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High-dose-rate brachytherapy of rhabdomyosarcoma limited to the external auditory canal

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Abstract

PURPOSE—To report on the single-catheter high-dose-rate brachytherapy treatment of a 21-month-old girl child with an embryonal, botryoid-type, rhabdomyosarcoma limited to the external auditory canal (EAC).

METHODS AND MATERIALS—A 2.4-mm diameter catheter was inserted into the right EAC and placed against the tympanic membrane. A computed tomography simulation scan was acquired. A brachytherapy treatment plan, in which 21 Gy in seven fractions was prescribed to a 1-mm depth along the distal 2 cm of the catheter, was generated. Treatments were delivered under anesthesia without complication. A dosimetric comparison between this plan and an intensity-modulated radiation therapy (IMRT) plan was then conducted. A clinical target volume (CTV), which encompassed a 1-mm margin along the distal 2 cm of the catheter, was delineated for both plans. Given positioning uncertainty under image guidance, a planning target volume (PTV = CTV + 3-mm margin) was defined for the IMRT plan. The IMRT plan was optimized for maximal CTV coverage but subsequently normalized to the same CTV volume receiving 100% of the prescription dose (V_{100}) of the brachytherapy plan.

RESULTS—The IMRT plan was normalized to the brachytherapy CTV V_{100} of 82.0%. The PTV V_{100} of this plan was 34.1%. The PTV exhibited dosimetric undercoverage within the middle ear and toward the external ear. Mean cochlea doses for the IMRT and brachytherapy plans were 26.7% and 10.5% of prescription, respectively.

CONCLUSIONS—For rhabdomyosarcomas limited to the EAC, a standard brachytherapy catheter can deliver a highly conformal radiation plan that can spare the nearby cochlea from excess radiation.

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Keywords

Rhabdomyosarcoma; High-dose rate; External auditory canal; Pediatrics

Purpose

Rhabdomyosarcoma of the nonparameningeal head and neck is associated with favorable disease control outcomes (1). However, prolonged chemotherapy and radiation therapy treatments are associated with long-term disease morbidity, including growth retardation, facial hypoplasia, poor dentition, impaired vision, decreased auditory acuity, hypothyroidism, cognitive disability, and secondary malignancy (2, 3). Methods for minimizing treatment toxicity are therefore of paramount importance for these patients. One such method is high-dose-rate (HDR) brachytherapy, which can provide highly conformal dose distributions to target lesions, while minimizing dose to surrounding structures (4).

Here, we report on the usage of HDR brachytherapy for treating a 21-month-old girl child with an embryonal, botryoid-type, rhabdomyosarcoma limited to the right external auditory canal (EAC). Our first objective is to describe the technical aspects of HDR brachytherapy for treating disease limited to the EAC. Our second objective is to perform a dosimetric comparison between HDR brachytherapy and intensity-modulated radiation therapy (IMRT) plans.

Methods and materials

Patient presentation

The patient initially presented with “white caviar”-like material protruding from the right EAC, as shown in Fig. 1a. The mass persisted despite antibiotic treatment. Biopsy showed embryonal rhabdomyosarcoma, botryoidtype. A MRI scan (Fig. 1b) revealed a T1 hypointense, T2 hyperintense mass in the right EAC, spanning 1.7×0.8 cm. There was no invasion of the middle ear, mastoid, or parotid space. A CT scan (Fig. 1c) confirmed that there was no bony erosion. She was assigned stage I (T1aN0M0), group 3 disease. She then underwent chemotherapy with vincristine, actinomycin D, and cyclophosphamide. Repeat biopsy after 12 weeks of chemotherapy showed persistent embryonal rhabdomyosarcoma. However, residual disease was not visualized during the radiation oncology consultation after biopsy. The patient was recommended to undergo HDR brachytherapy to the EAC.

