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Teaching Case

Magnetic Resonance Guided Radiation Therapy for High-Grade Glioma in Pregnancy: Planning, Validation, and Adaptive Fetal Dose Monitoring

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Introduction

The diagnosis of cancer during pregnancy is a rare clinical challenge, occurring in approximately 1 in 1000 pregnancies.[1] High-grade gliomas in this population necessitate prompt treatment, creating an ethical and physical dilemma: balancing maternal survival against the potential for radiation-induced fetal harm.[2]

The fetus is highly sensitive to ionizing radiation. Risks such as teratogenesis, growth restriction, and central nervous system damage are dose and gestational age-dependent.[3,4] While stochastic risks (eg, secondary carcinogenesis) have no known threshold, a cumulative fetal dose of <5 cGy is often accepted as a practical safety limit when radiation therapy (RT) is unavoidable.[3,5] Fetal dose from cranial irradiation originates primarily from head leakage and internal patient scatter.[6] Historically, minimizing this dose involved physical shielding and plan optimization on conventional linear accelerators (LINACs).[6,7]

The advent of magnetic resonance (MR) guided linear accelerators (MR-LINACs) introduces a new paradigm. These systems offer potential dosimetric advantages regarding peripheral dose and, crucially, eliminate ionizing radiation from setup imaging. We present a teaching case—to our knowledge, the first report of a pregnant patient with a high-grade glioma treated on an MR-LINAC—detailing the treatment planning, validation, and the critical role of adaptive fetal dose monitoring.

Case Presentation

A 21-year-old female (G1P0) presented at 14 weeks gestation with new-onset seizures and speech impairment. A noncontrast brain MR imaging revealed a large, 8.3 × 4.3 × 5.1 cm (AP × TV × CC) expansile T2/FLAIR hyperintense mass in the high parasagittal left frontal lobe. The mass caused a 3-mm rightward midline shift, regional sulcal effacement, and mass effect on the left lateral ventricle.

Following multidisciplinary consultation with neurosurgery and maternal-fetal medicine (MFM), the patient underwent an awake left-sided craniotomy for maximal safe resection. Postoperative imaging showed expected

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Research data are stored in an institutional repository and will be shared on request to the corresponding author.

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vasogenic edema and residual tumor. Pathology confirmed a WHO Grade III IDH R132H mutant astrocytoma with a Ki-67 rate of 3.2% and loss of ATRX nuclear immunoreactivity.

The care team elected to proceed with adjuvant RT immediately to maximize the distance between the target and the fetus before further gestational growth. The MFM team established a cumulative fetal dose limit of 5 cGy (acceptable) and 1.5 cGy (ideal). The patient tolerated the treatment well, completing the RT course in the 24th week of pregnancy, with no acute toxicities exceeding Grade 1. At 35 weeks gestation, she presented to an outside hospital fully dilated and in breech presentation. She underwent a stat C-section, delivering a healthy baby without complications, followed by a normal neonatal course.

MR-LINAC selection

A 1.5T Elekta Unity MR-LINAC was selected over a conventional C-arm LINAC to minimize fetal exposure through several inherent design advantages. First, the system's MR cryostat provides significant passive self-shielding against head leakage, which is further complemented by the 7MV flattening-filter-free (FFF) beam that ensures sharp dose falloff and reduced scatter.[8] Additionally, the extended 143.5-cm source-to-axis distance physically reduces peripheral dose at the fetal depth compared to standard isocenter geometries. Crucially, the integrated MR imaging capability allowed for daily setup and monitoring without the cumulative ionizing radiation dose associated with cone beam computed tomography (CT) or kV imaging necessitated by conventional systems.

Simulation and planning

A "zero CT-sim" workflow was adopted. Electron density (ED) values were derived from a pre-existing diagnostic CT using a validated Hounsfield unit-to-ED calibration. For MR simulation, standard cranial sequences were followed by overlapping T2 scans of the abdomen. Using MIM Maestro software, these were stitched to create a single 768-slice composite MR data set (Fig. 1) for dimensional evaluation.

