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A novel rectal applicator for contact radiotherapy with HDR ^{192}Ir sources

Murillo Bellezzo[1,2], Gabriel P. Fonseca[1], An-Sofie Verrijssen[1], Robert Voncken[1], Michiel R. Van den Bosch[1], Hélio Yoriyaz[2], Brigitte Reniers[3], Maaike Berbée[1], Evert J. Van Limbergen[1], Frank Verhaegen[1,*]

[1]*Department of Radiation Oncology (MAASTRO), GROW School for Oncology and Developmental Biology, Maastricht University Medical Center, Maastricht, The Netherlands*

[2]*Centro de Engenharia Nuclear, Instituto de Pesquisas Energéticas e Nucleares IPEN-CNEN/SP, São Paulo, Brazil*

[3]*Research group NuTeC, Centre for Environmental Sciences, Hasselt University, Diepenbeek, Belgium*

ABSTRACT

PURPOSE: Dose escalation to rectal tumors leads to higher complete response rates and may thereby enable omission of surgery. Important advantages of endoluminal boosting techniques include the possibility to apply a more selective/localized boost than using external beam radiotherapy. A novel brachytherapy (BT) rectal applicator with lateral shielding was designed to be used with a rectoscope for eye-guided positioning to deliver a dose distribution similar to the one of contact x-ray radiotherapy devices, using commonly available high-dose-rate ^{192}Ir BT sources.

METHODS AND MATERIALS: A cylindrical multichannel BT applicator with lateral shielding was designed by Monte Carlo modeling, validated experimentally with film dosimetry and compared with results found in the literature for the Papillon 50 (P50) contact x-ray radiotherapy device regarding rectoscope dimensions, radiation beam shape, dose fall-off, and treatment time.

RESULTS: The multichannel applicator designed is able to deliver 30 Gy under 13 min with a 20350 U (5 Ci) source. The use of multiple channels and lateral shielding provide a uniform circular treatment surface with 22 mm in diameter. The resulting dose fall-off is slightly steeper (maximum difference of 5%) than the one generated by the P50 device with the 22 mm applicator.

CONCLUSIONS: A novel multichannel rectal applicator for contact radiotherapy with high-dose-rate ^{192}Ir sources that can be integrated with commercially available treatment planning systems was designed to produce a dose distribution similar to the one obtained by the P50 device.

Keywords: Brachytherapy; Monte Carlo; Contact radiotherapy; Rectal applicator

Introduction

Worldwide, colorectal cancer is the third most commonly diagnosed cancer in males and the second in females, with 1.65 million new cases and almost 835,000 deaths in 2015 (1). About one-third of these cancers is located in the rectum (2). The mainstay of curative rectal cancer treatment involves total mesorectal excision, where the tumor together with the rectum and surrounding mesorectal fat is removed. Total mesorectal excision surgery may result in significant long-term morbidity, such as urgency and fecal incontinence, as well as sexual and urinary dysfunction (3). Moreover, patients with low-seated tumors are often facing resection of the anal complex, resulting in a permanent colostomy (4). Recent studies however show that in selected patients, with complete remission after initial radiotherapy and surgery, associated toxicity can be safely omitted (5). However, only 15−20% of patients achieve a complete clinical remission after standard adjuvant chemoradiotherapy treatment (6).

Dose escalation to a rectal tumor leads to higher complete response rates and may thereby further enable omission of surgery (7). Dose escalation within the rectum in general leads to increased toxicity and decreased functional outcome,

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* Corresponding author. Department of Radiation Oncology (MAASTRO), GROW School for Oncology and Developmental Biology, Maastricht University Medical Center, 6201 BN Maastricht, The Netherlands. Tel.: +31 0 88 4455792; fax: +31 88 44 55 667.

E-mail address: frank.verhaegen@maastro.nl (F. Verhaegen).

