Is intraoperative MRI use in malignant brain tumor surgery a health care burden? A matched analysis of MarketScan Database

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Abstract

Background Intraoperative magnetic resonance imaging (iMRI) is a useful adjunct for resection of primary malignant brain tumors (MBTs). The aim of our study is to investigate the impact of iMRI on health care utilization in patients who underwent craniotomy for resection of MBTs.

Materials and methods MarketScan database were queried using the ICD-9/10 and CPT 4th edition, from 2008 to 2020. We included patients ≥18 years of age who underwent a craniotomy with at-least one year follow-up. Outcomes were length of stay (LOS), discharge disposition, hospital/emergency room (ER) re-admissions, outpatient services, medication refills and corresponding payments.

Results Of 6,640 patients who underwent craniotomy for MBTs, 465 patients (7%) had iMRI used during the procedure with 0.7% per year increase in iMRI use during the study period. Patients without iMRI use had higher complications at index hospitalization compared to those with iMRI use (19% vs. 14%, p = 0.04). There was no difference in the ER admission rates among the patients who underwent surgery with and without iMRI use at 6-months and 1-year after the index procedure. In terms of post-discharge payments, no significant differences were noted among the patients without and with iMRI use at 6-months ($81,107 vs. $ 81,458, p = 0.26) and 1-year ($132,657 vs. $ 118,113, p = 0.12).

Conclusion iMRI use during craniotomy for MBT gradually increased during the study period. iMRI did not result in higher payments at index hospitalization, 6-months, and 1-year after the index procedure.

Keywords Intraoperative MRI · Malignant brain tumor · Healthcare utilization · Surgery · National database

Introduction

Integration of image guidance navigation with intra-operative magnetic resonance imaging (iMRI) offers the potential for improvement of clinical outcomes through surgical decisions and maneuvers based on real-time imaging data [1–3]. iMRI further facilitate minimally invasive procedures affording treatment of deep-seated lesions that are difficult to access through conventional neurosurgery [4–6]. Early adopters of iMRI pioneered its application in facilitating stereotactic biopsies [7, 8], maximizing the extent of tumor resection [9, 10], and aiding stereotactic electrode placement [11]. Since its inception at the University of Minnesota and Brigham & Woman’s Hospital (BWH), there is growing enthusiasm for the potential of technology and its adaption [12–15]. It is estimated that by 2026, >1,600 units of iMRI will be adopted for neurosurgical applications.
Pertaining to brain tumors, iMRI has been used primarily in glioma [4, 14, 16–21] and pituitary [22–25] surgeries to maximize the extent of tumor resection (EOR). Published results from completed [1] and on-going randomized trials [26] have demonstrated the utility of iMRI in this regard. Meta-analysis of the available non-randomized clinical series (n = 15 studies) similarly reported that iMRI improved the EOR for both low-grade and high-grade gliomas [13, 21]. However, the level of evidence supporting the clinical benefit of iMRI in tumor resection is considered limited by a recent Cochrane systematic review [12], given incomplete reporting of adverse events as well as concerns for reporting bias. The importance of investigations into the cost-effectiveness of iMRI is magnified in this context.

The major challenges associated with iMRI use involve the significant upfront installment costs, maintenance expenses, increased operative time and need for a trained staff, all contributing to increased health care burden. Other modalities such as intra-operative ultrasound or tumor-fluorescence have been shown to have competing sensitivity with less health care costs [27, 28]. Limited studies including retrospective observational [29–32], microsimulation model[33], systematic review or meta-analysis [12, 27] address the cost-effectiveness of iMRI in cranial procedures. A recent systematic review reported uncertain effects of iMRI on costs [12] and another reported $32,954/quality-adjusted life year (QALY) with iMRI [27].

There is a gap in the literature regarding the impact of iMRI use on health-care utilization in patients who undergo craniotomy for malignant brain tumors (MBTs). To address this gap, we designed this study to analyze real-world clinical data using a large national administrative database. We hypothesized that patients who underwent surgery using iMRI are likely to have higher utilization of health care resources, which is likely to offset at a year follow-up compared to patients who had surgery without iMRI.