A 30-fraction simultaneous integrated boost (SIB) plan was prescribed to 57 Gy (190 cGy/fraction) to the high-dose planning target volume (PTV) and 50 Gy (167 cGy/-fraction) to the low-dose PTV. The plan used 6 Intensity Modulated Radiotherapy (IMRT) beam angles and 25 total segments (255 MU).

Pretreatment validation (Phantom)

To validate fetal dose estimates, a custom "Maternal Anthropomorphic Analogue" (MAMA) phantom was designed (Fig. 2). It consisted of an Sun Nuclear (SNC) ArcCheckMR and solid water arranged to mimic the patient's torso. The MAMA phantom was placed at the treatment isocenter, with an A12 ion chamber positioned at a conservative 3 cm depth (plus 1 cm bolus) corresponding to the location of the uterine fundus. The phantom was exposed to the final treatment plan.

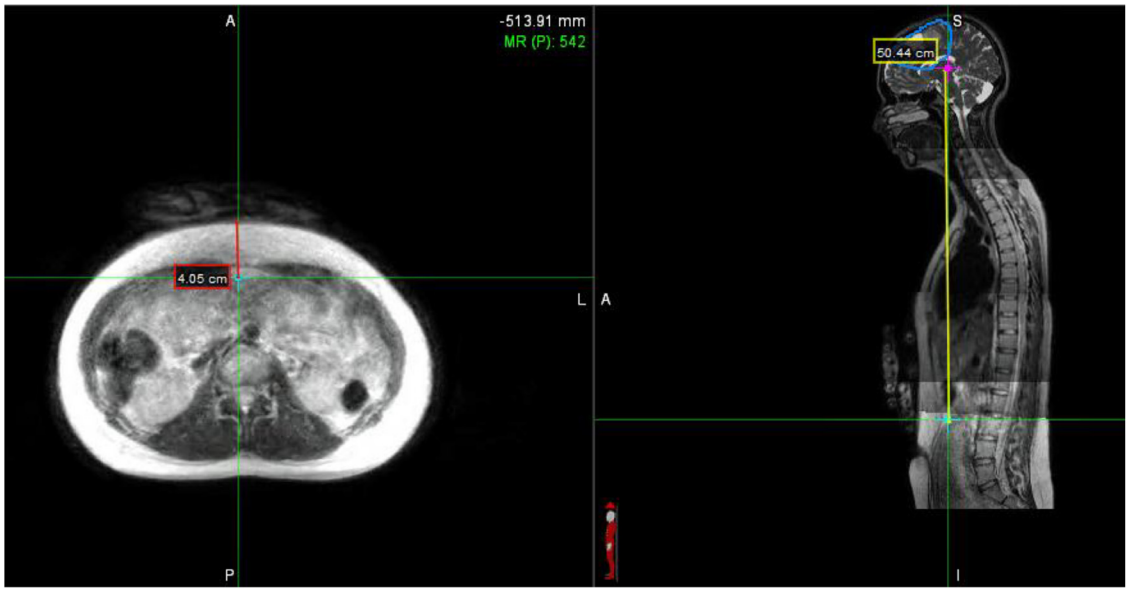
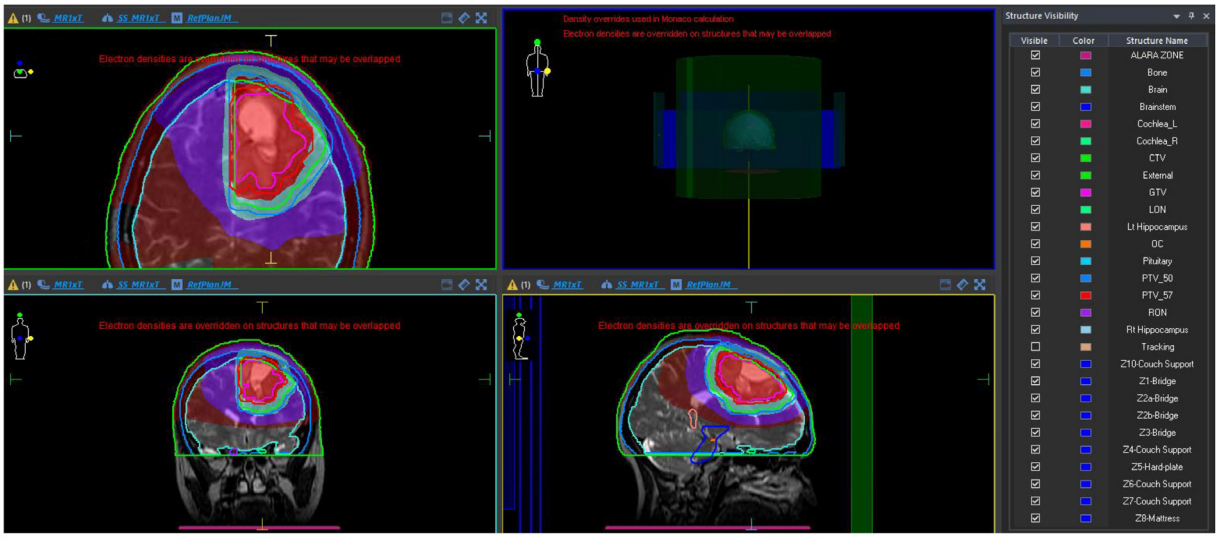


