

Importance of intraoperative magnetic resonance imaging for pediatric brain tumor surgery

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Abstract

Background: High-field intraoperative MRI (IoMRI) is gaining increasing recognition as an invaluable tool in pediatric brain tumor surgery where the extent of tumor resection is a major prognostic factor. We report the initial experience of a dedicated pediatric 3-T intraoperative MRI (IoMRI) unit with integrated neuronavigation in the management of pediatric brain tumors.

Methods: Seventy-three children (mean age 9.5 years; range 0.2–19 years) underwent IoMRI between October 2009 and January 2012, during 79 brain tumor resections using a 3-T MR scanner located adjacent to the neurosurgical operating theater that is equipped with neuronavigation facility. IoMRI was performed either to assess the extent of tumor resection after surgical impression of complete/intended tumor resection or to update neuronavigation. The surgical aims, IoMRI findings, extent of tumor resection, and follow-up data were reviewed.

Results: Complete resection was intended in 47/79 (59%) operations. IoMRI confirmed complete resection in 27/47 (57%). IoMRI findings led to further resection in 12/47 (26%). In 7/47 (15%), IoMRI was equivocal for residual tumor and no evidence of residual tumor was found on re-inspection. In 32/79 (41%) operations, the surgical aim was partial tumor resection. In this subset, surgical resection was extended following IoMRI in 13/32 (41%) operations. None of the patients required early second look procedure for residual disease.

Conclusions: At our institution, IoMRI has led to increased rate of tumor resection and a change in surgical strategy with further tumor resection in 32% of patients. While interpreting IoMRI, it is important to be aware of the known pitfalls.

Key Words: Magnetic resonance imaging, neuronavigation, pediatric brain tumor

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INTRODUCTION

Brain tumors are a major cause of mortality and long-term morbidity in the pediatric population. Surgery is a vital part of management, and the degree of primary surgical resection is a major prognostic factor in several

tumor types, including the more common malignant tumors such as medulloblastoma, high-grade glioma, and ependymoma.^[1,8,10] For low-grade glioma, the most common brain tumor in childhood, complete surgical excision is generally curative without the need for further adjuvant therapy.

High-field intraoperative MRI (IoMRI) is rapidly developing as an aid to safe and effective neurosurgery. The use of neuronavigation systems and operating microscopes is well established in aiding tumor resection. Whilst the role of IoMRI is well documented in adult neurooncology practice, there is limited published literature on its role in the management of pediatric neurosurgical management.

HIGH-FIELD IOMRI FACILITY: DESIGN AND SAFETY CONSIDERATIONS

The IoMRI system at Alder Hey Children's Hospital involves a two-room solution which allows independent function of individual components. It is equipped with a Philips Achieva® 3-T scanner (Philips Healthcare, Best, the Netherlands) with a length of 157 cm and an inner bore of 65 cm. The facility design allows for diagnostic MRI when not needed for IoMRI, making the facility economically viable and allowing for optimal use of this expensive technology. The IoMRI suite is located next to the neurosurgical operating theater, separated by double doors. This arrangement enables independent use of the neurosurgical operating theater and the MRI scanner when IoMRI is not needed.

Special coils and hardware are necessary to facilitate maintenance of sterility of the operative field. IoMRI can be performed using the standard Philips parallel imaging FLEX L coil, with a carbon fiber head clamp, but optimal results are obtained with a dedicated intraoperative head coil (NORAS MRI Products, Hochberg, Germany). The NORAS 8-channel intraoperative head coil contains an integral head clamp with five fixation points (titanium pins) and 14 fiducial markers, allowing accurate intraoperative updating of neuronavigation with automatic registration. Safe transfer of the patient into the MRI scanner is achieved by an MRI-compatible patient transfer table (Maquet, Rastatt, Germany), which docks securely with the MRI platform.

IoMRI poses certain challenges in terms of safe use, both for the theater staff and for the anesthetized patient. The general safety and anesthetic considerations for IoMRI are outlined in Boxes 1 and 2, respectively.