Materials and methods

Data source

IBM MarketScan Research Databases is a healthcare research database with de-identified medical, drug, and dental claims for more than 265 million patients. Data from 2008 to 2020 were used in this study. Our neurology/neurosurgery custom subset includes inpatient, outpatient and prescription data, with diagnoses and procedures, insurer, and patient payment information, linked by a unique patient identification number [34]. Claim records in MarketScan represent patients’ trajectories through the healthcare system.

International Classification of Diseases, Ninth Revision (ICD-9) and Tenth Revision (ICD-10) codes and Current Procedural Terminology 4th edition (CPT-4) codes were used to identify patients ≥ 18 years of age who underwent craniotomy for resection of primary MBTs using iMRI from 2008 to 2020, Table 1.

We included patients who had ≥ 12 months of follow-up data available after craniotomy. Post-surgery follow-up time was calculated as the difference between the index procedure discharge date and the enrollment end date (or last claim date in the dataset). Prior to 2008, data was available for < 10 patients/year and therefore was excluded from the analysis.

Patient characteristics and outcomes

Patients’ demographics such as age, sex, insurance type (e.g., commercial, Medicaid or Medicare) and comorbidities, at the time of index procedure, were included in the study. The Elixhauser score was used to account for the burden of comorbidities [35]. We used the adaptation to ICD-9-CM codes developed by Quan et al [36].

Index hospitalization, length of hospital stay (LOS), discharge home status, index hospitalization complications, (renal, cardiac, neurological/neurosurgical, deep vein thrombosis or pulmonary embolism (DVT/PE), pneumonia/pulmonary infection, wound infection, myocardial infarction, acute kidney injury, pressure ulcers and sepsis) were extracted and analyzed. We also evaluated emergency room (ER)/hospital readmission, outpatient services, and outpatient medication refills at 6 months and 1-year follow up. Health-care utilization at all time points were analyzed from the database. Inflation adjustments were made for payments to 2020 US dollars using the medical component of the consumer price index (accessible through the United States Bureau of Labor Statistics) [37].

### Table 1 ICD-9/ICD-10/CPT codes used for iMRI for resection of malignant brain tumors

| Primary malignant brain tumor Craniotomy | ICD-9 Code | ICD-10 Code | CPT Code |
|------------------------------------------|------------|-------------|----------|
| B030YZZ                                  | 70,557–   | 70,559     | B030ZZZ  |
| Intraoperative MRI                       | B030YOZ,  | 70,557–   | B030ZZZ  |

- Represent patients’ trajectories through the healthcare system.
Statistical analysis

Continuous variables were summarized with means and standard deviations, median and interquartile ranges as well as the full range (minimum to maximum) and compared using Kruskal-Wallis test. Categorical variables were summarized counts with corresponding percentages and compared with Chi-square tests. Exact match was used which matched all baseline characteristics (age, sex, insurance and Elixhauser index) for the two groups. Paired test was used for outcomes after exact matching. The Wilcoxon matched pairs signed ranks test was used for continuous outcomes and McNemar’s Test for categorical outcomes. Covariate balance before and after matching was evaluated using p-values. A p-value less than 0.05 was considered statistically significant. We used the software SAS 9.4 (SAS Institute, Inc, Cary, NC) for data pre-processing and statistical analysis.

Results

Trends and patient demographics

A cohort of 6,640 adult patients who underwent craniotomy for MBTs with 1-year follow-up was identified from the database. Of these, 465 patients (7%) underwent craniotomy using iMRI. The trends of iMRI use during craniotomy for MBT gradually increased from 2008 (2.87%) to 2019 (9.18%) with highest use in 2016 (11.92%). There was 0.66% increase in iMRI use per year during the study period (p = 0.0007), Fig. 1.

