

3D Printed Patient-Specific Applicator for HDR Brachytherapy of the Orbit

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Case report

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Abstract

BACKGROUND This report describes a process for designing a 3D printed patient-specific applicator for HDR brachytherapy of the orbit.

CASE PRESENTATION A 34-year-old man with recurrent melanoma of the orbit was referred for consideration of re-irradiation. An applicator for HDR brachytherapy was designed based on the computed tomography (CT) of patient anatomy. The body contour was used to generate an applicator with a flush fit against the patient's skin while the planning target volume (PTV) was used to devise channels that allow for access and coverage of the tumor bed. An end-to-end quality assurance test was devised to determine feasibility for clinical use. The applicator was designed to conform to the volume and contours inside the orbital cavity. Support wings placed flush with the patient skin provided stability and reproducibility, while 16 source channels of varying length were needed for sufficient access to the target. A solid sheath, printed as an outer support-wall for each channel, prevented bending or accidental puncturing of the surface of the applicator.

CONCLUSIONS Quality assurance tests demonstrated feasibility for clinical use. Our experience with available 3D printing technology used to generate an applicator for the orbit may provide guidance for how materials of suitable biomechanical and radiation properties can be used in brachytherapy.

Background

The delivery of high dose-rate (HDR) brachytherapy can be complicated by irregular tissue contours, lack of appropriate patient-specific applicators, and deformable changes in patient anatomy. Currently, the fabrication of patient-specific devices is expensive and labor intensive. Additive and subtractive manufacturing, commonly known as 3D printing, has evolved from a broad discipline focusing primarily in research and development to one that allows for rapid and affordable fabrication of high-precision devices (Rengier et al. 2010; Patra and Young 2016; Melchels et al. 2010). This report describes a process for designing a patient-specific applicator for HDR brachytherapy of the orbit.

Case Presentation

Clinical history

A 34-year-old man received proton-beam radiation therapy in 2003 for a 17.0x14.0x10.5 mm melanoma involving the left choroid and ciliary body. He was treated with proton-beam therapy to a dose of 70 Cobalt Gray Equivalent, in five fractions, over ten days. In 2017, the patient was in a motor vehicle accident, which resulted in rupture of his left globe. He underwent enucleation of the left globe and was found to have recurrent melanoma. The patient healed well from surgery and a left eye prosthesis was fitted. However, over the next nine months the patient reported that the prosthesis became progressively displaced and increasingly painful to wear. A diagnostic CT revealed a heterogeneous lobular soft tissue mass in the anterior and inferior left orbit measuring 27.0x26.0x19.0 mm. He underwent salvage left

orbital exenteration in March 2018. Surgical pathology confirmed multiple recurrent melanoma with a positive inferior-medial surgical margin. Restaging imaging revealed no evidence of metastatic disease and he was referred for consideration of re-irradiation.

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Applicator design

An applicator for HDR brachytherapy was designed in the AutoCAD Inventor Suite (Autodesk, San Rafael, CA) based on the latest diagnostic CT. The primary contours of interest were the patient's surface and the PTV. The patient surface was used to generate an applicator with a flush fit against the left orbital cavity and a protruding horizontal surface 10.0 mm anteriorly from the supraorbital ridge. Support wings with a thickness of 5.0 mm were designed to extend superiorly and inferiorly by 15.0 mm and laterally by 60.0 mm. The wings were designed to be flush against the patient's skin in order to provide a stable and reproducible fit.