ALDER HEY EXPERIENCE WITH IOMRI

MATERIALS AND METHODS

Patients

Between October 2009 and January 2012, IoMRI was performed on 73 patients during 79 cranial tumor resections. The mean age was 9.5 years (range 0.2–19 years).

Box 1: Intraoperative magnetic resonance imaging: General safety considerations

- No metallic objects should be carried into the high-field area
- Scrubs without pockets are recommended to help prevent inadvertent carrying of ferromagnetic objects into the high-field area
- All instruments must be accounted for and checked for MR compatibility before IoMRI
- Hearing protection is necessary for the patient (even when anesthetized) and all support staff who remain in the MRI suite whilst imaging is in progress

Box 2: Intraoperative magnetic resonance imaging: Anesthetic considerations

- Every transfer must be carefully managed to minimize the risk of dislodging the endotracheal tube, and arterial, central venous, and peripheral venous catheters
- No metallic surgical or anesthetic instrument should be left on the table or under drapes during preoperative positioning
- All monitoring equipments inside the MRI room must be MRI compatible, including ECG electrodes and leads, blood pressure cuffs, and pressure transducer cables
- Endotracheal tube should be fixed securely before the patient is positioned
- The cuff of the endotracheal tube should be kept as far as possible from the field of view to minimize artifacts
- Fluid and drug infusion pumps should be MRI compatible
- All non-MRI-compatible material including conventional ECG electrodes, temperature probes, and diathermy plates must be removed before transfer into the MRI scanner

Imaging

IoMRI was performed on a Philips Achieva 3-T scanner (<http://www.healthcare.philips.com>) located alongside the neurosurgical operation theater and equipped with neuronavigation facility using BrainSUITE® (Brain-LAB, Feldkirchen, Germany; <http://www.brainlab.com>). Preoperative imaging was performed either on the 3-T scanner or a Philips Achieva 1.5-T scanner.

The surgical aim (complete, subtotal, near-total resection) was defined preoperatively by a multidisciplinary team. The indications of IoMRI have been summarized in Box 3.

The intraoperative imaging sequences were tailored to tumor characteristics and surgical aims. Standard IoMRI sequences performed at our institution are summarized in Box 4. In complex operations, more than one intraoperative scan may be required. The specific parameters for the MR sequences have been described by Abernethy *et al.*^[2] High-field IoMRI also allows for advanced multimodal imaging [Box 5] to be performed, which can aid in surgical decision making.

IoMRI was limited to the precontrast sequences if there was unequivocal evidence of residual tumor. The

Box 3: Indications for Intraoperative magnetic resonance imaging

Intraoperative

- To update neuronavigation where the navigation accuracy has been lost
- To assess the extent of tumor resection where subtotal tumor resection is intended
- To confirm surgical impression where complete tumor resection is intended
- To confirm correct biopsy tract/specimen for MRI-guided biopsies

Box 5: Intraoperative advanced magnetic resonance imaging techniques

Diffusion tensor imaging (DTI)

- DTI can provide preoperative and intraoperative mapping of deep white matter tracts
- When used with neuronavigation, it can help the surgeon to avoid damage to these important structures while maximizing resection of deep-seated tumors

Perfusion imaging

- Perfusion imaging by direct contrast enhancement makes it possible to acquire physiological measurements of relative cerebral blood flow
- Can be applied intraoperatively for early resection control, and is as reliable as preoperative perfusion mapping
- Integrating perfusion imaging into the IoMRI protocol can yield additional physiological information and help to overcome the problem of intraoperative brain shift caused by resection of the tumor

MR spectroscopy (MRS)

- MRS can provide biochemical information about relative metabolite concentrations
- MRS can be time consuming but has been helpful in evaluating for residual tumour on some challenging ioMR cases. The presence/absence of abnormal metabolites aid in the interpretation of the ioMR imaging

IoMRI scan served as the early postoperative MRI if the IoMRI revealed complete tumor resection or satisfactory degree of subtotal/near-total resection. Repeat IoMRI was performed if further tumor resection was performed after the first IoMRI. Gadopentetate dimeglumine (Magnevist®; Schering, Berlin, Germany) at 0.2 ml/kg bodyweight was used as contrast agent during IoMRI if the tumors demonstrated enhancement on preoperative imaging. The majority of the children received only one dose of contrast during the first and only IoMRI study. The duration of the IoMRI varied between 10 min for a limited study to update neuronavigation and 40 min for a complete early postoperative study.