Figure 1 Stitched MR with MR-Sim Separation + Depth. Sagittal and transverse MR images from the stitched 768-slice data set. This allowed for precise measurement of the separation (51.4 cm) between the inferior extent of the target and the uterine fundus, as well as the fundus depth (4.0 cm).



DVH Statistics

Dosimetric Criteria | Statistics | Display

Structure	Dosimetric Criterion	Actual Value
PTV_57	V5700cGy > 95 % (-3 %)	95.11 %
PTV_50	V5000cGy > 95 %	98.74 %
Lt Hippocampus	Dmax < 1600 cGy	1323.4 cGy
	V900cGy < 99.9 %	22.16 %
Rt Hippocampus	Dmax < 1600 cGy	1309.0 cGy
	V900cGy < 99.9 %	12.76 %
Brain	V3000cGy < 50 %	26.17 %
	Dmean < 3000 cGy	1935.5 cGy
Brainstem	V5500cGy < 0.5 cm³	0.000 cm³
	V3000cGy < 33 %	0.00 %
	Dmax < 6000 cGy	813.9 cGy
Cochlea_L	Dmax < 4500 cGy	142.1 cGy
	Dmean < 3000 cGy	117.3 cGy
Cochlea_R	Dmax < 4500 cGy	101.0 cGy
	Dmean < 3000 cGy	86.8 cGy
GTV	V100cGy > 99.6 %	100.00 %
LON	Dmax < 5400 cGy	194.5 cGy
OC	Dmax < 5400 cGy	244.6 cGy
Pituitary	Dmean < 3600 cGy	174.2 cGy
RON	Dmax < 5400 cGy	181.7 cGy

Figure 2 Monaco IMRT plan. Coronal, sagittal, and transverse views of the 57/50 Gy SIB treatment plan in the Monaco Treatment Planning System (TPS), demonstrating target coverage and the As Low As Reasonably Achievable (ALARA) avoidance zone inferiorly. The Dose-Volume Histogram (DVH) shows constraints were met.

Plan quality and dose estimates

The IMRT plan met all standard clinical constraints based on QUANTEC[9] and included an As Low As Reasonably Achievable (ALARA) avoidance zone at the inferior aspect of the scan to assist the optimizer (Fig. 3). The initial pretreatment MAMA phantom validation, based on the static MR-Sim separation of 51.4 cm, projected a total fetal dose of

Figure 3 MAMA phantom. The "Maternal Anthropomorphic Analogue" (MAMA) validation phantom, consisting of an ArcCheckMR and solid water, shown on the Elekta Unity couch.