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but this can be controlled as long as the treated volumes are kept small (8). Important advantages of endoluminal boosting techniques, such as 50 kV contact x-ray radiotherapy (CXRT) or brachytherapy (BT), include the possibility to apply a more selective/localized boost than using external beam radiotherapy. These techniques have been shown to increase the rate of pathological complete response, allowing for organ preservation with a favorable toxicity profile (9). Compared with the currently existing BT techniques (10–12), favorable characteristics of CXRT include more accurate positioning of the applicator; steeper depth-dose profile and a more selective treatment surface. Unfortunately, the widespread introduction is hampered by the limited availability of the device and the lack of treatment planning tools. Hence, a novel applicator was designed to deliver a dose distribution similar to the one delivered by the Papillon 50 CXRT device (P50) (13), but using commonly available ^{192}Ir high-dose-rate (HDR) BT afterloaders and sources brought in close contact with the tumor, enabling the integration with existing treatment planning systems.

Methods and materials

Design of the applicator

An HDR BT rectal applicator was designed to be used with a rectoscope for visual guided positioning, using the tip of the applicator as radiation exit surface. Considering a maximum rectoscope diameter of 30 mm [biggest P50 applicator (13)] and the requirement of having lateral shielding to spare healthy tissues, a cylindrical region with 22 mm in diameter was defined as the region inside the applicator where the BT sources could be positioned. Within this region, several configurations with a different number of channels and catheter shapes were evaluated with Monte Carlo (MC) simulations to find a configuration that fulfills the clinical requirements (dose distribution, treatment time, applicator dimensions). Given the geometrical restrictions and seeking a high dose rate with a steep dose fall-off, a design with multiple straight channels in circular patterns brought in close contact with the tumor was adopted for further investigation and will be presented in this work.

Figure 1 shows the initial applicator design, consisting of a 22 mm diameter polymethyl methacrylate cylindrical core, with 2 mm pure tungsten (19.25 g/cm^3) lateral shielding and a 1 mm plastic cap at the exit surface for electron absorption (14, 15) (composition by weight 37.5% C, 3.2% H, 59.3% F, with a density of 1.8 g/cm^3, as used in the Leipzig and Valencia applicators).

Design optimization

The design of the applicator was optimized by MC simulations using a GammaMed Plus HDR ^{192}Ir source (Varian Medical Systems, Palo Alto, CA) (16–18) that was validated against TG-43 (19) dose data available in the literature (20, 21) (data not shown). The MCNP6.1 MC code (22) was used in all simulations of this work.

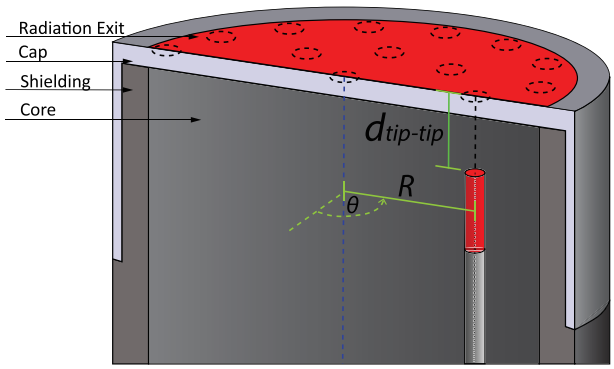

Fig. 1. Model for the multichannel HDR contact applicator: a central core holding a number of straight channels positioned in cylindrical patterns surrounded by lateral shielding with a plastic cap on top to stop secondary electrons. The tip of the source (2.5 mm from the center) was used as positioning reference because $d_{tip-tip}$ was easier to measure during experimental validations. HDR = high dose rate.

The design was optimized considering the dose distribution fall-off, dose uniformity, dose rate, and estimated treatment time, using the P50 device as a reference.

Dose fall-off and dose rate. The P50 device has a steep dose fall-off (30–50% of the surface dose at 10 mm depth) and high dose rate (20–35 Gy/min at the treatment surface) where the different values refer to different rectoscope diameters (13, 23). For the HDR BT applicator, both characteristics are primarily dictated by the distance of the sources to the end surface of the applicator ($d_{tip-tip}$, Fig. 1) due to the inverse-square law. The range of $d_{tip-tip}$ values where the dose fall-off from the applicator end surface is encompassed by the ones generated by P50 with different rectoscopes (22, 25, and 30 mm) was obtained by MC simulations in water. The dose fall-off was characterized using 1 mm^3 voxels at the applicator central axis.

