Advances in Radiation Oncology (2025) **10**, 101673

advances in radiation oncology

www.advancesradonc.org

Teaching Case

Treatment of a Pregnant Patient With a Brain Tumor Using Pencil Beam Scanning Proton Therapy

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Received 22 September 2023; accepted 25 October 2024

Background

Radiation therapy plays a crucial role in the treatment of patients with cancer, including those who are pregnant.[1] However, balancing maternal prognosis and fetal risk can be challenging.[2,3] The majority of fetal dose deposition is attributed to head leakage and patient scatter, necessitating specialized approaches to mitigate these contributions.[1,4] In x-ray therapy (XRT), a lead fetal shield and planning modifications are often employed to reduce fetal exposure.[1,5-7]

Traditionally, XRT has been the standard for treating pregnant patients when radiation therapy is medically necessary. Case studies have reported fetal dose estimates ranging from 0.5 to 2 cGy in patients with brain tumors.[6,8-10] Some centers use a shielding device to achieve lower doses, albeit at the cost of practical challenges.[1,11,12] Shield placement over the abdomen can pose clearance issues and restrict gantry rotation to partial anterior arcs to maintain the primary beam within the shielded region. These restrictions in beam angles can increase the dose to normal tissues and increase the risk of acute and late side effects in these young patients. Alternatively, certain centers forgo fetal shields, accepting a higher fetal dose.

Pencil beam scanning proton therapy (PBS-PRT) emerges as a promising alternative for pregnant patients, and previous case studies have reported favorable results.[13-17] The main contributor to fetal exposure from PBS-PRT is internal neutrons, produced when protons interact with the patient.[4] We previously conducted a retrospective study at our institution to determine the total fetal equivalent dose from PBS-PRT compared with XRT when treating brain and head and neck cancers.[18] Fetal equivalent dose was reduced by a factor of 10 with PBS-PRT compared with XRT for all 7 cases that were investigated without making any compromises to the patient's treatment. These findings highlight the potential of PBS-PRT in effectively treating pregnant patients while minimizing fetal radiation exposure and led to a change of practice at our institution. Herein, we describe the case of the first pregnant woman with a brain tumor we treated with PBS-PRT after comparison with an XRT plan.

Case

A 34-year-old pregnant woman initially presented with left-sided hearing loss and facial weakness at 17 weeks gestation. A brain magnetic resonance imaging (MRI) was performed (without contrast because of her pregnant status), which showed a T1 hypointense brain lesion at the left cerebellopontine angle. This was thought to most likely represent a schwannoma or meningioma given the

Sources of support: This work had no specific funding.

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

The patient involved in the case report has provided informed written consent to publish their case information. The signed consent form may be provided if requested.

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https://doi.org/10.1016/j.adro.2024.101673

imaging findings and growth during pregnancy. At 22-weeks of gestation, the patient underwent a left suboccipital craniotomy to remove the tumor, with a subtotal resection with residual disease infiltrating the brainstem with a finding of high-grade B-cell lymphoma on pathology. There was no evidence of disease elsewhere in the body. After multidisciplinary evaluation and in line with the patient's aim to avoid systemic therapy before delivery, the patient was recommended focal radiation therapy to provide durable local control to the residual brainstem disease and prevent symptomatic local progression before initiation of systemic therapy postdelivery.

At 23-weeks of gestation, a computed tomography (CT) simulation and brain MRI without contrast were conducted, revealing 6.8 cm^3 residual tumor invading the brainstem. The CT scan encompassed the top of head to 1 cm below the chin, without any additional fetal shielding. Fetal shielding for diagnostic imaging has been shown to potentially increase dose and have negligible benefit therefore it was avoided in this case.[19] During simulation, the distance from the patient's eyes (the approximate isocenter location) to fundus (55 cm) and the anterior-to-posterior patient thickness at the fundus was measured.