Overall, patients in the iMRI use cohort were younger (median age 45 vs. 50 years), with lower Medicare insurance enrollment (5% vs. 8%) and higher 3+ comorbidity index (43% vs. 41%) compared to patients without iMRI use. No statistically significant difference in sex was identified across cohorts, Table 2. A subset of 439 patients without and with iMRI following exact matching was identified in each cohort.

Outcomes at index hospitalization after the procedure

No differences in LOS (median 3 days each) and discharge to home (84% vs. 87%) were noted among patients without and with iMRI use for craniotomy respectively, p > 0.05. Similarly, no difference in payments at index hospitalization was noted among the cohorts (median $57,910 vs. $58,067). However, all complications were higher in the cohort without iMRI use for craniotomy compared to patients with IMRI use (19% vs. 14%, p = 0.04), Table 3.
ER admissions and Health care utilization at 6 months and 1-year after the procedure

There was no difference in the ER re-admission rates at 6-months (43% vs. 40%) and at 1-year (56% vs. 55%) after the index procedure among the patients without and with iMRI use for craniotomy. Although hospital admissions and corresponding payments were higher among the patients without iMRI use at both 6-months and 1-year compared to those with iMRI, no differences in outpatient services and related payments were noted among the cohorts.

Table 3 Outcomes comparisons among the groups with and without iMRI following exact match

| Outcome                                      | Craniotomy for MBT, exact matched cohort | p Value   |
|-----------------------------------------------|------------------------------------------|-----------|
| **Index hospitalization**                     |                                          |           |
| LOS in days, median (IQR)                     | Without iMRI (n=439)                     | With iMRI (n=439) | 0.0918 |
| Index, Median payments (IQR)                  | 3 (2, 6)                                 | 3 (2, 4)  | 0.8126 |
| Discharge home n (%)                          | 368 (84%)                                | 383 (87%) | 0.1394 |
| Complications at index hospitalization, n (%) | 83 (19%)                                 | 60 (14%)  | **0.0365** |
| **1/2-year post discharge**                   |                                          |           |
| ER admissions                                 |                                          |           |
| Admitted, n (%)                               | 190 (43%)                                | 177 (40%) | 0.3592 |
| Payments for admitted only, median (IQR)      | 1737 (221, 4296)                         | 1489 (312, 3900) | 0.3779 |
| Hospital admissions                           |                                          |           |
| Admitted, n (%)                               | 124 (28%)                                | 97 (22%)  | **0.0344** |
| Payments for admitted only, median (IQR)      | 30,241 (12,517, 70,663)                  | 20,697 (10,360, 42,343) | **0.0017** |
| Outpatient services                           |                                          |           |
| No of services, median (IQR)                  | 138 (74, 197)                            | 139 (78, 188) | 0.3995 |
| Payments, median (IQR)                        | 50,540 (11,684, 98,208)                  | 58,076 (13,817, 99,818) | 0.8904 |
| Medication refills                            |                                          |           |
| No of refills, median (IQR)                   | 20 (7, 31)                               | 19 (9, 30) | 0.5943 |
| Payments, median (IQR)                        | 7305 (124, 26,263)                      | 10,419 (229, 23,818) | 0.905 |
| Combined payments, median (IQR)               | 81,107 (25,572, 139,150)                | 81,458 (25,514, 127,875) | 0.2619 |
| **1-year post discharge**                     |                                          |           |
| ER admissions                                 |                                          |           |
| Admitted, n (%)                               | 245 (56%)                                | 243 (55%) | 0.8918 |
| Payments for admitted only, median (IQR)      | 1967 (409, 5455)                         | 2289 (583, 5287) | 0.9588 |
| Hospital admissions                           |                                          |           |
| Admitted, n (%)                               | 177 (40%)                                | 146 (33%) | **0.032** |
| Payments for admitted only, median (IQR)      | 42,728 (17,623, 89,429)                 | 25,494 (13,122, 63,338) | **0.0006** |
| Outpatient services                           |                                          |           |
| No of services, median (IQR)                  | 218 (117, 304)                           | 212 (141, 293) | 0.5531 |
| Payments, median (IQR)                        | 79,079 (24,750, 140,487)                | 77,758 (28,901, 140,369) | 0.5224 |
| Medication refills                            |                                          |           |
| No of refills, median (IQR)                   | 37 (16, 60)                              | 36 (18, 57) | 0.6553 |
| Payments, median (IQR)                        | 14,738 (283, 43,531)                    | 16,065 (582, 40,234) | 0.802 |
| Combined payments, median (IQR)               | 132,657 (51,367, 217,466)               | 118,113 (54,449, 189,963) | 0.1225 |