The involved left orbital surfaces, including the residual mucosa and soft tissue abutting the mass found on pre-operative imaging and the sites with positive margins, were contoured as the clinical target volume (CTV; Volume~4.0 cm³) and radially expanded by 2.0 mm to generate a PTV. The PTV was used to devise channels that allowed for access and sufficient coverage of the target with the Ir-192 HDR source. The channels were constructed to fit an endobronchial HDR source guide tube with an outer diameter of 2.0 mm (Varian Medical Systems, Palo Alto, CA). While considering the size of the orbital cavity and the distance of the PTV to the cavity surface, it was found that sufficient target access would be provided when all channels were tilted 15° toward the patient's right and 10° superiorly. For the most superior channel, patient anatomy did not allow for the 10° tilt. Under these constraints, the applicator was designed with 16 channels of varying length. The tip of the channels, corresponding to the location of the first possible dwell position, was chosen to be at 5.0 mm from the surface of the orbital cavity. Figure 1 shows the applicator geometry overlaid on patient anatomy. The material for printing the applicator, an acrylic photopolymer (Polymerized TangoPlus and Agilus30 Family, Stratasys Ltd., Eden Prairie, MN), was selected based on similarity with the biomechanical properties of human skin (Edwards and Marks 1995). Note that these materials are not approved per the International Standard ISO-10993-1 as a biocompatible material. The applicator was covered in a sterile wrap to prevent any contact with patient skin. Given the flexibility of this material, a solid sheath with a thickness of 2.0 mm was designed as an outer support-wall for each channel to prevent bending or accidental puncturing of the surface of the applicator. The assembly was created using a PolyJet 3D printer (Stratasys Ltd., Eden Prairie, MN) which allows for simultaneous printing of materials with varying physical properties. The primary applicator was designed as 80/20% mixing of polymers in the Agilus30/TangoPlus family; the sheath was 80/20% mixing of TangoPlus/Agilus30. Print time was ~20 hours, while cost was ~400\$. Figure 2 presents the

design of the applicator and a model of the channel sheath. Prior to use in the patient, the applicator was imaged with a helical CT scanner (120kVp, 1.0 mm³ isotropic voxels). The mean Hounsfield unit (HU) values were measured in a large region-of-interest in the applicator and found to be (mean ± std.dev.) 85±11 HU, rendering it tissue-equivalent for dose calculations.

Testing and validation

At the time of treatment simulation, the patient was immobilized supine with a custom thermoplastic mask and head holder. Serial axial CT images were obtained for treatment planning after placing the patient-specific applicator, covered in a plastic and sterile latex wrap, inside the left orbital cavity and securing it using self-adherent wrap. Treatment planning and dose calculation were performed in the Brachytherapy Planning module of Eclipse (Varian Medical Systems, Palo Alto, CA) based on the AAPM TG-43 (Rivard et al. 2004) formalism, using Ir-192 at a nominal source strength of 10 Ci. The planned prescription was 3400 cGy, to be delivered in 10 fractions, twice daily, over five consecutive days (Finger et al. 2014). Figure 3 shows the dose-volume histogram for the PTV, orbit bones, right eye, right lens, and brain.

An end-to-end quality assurance test was designed to determine feasibility for clinical use. Two calibrated pairs of optically stimulated luminescence dosimeters (OSLDs) were firmly placed on the surface of the applicator at two locations representing dose to PTV and another high-resolution CT was acquired. The clinical HDR plan was transferred to the CT containing the OSLDs in order to calculate the mean dose to the dosimeters. The applicator was then immersed in a water-filled container to mimic scattering conditions, and the clinical HDR plan was delivered. In the two sampled positions on the surface of the applicator, the mean difference in measured and calculated dose was 12% and 18%. Finally, all ten fractions of the clinical HDR plan were consecutively delivered, amounting to a dose of at least 300 Gy to the surface of the applicator, and the applicator was monitored for structural damage. No damage was found over the course of two weeks.

Treatment

A second CT simulation scan was obtained without the brachytherapy applicator for the purpose of generating an alternative stereotactic body radiotherapy (SBRT) plan. The orbital air density was assigned to water (i.e., 0 HU) in the treatment planning system to simulate a fluid filled cavity. A 4-arc volumetric modulated arc therapy plan with 6MV photons, utilizing superiorly oriented non-coplanar beams to avoid entry or exit into the contralateral eye, was created in Eclipse version 13.6 (Varian Medical Systems, Palo Alto, CA). The prescription dose was 2500 cGy, in 5 daily fractions.

Although most of the previously irradiated soft tissue was resected, the patient was consented for osteoradionecrosis and non-healing wounds. He was treated with SBRT instead of brachytherapy because the 3D printed material was not approved for biocompatibility and because filling the orbital cavity with sterile saline provided a reproducible bolus with fewer air gaps. To confirm consistency with treatment planning, daily cone-beam CT was performed after filling the orbit with sterile saline.

