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Fabrication and Application of 3D Printed Bolus for Optimizing Radiotherapy in Superficial Tumor

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1. Abstract

Purpose To evaluated the feasibility and application of using 3-dimensional (3D) printed bolus for optimizing radiotherapy in superficial tumors.

1.1. Materials and Methods

A customized compensator was fabricated by 3D printed for a patient with recurrent basal cell carcinoma around the ear. The information of patient for constructing the 3D printed bolus arise from CT scanning, and PLA and TPU material are selected for generating 3D printed bolus and compared to conventional boluses. MONACO 5.11 planning system was adopted to the 3 groups simulation CT for comparing the body surficial fit effect, repeatability, dosimetric parameters Dmax (cGy), Dmean (cGy), D2% (cGy), D50% (cGy), D98 of plans % (cGy), uniformity index (HI), conformity index (CI) in the target area.

1.2. Results

The patient-specific 3D printed bolus is designed and fabricated successfully. Compared with the conventional bolus, the 3D printed bolus (TPU material) shows better repeatability and conformability, it has less air gap and most of target region covered by the 95% isodose line. 3D printed bolus also shows better surface dose and dose distribution uniformity, and improve the therapeutic efficacy significantly in clinical practice.

1.3. Conclusion

The 3D printed bolus exhibits significant enhancement of radiotherapy in superficial tumor, and lay foundations for personal enhanced radiotherapy in superficial tumor.

2. Introduction

Cancers are the leading non-communicable disease-related cause of mortality around the world, and are among the most difficult diseases to treat completely [1]. Although endeavors have been made to improve the treatment outcomes, the new therapeutic modalities, such as immunotherapy [2], gene therapy [3], gas therapy [4], phototherapy [5], TTFields [6] and so on, have improved the outcome significantly. However, the conventional therapeutic methods, such as chemotherapy, surgical operation and radiotherapy (RT), are still the mainstream of clinical practice for many different tumors and patient populations, especially for the application of RT, which is used to treat an estimated 70% of solid cancers in humans, and can achieve curative outcomes in up to 40% of cases.

In clinical practices or fundamental researches, RT functions by delivering directed forms of high-energy IR including X-rays, γ-rays, electrons, neutrons, and charged particles to tumor tissues and induced the death of cancer cells, including external beam RT (EBRT) and internal radioisotope treatment (RIT) approaches [7]. Especially, the linear accelerators can provide megavolt-level photon lines for the treatment of deep tumors and megavolt-level electron lines for superficial tumors, which could improve the therapeutic effects significantly and decrease the health hazard, and with the development of computer and bioimaging technology, the better therapeutic effect is achieved now. However, with the difference of lesion and high-dose intraoperative ionizing radiation often also damage to normal tissues, which could initiate the negative physical response when irradiated to the tumor spot [8, 9]. For the superficial tumors, electron beams are often used for skin irradiation for their rapid depth dose fall-off over photons due to the limited range of electrons, which greatly reduces the dose delivered to the surrounding normal tissue [10]. And similar to deep tumors, the improvement of radiotherapy (electron beams irradiation) in superficial tumors is hindered by the build-up effects, which reduces the located radiotherapy dose and uniformity. Thus, the build-up effects have attracted much attention in clinical researches.