Technical aspects of HDR applicator insertion

The patient was taken to the CT simulation room. She was anesthetized under propofol anesthesia in the supine position by the pediatric anesthesiology team. Her head was tilted toward the left, such that the right ear faced upward. A 2.4-mm diameter brachytherapy catheter was gently lubricated and inserted into the right EAC and against the tympanic membrane. Care was taken to avoid puncture of the tympanic membrane. Once in place, a button was fixed to the catheter at the ear opening to ensure safe and reproducible insertion during treatments. The catheter was removed, and the distance from the button to the tip of the catheter was measured as 2.0 cm (Fig. 2a). The depth of insertion was confirmed via

measurement on the patient's prior diagnostic CT scan. The catheter was then reinserted, and a planning CT scan was then acquired with the catheter in place (Fig. 2b).

The CT scan was then downloaded onto the treatment planning system (BrachyVision, Varian Brachytherapy, Charlottesville, VA). A prescription dose of 21 Gy in seven fractions was prescribed to 1 mm from the catheter surface. Dose was prescribed to the distal 2 cm of the catheter. Organs at risk (e.g., right cochlea, right temporal lobe, and brainstem) were then contoured. The medical physics team digitized the catheter and adjusted the dwell times along the catheter to develop a radiation treatment plan.

The first treatment was delivered according to this plan. For the second through seventh treatments, the prescription depth was changed from 1 mm to 0.5 mm from the catheter surface, to decrease the dose to the surface of the EAC. All treatments were delivered under propofol anesthesia without any complications.

Dosimetric comparison between HDR brachytherapy and IMRT

A dosimetric comparison between the HDR brachytherapy and IMRT plans was then conducted. For the HDR brachytherapy plan, a clinical target volume (CTV) was defined by placing a 1-mm margin around the distal 2 cm of the catheter to create a 4.4-mm diameter structure. The CTV volume receiving 100% of the prescription dose (V_{100}) and minimum dose received by 90% of the volume (D_{90}) were then estimated.

The IMRT plan used the same CTV and prescription dose on the brachytherapy planning CT. Although a patient treated with IMRT likely would not have undergone catheter placement and would have been treated with a different dose fractionation scheme (e.g., 36 Gy in 20 fractions), accounting for these differences could have introduced additional dosimetric bias. All doses were expressed in terms of the percent prescription. A planning target volume (PTV) was generated by placing a 3-mm margin around the CTV to account for positioning error under daily image guidance. Then, an IMRT plan was created on a commercial treatment planning system (Eclipse, Varian Medical systems) using a mini multi-leaf collimator (2.5-mm width). The objective was to maximize coverage of the CTV, while minimizing dose to the organs at risk. The PTV, which extended close to the external auditory meatus, was not included within the objective function, due to the sensitivity of the optimization algorithm to air pockets near this complex tissue interface. Simulated bolus was not placed over the external auditory meatus, due to the presence of the catheter button (Fig. 2b) and the high likelihood of residual air gaps after bolus placement.

The IMRT plan was normalized to the same CTV V_{100} of the brachytherapy plan. Dosimetric indices for the brainstem, right cochlea, CTV, and right temporal lobe were computed for both plans. The PTV V_{100} for the IMRT plan was also calculated.

Results

After brachytherapy, the patient continued vincristine, actinomycin D, and cyclophosphamide chemotherapy for a total of 46 weeks. CT scan 3 months after

brachytherapy revealed no abnormalities. The patient followed up in clinic 8 months after brachytherapy completion, and there was no clinical evidence of disease.

HDR brachytherapy treatment plan

The HDR brachytherapy treatment plan is shown in Fig. 3a. For the CTV, the V_{100} and D_{90} were 82.0% and 87.9% of prescription, respectively. The dose fall off was rapid across the middle ear cavity, such that the right cochlea received a mean dose of 10.5%.