Discussion

In this report we describe a process for designing a 3D printed patient-specific applicator for HDR brachytherapy of the orbit. The physical properties of the polymers provided by the manufacturer are comparable to the relevant biomechanical properties of human tissue (Edwards and Marks 1995). This similarity allows for a comfortable, stable, and reproducible fit in challenging locations in the body. When deciding on the material to use for 3D printing of brachytherapy applicators, biocompatibility and sterilization should also be considered (Fowler et al. 2016; Zhao et al. 2017; Imber et al. 2019). Manufacturers are increasingly supporting the need for 3D printing of biocompatible materials that pass the ISO 10993-1 International Standard, as well as the United States Pharmacopeia standards of biocompatibility (Cunha et al. 2015). The medical physics and radiation oncology community have ongoing working groups to develop consensus guidelines for manufacturing and quality assurance of 3D printed applicators.

Abbreviations

CT = computed tomography

CTV = clinical target volume

HDR = high dose-rate

HU = Hounsfield unit

OSLD = optically stimulated luminescence dosimeters

PTV = planning target volume

SBRT = stereotactic body radiation therapy

Declarations

- Ethics approval and consent to participate: NA
- Consent for publication: Written informed consent was obtained from the patient for publication of this case report and accompanying images.

- Availability of data and materials: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.
- Competing interests: None
- Funding: DGK is supported by an Outstanding Investigator Award from the NCI (R35 CA197616).
- Conflicts of Interest: None
- Authors' contributions: All authors contributed to applicator design, ES/OC printed applicator and devised end-to-end quality assurance tests, DGK/CJ identified clinical need, ES/CJ prepared manuscript.

References

- Cunha JAM, Mellis K, Sethi R, Siau T, Sudhyadhom A, Garg A, Goldberg K, Hsu IC, Pouliot J (2015) Evaluation of PC-ISO for customized, 3D printed, gynecologic HDR brachytherapy applicators. *Journal of Applied Clinical Medical Physics* 16 (1):246-253. doi:10.1120/jacmp.v16i1.5168
- Edwards C, Marks R (1995) Evaluation of biomechanical properties of human skin. *Clinics in Dermatology* 13 (4):375-380. doi:[https://doi.org/10.1016/0738-081X\(95\)00078-T](https://doi.org/10.1016/0738-081X(95)00078-T)
- Finger PT, Tena LB, Semenova E, Aridgides P, Choi WH (2014) Extrascleral extension of choroidal melanoma: Post-enucleation high-dose-rate interstitial brachytherapy of the orbit. *Brachytherapy* 13 (3):275-280. doi:10.1016/j.brachy.2013.09.002
- Fowler TL, Buyyounouski MK, Jenkins CH, Fahimian BP (2016) Clinical Implementation of 3D Printing for Brachytherapy: Techniques and Emerging Applications. *Brachytherapy* 15:S166. doi:10.1016/j.brachy.2016.04.297
- Imber BS, Wolden SL, Stambuk HE, Matros E, Wexler LH, Drew AS, Rosen EB, Ganly I, Cohen GaN, Damato AL (2019) Novel intraoperative radiotherapy utilizing prefabricated custom three-dimensionally printed high-dose-rate applicators. *Brachytherapy* 18 (3):277-284. doi:<https://doi.org/10.1016/j.brachy.2019.01.012>
- Melchels FPW, Feijen J, Grijpma DW (2010) A review on stereolithography and its applications in biomedical engineering. *Biomaterials* 31 (24):6121-6130. doi:<https://doi.org/10.1016/j.biomaterials.2010.04.050>
- Patra S, Young V (2016) A Review of 3D Printing Techniques and the Future in Biofabrication of Bioprinted Tissue. *Cell Biochemistry and Biophysics* 74 (2):93-98. doi:10.1007/s12013-016-0730-0
- Rengier F, Mehndiratta A, von Tengg-Kobligk H, Zechmann CM, Unterhinninghofen R, Kauczor H-U, Giesel FL (2010) 3D printing based on imaging data: review of medical applications. *International Journal of*

Rivard MJ, Coursey BM, DeWerd LA, Hanson WF, Saiful Huq M, Ibbott GS, Mitch MG, Nath R, Williamson JF (2004) Update of AAPM Task Group No. 43 Report: A revised AAPM protocol for brachytherapy dose calculations. Medical Physics 31 (3):633-674. doi:10.1118/1.1646040

