variety of diagnoses included in this review also generalizes our results and outcomes, which should be applied specifically to the causative diagnosis. Of note, patients #18 and 19 who are still alive with leptomeningeal breast cancer had their surgeries within the past 15 months, and there is an expected survival bias towards patients with more recent surgeries. In addition, two patients were lost to long-term follow-up after initial treatment which influences our outcome analysis.

## Conclusions

Ommaya reservoirs are effective intraventricular delivery mechanism for chemotherapy in patients with central nervous system leukemias, lymphomas and leptomeningeal metastases. Endoscopy-assisted placement of Ommaya catheters provides a real-time, visual confirmation of adequate placement. Immediate intraoperative intraventricular infusion of chemotherapy after Ommaya placement is safe, effective, and may increase efficiency in time to treatment for patients.

## Abbreviations

ALL, Acute Lymphocytic Leukemia; CNS, Central Nervous System; CSF, Cerebrospinal Fluid; CT, Computed Tomography; MRI, Magnetic Resonance Imaging;

## Declarations

**Funding:** The authors did not receive support from any organization for the submitted work.

**Conflicts of interest/Competing interests:** The authors have no conflicts of interest to declare that are relevant to the contents of this article.

**Availability of data and material** (data transparency): The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

**Code availability** (software application or custom code): not applicable

**Authors' contributions:** All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Oluwaseun A. Omofoye and Ray M. Chu. The first draft of the manuscript was written by Oluwaseun A. Omofoye and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

**Ethics approval:** This research study was conducted retrospectively from data obtained for clinical purposes. Ethical approval was waived by the local Ethics Committee of Cedars-Sinai Medical Center in view of the retrospective nature of the study and all the procedures being performed were part of the routine care.

**Consent to participate:** not applicable

**Consent for publication:** not applicable

## References

1. Taillibert S, Chamberlain MC. Leptomeningeal metastases. In: Schiff D, Van den Bent MJ, eds. *Handbook of Clinical Neurology*. Elsevier (149);2018:169-204.
2. Kokkoris CP. Leptomeningeal carcinomatosis. How does cancer reach the pia-arachnoid?. *Cancer*. 1983;51(1):154-160. doi:10.1002/1097-0142(19830101)51:1<154::aid-cnrcr2820510130>3.0.co;2-k
3. Le Rhun E, Taillibert S, Chamberlain MC. Carcinomatous meningitis: Leptomeningeal metastases in solid tumors. *Surg Neurol Int*. 2013;4(Suppl 4):S265-S288. Published 2013 May 2. doi:10.4103/2152-

7806.111304

4. Rosen ST, Aisner J, Makuch RW, et al. Carcinomatous leptomeningitis in small cell lung cancer: a clinicopathologic review of the National Cancer Institute experience. *Medicine (Baltimore)*. 1982;61(1):45-53. doi:10.1097/00005792-198201000-00005
5. Aroney RS, Dalley DN, Chan WK, Bell DR, Levi JA. Meningeal carcinomatosis in small cell carcinoma of the lung. *Am J Med*. 1981;71(1):26-32. doi:10.1016/0002-9343(81)90254-0
6. Omofoye OA, Binello E. Intraventricular metastases from rectal carcinoma: case report and literature review. *J Biomed Res*. 2019;34(4):318-322. doi:10.7555/JBR.33.20180133
7. Bokstein F, Lossos A, Siegal T. Leptomeningeal metastases from solid tumors: a comparison of two prospective series treated with and without intra-cerebrospinal fluid chemotherapy. *Cancer*. 1998;82(9):1756-1763.
8. Chamberlain MC. Leptomeningeal metastasis. *Curr Opin Neurol*. 2009;22(6):665-674. doi:10.1097/WCO.0b013e3283322a92
9. Glantz MJ, Van Horn A, Fisher R, Chamberlain MC. Route of intracerebrospinal fluid chemotherapy administration and efficacy of therapy in neoplastic meningitis. *Cancer*. 2010;116(8):1947-1952. doi:10.1002/cncr.24921
10. Shapiro WR, Young DF, Mehta BM. Methotrexate: distribution in cerebrospinal fluid after intravenous, ventricular and lumbar injections. *N Engl J Med*. 1975;293(4):161-166. doi:10.1056/NEJM197507242930402
11. Sandberg DI, Bilsky MH, Souweidane MM, Bzdil J, Gutin PH. Ommaya reservoirs for the treatment of leptomeningeal metastases. *Neurosurgery*. 2000;47(1):49-55. doi:10.1097/00006123-200007000-00011
12. Takahashi M, Yamada R, Tabei Y, Nakamura O, Shinoura N. Navigation-guided Ommaya reservoir placement: implications for the treatment of leptomeningeal metastases. *Minim Invasive Neurosurg*. 2007;50(6):340-345. doi:10.1055/s-2007-993162
13. Wang A, Tenner MS, Schmidt MH, Bowers C. Placement of Ommaya Reservoirs Using Electromagnetic Neuronavigation and Neuroendoscopy: A Retrospective Study with Cost-Benefit Analysis. *World Neurosurg*. 2019;122:e723-e728. doi:10.1016/j.wneu.2018.10.127
14. Lau JC, Kosteniuk SE, Walker T, Iansavichene A, Macdonald DR, Megyesi JF. Operative Complications with and without Image Guidance: A Systematic Review and Meta-Analysis of the Ommaya Reservoir Literature. *World Neurosurg*. 2019;122:404-414. doi:10.1016/j.wneu.2018.11.036
15. Peyrl A, Chocholous M, Azizi AA, et al. Safety of Ommaya reservoirs in children with brain tumors: a 20-year experience with 5472 intraventricular drug administrations in 98 patients. *J Neurooncol*. 2014;120(1):139-145. doi:10.1007/s11060-014-1531-1
16. Lane J, Zacharia BE. Endoscopic-Assisted Ommaya Reservoir Placement: Technical Note. *Cureus*. 2017;9(7):e1490. Published 2017 Jul 19. doi:10.7759/cureus.1490
17. Chamberlain MC, Kormanik PA, Barba D. Complications associated with intraventricular chemotherapy in patients with leptomeningeal metastases. *J Neurosurg*. 1997;87(5):694-699. doi:10.3171/jns.1997.87.5.0694