Dosimetric comparison between HDR brachytherapy and IMRT

Fig. 3b shows the IMRT treatment plan. After normalization to a CTV V_{100} of 82.0%, the CTV D_{90} was 96.9%. However, the V_{100} for the PTV was only 34.1%, partially due to air within the middle ear and adjacent to the external auditory meatus. Furthermore, the cochlea, which was located approximately 4-mm away from the catheter, had a greater mean dose of 26.7% for the IMRT plan compared with 10.5% for the HDR brachytherapy plan. However, the brainstem and right temporal lobe doses were quite similar between the two plans. Table 1 summarizes dosimetric indices for both plans. Relevant dose-volume histograms are shown in Fig. 4.

Discussion

We have described the technical aspect of using HDR brachytherapy for treating embryonal rhabdomyosarcoma limited to the EAC. The technical setup was extremely simple, in that it involved the insertion of only a single-HDR catheter into the EAC. The HDR brachytherapy plan was also highly conformal, and the nearby cochlea was largely spared from high-dose radiation. The rapid dose fall off may have accounted for the lower CTV V_{100} of 82.0% on subsequent analysis. However, we also approached the spatial resolution limits of the contouring and dose calculation algorithms, while analyzing the dosimetry of the 4.4-mm diameter CTV. It is expected that this patient will achieve long-term local control with minimal toxicity using this customized treatment technique, which was completed under anesthesia over seven sessions rather than the 20 sessions required for IMRT.

Whereas the HDR brachytherapy plan was elegant in its simplicity, the IMRT plan was far more complex. First, a 3-mm PTV around the CTV was required to account for positioning errors associated with daily image guidance. Second, the PTV coverage of 34.1% was suboptimal. Although bolus over the external acoustic meatus would have improved PTV coverage near the external ear, PTV coverage of the air gap within the middle ear would not have improved. Third, maximizing PTV coverage would not have allowed for adequate sparing of the cochlea, especially given the overlap between the PTV and cochlea contours in Fig. 3b. Even with the undercovered PTV, the mean cochlea dose of 26.1% for the IMRT plan was markedly greater than the 10.5% mean dose for the HDR plan.

For this particular case, proton radiation therapy could have been used for irradiating the EAC, most likely with a single lateral beam. However, due to the close proximity (4 mm) of the EAC to the cochlea and the reported uncertainties of the proton range in tissue (5), we would not expect the cochlea dose for proton therapy to be as low as that for HDR brachytherapy. In fact, a dosimetric comparison study between proton and IMRT for

parameningeal rhabdomyosarcomas failed to yield a statistically significant difference in mean ipsilateral cochlea dose (6).

Brachytherapy has been shown to be a promising technique for treating rhabdomyosarcomas of the head and neck. The Ablative surgery, MOuld brachytherapy and surgical REconstruction (AMORE) trial of mold brachytherapy after radical resection for both parameningeal and nonparameningeal (excluding orbit) sites using low-dose rate or pulsed-dose rate techniques demonstrated good local control with an acceptable side effect profile (7). A subsequent report concluded that patients who underwent mold brachytherapy experienced fewer adverse events but exhibited a similar overall survival compared with patients who underwent external beam radiation therapy (8). Mold brachytherapy has also been well tolerated for the treatment of orbital rhabdomyosarcomas (9).

Rhabdomyosarcomas of the head and neck have also been included in institutional reports of pediatric soft-tissue sarcomas treated with HDR brachytherapy techniques. Fractionated-HDR brachytherapy, either administered alone or in combination with external beam therapy, can provide good-to-excellent long-term local control rates (10, 11), although long-term toxicities have been observed (12, 13). Single-dose intraoperative HDR brachytherapy can also achieve excellent long-term local control with a relatively low risk of late toxicity (14). However, children aged ≥ 6 years may be more susceptible to late grade 3 + toxicity at doses ≥ 12 Gy (15). HDR brachytherapy is also a viable treatment option for refractory orbital rhabdomyosarcomas, with most patients maintaining vision preservation in one series (16). More recently, a customized mouthpiece for the noninvasive HDR brachytherapy treatment of a soft palate rhabdomyosarcoma has been described (17). The promising results from these studies and others have facilitated the inclusion of both low-dose rate and HDR brachytherapy techniques for the treatment of pediatric sarcomas in the recent American Brachytherapy Society guidelines (18).