QA Phantom Comparison Measurement

Date:

Phantom: Solid water 4cm + 2cm (holder) + 5 + 5 + 3 cm

Chamber: A12

Performed by:

Field Size: 10x10 cm

MUs delivered: 200 MU

QA AT 2673 CHANGED TO 1350 FOR THIS TO MATCH COUCH INDEX OF 5

	Reading 1	Reading 2	Reading 3	Average
	41.270 nC	41.260 nC	41.260 nC	41.263 nC

10x10 in SW: 41.263 nC 41263.33 pC

Cal. Factor: 0.004847 cGy/pC

0.05 cGy/fx acceptable	
10.31583 pC/fx acceptable/expected	
5.83 pC measured plan	
0.31 pC of leakage current	
5.52 pC estimated	0.803 cGy estimated

Patient Name:

Plan: Brain

Phantom: Solid water plus arccheck (5+5+5+2+1+1) = 17 cm at sensitive point from couch, 3 cm depth for conservative approach (4 cm anatomical), 1 cm of bolus on top to represent clinical setup)

Setup: Chamber 50.4 cm from iso

Figure 4 QA phantom calibration and measurement. The calibration and ion chamber measurement calculations for the pretreatment validation, resulting in the 0.803 cGy total dose estimate.

0.803 cGy (Fig. 4). Thermoluminescent detector (TLD) measurements from the first week extrapolated to a total skin surface dose of 0.6 cGy.

In vivo verification and adaptive monitoring

For in vivo verification, 5 TLDs (UW Madison Radiation Calibration Laboratory) were placed on the patient's skin (3 above the fundus, 2 above the umbilicus, all beneath a 1-cm bolus) for the first 5 fractions.

Critically, recognizing that fetal growth would decrease the target-to-fetus separation, a weekly adaptive monitoring protocol was instituted. Every 5 fractions, a T2 scan of the abdomen was acquired and stitched to the original MR-Sim scan. The MAMA phantom geometry was updated to match the new separation, and the weekly dose was estimated.

Adaptive monitoring results

Weekly MR stitching revealed significant anatomic changes. Over the 6-week course, the fetus grew, and the uterine fundus migrated superiorly by 7.0 cm. The separation distance decreased from 51.4 cm at simulation to 44.3 cm by the final week. This anatomic shift invalidated the initial 0.803 cGy estimate. As the fetus moved closer to the scatter source, the measured dose per fraction increased (Table 1). The weighted average of these weekly measurements yielded a final, clinically adjusted cumulative fetal dose of 1.54 cGy.

Discussion

The decision to proceed with RT during pregnancy is the first major teaching point. While delaying treatment

Table 1 Adjusted final uterine fundus dose estimate

Timepoint	Separation	Depth	Dose to point
Sim	51.4 cm	4.0 cm	0.803 cGy
Week 1	47.6 cm	3.7 cm	1.257 cGy
Week 2	46.1 cm	3.7 cm	1.485 cGy
Week 3	44.7 cm	3.4 cm	1.715 cGy
Week 4	44.6 cm	3.3 cm	1.734 cGy
Week 5	44.5 cm	3.2 cm	1.744 cGy
Week 6	44.3 cm	3.1 cm	1.778 cGy
Week 7	44.3 cm	3.0 cm	1.785 cGy

This table documents the critical finding of anatomic change. As the separation distance decreased due to fetal growth, the measured dose to the uterine fundus (via the reconfigured MAMA phantom) increased weekly. The final weighted average provides the most accurate dose estimate.

until postpartum is often preferred to avoid fetal risk, as described by Khandaker,[10] the aggressive nature of this patient's WHO Grade III glioma and the timing (early second trimester) necessitated immediate intervention.