A proton therapy plan was created in Eclipse with a prescription of 25 Gy in 5 fractions to the residual tumor with a 20 Gy in 5 fractions low dose clinical target volume (CTV) including a 1 cm anatomically constrained expansion from the residual tumor and operative cavity. This hypofractionated course was selected for several reasons, including minimizing total radiation exposure from daily image-guided radiation therapy, and the extensive literature demonstrating safety of hypofractionation for cerebellopontine angle tumors. The treatment plan comprised 3 axial fields including a left posterior oblique, left anterior oblique, and right posterior oblique beams. The contralateral right posterior oblique beam was added to break up end of range biologic enhancement from the left-sided beams. No vertex beam or additional beam accessories were deemed necessary for achieving adequate coverage. Following institutional standard of practice for PBS-PRT patients, the calculations were verified with an in-house Monte Carlo dose calculation.[20]

A comparison plan was generated in Eclipse using XRT with the same CT simulation and dose prescription as the PBS-PRT plan. This XRT comparison plan employed volumetric modulated arc therapy with 3 partial anterior arcs and a flattening filter free beam energy of 6 MV. In adherence to our standard of practice for treating pregnant patients with XRT, a lead fetal shield was positioned between the gantry and fetus, necessitating limiting gantry rotation to the angles 85° to 275° and both a shift to the superior edge of the field and an anterior shift to accommodate gantry rotation clearance of the shield. Dose distributions and beam geometries for both the PBS-PRT and XRT plans are illustrated in Fig. 1, with decreased low dose bath from the PBS-PRT plan as expected.

Pretreatment measurements were performed for both plans using the setup depicted in Fig. 2, with an anthropomorphic RANDO phantom representing the patient's body. Measurements for the proton plan were performed on a Hitachi Probeat V PBS-PRT system with a WENDI-2 neutron meter placed at the phantom's abdomen to measure dose at the location of the fetus. This neutron detector was selected because its response function was designed specifically to match a fluence-to-ambient dose conversion function to provide accurate measurements of ambient dose equivalent, accounting for the biologic effect of neutrons.[21] Therefore, the measured neutron dose is reported in sieverts as opposed to gray. Slices of acrylic were introduced into the setup, inferior to the RANDO phantom, to obtain measurements at various distances from isocenter to the detector's center in 5 cm increments over the range of the estimated fundus position. A similar arrangement was employed to assess the imaging dose resulting from 2-dimensional (2D) kilovoltage radiographs used for patient positioning with a Fluke 451 meter, which is capable of measuring leakage and scatter around diagnostic radiograph and radiation therapy suites.

The XRT plan was delivered to the phantom using a Varian TrueBeam. A solid water block was placed at the phantom's abdomen, 30 cm in height, with a Farmer-type ion chamber (the standard for absolute photon dose measurements) oriented crossline at a 5 cm depth within the block. Multiple measurements were obtained at various distances from isocenter to the ion chamber using solid water representing potential daily variations in the location of the apex of the fundus.

Fetal position was estimated from patient measurements and fetal growth predictions of 1 cm growth superiorly per week of gestation.[1] The distances from isocenter to fundus were first converted to distance from inferior edge of CTV to fundus to provide a direct comparison between the XRT and PBS-PRT measurements. Next, the acquired measurements at various distances, now converted to inferior edge of CTV to fundus, were plotted to generate a curve from which fetal dose could be interpolated at distances not directly measured, shown in Fig. 3. This curve was used to estimate fetal dose at the time of treatment. For the entire treatment course, the estimated total fetal equivalent dose from phantom measurements was 0.04 mSv for PBS-PRT and 1.1 mSv for XRT. Two-dimensional kilovoltage imaging contributed an additional 0.005 mSv for PBS-PRT and the simulation CT added 0.08 mSv. Two-dimensional kilovoltage imaging dose in XRT was undetectable with the Fluke meter under the fetal shield.