Dose distribution uniformity at the radiation exit surface. Software was developed to calculate the 2D dose distribution at the applicator exit surface by combining MC presimulated dose distributions of the model shown in Fig. 1 to evaluate the relation between dose uniformity and the number of channels in the applicator. For setups containing from 1 to 20 channels, each source could be positioned at R = 0 to 10 mm in 1 mm steps, $d_{tip-tip}$ could range from 1.5 to 3.5 mm in 1 mm steps, and θ from 0 to 360° with 1° steps. There was no dwell time restriction, and the resulting dose rate (Gy/min) was calculated considering a 10 Ci source. The resulting dose distribution uniformity was evaluated considering the relative standard deviation (RSD), defined as the ratio of the standard deviation to the mean, in the scoring region with acceptance criteria of RSD lower than 2%.

For each MC simulation, 1e10 photons were transported and secondary electrons had their energy deposited locally.

The dose was scored in water assuming charged-particle equilibrium using a cylindrical grid at the applicator exit surface with 26 mm diameter and 0.1 mm thickness, radial resolution of 0.1 mm and the angular resolution of 1°, resulting in a statistical dose uncertainty lower than 1% (type A $\pm$ 1σ) in all scoring regions.

Treatment time. The total treatment time consists of two components: the dummy check time and the irradiation time. For the GammaMed Plus iX afterloader (Varian Medical Systems, Palo Alto, CA), a dummy source is sent twice to the end of each catheter that is going to be used during a treatment to check for obstructions, taking nearly 30 s per channel, the second dummy run can be dismissed depending on the system used, but keeping it is a safer clinical practice. The irradiation time is dose rate dependent and will change according to the applicator design and source activity.

Treatments with the P50 device usually deliver fractions of up to 30 Gy at the tumor surface (24). The treatment times to deliver the same dose with the different setups of the HDR applicator were evaluated considering a source of 5 Ci, representing a low activity source, close to a worst-case scenario regarding dwell times.

Virtual shielded model evaluation

A second MC model of the applicator (including more details such as shielding, plastic cap, optimized channel positions, and the $d_{tip\text{-}tip}$ resulting from the previous section) was built to simulate the 3D dose distribution in water, which was evaluated considering surface dose distribution, dose profiles at different depths for regions with higher and lower dose uniformity, depth-dose profiles and dose fall-off. The results were compared with values found in the literature (25) for the P50 device using the 22 mm rectoscope that generates a similar irradiation area at the treatment surface.

Experimental validation

The experimental validation using a simplified prototype of the applicator is described in Appendix A.

Results

Design optimization

MC simulations in water showed that the dose fall-off in the applicator central axis is not only $d_{tip\text{-}tip}$ dependent, but also depends on the number of channels used. For designs having from 1 to 20 channels, $d_{tip\text{-}tip}$ between 1.5 and 3.5 mm resulted in dose fall-off fairly similar to the one of the P50 device.

As the number of channels in the applicator increases, it becomes possible to add more concentric rings to accommodate the channels and move the sources closer to the applicator exit surface without violating the dose uniformity criterion RSD.

The channels were distributed as follows: 1 channel—a central channel with $d_{tip\text{-}tip}$ = 3.5 mm; 2−5 channels—a ring (without central channel) with $d_{tip\text{-}tip}$ = 3.5 mm; 6−13 channels—a central channel and one ring with $d_{tip\text{-}tip}$ = 2.5 mm; 14−20 channels—a central channel and two rings with $d_{tip\text{-}tip}$ = 1.5 mm.

The transition when there were enough channels to add a new ring results in steps in RSD (from to the change in number of rings) (Fig. 2a) and irradiation time (from the change in dose rate due to $d_{tip\text{-}tip}$) (Fig. 2b).

The horizontal dashed lines in Fig. 2a show the maximum value allowed for RSD (2%), where models with eight channels or more were acceptable. The same criterion (lower limit of eight channels) is represented by the vertical dashed line in Fig. 2b, showing the treatment delivery time for a 5 Ci source lower limit of eight channels. As the number of channels increases, the irradiation time has the tendency to be lower due to the higher dose rate as the sources are brought closer to the surface; however, the total treatment time has the tendency to keep rising due to the dummy check time component.