18. Ommaya AK. Subcutaneous reservoir and pump for sterile access to ventricular cerebrospinal fluid. *Lancet*. 1963;2(7315):983-984. doi:10.1016/s0140-6736(63)90681-0
19. Witorsch P, Williams TW Jr, Ommaya AK, Utz JP. Intraventricular administration of amphotericin B. Use of subcutaneous reservoir in four patients with mycotic meningitis. *JAMA*. 1965;194(7):699-702. doi:10.1001/jama.194.7.699
20. Kuramoto T, Uchikado H, Tajima Y, Tokutomi T, Shigemori M. *No Shinkei Geka*. 2005;33(12):1207-1212.
21. Mori R, Joki T, Nonaka Y, Ikeuchi S, Abe T. Parallel insertion endoscopic technique for precise catheter placement in cystic craniopharyngiomas. *J Neurol Surg A Cent Eur Neurosurg*. 2014;75(6):442-446. doi:10.1055/s-0033-1349341
22. Joki T, Oi S, Babapour B, et al. Neuroendoscopic placement of Ommaya reservoir into a cystic craniopharyngioma. *Childs Nerv Syst*. 2002;18(11):629-633. doi:10.1007/s00381-002-0638-4
23. Figura NB, Rizk VT, Mohammadi H, et al. Clinical outcomes of breast leptomeningeal disease treated with intrathecal trastuzumab, intrathecal chemotherapy, or whole brain radiation therapy. *Breast Cancer Res Treat*. 2019;175(3):781-788. doi:10.1007/s10549-019-05170-7
24. Schlegel U, Pels H, Glasmacher A, et al. Combined systemic and intraventricular chemotherapy in primary CNS lymphoma: a pilot study. *J Neurol Neurosurg Psychiatry*. 2001;71(1):118-122. doi:10.1136/jnnp.71.1.118
25. Glantz MJ, Cole BF, Recht L, et al. High-dose intravenous methotrexate for patients with nonleukemic leptomeningeal cancer: is intrathecal chemotherapy necessary?. *J Clin Oncol*. 1998;16(4):1561-1567. doi:10.1200/JCO.1998.16.4.1561