Boldface type indicates statistical significance

Complications at index hospitalization

Overall, rate of any complication was higher in patients who underwent craniotomy without iMRI compared to those with iMRI (19% vs. 14%, p = 0.04). Among different complications, only pneumonia or pulmonary complication rates were found to be higher in patients who underwent craniotomy without iMRI compared to those with iMRI (7.3% vs. 3.6%, p = 0.02). No difference in rates of other complications such as neurological or DVT/PE were noted among the cohorts, Table 4.
Discussion

In our study of 6,640 patients who underwent craniotomy for MBT during the study period, iMRI was used in 7% of patients. There was a statistically significant increase in iMRI use for MBT during the study period (0.66% increase per year). Our finding that patients who underwent craniotomy for MBT with iMRI suffered lower rates of post-operative morbidity relative to those who underwent craniotomy without MRI (14% vs. 19%, \( p=0.04 \)), suggest that iMRI improved the safety of tumor resection. There was no difference in the ER admission rates or payments at index hospitalization at 6-months or at 1-year after the procedure.

Use of iMRI has gradually evolved from low field [Signa SP (0.5T, GE Medical Systems, Milwaukee, WI), Odin system (Polestar, Israel) etc.] to high field magnet solutions [IMRIS (1.5T, Calgary, Canada), Siemens’ Brain suite system (1.5T, need to reflect the availability of 3T and 7T will be available soon) etc.] with improved resolution of images [31, 38].

Comparison with retrospective observational studies

One of the initial retrospective observational studies focusing on costs associated with iMRI guided brain tumor resections was reported by Kowalik et al. [29] in 2000 at the University of Minnesota using 1.5T Philips Gyroscan ACS-NT iMRI system. In this study, authors compared the costs associated with surgeries in the interventional MRI suite compared to the conventional OR suite. The mean LOS for first (3.7 vs. 8.2 days) and repeat resections (6.0 vs. 8.7 days) was significantly shorter for iMRI guided resection compared to non-iMRI guided resections. Also the repeat resection rates for non-iMRI users was 20% compared to 0% with iMRI users. In terms of hospital charges, iMRI users had 12.2% ($4063) lower charges compared to non-users for first procedure and 4.1% lower ($922) for recurrent procedures. For hospital costs, iMRI users incurred 14.4% lower ($3415) costs at first resections and 3.3% lower ($723) for repeat resections with iMRI use compared to non-iMRI users. The cost to charge ratio for first surgery was 69.6% for iMRI users compared to 71.4% for non-iMRI users for first resections. This study supports iMRI use for cranial procedures for improved financial margins for the hospitals. The authors did not clearly state the reason for decreased health care utilization with iMRI users compared to non-iMRI use in the manuscript. This difference may be attributed to the fact that the brain tumor resections were performed in the interventional suites compared to conventional OR, which may have offset the iMRI costs and charges.
Similarly, Schulder et al. [31] in 2003, reported the impact of using iMRI (PoleStar N-10 system) in 112 patients with brain tumors (high grade glioma = 25, low grade glioma = 12, pituitary tumors = 24, meningioma = 26). In this study, they reported a shorter LOS for patients with iMRI compared to non-iMRI users (9.4 vs. 5.1 days) with no impact on hospital charges among the groups. The mean increase in operative time associated with iMRI use was 1.6 h in this study. Hospital charges as costs were not available in this study [31]. In contrast, we found that iMRI users incurred marginally higher costs compared to non-users at index hospitalization (median difference: $157). The difference in LOS compared to our study can be attributed to improved neurosurgical critical care in recent years resulting in overall shortened LOS in patients with brain tumors.