With the development of materials technology and associated technologies, bolus materials are applied to overcome the build-up effects in conventionally radiotherapy practice to alter the delivered dose to the skin surface and compensate for irregular patient contours. Naturally or designed synthetically developed materials have been used such as wet gauze and vinyl gels among others [11]. Synthetic gel - type commercial bolus (Superflab, Civco, Orange City, IA, USA) is in common use owing to its tissue equivalency and being latex free. In clinical practice, the bolus must meet the demand for the positioning of bolus should be reproducible, and maintain its shape and properties throughout the course of treatment [12]. Especially, Direct contact of bolus with the surface of the skin is ideal to be more efficient by increasing the dose to superficial tissues and by improving dose uniformity. At present, the commercial (such as Superflab (Eckert & Ziegler, Hopkinton, Massachusetts, USA), or home-made bolus are put into use for the compensation of superficial tissues, for instance, head, face and chest wall after breast cancer surgery, during the electron beams irradiation. Worryingly, the dose decreased sharply (~34%) due to the different thickness of air cavities after the bolus is unable to fit with superficial tissues completely [13, 14]. For instance, Kong and Holloway's result revealed that the impact of air gaps on electron beams is dependent on field size, beam energy, bolus thickness and air gap size (most important). For a 3 cm diameter circular field, 6 MeV beam, 20 mm air gap, and 1.5 cm bolus, both the maximum dose and surface dose were reduced by approximately 60%, and the depth of the dose maximum shifted by 3.5 mm [15]. Butson and colleages assessed the impact of air gaps for 6 MV beams using field sizes of 8 × 8 cm and 10 × 20 cm, the results shows that the small air gaps (<10 mm) slightly decreased the surface and skin dose, but it still allowed for at least 90% of the maximum dose being delivered to the skin regions [13]. Therefore, the air gaps should be avoided to improve the accuracy of treatment delivery when radiotherapy is applied in superficial tumors.

Currently, with the rapid development of 3D printed technologies, which enable the creation of different shapes, sizes and individualized and precise customization from a 3D software model [16]. Until now, the utilization of 3D printed bolus attracts enormous interests in radio-medicine [17, 18]. For instance, for creating a proton range compensator [19] and for bolus in electron beam radiotherapy [20]. In superficial tumors radiotherapy with 3D printed bolus, it enhances the fitness to enhance the electron beams irradiation dose and uniformity of distribution [21], and exhibits excellent applicational prospects.

In this study, we evaluate a new 3D printed of with patient specific bolus generated from different materials, in which is designed as CT scanning guided radiotherapy for basal cell carcinoma, and examine the dosimetry evaluation. We describe our first clinical experience with the 3D printed bolus, describing the geometrical accuracy of the produced bolus and the resulting tumor coverage to improve the outcome of radiotherapy.

3. Materials and Methods

3.1 Patients

The patient is consented to an institutional review board-approved protocol that allows comprehensive analysis of tumor samples (Ethics Committees of Shenzhen People's Hospital).

Case information: Male, 66 years old, an surgical operation of anterior basal cell carcinoma, internal thigh skin removal and free flap repair due to basal cell carcinoma of left front ear in 2014, and no other adjuvant therapies are conducted after the surgical operation. In 2019, local biopsy and pathology confirmed local recurrence of basal cell carcinoma, and with symptoms of skin pruritus and ulcers appeared in the front of the left ear and auricle, then, the skin lesions were identified, including the left front of the ear, external auditory canal, auricle and earlobe.

3.2 Generation of 3D printed of bolus

The 3D printed of bolus was prepared by following steps: (1) The patient first performed a CT scanning without wearing a bolus to obtain a tomographic image of the lesion, and reconstructed the facial skin contour model with imaging information; (2) Then, the 3D printed bolus is constructed with 3D printed technology with different type of materials that the thickness of bolus is 1 cm, including thermoplastic polyurethane elastomer (TPU) and polylactic acid (PLA).

3.3 The schedule of radiotherapy with the 3D printed bolus

The schedule of radiotherapy with the 3D printed bolus generated from following steps: (1) The CT scanning of patient is conducted with 3D printed bolus or not; (2) Target delineation of superficial tissue is originated from the information of CT positioning scanning, the gross tumor volume (GTV) of tumors contains a clinical target volume margins (CTV, extend 1.5 cm from GTV) and planned target volume margins (PTV, extend 0.3 cm from GTV), and calculates the potential damaged organs, then, readjust the position to enhance the therapeutic effects and minimize the side effects; (3) The treatment plan is divided into two sections: the first stage applies a 7-field intensity-modulated radiotherapy (IMRT) technology, the PTV dose is 48 Gy/24 fraction; the second stage applied a the reduced field push (12 Gy/6 fraction) five times, and the total target dose is 60 Gy/30 fraction.