Despite the advantages of brachytherapy, IMRT remains the *de facto* standard for treating rhabdomyosarcomas of the head and neck. First, specialized resources in a tertiary center are required for a successful head-and-neck brachytherapy program, whereas IMRT is readily available in most radiation oncology centers. Second, IMRT can provide good local control, even for parameningeal sites, while sparing nearby normal structures (19). Recent studies have yielded promising results for proton therapy, especially given its ability to lower integral dose and improve normal tissue sparing when compared to IMRT (20, 21). However, for the rare patient with an extremely favorable anatomic presentation, such as the patient presented here, a customized brachytherapy regimen may be the optimal solution for providing an efficacious treatment, while minimizing long-term toxicity.

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Fig. 1.

A photograph of (a) rhabdomyosarcoma protruding from the right EAC before induction chemotherapy. (b) T2-weighted MRI, and (c) CT showing tumor within the external auditory canal. No evidence of middle ear involvement or temporal bone invasion was noted. Red arrows point to the tumor. EAC, external auditory canal. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Fig. 2. Photographs of (a) 2.4-mm diameter HDR brachytherapy catheter with a button attached and (b) catheter inserted into the right EAC after induction chemotherapy and before HDR brachytherapy treatment under anesthesia. EAC, external auditory canal; HDR, high-dose rate. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Fig. 3.

Treatment planning images for (a) HDR brachytherapy and (b) IMRT. The red contour around the applicator represents the CTV. The CTV was defined as a 1-mm margin around the 2.4-mm catheter to match the brachytherapy prescription depth of 1 mm. The orange contour in (b) represents the PTV (PTV = CTV + 3-mm margin). The brown contour represents the right cochlea (4-mm away from the catheter). Isodose lines: yellow, 150%; green, 100%; magenta, 70%; blue, 50%; cyan, 25%. CTV, clinical target volume; HDR, high-dose rate; IMRT, intensity-modulated radiation therapy; PTV, planning target volume. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Fig. 4.
Dose-volume histograms of HDR brachytherapy (solid line) and IMRT (dashed line) plans. Black lines, CTV. Dark gray line, PTV (IMRT only). Light gray lines, right cochlea. CTV, clinical target volume; HDR, high-dose rate; IMRT, intensity-modulated radiation therapy; PTV, planning target volume.

Table 1

Dosimetric parameters for HDR brachytherapy and IMRT plans

Technique	Brachytherapy					IMRT				
	Brainstem	Right cochlea	CTV	Right temporal lobe	Brainstem	Right cochlea	CTV	PTV	Right temporal lobe	
Volume (cm ³)	13.2	0.1	0.3	46.7	13.2	0.1	0.3	2.1	46.7	
Mean dose (%)	0.8	10.5	159.3	2.2	0.6	26.7	103.9	93.4	0.5	
Standard deviation dose (%)	0.2	3.6	68.6	1.7	1.0	7.0	4.7	12.3	1.2	
Minimum dose (%)	0.4	5.4	41.0	0.4	0.1	14.4	83.6	3.7	0.0	
Maximum dose (%)	1.8	23.7	668.3	16.7	13.7	49.1	110.8	110.8	21.4	
D_{90} (%)	0.6	6.6	87.9	0.8	0.2	18.6	96.9	78.0	0.1	
V_{100} (%)	0.0	0.0	82.0	0.0	0.0	0.0	82.0	34.1	0.0	

CTV = clinical target volume; D_{90} = minimum dose received by 90% of the target volume; HDR = high-dose rate; IMRT = intensity-modulated radiation therapy; PTV = planning target volume; V_{100} = volume received by 100% of the prescription dose.

For HDR brachytherapy, the dose was prescribed to a 1-mm depth from the surface of the 2.4-mm diameter catheter. The IMRT plan was normalized to the brachytherapy CTV V_{100} of 82.0%. All doses are expressed as the percent prescription dose.