## Tables

Table 1: Patient characteristics, diagnosis and treatment summary

Patient #	Age (years)	Sex	Diagnosis	Catheter depth (cm)	# of I-CSF infusions	I-CSF chemotherapy	Ommaya days
1	63	F	NSCLC	7.5	1	MTX	475
2	60	F	Breast cancer	7.5	4	MTX	16
3	79	F	NSCLC	8.5	5	Cytarabine, MTX	77†
4	52	M	Rhabdomyosarcoma	7.5	7	Thiotepa	53
5	67	F	SCLC	8.5	5	Thiotepa, MTX	81
6	67	M	NSCLC	8	1	Thiotepa	20
7	30	F	Hodgkin Lymphoma	8	9	Rituximab	2177*
8	31	F	ALL	8	1	MTX	7*
9	65	M	NSCLC	7.5	23	MTX	311
10	55	F	Breast cancer	8	1	MTX	75
11	36	F	Breast cancer	7.5	20	MTX, Topotecan	376
12	47	F	Ovarian cancer	8.5	23	MTX, Cytarabine	228
13	53	F	Breast cancer	7.5	21	Herceptin, Cytarabine	167
14	40	F	Breast cancer	8	23	Herceptin, Topotecan	1421*
15	72	M	DLBCL	8	6	MTX, Rituximab	273
16	57	M	ALL	8	5	Cytarabine	52
17	53	F	Breast cancer	8	4	Herceptin	92
18	68	F	Breast cancer	8	8	Cytarabine	435*
19	57	F	Breast cancer	8	21	Herceptin	162*
20	49	F	ALL	7	13	Cytarabine, MTX, Hydrocortisone	32†
<b>Mean</b>	<b>55.1</b>		NSCLC	<b>7.875</b>	<b>10.05</b>		<b>326.5</b>

Abbreviations:

ALL, Acute lymphocytic leukemia; DLBCL, Diffuse large B-cell lymphoma; F, Female; I-CSF, Intra-cerebrospinal fluid; M, Male; MTX, Methotrexate; NSCLC, Non-small cell lung cancer; SCLC, Small cell lung cancer