4. Results

4.1 Generation of 3D Printed Bolus

We successfully constructed the 3D printed bolus with a consumer-grade 3D printer according to the information of CT scanning from patient. First, we applied the CT scanning of lesion with patient (Figure 1a), and reconstruct the skin contour model of the lesion (Figure 1b), which indicated that the skin contour model with CT scanning is high similarity to patient lesion, suggesting the good body surface fit effect. Then, as inspired by previous studies of radiotherapy with 3D printed bolus [22-25], two materials, thermoplastic polyurethane elastomer (TPU) and polylactic acid (PLA), are chose for constructing the bolus, the results show that both materials are capable for constructing the 3D printed of bolus successfully (Figure 1c and d), the thickness of both boluses are 1 cm.

4.2. Comparison Body Surface Fit Effect

After generation of 3D printed bolus with two materials, we compared the advantage between two 3D printed bolus (TPU and PLA). The value of CT is -506、 and +327, respectively, which shows better capability of TPU than PLA, and taking the high density of PLA has a great influence on the dose distribution of the photon line, and it brings inconvenience to loading and unloading into consideration, the 3D printed bolus generated from TPU is selected for the treatment of patients.

For elucidating the enhancement of body surface fit effect with 3D printed bolus, the conventional bolus is set as control. As shown in Figure 2a and 2b, the CT positioning scanning reveal that the body surface fit effect is increased significantly (Table 1). In details, 3D printed bolus covered the surface of superficial recurrent tumor lesions and tissue defects, and the maximum air gap with the skin around the ear was 0.41 cm. The gap is located behind the ear and the head, which is within the PTV range. However, the conventional bolus has a maximum gap of 2.12 cm due to the irregular protrusion of the auricle, which the volume of 3D printed bolus is over 20 times than conventional bolus, suggesting that it is more capable for clinical application due to the effectively cover areas and filled.

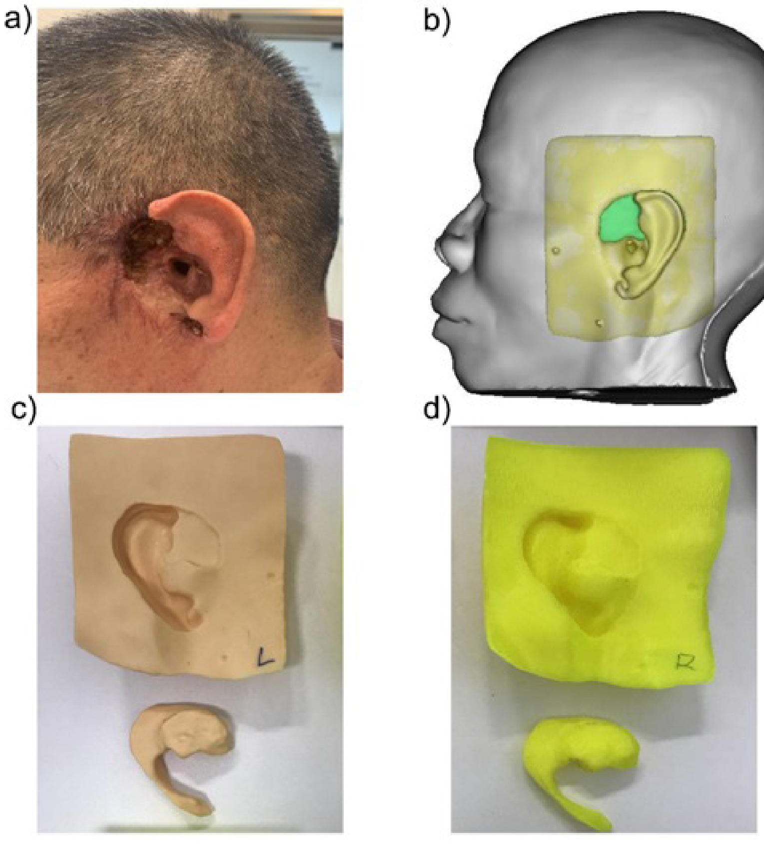

Figure 1. Generation of 3D printed bolus. a) Lateral view of patient's superficial lesions; b) Reconstruct the skin contour model of the tumor lesion; c) 3D printed bolus with PLA material; d) 3D printed bolus with TPU material.