The PBS-PRT plan was determined by the physician to provide superior target coverage and normal tissue

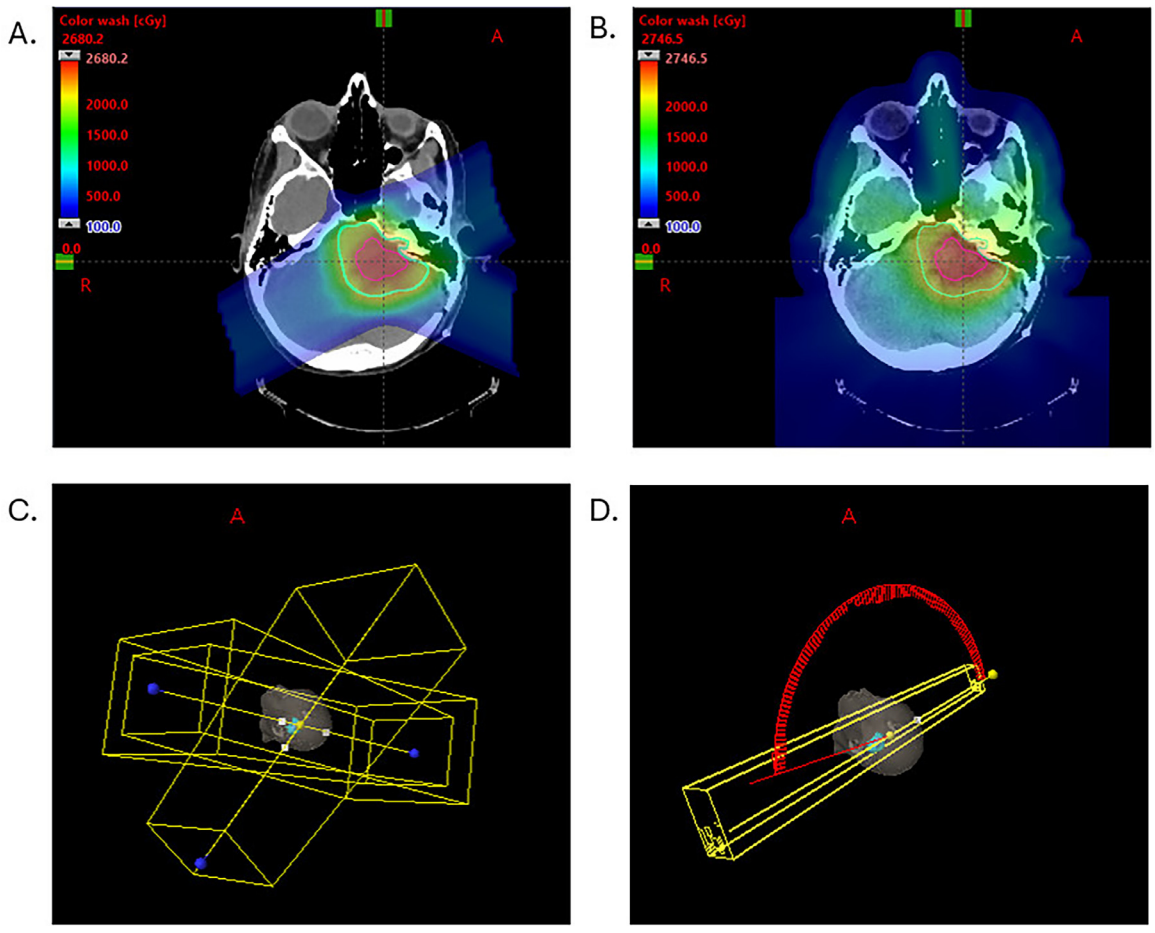

Figure 1 Representative axial computed tomography slices showing dose distributions of the (A) proton therapy (PRT) and (B) x-ray radiation therapy (XRT) comparison plans for the pregnant patient. Beam configurations including (C) PRT static fields and (D) XRT partial anterior arcs.

sparing. Even when considering potential uncertainties and additional imaging dose, the total fetal equivalent dose remained significantly lower for PBS-PRT. Based on this data, the physician concluded PBS-PRT was the best treatment option for the patient. The patient subsequently received PBS-PRT at 25 weeks gestation.