The IoMRI interpretation was performed by the operating neurosurgeon and a pediatric neuroradiologist in consensus. If the IoMRI findings led to further tumor resection, tissue samples were obtained for histopathologic analysis.

Box 4: Intraoperative magnetic resonance imaging sequences

Standard sequence

- T2-weighted turbo spin echo (T2-TSE) in three planes
- T1-weighted 1-mm isotropic 3-D gradient-echo (T1-TFE) pre- and post-contrast medium administration
- Coronal T2-weighted fluid-attenuated inversion recovery (FLAIR) sequence
- Diffusion-weighted imaging (DWI) or diffusion tensor imaging (DTI)

To update neuronavigation

- T1-weighted 1-mm isotropic 3-D gradient-echo (T1-TFE)
- Additional sequences depending on tumor characteristics to assess the degree of resection

Following the IoMRI, the patient is transferred back to the operating theater, where the images are immediately available to the neurosurgeon using advanced multimodal image display technology.

This study was approved by the research department of our institution as a service evaluation, as defined by the United Kingdom National Patients Safety Agency.

RESULTS

IoMRI was used during 79 cranial tumor resections in 73 children. Overall, IoMRI scan led to further surgery in 25 cases (32%). The results are summarized in Table 1.

Complete resection intended

Complete surgical resection [Figures 1a and b] was intended in 47/79 (59%) operations. IoMRI findings suggested complete resection in 27/47 (57%), residual disease in 12/47 (26%), and equivocal residual disease in 7/47 (15%) patients. Twelve children with definite residual tumor underwent further surgery, and complete resection was achieved and confirmed on the subsequent IoMRI scan. In seven children with equivocal residual disease on IoMRI, at re-inspection, it was not possible to identify any obvious residual tumor and the patients were therefore closed and no further imaging was performed. Follow-up MRI scans at 3 months in 6/7 patients with equivocal IoMRI did not show any evidence of residual tumor, and therefore these patients could be classified as complete tumor resection, making the total number in this category as 34/47 (72%).

Partial resection intended

Partial resection [Figures 2a–c] was intended in 32/79 (41%) operations. The majority of these were midline chiasmatic/hypothalamic, brainstem gliomas or high-risk craniopharyngiomas involving the hypothalamus where the surgical aim was subtotal tumor resection to preserve vital structures. Surgical resection was extended in 13/32 (41%) operations following IoMRI.

Follow-up

Since the use of IoMRI facility at Alder Hey, there has

Table 1: Results

Aim	No. of cases	Intraoperative magnetic resonance imaging outcome		
		Completion of surgery	Further resection	No further resection Equivocal
Complete resection	47	27	12 + 1 excision biopsy	7
Partial resection	32	19	13	0
Total	79	47	25	7

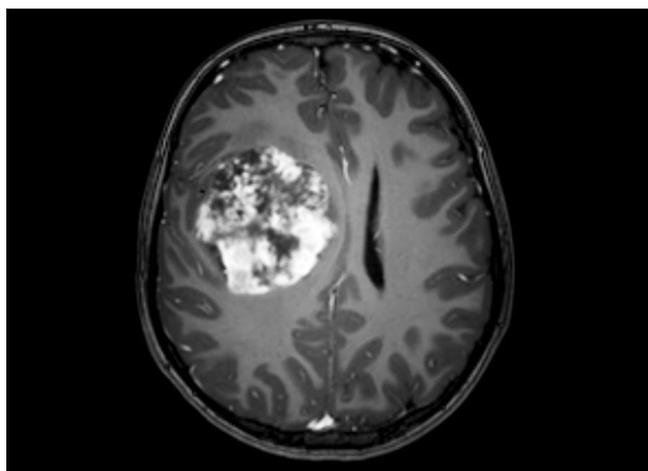


Figure 1a: Axial T1-weighted Gadolinium-enhanced preoperative MRI image showing a large heterogeneously enhancing tumor in the right posterior frontal region with associated mass effect and midline shift (histology confirmed the tumor to be an atypical teratoid rhabdoid tumor, WHO Grade 4)