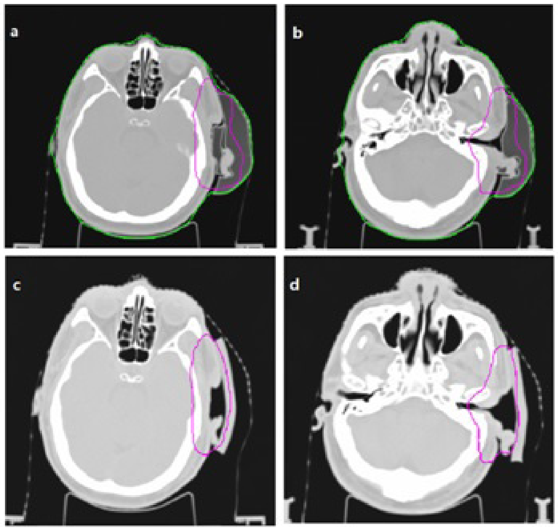

Figure 2. Comparison of body surface fit effects of different bolus. a) and b) are 3D printed bolus CT positioning scan images; c) and d) are conventional bolus CT positioning scan images.

Table 1: The comparision of body surface fit effect between 3D printed bolus and conventional bolus.

Bolus	maximal gap distance（cm）	minimal gap distance（cm）	Volume（cm^3）
3D-TPU bolus	0.41	0.16	1.9
Conventional bolus	2.12	1.74	20.2

4.3 Comparision of Radiotherapy Dose

We then examine the radiotherapy dose of 3D printed bolus compared to conventional bolus. As shown in Figure 3 and Table 2 (3D printed bolus: solid line; conventional bolus: thick dashed line; without bolus: thin dashed line). The results showed that the schedule of radiotherapy with 3D printed bolus is better than conventional bolus and control group, which arise from the formula of HI=D5%/D95%，CI=V2Rx/(TV*VRI) from V5.11 of MONACO. The three dosimetry parameters of IMRT plan, heterogeneity index (HI) with 3D printed bolus is lower than conventional bolus and control group, and conformity index (CI) is similar to other groups. In detail, application results show that 3D printed bolus is not only significantly better than conventional bolus in fitting effect, but also can fix and support the auricle. The DVH histogram shows that the dose curve of 3D printed bolus is prior than that of conventional bolus and non-bolus, and 98% of the target volume reaches 4820 cGy, which fully meets the prescribed dose. However, there is 4603 cGy and 4156 cGy, respectively, in the case of conventional bolus and without bolus, suggesting the ungratified dosage requirement. After examination, the Dmax of the three groups of plans are 5263 cGy, 5614 cGy and 5688 cGy, respectively. In terms of the dose received for 2% of the target volume, the 3D printed bolus is closer to the prescribed dose. For the uniformity index (HI) and conformity index (CI) of target area, the HI of 3D printed bolus is 1.05, which is closer to 1 than the other two treatment groups, which suggests that the 3D printed bolus dose distribution is more uniform. The CI of 3D printed bolus is 0.73, which is slightly lower than the 0.77 of conventional blouses. By analyzing carefully, the isodose curve shows that the volume is 4800 cGy on bolus outside the 3D-TPU target area, it is more than that of conventional boluses, and it is consistent with that reported by Park from the paraffin-printed compensator [26]. The result is the same, but the prescription dose coverage in the target area is still better than the conventional blouse and the better.

Table 2: The comparision of three dosimetry parameters of IMRT plan (cGy).