Another retrospective study by Makary et al. [30] compared low-field iMRI (0.15 T) with conventional MRI (cMRI) use (within 48 h of tumor resection) in 65 patients who underwent tumor resection. Authors reported that complication rates were lower for iMRI users compared to cMRI users (44% vs. 72%) and the repeat resection interval was longer for iMRI users compared to cMRI users (20.1 vs. 6.7 months). iMRI was found to be cost-effective compared to cMRI only in patients who had repeat resections ($10,690 vs.$76,874/ resection free years). No differences in total costs, direct/indirect costs, total charges, net profits, cost/charge ratio or cost/investment ratio were noted among the iMRI and cMRI cohorts. There was no difference in reimbursement for initial resection in this study ($48,018 for iMRI compared to $52,522 for cMRI cohorts). Similarly, we did not note any significant difference in payments at index hospitalization among the cohorts (median: $58,067 vs. $57,910). Garcia-Garcia et al. [32] in a recent retrospective study (n=50 iMRI and n=146 control arm) reported an incremental cost per patients of €789 with iMRI use. Authors used Karnofsky-Performance score (KPS) in this study and reported an incremental cost-effectiveness ratio of €111 for each increase in post-operative KPS. It is critical to be cognizant that the image quality of low-field MRI is likely to be poor and may not be clinically useful. Therefore, this factor should be considered while convincing hospitals to invest in this modality. The information related to the field strength of the MRI (low vs. high field) cannot be extracted from the database.

**QALYs and iMRI use**

In a systematic review, Eljamel et al. [27] compared the cost of various intraoperative modalities such as 5-aminolevulinic acid/fluorescein, intraoperative ultrasound (iUS) and iMRI in high-grade glioma resection. Authors used additional capital cost (ACC) which was calculated as the purchase cost/(depreciation × number of cases per year). They assumed at least 20 cases per year of high-grade tumor resection and depreciation period of 8 years. Also, they took into account the use of iUS and iMRI for other tumor resections such as low-grade glioma, pituitary, meningioma etc. and assumed these modalities to be used in approximately 20% of high-grade tumors. Therefore, ACC was calculated as 0.20X purchase price/160. Gain in QALY was defined as an increase in PFS following GTR using an intraoperative modality compared to standard modality. This study reported additional cost per QALY was about $32,954 for iMRI compared to $6049 for iUS, $16,218 for 5-ALA and $3181 for fluorescein. Tumor heterogeneity, patient demographics and clinical effectiveness (OS/PFS) of a particular intraoperative modality was not correlated in this study [27]. In another study, Abraham et al. [33] used a microsimulation model to determine the cost-effectiveness of iMRI in 200,000 patients with high-grade gliomas (100,000 in each arm with iMRI and without iMRI). Cost efficacy was defined at a threshold of $100,000 per QALY in this study. Authors reported a benefit of 0.18 QALY using iMRI (1.34 vs. 1.16 QALYs) at an incremental cost of $13,447 ($176,460 with iMRI vs. $163,013 without iMRI). Authors reported a cost-effectiveness ratio of $76,442 per QALY which was below the threshold of $100,000. Based on probabilistic sensitivity analysis, this study reported that iMRI use was associated with a 99.5% chance of cost-effectiveness at willingness to pay threshold of $100,000/QALY [33]. Based on these studies, we can conclude that iMRI use provides cost effective improvement in QALYs. Although, iMRI is expensive compared to other intraoperative imaging tools, the image quality and safety of resection provided by iMRI is superior to other tools and should be considered.