The RSD for applicator designs with 8, 9, 10, and 11 channels were 1.93%, 1.88%, 1.88%, and 1.88%, respectively. The nine-channel model (one ring of eight channels and one central channel) was found to be the best compromise between RSD and treatment time.

Figure 3a shows the applicator's final design, with nine channels, 3 mm of pure tungsten (19.25 g/cm^3) for lateral shielding (1.5 mm around the applicator core and 1.5 mm belonging to the rectoscope) and a 1 mm thick plastic cap to absorb secondary electrons (14, 15) (composition by weight 37.5% C, 3.2% H, 59.3% F, with a density of 1.8 g/cm^3, as used in the Leipzig and Valencia applicators). Figure 3b shows the applicator positioning inside the rectum against the tumor. The knee-chest position is adopted for treatments with the P50 machine; however, lateral and lithotomy positions may be also an option for the new applicator. Possible treatment positions will be subject of further studies.

Virtual shielded model

Figure 4a shows the simulated dose at the virtual shielded applicator's exit surface (Fig. 3), where hotspots are noticeably close to the source channels. Figure 4b shows the depth isodoses in front of the applicator. The dose profiles in Fig. 4c at the applicator's surface and at 1 mm depth along line 1 from Fig. 4a (connecting the center of the central source and the center of two other sources) show that the effects of these hotspots are greatly reduced at 1 mm depth and are also reduced for the dose profile along line 2 from Fig. 4a passing in between two sources (rotated 22.5°; Fig. 4d).

Figure 5 shows a comparison of dose profiles at different depths and dose fall-off simulated in water between the P50

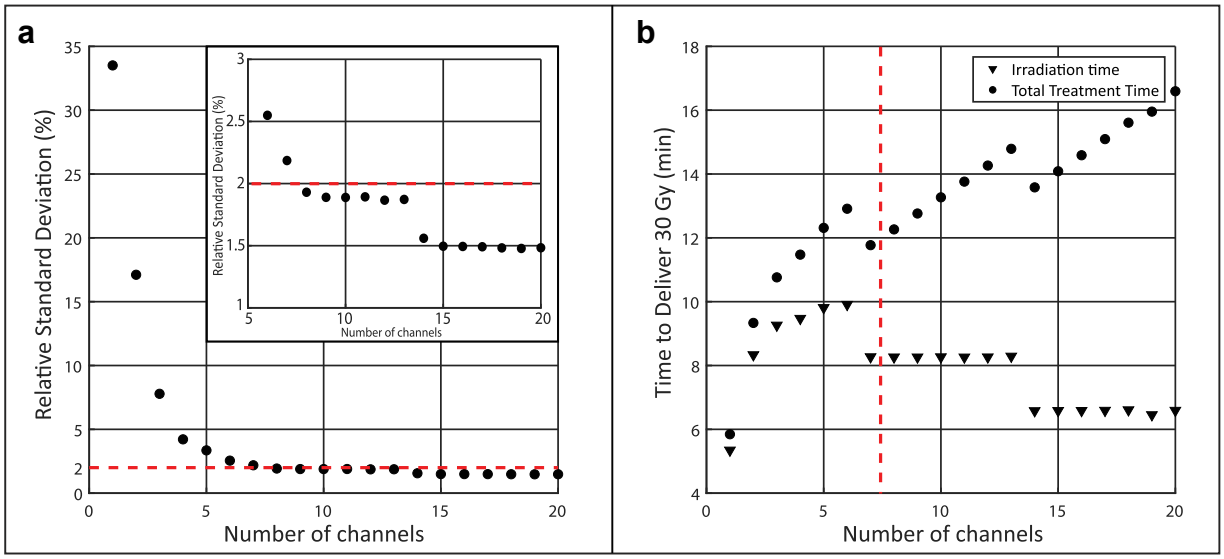

Fig. 2. RSD at the applicator's exit surface with a rescaled insert to better evaluate applicators with more than five channels (a) and treatment time to deliver 30 Gy with a 20350 U (5 Ci) source (b) obtained from optimizing applicators with a number of channels ranging from 1 to 20. The reference line in (a) (horizontal dashed line) for RSD of 2% represents the arbitrary dose uniformity criterion. The vertical dashed line in (b) represents the applicators accepted by the same criterion. RSD = relative standard deviation.

contact therapy device with the 22 mm rectoscope [data from Croce *et al.* (25)] and the HDR applicator. The dose profiles from Fig. 5a–c show that the radiation beam resulting from the HDR applicator has a wider aperture than the one generated by the P50 machine, nevertheless with a similar dose fall-off (maximum difference of 4.5% at 12 mm depth) shown in Fig. 5d.