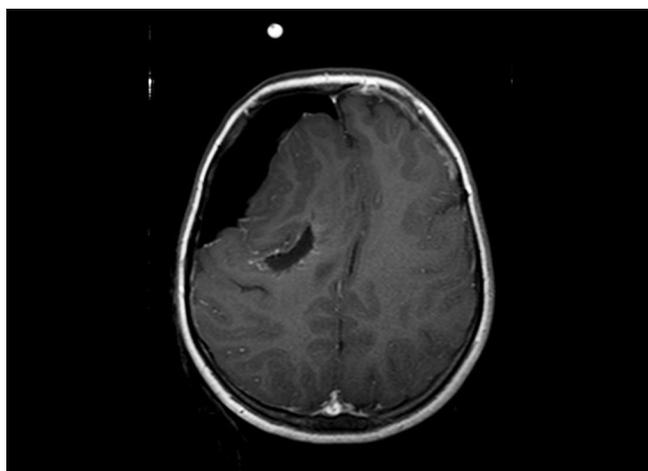


Figure 1b: Axial T1-weighted, Gadolinium-enhanced intraoperative MRI image showing complete excision of the right frontal tumor. This served as the final intraoperative/early postoperative scan

been no avoidable early second look procedure for residual disease within 1 year of surgery.

DISCUSSION

IoMRI has become increasingly important as a tool to aid safe and complete resection of brain tumors in adults, and is expected to make a major contribution to neurosurgery for pediatric brain tumors. In a study of adults with low-grade gliomas, Pamir *et al.* have reported that 3-T IoMRI led to further resection in up to 40% of cases and increased the proportion of complete tumor resections by over 30%.^[7] In another study of adult patients with high-grade gliomas, the use of a low-field IoMRI increased the proportion of complete macroscopic tumor resection from 36 to 75%.^[4] Computer-assisted neuronavigation using preoperative MRI is now considered standard care and has facilitated radical tumor resection and increased survival in adults. In a study of 104 adults with glioblastoma treated surgically, the use of image-guided neuronavigation led to complete macroscopic tumor resection in 31% using neuronavigation, but only 19% without neuronavigation. The use of neuronavigation and complete tumor resection were associated with a highly significant increase in patient survival.^[9]

Other than high-field MRI, other modalities for intraoperative brain imaging include ultrasound (US), computed tomography (CT; using either fixed or mobile scanners), and low- and medium-field MRI. Their relative merits and demerits are discussed in Box 6. It is important to note that none of these alternative intraoperative modalities can match the diagnostic accuracy of high-field MRI in the evaluation and documentation of completeness of tumor resection now required for modern treatment protocols. In addition, IoMRI can obviate the need for postoperative MRI imaging which will otherwise be needed within 24 h of surgery to document the extent of tumor excision. This is particularly useful if the child is in an unstable clinical condition in the postoperative period and in children who would otherwise require a second general anesthetic for postop high-field MRI scan to document the extent of tumor excision.

A dedicated pediatric 3-T IoMRI facility has a number of advantages and challenges. In our initial experience with IoMRI, it has positively influenced our neurosurgical outcome and practice, in particular, the way in which we perform surgery and evaluate our surgical results.

The extent of resection is an important predictor of prognosis in children with medulloblastoma, ependymoma, and high-grade glioma.^[1,8,10] Traditionally, this has led to reoperation following early postsurgical scan. IoMRI now provides the opportunity to identify cases where the surgical aim has not been met and extended resection is possible. In our initial experience, IoMRI has resulted in extended surgical resection in 32% of all operations, including 26% where complete resection was intended and 41% where partial resection