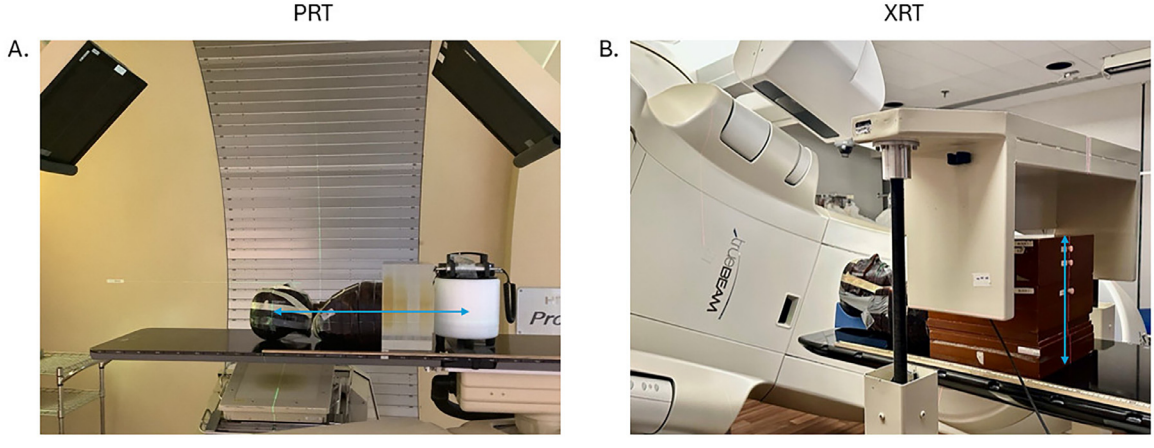

Figure 2 (A) PRT setup for fetal dose measurements using a WENDI-2 meter, anthropomorphic phantom, and acrylic. The arrow represents the isocenter to fundus distance. (B) XRT setup with an ion chamber, anthropomorphic phantom, solid water block, and fetal shield. The arrow represents the anterior-to-posterior patient thickness at the fundus.
Abbreviations: PRT = proton therapy; XRT = x-ray radiation therapy.

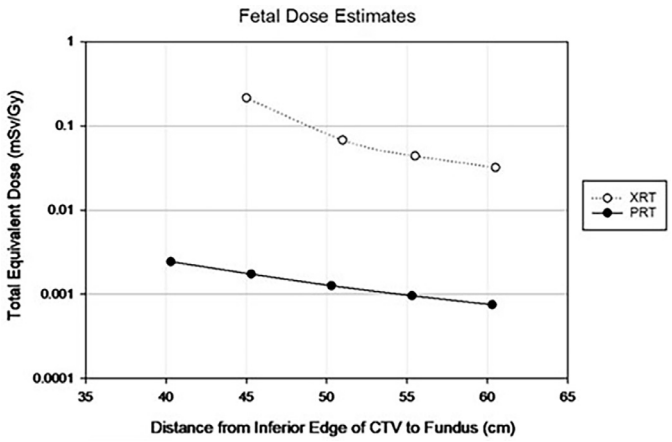

Figure 3 Measured total equivalent dose in millisieverts per prescription gray as a function of distance from the inferior edge of the CTV in centimeters cm to the center of the detector (fundus) from the PRT and XRT brain plan.
Abbreviations: CTV = clinical target volume; PRT = proton therapy; XRT = x-ray radiation therapy.

The patient's radiation exposure was monitored with Landauer badges, Luxel+ and Neutrak CR-39 plastic nuclear track detectors (Landauer, Glenwood, IL), at the sternum and umbilicus for the patient's simulation CT and during the imaging and treatments of all fractions. These locations were selected to encompass the range within which the fundus may be located. The Luxel+ measures beta and photon radiation, whereas the Neutrak, sealed inside the Luxel+, is insensitive to these types of radiation and is capable of measuring exposure due to neutrons. Landauer reported an x-ray deep dose equivalent of 0.7 mSv from the badge at the sternum and the badge at the umbilicus registered an undetectable dose level, below the detection range of 0.1 mSv. The neutron dose was also at an undetectable level by the badges at both the sternum and umbilicus. We had estimated a total dose of 0.3 mSv at the sternum and 0.05 mSv at the umbilicus from the phantom measurements.