Discussion

Design and clinical implementation

The applicator can be integrated to currently available treatment planning systems with model-based dose calculation algorithms (MBDCAs), such as Acuros BV in BrachyVision (Varian) and Oncentra Brachy ACE (Elekta, Stockholm, SE). Studies have shown small deviations in dose distribution between Monte Carlo simulations and these treatment planning systems (26, 27) for shielded applicators. The use of multiple channels and the possibility of TPS integration enables a better control of dose distribution, which is an advantage comparing with current CXRT techniques. However, the time required to send the dummy sources was the main factor that limited modeling an applicator with more than nine channels (Fig. 2b); having more channels in the applicator would increase the degrees of freedom available for the TPS. Another limiting factor to use more channels was the transit dose contribution to the total dose

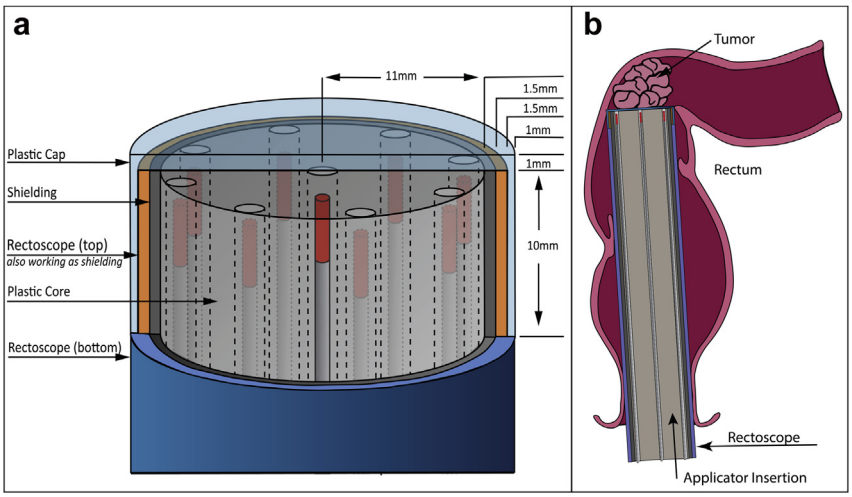

Fig. 3. (a) Model for the nine-channel HDR contact applicator. A central channel surrounded by a ring of eight equally distributed channels at 10 mm radii. (b) Applicator positioning inside the rectum against the tumor. HDR = high dose rate.