**Future directions**

Makary et al. [30] reported the total implementation and operation cost to be ~3.8 million over iMRI 5-year useful life. The depreciation cost per iMRI procedure increased 3-fold during the 5-year useful span, which was related to decreased use of iMRI at the authors’ institution. Although there is an enormous upfront and maintenance cost associated with iMRI, we found no differences in health-care utilization in patients with MBTs for up to 1 year after the index procedure. There is evidence (albeit low-level) supporting the utility of iMRI in patients with MBTs to improve EOR and overall clinical outcomes. Justifying the clinical necessity of iMRI for improved patient care with the current lack of high-quality evidence supporting the cost-effectiveness of the modality makes it difficult to convince health-care systems to invest in the costly technology. We believe that the availability of iMRI is also beneficial in recruitment of...
cancer patients and also supports the work of physicians-scientists which tends to offset the initial installation and maintenance costs. Also technologies such as iMRI help cancer centres to maintain the status of “center of excellence” with latest technology available which help them to be at the forefront of cancer care and therefore procure grants or research funding. Using iMRI in the inpatient and outpatient settings for diagnostic studies is another way to offset some of the costs associated with this technology. Physicians and policy makers need to be aware of the costs associated with iMRI, so that they can plan ahead to optimize and offset initial costs and provide high quality care to patients. With emphasis on surgical precision, > 5500 iMRI units (> 1600 for neurosurgical indications) are likely to be installed worldwide by 2026 with compound annual growth rate of 7.5% amounting to ~315 million dollars US from 2017 to 2026. Therefore, the upfront installation costs of iMRI cannot be neglected and should be taken into account when considering health care economics related to this technology. Further prospective research is needed to determine the impact of iMRI use on clinical outcomes.

Strength and limitations

Market Scan database provides longitudinal data for an individual diagnosis, intervention, and related health care utilization [39, 40]. This database provides information regarding the real-world situation of a given pathology in terms of trends, readmissions, and health care utilization.

Limitations of our study include its retrospective design, selection bias and coding errors. The location and surgical details about the craniotomy cannot be extracted from the database. Furthermore, patient symptoms, imaging characteristics, clinical outcomes (extent of tumor resection, overall or progression free survival), patient satisfaction, health related quality of life and quality adjusted life years (QALYs) cannot be extracted from this database. Lack of codes to differentiate between grades of tumor (low-grade vs. high grade), molecular profile and pathological characteristics of malignant tumors that may have an impact on clinical outcomes, hospital readmissions and need for additional treatment and corresponding health care utilization cannot be extracted from the database. Information regarding the type and strength of magnet used for iMRI (low field vs. high field) cannot be extracted. Also, there is no documentation of OR times related to the procedures (with and without iMRI), however the index hospitalization payments are likely to indirectly represent the costs incurred related to the OR. Despite these limitations, we did not find any differences in payments at all time-points without and with iMRI use for the surgical procedure. We would also like to emphasize that our study may not reflect the complete picture of US health care related to iMRI and there may be some hidden costs which are not captured by this database. Future studies are needed to better elucidate this data at multi-institutional level. This is the first study to report the health care utilization with iMRI use during craniotomy for MBTs using a large administrative database.

Conclusions

iMRI use during craniotomy for MBT increased during the study period. iMRI was likely to be used in younger patients with higher comorbidities. iMRI use was associated with fewer post-operative complications at index hospitalization compared to without iMRI. iMRI use did not result in higher payments at index hospitalization, 6-months and 1-year after the index procedure. Following upfront installation cost of iMRI for the hospitals (which may be up to few million dollars), iMRI did not incur higher health care utilization for up to 1-year after the index procedure. These findings can be used to guide the neurosurgeons and policy makers regarding the utilization of iMRI in patients with MBTs without the additional burden of increased cost on the health care.

Declarations

Disclosures: The authors have no conflicts of interest or financial disclosures.

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