Bolus	Dmax	Dmean	D2%	D98%	D5%	D95%	HI	CI
CCI3D-TPU	5263	5011	5136	4820	5109	4867	1.05	0.73
Conventional bolus	5614	5108	5353	4603	5311	4757	1.12	0.77
Without bolus	5688	5120	5476	4156	5426	4529	1.20	0.73

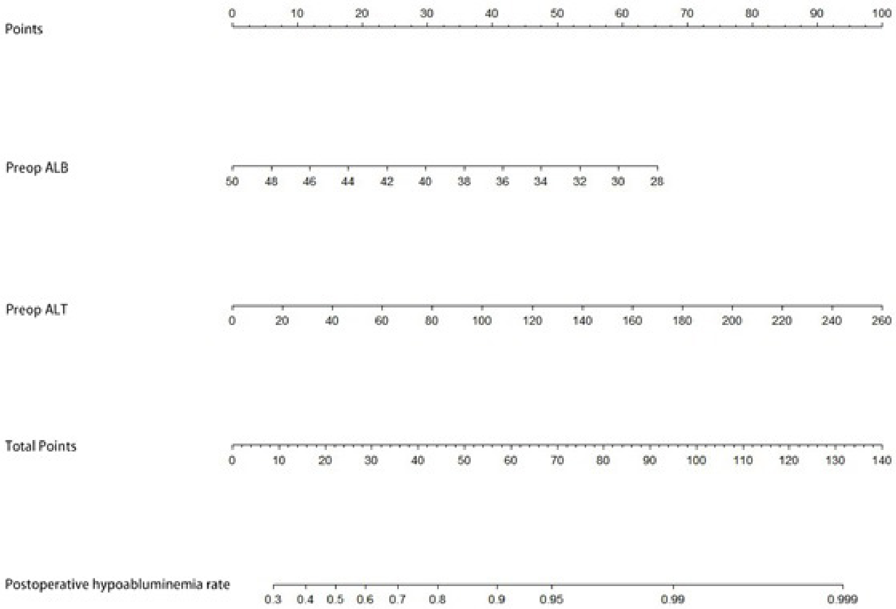

Figure 3. Dose-volume histograms for 3 types of IMRT plans (3D printed bolus: solid line; conventional bolus: thick dashed line; without bolus: thin dashed line).

4.4. The Therapeutic Efficacy with 3D Printed Bolus

Finally, we applied the radiotherapy (40 Gy) with 3D printed bolus in superficial tumors patients with, as shown in Figure 4, the 3D printed bolus helps to improve the therapeutic efficacy significantly, after the treatment for a month, the lesion become escharosised and small than before treatment, which shows excellent enhancement in radiotherapy.

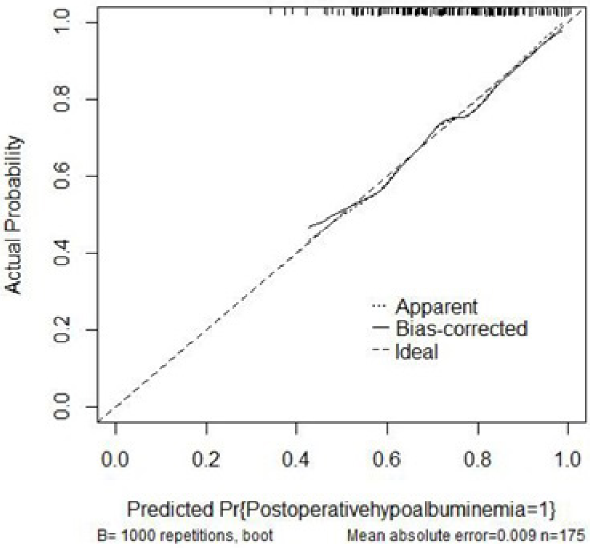

Figure 4: Representive image of radiotherapy with 3D printed bolus.

5. Discussion

The aim of this work was to evaluated a 3D printed bolus with TPU materials to enhance the therapeutic efficacy of radiotherapy in superficial tumors comparable to traditional radiotherapy bolus. In radiotherapy of superficial tumors, the dose build-up effect of the distance between electron beams decreases the dose of tumor lesion and the uniformity of distribution.

Currently, in clinical practices of radiotherapy, 3D printed boluses have been applied for enhanced radiotherapy in various tumors due to the higher irradiation dose over conventional boluses [27, 28], and the thickness of 3D printed bolus is usually 0.4 to 0.8 mm. In this study, we generate a 3D printed bolus with the thickness is 1 cm, which not only fills the contour of the superficial part of the defect, but also supports and fixes the damaged auricle. Then, we evaluate the body surface fit effect and the radiotherapy dose compared to conventional bolus, which show better body surface fit effect and high dose index in the lesion, moreover, it is efficient to enhance the therapeutic outcome of radiotherapy in clinical practice.