The patient completed treatment with PBS-PRT without complications. No compromises were required in the planning or delivery in order to further minimize fetal dose, resulting in the same treatment plan that would be given had the patient not been pregnant. The patient later gave birth to a healthy baby weighing 2.26 kg with an Apgar score of 8 at 1 minute and 9 at 5 minutes. At last follow up 6 months posttreatment, the patient was doing well without evidence of active disease, with a healthy infant.

Discussion

This case study demonstrates the significant advantage of PBS-PRT over XRT in reducing fetal radiation exposure for treating brain tumors. In this specific case, the fetal dose from PBS-PRT was a factor of 27.5 times less than XRT.

A detailed analysis of measurement uncertainty in XRT compared with PBS-PRT was explored in our previous study.[18] XRT measurements were found to be sensitive to setup changes, including fetal shield placement, leading to an uncertainty of about 15%. Conversely, the main cause of uncertainty in PBS-PRT is related to the uncertainty in fetal relative biological effectiveness (RBE) of neutrons (2-10) and calibration of the WENDI-2 neutron detector (accurate to within a factor of 2).[22,23] The WENDI-2 meter has an implicit quality factor of about 4 to 5.[19] Therefore, the upper limit to the uncertainty between fetal equivalent dose and measurement is about a factor of 5. Even when accounting for the uncertainties attributed with neutron RBE of fetal dosimetry, PBS-PRT is still favorable.

No beam-modifying accessories were required for this patient's treatment. However, for more superficial tumors, a range shifter might have been necessary, which would increase the fetal dose because of increased neutron production in the range shifter. Larger treatment volumes would require additional monitor units, further increasing dose. If conventional fractionation was prescribed, the fetus would have grown significantly closer to the target throughout the treatment course and additional imaging would be necessary for patient alignment. The total dose to the fetus would also be higher because of the increased prescription dose compared with hypofractionated treatments.

A Hitachi Probeat V PBS-PRT system was used for the patient's treatment. The system was designed to minimize beam spot size and has a vacuum up to the steering magnets with minimal material in the beamline.[24] Consequently, this design minimizes neutron production, achieving lower neutron levels compared to other PBS-PRT systems.

Imaging was found to be the greatest contributor of dose to the fetus in PBS-PRT and should be used

carefully. An option for minimizing imaging dose is to limit imaging to coplanar angles relative to the imaging system for patient setup and then rotate the couch to the treatment position. Surface tracking methods such as Align VisionRT could then be used to verify the couch position throughout treatment.

Conclusions

This case study demonstrates PBS-PRT significantly minimized fetal dose for a pregnant patient with a brain tumor compared with XRT. No compromises were made to the PBS-PRT plan, ensuring the patient received the same plan quality as a patient who is not pregnant. PBS-PRT has been adopted as a treatment option for pregnant patients at our institution following our retrospective study, and this case details the first pregnant patient we treated with PBS-PRT.

Disclosures

John Lucido receives consulting fees from Varian, paid to his institution, which is not related to this work, however it was related to some equipment (linear accelerator) that was mentioned (but not endorsed or evaluated); receives payment from Global Bridges Oncology Referee for educational travel grant RFA, paid to his institution, which is not related to this work. William Breen receives consulting fees from GE Healthcare, paid to his institution; participates on a data safety monitoring board/advisory board for GE Healthcare, paid to his institution. Nicholas Remmes holds investments in many individual stocks, each valued at <$5000, including some health care stocks. To the best of his knowledge, he has no conflicts of interest between these holdings and his professional responsibilities. Additional details can be made available on request. Justine Dupere declares no conflicts of interest.

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