Zhao Y, Moran K, Yewondwossen M, Allan J, Clarke S, Rajaraman M, Wilke D, Joseph P, Robar JL (2017) Clinical applications of 3-dimensional printing in radiation therapy. Medical Dosimetry 42 (2):150-155. doi:<https://doi.org/10.1016/j.meddos.2017.03.001>

Figures

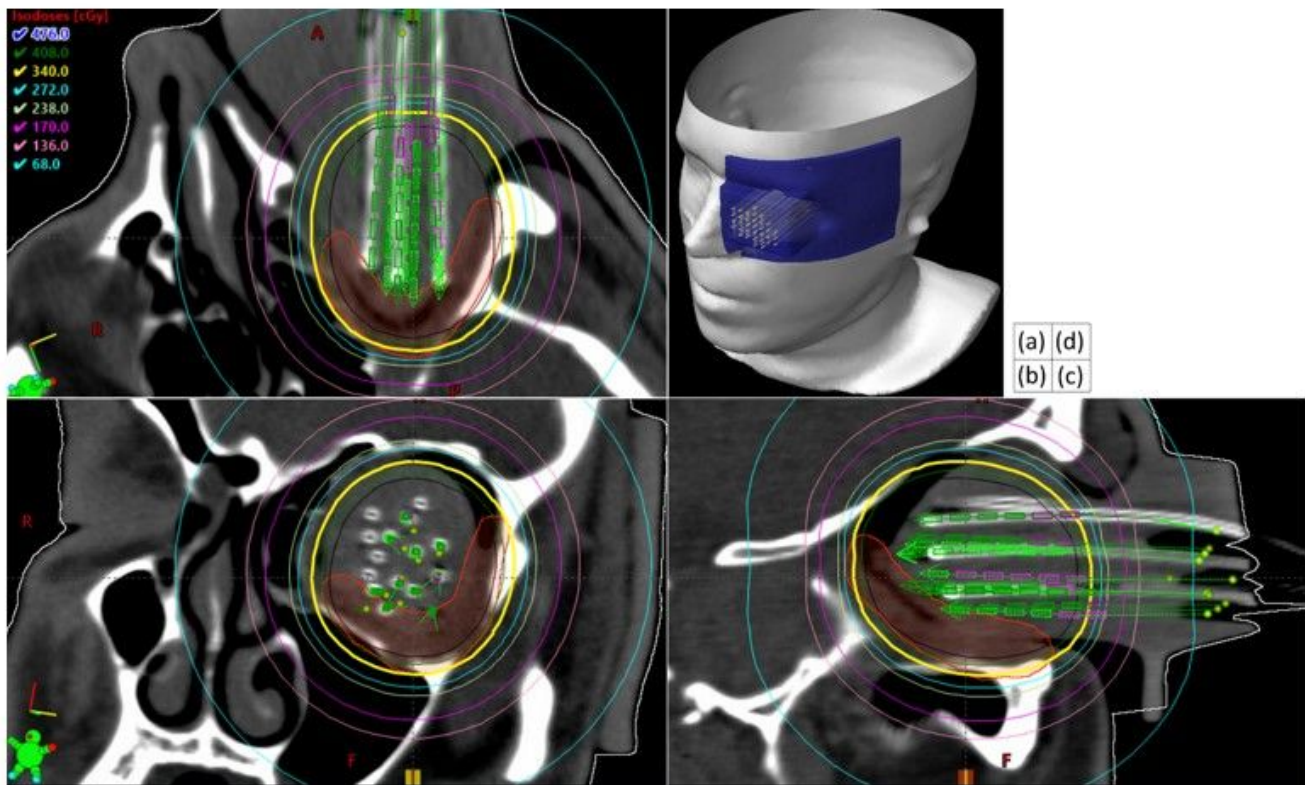


Figure 1

Applicator geometry overlaid on patient anatomy in (a) axial, (b) coronal, (c) sagittal, and (d) model view. Patient surface, PTV, and applicator are represented in white, red, and blue, respectively. Note that this CT scan contains the custom applicator in the patient's orbit. Isodose lines are shown for a prescription of 340 cGy (yellow line).