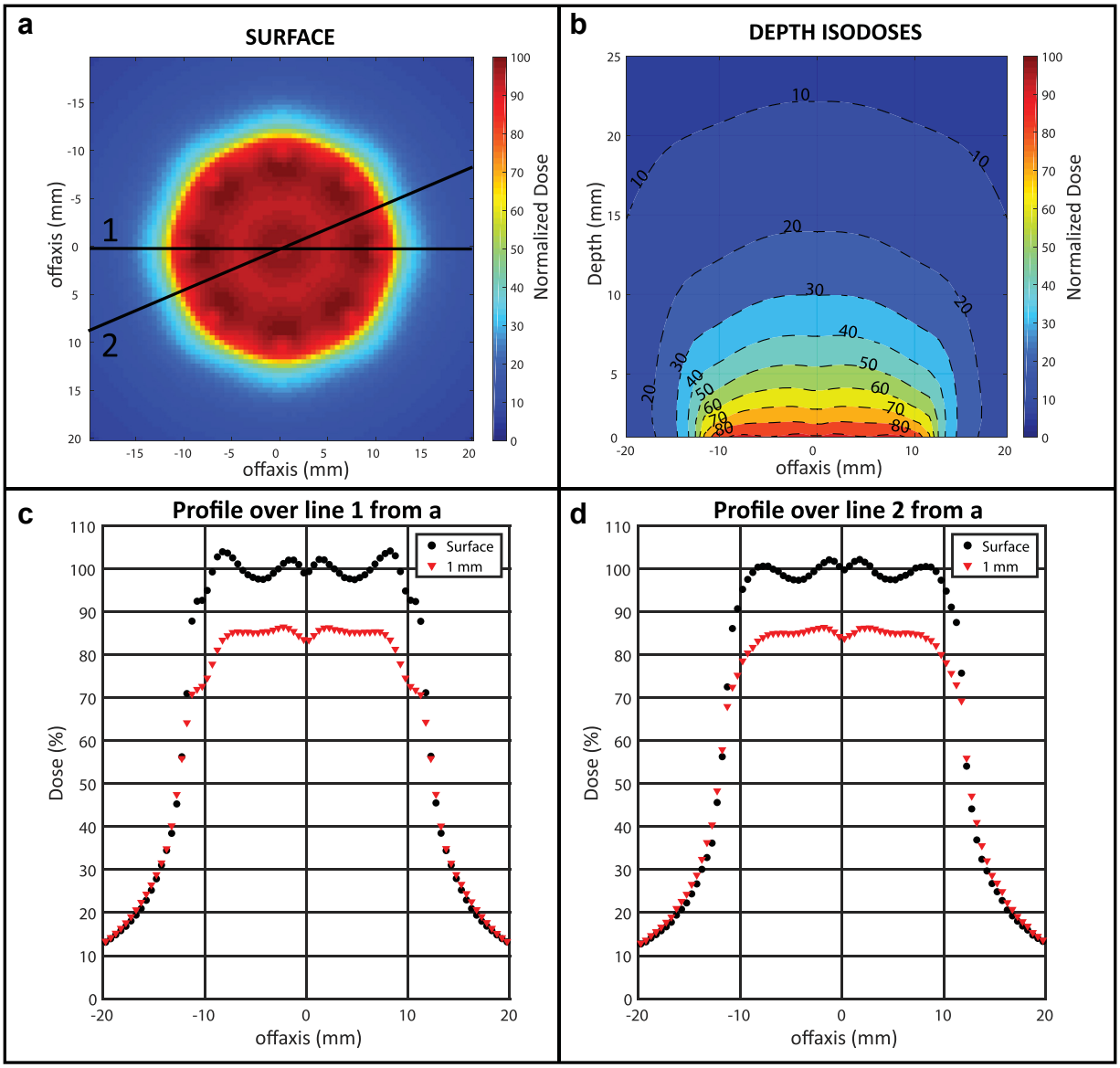

Fig. 4. Simulated normalized dose at the applicator surface for a region of 40 × 40 mm^2 (a), depth isodoses distribution (b), dose profiles at the applicator surface and at 1 mm depth in water along the line 1 (c) and line 2 (d) from (a).

(contribution equivalent to extra dwell time of 0.84 ± 0.09 s for the first dwell position using a 10 Ci source) (28). Increasing the number of channels would reduce the dwell time per channel, and the transit dose contribution would be higher, especially for the most distal dwell positions that have no transit time correction in current afterloaders. Moreover, the literature mentions a range of transit times for afterloaders of the same model, as summarized by Fonseca *et al.* (29). Ideally, an afterloader with transit dose correction for the most distal position and reduced dummy time would enable a design with more channels.

Validation

For a total of 12 irradiations using nine channels (Table A1 from Appendix A), the three irradiations where less than 90% of the voxels passed a gamma analysis with 1 mm/1% acceptance criteria had dwell times of 10 s per channel (irradiations 5, 6, and 9) with a transit dose contribution of 6.5% to the total dose. For dwell times of 20 s or higher (average transit dose contribution of 2.5%), an average of 96% of the voxels passed using the same criteria. This deviation is due to a higher uncertainty on the transit time correction for lower dwell times, and the fact that transit time correction applied for the HDR applicator was measured for a different geometry (28) and may not be correct for the present applicator. The usual dose delivered in clinical practice for rectal cancer patients using CXRT is 30 Gy (24), which requires an average dwell time per channel of 25 s to be delivered with the HDR applicator using a 10 Ci source. Therefore, applying the transit dose correction from Jeong *et al.* (28)