In clinical radiotherapy of tumor, the accuracy of irradiation is another crucial factor of the therapeutic outcome, using the CT scanning for generating the 3D printed bolus not only a reduction in total air gap volume between the skin and tumor lesion, more importantly, it leads to air gap volume in irregular that focus on the target areas and reduces the damage to normal tissue around the irradiation. On the other hand, the irradiation uniformity is improved sharply with 3D printed bolus, and it is also more convenient for the loading and uploading with 3D printed bolus than commercial bolus and achieves personal generation of bolus.

Despite the demonstrable benefits of 3D printed bolus for complex geometries, the primary consideration in implementing such a program clinically is selection of a 3D printed platform and material and the enhancement to radiotherapy. Based on our results, TPU material which facilitates reproducible clinical placement, provides excellent superficial dose, and is highly conformal, which pave a way to personal 3D printed bolus. And the generation and printed of the 3D printed bolus can be accompanied with CT scanning or more bioimaging technologies, and providing a viewpoint for individual-based treatment in superficial tumors.

6. Conclusion

3D printed bolus provides an individualized bolus solution to unique and/or irregular patient anatomy for radiotherapy in superficial tumors, which bring more advantages over conventional bolus in patient-specific conformality, optic clarity and flexibility, and significant radiotherapeutic outcomes is emerged. Our results show improved radiotherapy plan dose conformity, body surface fit effect with 3D printed bolus and lower toxicity to surround tissue. More important, in vivo measurements on treated patients confirming better therapeutic outcome. Based on our continued 3D printed bolus experience, which could improve the therapeutic efficacy personally.