The primary key concept of this case is that for pregnant patients undergoing fractionated RT, pretreatment fetal dose validation is necessary but not sufficient. Our initial phantom measurement (0.803 cGy) and TLD extrapolation (0.6 cGy) were significant underestimates because they assumed static anatomy. The 7-cm superior migration of the uterine fundus nearly doubled the weekly dose intensity by the end of treatment. The final weighted dose of 1.54 cGy, while slightly exceeding the "ideal" 1.5 cGy goal, remained well below the "acceptable" 5 cGy safety limit. Without adaptive monitoring, the true dose accumulation would have been unknown.

The second teaching point is the unique utility of the MR-LINAC in this scenario. The "zero CT-sim" workflow, leveraging a diagnostic CT and stitched MR scans, completely avoided simulation-related ionizing radiation, ensuring that all ionizing radiation received by the patient originated solely from the therapeutic beam. The MR-guided radiotherapy (MRgRT) system not only offered dosimetric advantages (self-shielding, FFF beam) that contributed to the low fetal dose, but its integrated MR imaging was the enabling technology for the adaptive monitoring protocol. This weekly, nonionizing anatomic verification would not have been possible on a conventional LINAC without repeated, and likely unacceptable, CT imaging.

This case builds on previous work by the American Association of Physicists in Medicine (AAPM) Task Group 36 guidelines[5] and Labby et al,[6] which established protocols for phantom-based dose estimation on conventional LINACs. Our workflow advances these methods by using the unique capabilities of the MR-LINAC. The integrated MR imaging allowed for weekly, nonionizing verification of the dynamic separation between target and fetus—a workflow that would be clinically impractical with CT-based image-guided radiotherapy due to the associated radiation dose.

The use of MR-LINACs for pregnant patients is emerging. Wooten et al[11] recently reported MRgRT for rectal cancer, highlighting soft-tissue management near the fetus. Our case expands this application to cranial targets, where the primary benefit shifts to monitoring the dynamic fetal separation.

Our approach can be contrasted with other modern modalities. Soon et al[12] recently reported using Gamma Knife (GK) radiosurgery for a pregnant patient, achieving a negligible fetal dose. While GK offers superior sparing for single-session treatment of small targets, it is not suitable for large, infiltrative gliomas requiring fractionated therapy. Intensity modulated proton therapy (IMPT) is widely recognized as an optimal modality for minimizing out-of-field fetal dose due to the Bragg peak effect and substantially reduced scatter compared to photon therapy.[13] Furthermore, when photon therapy is used, 3D conformal RT has historically been preferred over IMRT to minimize monitor units and the associated head scatter.[14] In this case, an MR-LINAC using a coplanar IMRT approach was selected. While IMRT inherently increases monitor units, the 1.5T MR-LINAC design mitigates peripheral dose through its self-shielding cryostat, extended 143.5 cm source-to-axis distance, and FFF beam. Although IMPT offers superior baseline dosimetry and lower theoretical fetal doses than photon-based IMRT, static dose simulations cannot account for the dynamic superior migration of the fetus over a multiweek fractionated course. Our findings demonstrate that the MR-LINAC's nonionizing, weekly volumetric imaging provides critical dynamic verification.

Conclusion

We report the first successful treatment of a pregnant patient with a high-grade glioma on an MR-LINAC. This case highlights that static pretreatment dose validation is insufficient for fractionated courses due to significant fetal growth. While modalities such as IMPT offer superior baseline dosimetric sparing of the fetus, the MR-LINAC's ability to perform adaptive, nonionizing anatomic monitoring allowed for the accurate tracking and verification of cumulative fetal dose, ensuring it remained within safe limits. This adaptive workflow represents a valuable and innovative clinical paradigm for managing dynamic anatomic changes and ensuring fetal safety when using fractionated photon RT.

Disclosures

None.

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