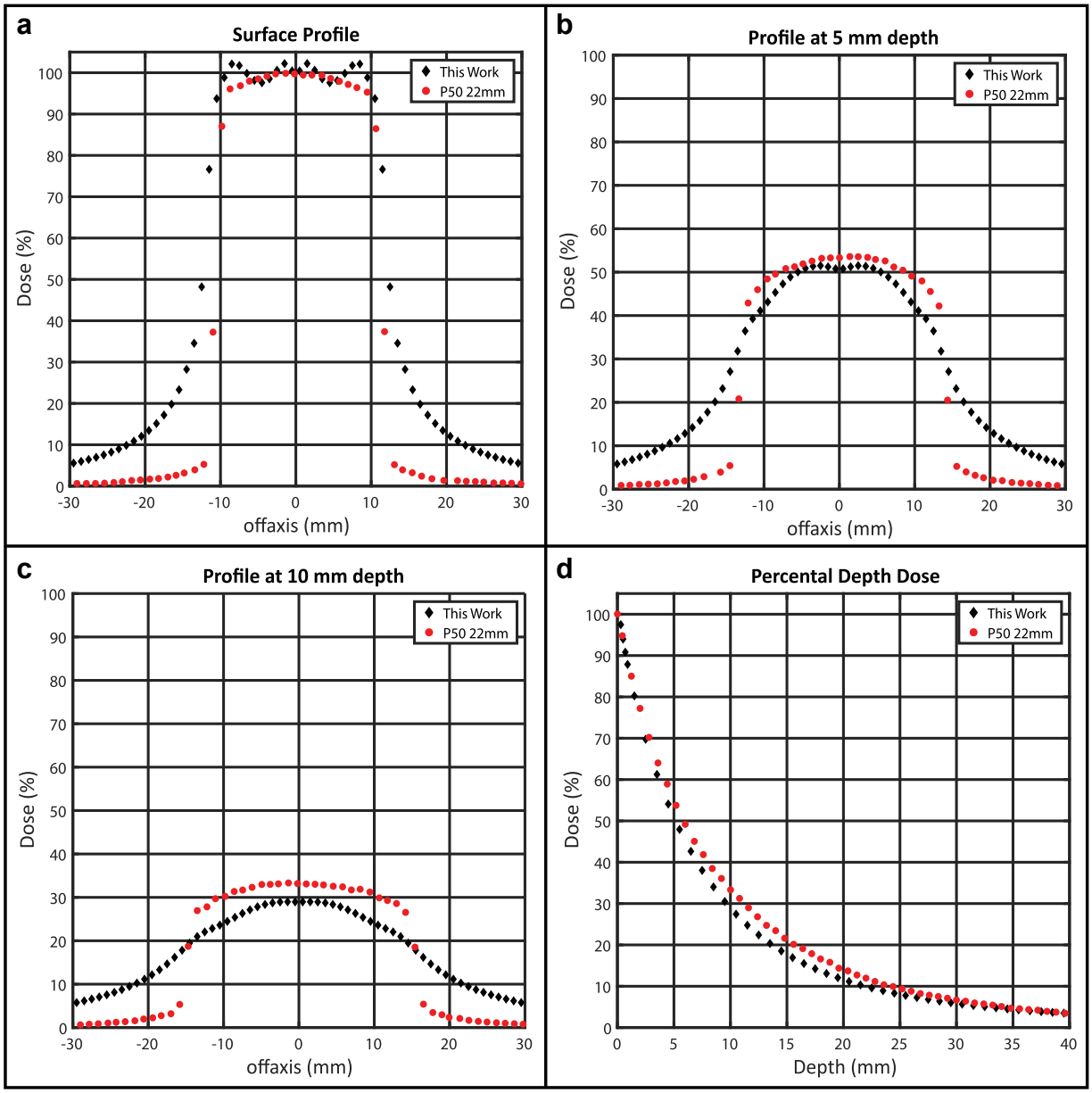

Fig. 5. Showing the dose profiles at the surface (a), 5 mm (b) and 10 mm (c) depth, and the percentage depth dose (d) in water.

is precise enough for typical treatment doses; however, further investigation of transit dose specific for the HDR applicator is required for low-dose treatments with a high activity source, which is the worst-case scenario for the transit dose correction.