\* Patient still alive at the time of result analysis

†Patient lost to follow-up after initial treatment

## Figures

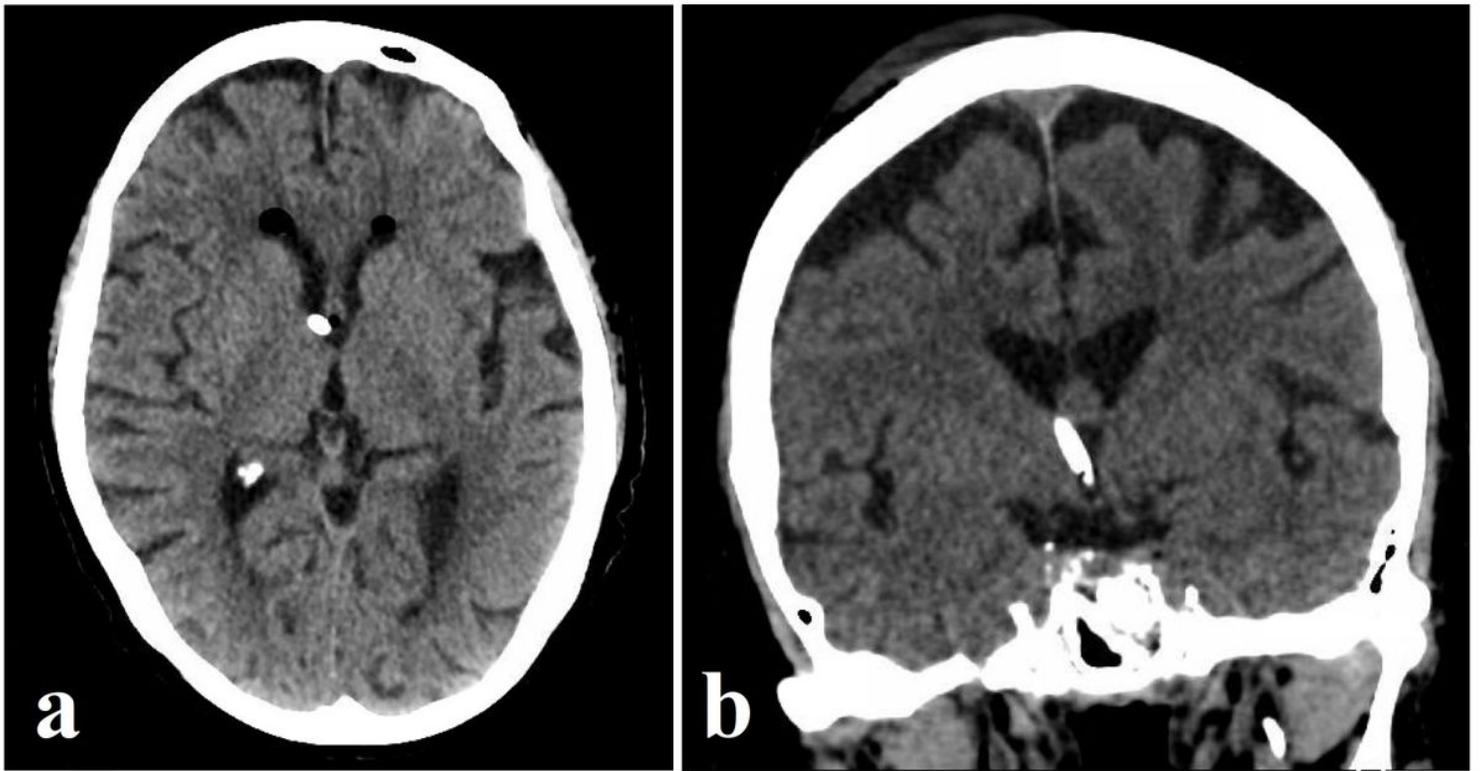
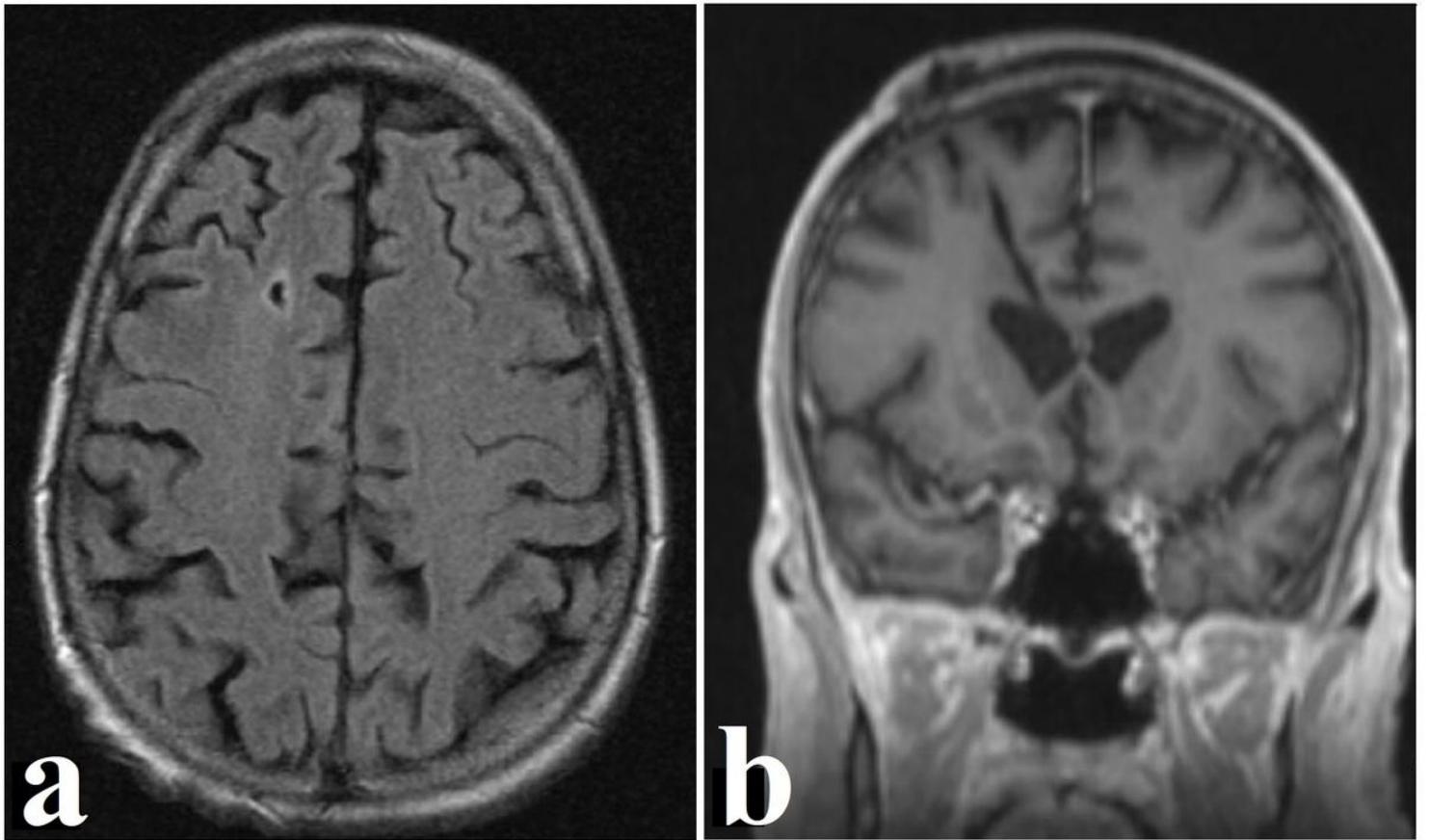