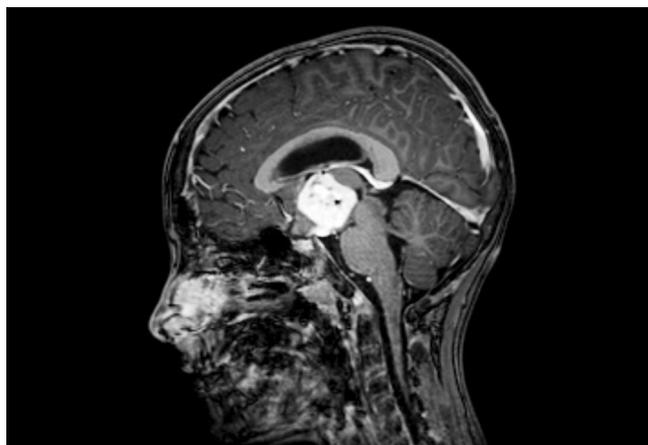


Figure 2a: Sagittal T1-weighted, Gadolinium-enhanced preoperative MRI image showing an enhancing suprasellar mass (histology confirmed it as pilocytic astrocytoma, WHO Grade 1) extending superiorly into the third ventricle and posteriorly between the cerebral peduncles. There is thickening of the optic chiasm



Figure 2b: Sagittal T1-weighted, non-contrast intraoperative MRI image showing partial resection of the posterosuperior aspect of the third ventricle tumor. The imaging was used to update neuronavigation and fine-tune further surgical debulking

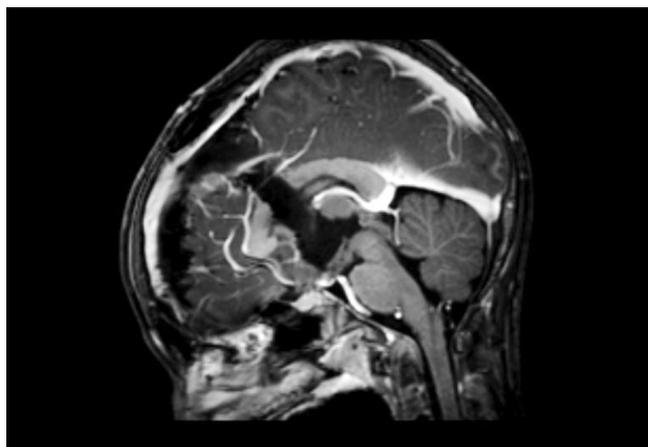


Figure 2c: Sagittal T1-weighted, Gadolinium-enhanced intraoperative MRI image showing almost complete resection of suprasellar tumor with small intended residual tumor in the hypothalamus. No further tumor resection was performed and this served as the final intraoperative/early postoperative scan

was intended [Table 1]. In literature, the reported rates of extended resection vary between 27.5 and 60%. Our results are similar to those reported by Nimsy *et al.*^[6] in their initial experience with 1.5-T IoMRI, where the surgical strategy was modified in 27.5% of the first 200 patients (both children and adults). In a recent paper, Levy *et al.* have reported their experience in 98 children who underwent IoMRI using a 1.5-T scanner. In this study, 55 children underwent surgery for brain tumors, and in 49% of these, IoMRI led to further surgery.^[5] Variations in the rate of extended resection are likely to occur given the diverse patient groups, tumor types, and surgical and radiological expertise. On balance, the results to date, including ours, indicate that IoMRI has led to improved tumor resection and further research is required to assess the clinical outcome for individual patient groups.

In our experience, high-field IoMRI has not only improved the percentage of gross total resection in keeping with the surgical goal, but also proven invaluable in the surgical management of deep-seated tumors in eloquent areas where the surgical goal had been limited resection. In 41% of our patients where the surgical goal was subtotal resection, further resection was carried out following IoMRI. This is particularly relevant in surgical management of deep-seated chiasmatic/hypothalamic gliomas where a midline approach (transcallosal interformiceal) gives a minimally invasive but limited view of often very large tumors. In these cases, a planned IoMRI [Figures 2a–c] at the halfway stage to evaluate progress and fine-tune the final resection has been very useful. IoMRI adds safety to this type of surgery and allows the surgeon to make an informed decision about the amount of residual tumor to be left, while minimizing the damage to functionally important structures such as the hypothalamus and optic chiasm. Another application of IoMRI is to confirm the biopsy tract and that representative tumor areas have been biopsied [Figures 3a and b].