7. Funding

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Reference

1. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer Statistics, 2021. Ca-Cancer. J Clin. 2021; 71: 7-33.
2. Cloughesy TF, Mochizuki AY, Orpilla JR, Hugo W, Lee AH, Davidson TB, et al. Neoadjuvant anti-PD-1 immunotherapy promotes a survival benefit with intratumoral and systemic immune responses in recurrent glioblastoma. Nature medicine. 2019; 25: 477.
3. Li CW, Samulski RJ. Engineering adeno-associated virus vectors for gene therapy. Nat Rev Genet. 2020; 21: 255-72.
4. Peng S, Song RY, Lin QG, Zhang YL, Yang YZ, Luo M, et al. A Robust Oxygen Microbubble Radiosensitizer for Iodine-125 Brachytherapy. Adv Sci. 2021.
5. Liu CH, Cao Y, Cheng YR, Wang DD, Xu TL, Su L, et al. An open source and reduce expenditure ROS generation strategy for chemodynamic/photodynamic synergistic therapy. Nature communications. 2020; 11.
6. Stupp R, Taillibert S, Kanner A, Read W, Steinberg DM, Lhermitte B, et al. Effect of Tumor-Treating Fields Plus Maintenance Temozolomide vs Maintenance Temozolomide Alone on Survival in Patients with Glioblastoma A Randomized Clinical Trial. Jama-J Am Med Assoc. 2017; 318: 2306-16.
7. Thariat J, Hannoun-Levi JM, Myint AS, Vuong T, Gerard JP. Past, present, and future of radiotherapy for the benefit of patients. Nature Reviews Clinical Oncology. 2013; 10: 52-60.
8. Verdecchia A, Baili P, Quaglia A, Kunkler I, Ciampichini R, Berrino F, et al. Patient survival for all cancers combined as indicator of cancer control in Europe. Eur J Public Health. 2008; 18: 527-32.
9. Grassberger C, Ellsworth SG, Wilks MQ, Keane FK, Loeffler JS. Assessing the interactions between radiotherapy and antitumour immunity. Nature Reviews Clinical Oncology. 2019; 16: 729-45.
10. Locke J, Karimpour S, Young G, Lockett MA, Perez CA. Radiotherapy for epithelial skin cancer. Int J Radiat Oncol. 2001; 51: 748-55.
11. Adamson JD, Cooney T, Demehri F, Stalnecker A, Georgas D, Yin FF, et al. Characterization of Water-Clear Polymeric Gels for Use as Radiotherapy Bolus. Technol Cancer Res T. 2017; 16: 923-9.
12. Vyas V, Palmer L, Mudge R, Jiang RQ, Fleck A, Schaly B, et al. On bolus for megavoltage photon and electron radiation therapy. Medical Dosimetry. 2013; 38: 268-73.
13. Butson MJ, Cheung T, Yu P, Metcalfe P. Effects on skin dose from unwanted air gaps under bolus in photon beam radiotherapy. Radiat Meas. 2000; 32: 201-4.
14. Baltz GC, Chi PCM, Wong PF, Wang CJ, Craft DF, Kry SF, et al. Development and validation of a 3D-printed bolus cap for total scalp irradiation. Journal of applied clinical medical physics. 2019; 20: 89-96.
15. Smilowitz JB, Mihailidis DN. Khan's The Physics of Radiation Therapy by John Gibbons. Medical physics. 2020.
16. Rosenzweig DH, Carelli E, Steffen T, Jarzem P, Haglund L. 3D-Printed ABS and PLA Scaffolds for Cartilage and Nucleus Pulposus Tissue Regeneration. International journal of molecular sciences. 2015; 16: 15118-35.
17. Choi JW, Kim N. Clinical application of three-dimensional printing technology in craniofacial plastic surgery. Arch Plast Surg. 2015; 42: 267-77.
18. Canters RA, Lips IM, Wendling M, Kusters M, van Zeeland M, Gerritsen RM, et al. Clinical implementation of 3D printing in the construction of patient specific bolus for electron beam radiotherapy for non-melanoma skin cancer. Radiotherapy and Oncology. 2016; 121: 148-53.
19. Ju SG, Kim MK, Hong CS, Kim JS, Han Y, Choi DH, et al. New Technique for Developing a Proton Range Compensator with Use of a 3-Dimensional Printer. Int J Radiat Oncol. 2014; 88: 453-8.
20. Su SQ, Moran K, Robar JL. Design and production of 3D printed bolus for electron radiation therapy. Medical physics. 2014; 41: 2.
21. Martin TW, Boss MK, LaRue SM, Leary D. 3D-printed bolus improves dose distribution for veterinary patients treated with photon beam radiation therapy. Can Vet J. 2020; 61: 638-44.

22. Robertson FM, Couper MB, Kinniburgh M, Monteith Z, Hill G, Pillai SA, et al. Ninjaflex vs Superflab: A comparison of dosimetric properties, conformity to the skin surface, Planning Target Volume coverage and positional reproducibility for external beam radiotherapy. Journal of applied clinical medical physics. 2021.

23. Van der Walt M, Crabtree T, Albantow C. PLA as a suitable 3D printing thermoplastic for use in external beam radiotherapy. Australas Phys Eng S. 2019; 42: 1165-76.

24. Burleson S, Baker J, Hsia AT, Xu ZG. Use of 3D printers to create a patient-specific 3D bolus for external beam therapy. Journal of applied clinical medical physics. 2015; 16: 166-78.

25. Zou W, Fisher T, Zhang M, Kim L, Chen T, Narra V, et al. Potential of 3D printing technologies for fabrication of electron bolus and proton compensators. Journal of applied clinical medical physics. 2015; 16: 90-8.

26. Park JW, Yea JW. Three-dimensional customized bolus for intensity-modulated radiotherapy in a patient with Kimura's disease involving the auricle. Cancer Radiother. 2016; 20: 205-9.

27. Kitamori H, Sumida I, Tsujimoto T, Shimamoto H, Murakami S, Ohki M. Evaluation of mouthpiece fixation devices for head and neck radiotherapy patients fabricated in PolyJet photopolymer by a 3D printer. Phys Medica. 2019; 58: 90-8.

28. Kim SW, Shin HJ, Kay CS, Son SH. A Customized Bolus Produced Using a 3-Dimensional Printer for Radiotherapy. PloS one. 2014; 9.