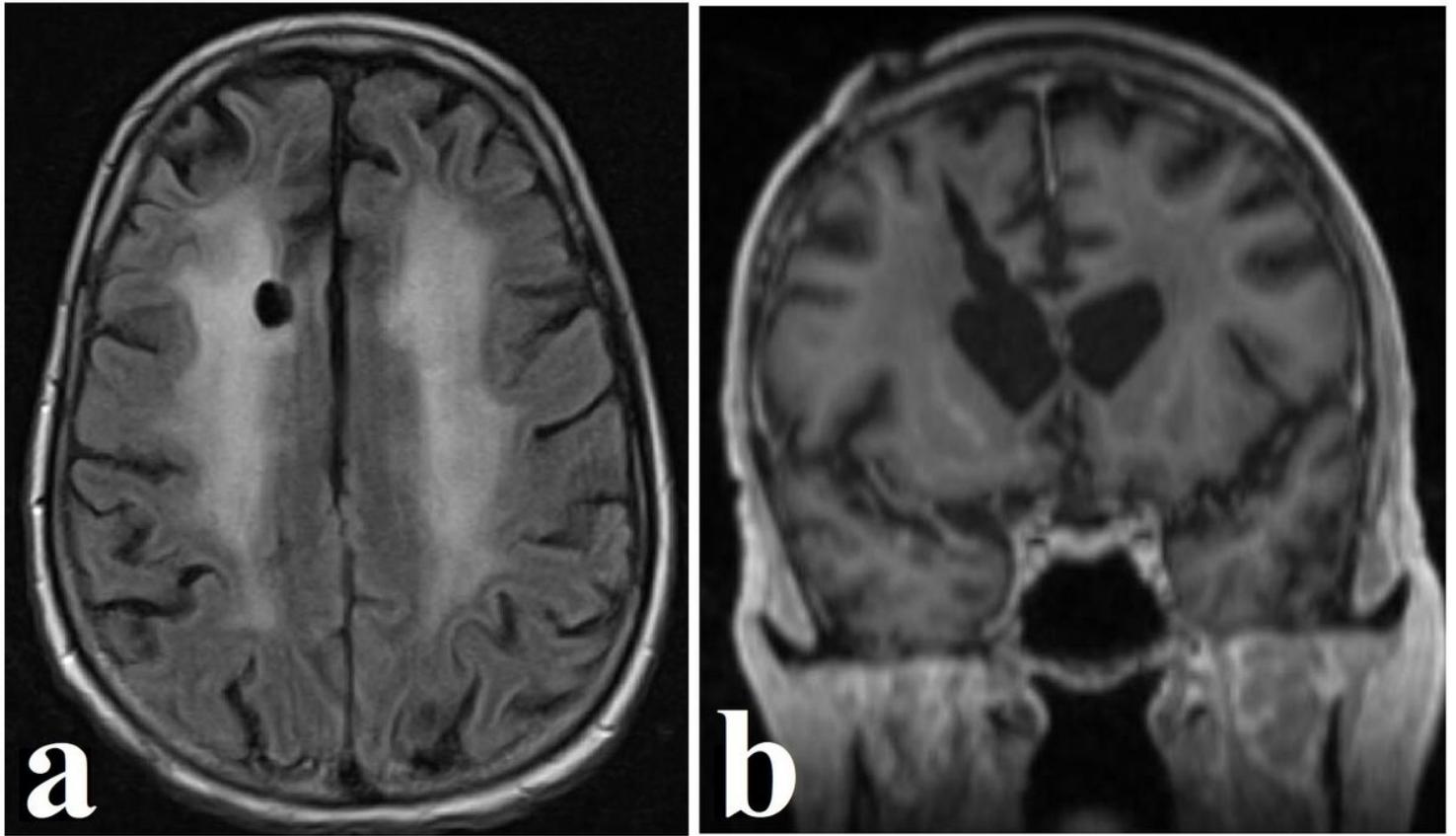
Figure 1

(a) Postoperative day 0 non-contrasted head CT (axial view) showing Ommaya catheter in the third ventricle through the right foramen of Monro (b): Coronal view showing Ommaya catheter in the third ventricle through the right foramen of Monro



**Figure 2**

(a) 1-month postoperative brain MRI (Pre-gadolinium axial image), revealing very minimal white matter changes immediately surrounding the catheter tract on FLAIR sequence (b): Post-gadolinium coronal image shows the catheter tract on post-contrast T1 sequence without any leukomalacia



**Figure 3**

(a) 10-month postoperative brain MRI (Pre-gadolinium axial image), revealing significantly increased white matter changes around the catheter tract on FLAIR sequence and enlarged encephalomalacia surrounding the catheter (b): Post-gadolinium coronal image revealing a significantly enlarged leukomalacia around the catheter tract on post-contrast T1 sequence