IoMRI has not only reduced the need for early reoperation, but also reduced the number of early postoperative MRI scans, previously performed routinely between 24 and 48 h post surgery. In our practice, the final IoMRI scan has replaced the postoperative MRI scan and helped to streamline patient care pathway.

Evaluation of IoMRI studies pose certain challenges, and although we have not encountered significant problems with interpretation of IoMRI, they are well described in literature. These include susceptibility artifacts, surgically induced contrast enhancement, and brain shift.

Susceptibility artifact can occur from external sources including metallic objects (even if nominally MRI compatible) such as head holder pins and endotracheal tubes or intracranial sources including hemorrhage and air introduced during surgery. Gradient- and echo planar-

Box 6: Modalities for Intraoperative imaging		
	Merits	Demerits
Intraoperative US	<ul style="list-style-type: none"> ➤ Real-time modality ➤ Minimal disruption to the operation ➤ Can provide real-time intraoperative situation, compensating for the effects of brain shift when used with advanced neuronavigation systems to update high-quality preoperative MRI data 	<ul style="list-style-type: none"> ➤ Field of view can be limited, depending on the tumor location ➤ Image quality can be inadequate for accurate evaluation of the extent of tumor resection ➤ High-field MRI will still be required postoperatively to document the extent of tumor resection
Intraoperative CT scan	<ul style="list-style-type: none"> ➤ Avoids the hazards of high magnetic field ➤ Both fixed and mobile CT scanners can be used 	<ul style="list-style-type: none"> ➤ Lacks the high intrinsic contrast and sensitivity of MRI ➤ Radiation protection issues for patient and theater staff ➤ Mobile CT scanners may be difficult to set up and calibrate effectively ➤ High-field MRI will still be required postoperatively to document the extent of tumor resection
Low-field intraoperative MRI	<ul style="list-style-type: none"> ➤ Open configuration magnets operating at field strengths up to 0.3 T ➤ Allows access to the patient's head without moving out of the scanner 	<ul style="list-style-type: none"> ➤ Signal-to-noise ratio (SNR) and T2 sensitivity are reduced ➤ Scan times may be inconveniently long ➤ Advanced MRI techniques are not possible ➤ High-field MRI will still be required postoperatively to document the extent of tumor resection

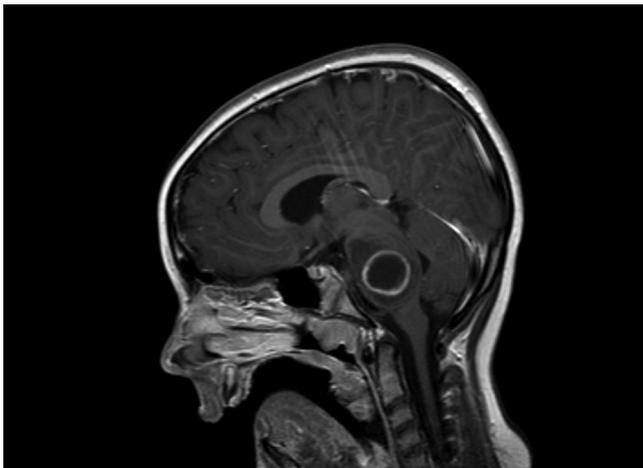


Figure 3a: Sagittal T1-weighted, Gadolinium-enhanced preoperative MRI image showing a peripherally enhancing pontine tumor (histology confirmed it as glioblastoma, WHO grade 4)