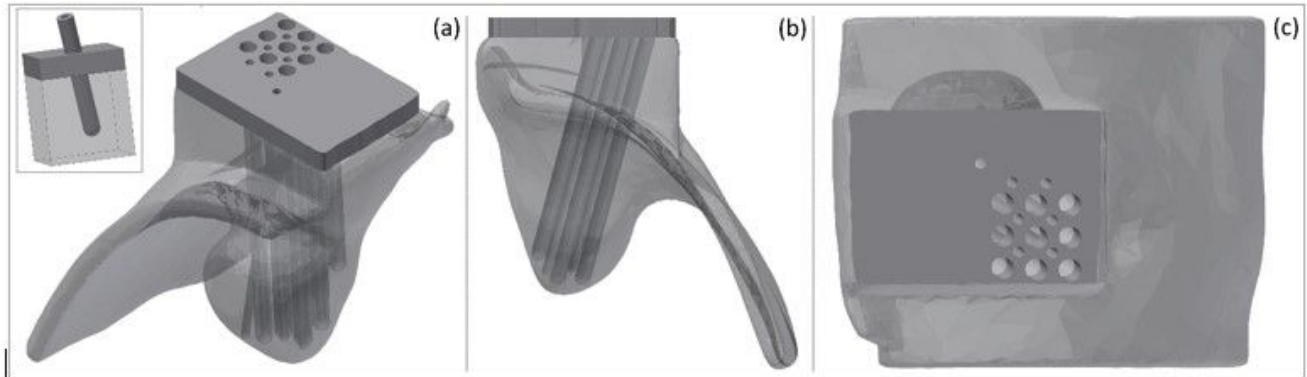


Figure 2

(a) Model view, (b) side view, and (c) top view of patient-specific applicator for HDR brachytherapy of recurrent melanoma of the ocular orbit. The material for printing was selected based on similarity with biomechanical properties of human skin. Insert in panel (a) shows model for the design of the sheath of the source guide tube intended to prevent bending or accidental puncturing of the surface of the applicator.

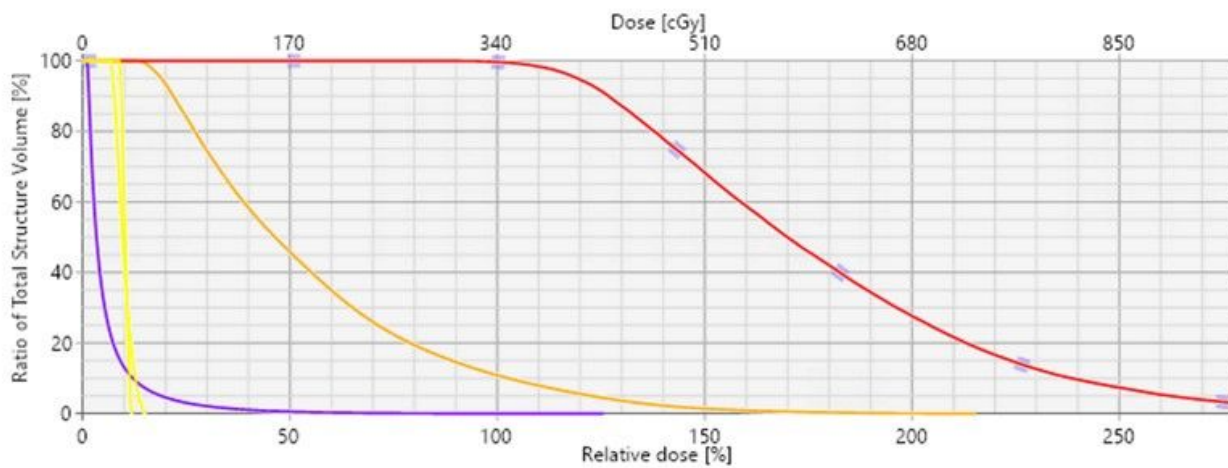


Figure 3

Dose-volume histogram for HDR plan with patient-specific applicator (shown for one fraction only). Red line represents PTV, orange is orbit bones, yellow lines are for right eye and lens, and purple line is brain.