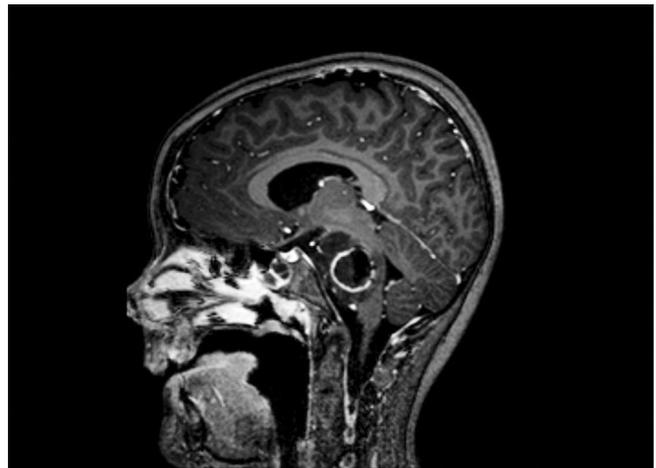


Figure 3b: Sagittal T1-weighted, Gadolinium-enhanced intraoperative MRI image confirming that representative biopsies have been performed, particularly from the enhancing edge of the tumor

sequences are the most affected. The use of titanium pins to hold the head minimizes susceptibility artifact. Also, the pins are usually placed away from the region of interest to minimize the influence of susceptibility artifact on image interpretation. Placing the cuff of the endotracheal tube on the chest rather than beside the head can reduce the associated artifact. Irrigation of surgical cavity reduces the amount of intracranial and intracavitary air.

Surgically induced contrast enhancement is a potential cause for misinterpretation during brain tumor resection. The following four types of contrast enhancement induced by surgery have been described:^[3]

1. meningeal enhancement,
2. increased enhancement of the choroid plexus,
3. delayed enhancement of the surgical margin, and

4. immediate intraparenchymal enhancement.

The latter two are thought to be caused by leakage of contrast material from surgically open vessels or transient blood brain barrier disruption and have a greater potential to be misinterpreted as residual tumor. This phenomenon is particularly important in tumors with cystic components and at a site where a bipolar cauterizing instrument has been used during surgery. Careful comparison with preoperative imaging is advisable in these circumstances.

Intraoperative brain tissue deformation (brain shift) [Figures 4a–c] is frequently multifactorial. These include reduction in tumor mass, collapse of the resection cavity, edema, hemorrhage, and drainage of cerebrospinal fluid. Careful comparison of anatomical landmarks including

the sulci, the gyri, the vessels, and the non-deformed parenchymal structures is useful in orientation. Diffusion tensor imaging with fiber tracking may be helpful in this situation.

Advances in multimodal neuronavigation have enabled the neurosurgeon's view through the operating microscope to be fused with MR images that may include diffusion tensor imaging (DTI) and functional imaging (Brain-LAB). For reliable tumor resection, a high degree of accuracy is essential for neuronavigation. Brain shift and registration errors are the major factors that may impair navigation accuracy if navigation is based on preoperative MRI. Further inaccuracies can be introduced if the head moves within the holding pins after registration. Progressive brain shift occurs as the bulk of the tumor decreases during the operation. In this situation, neuronavigation based on preoperative MRI may be misleading and potentially dangerous. Updating the navigation system with IoMRI is the most reliable method to overcome these problems. Our use of sophisticated automatic registration systems allows navigation update without using the original patient registration, thereby providing a straightforward and time-efficient method to compensate for brain shift and registration errors. Also, microscope-based image fusion and display can be used for precise localization of residual tumor and orientation within the resection cavity. Advanced display technology with superimposition of the operating microscope image with preoperative and IoMRI facilitates image interpretation.

Without automatic registration techniques, after acquiring new images, the accuracy of intraoperative updating is valid only if there is no positional shifting impairing the initial patient registration. In clinical practice, this can be avoided by taking proven landmark checks just after the first registration. After updating, a side-by-side display of preoperative and intraoperative images of the tumor remnant detection is possible, facilitating orientation, image interpretation, and evaluation of brain shift. In our experience, automatic re-registration, bespoke coils, and attached reference frames have improved speed, accuracy, and reliability.

Our initial results have been encouraging and further research is required to evaluate the clinical effectiveness of IoMRI in the management of specific tumors and the role of advanced MRI techniques in the intraoperative context.

CONCLUSION

In our experience, when managing children, the IoMRI provides us with the ability to illustrate, document, and discuss all aspects of surgery and is a significant improvement in the quality of patient care. Being

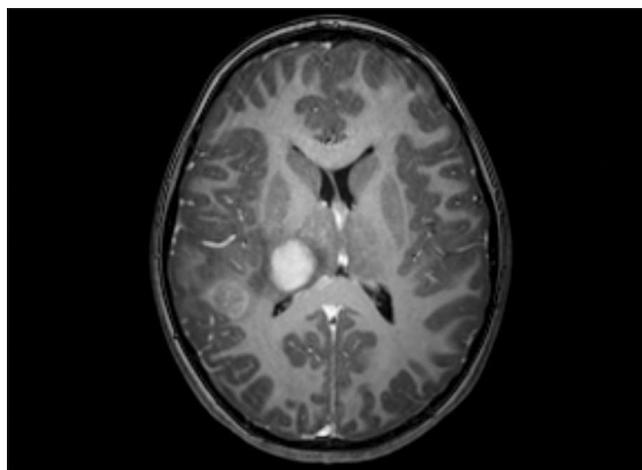


Figure 4a: Axial T1-weighted, Gadolinium-enhanced preoperative MRI image showing peripherally enhancing bilobed tumor (histology confirmed it as anaplastic astrocytoma, WHO Grade 3) in right thalamus and right posterior temporal lobe

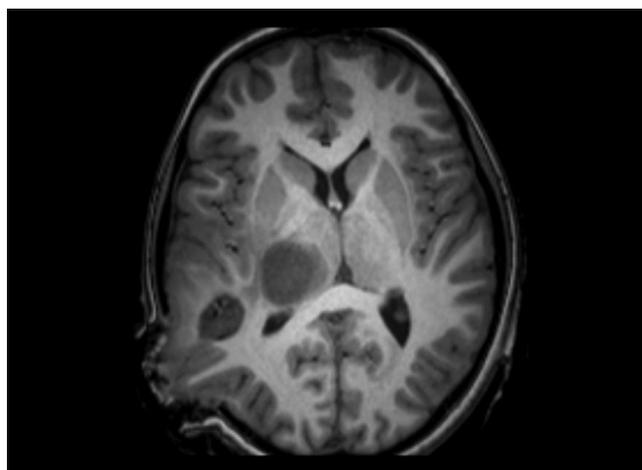


Figure 4b: Axial T1-weighted, non-contrast intraoperative MRI image showing herniation of brain parenchyma through the craniotomy defect. The imaging was obtained to update neuronavigation and guide further surgery as navigation had lost accuracy due to intraoperative brain shift

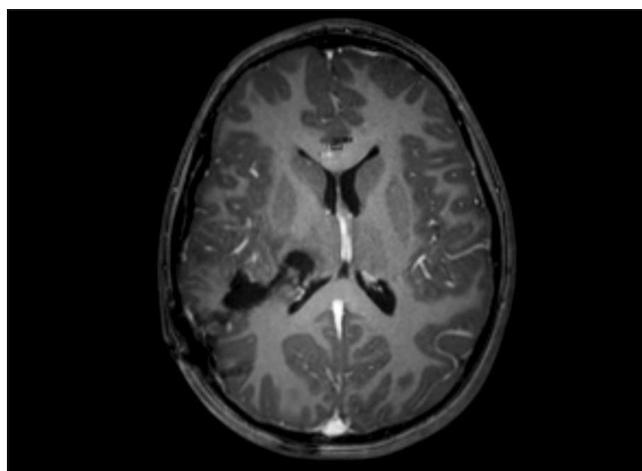


Figure 4c: Axial T1-weighted, Gadolinium-enhanced intraoperative MRI image showing complete tumor resection. This served as the final intraoperative/early postoperative scan

able to confirm the achievement of surgical aims immediately after surgery is an immeasurable quality leap in parent satisfaction and experience. This technology has transformed our management approach to brain tumor in children by influencing surgical decisions and increasing the rate of complete tumor resection and the extent of partial tumor resection. Optimal use of this expensive intraoperative facility requires careful planning and management. Equivocal findings resulting from postsurgical contrast enhancement can pose challenges. Further studies involving larger numbers of patients/procedures, outcome, and the use of advanced IoMRI techniques need to be encouraged.

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