Source position uncertainty

A $d_{tip\text{-}tip}$ between 2 and 3 mm is required to obtain a steep dose fall-off, mainly governed by the inverse-square law. However, due to the high-dose gradient close to the source, the mean dose difference at the applicator exit surface is approximately 1.7% for each 0.1 mm shifted from $d_{tip\text{-}tip}$ = 2 mm to 3 mm. The source position can be shifted due to transfer tube bending, and forcing the source against the end of the channel would remove the uncertainty of $d_{tip\text{-}tip}$; however, it would also increase the potential of snaking of the source cable inside the channel, causing a local dose distribution inhomogeneity due to the source inclination (see Appendix B), or it could cause an error on the afterloader due to obstruction detection. Since the designed applicator has straight rigid channels, the option of using smaller lumen sizes is under evaluation to reduce the snaking effect when the source reaches the tip of the channel. This would reduce the errors due to transfer tube bending that may occur during clinical practice.

Virtual shielded model

The dose distribution for an applicator with nine channels has the smallest RSD 3 mm away from the sources tip, and the dose fall-off will be similar to the one generated by P50 when $d_{tip\text{-}tip}$ is between 2 and 3 mm. Therefore, it is possible to choose $d_{tip\text{-}tip}$ with conventional treatment planning systems to control the tissue depth where the dose distribution will be most uniform and the shape of the dose fall-off. The HDR applicator has a wider radiation beam than the P50 machine due to the small $d_{tip\text{-}tip}$. If the rectoscope is also used as shielding, it can be placed around a protruding tumor providing better shielding for healthy tissues and shaping a narrower radiation field.

The material considered as shielding for all the MC simulations was pure tungsten (19.25 g/cm^3). In practice, tungsten is a material that is not easily machined and it is possible that a tungsten alloy will be adopted for the real applicator. Nevertheless, commonly used tungsten alloys often have up to 97% of tungsten in their composition, providing a similar shielding effect.

Clinical aspects of dose delivery

The designed applicator represents a new design in rectal cancer BT. The applicator can be positioned directly against the tumor by visual guidance through a rectoscope. This approach enables fast and reliable positioning on the tumor without the need for additional imaging devices. Furthermore, the rectoscope encompassing the applicator enables shielding in all directions except toward the treatment depth into the rectal wall containing the tumor, which is the main advantage of this applicator compared with other HDR techniques, the possibility to more selectively target the tumor (due to shielding and lower beam aperture). Having a steeper dose fall-off enables destroying the tumor cells layer by layer, which also preserves healthy tissues including organs such as the vagina/urethra, prostate, and bladder. This is extremely important as after conventional HDR BT, late toxicity, mainly rectal bleeding, is a common side effect (30). Late rectal bleeding occurs less frequently after treatment with the P50 machine. It has been hypothesized that this is due to limiting high doses only to small volumes using lateral shielding and a steep dose fall-off in the depth of the tissue.

Owing to its new design, clinical data of patients treated with this applicator is not yet available. For the first clinical applications, the patient eligibility criteria are expected to be similar to those applied for patients treated with the P50 machine [well to moderately well-differentiated rectal adenocarcinoma, cT1-3 tumors with less than 3 cm in diameter situated less than 12 cm from anal verge (31)] once the dose distributions are similar. Future studies will show whether the eligibility criteria should be adapted.

To date limited information is available about the dose distribution in the tumor of the treatments with the P50 device. There are no guidelines for dose prescription or reporting in rectal endoluminal contact BT. Questions include especially how the dose should be distributed among the volumes to increase tumor cure while avoiding significant toxicity. As a starting point, our team tried to mimic a dose distribution comparable with the Papillon 50 kV contact therapy, as much clinical experience is available for this approach (32–41) as monotherapy or combined with other forms of radiotherapy. Our approach mimics the 50 kV contact therapy well, although not perfectly, especially with an even somewhat steeper dose fall-off in depth and a somewhat less steep dose fall-off in the penumbra to the side. Although differences are small, clinical studies are needed to evaluate whether these are relevant or not.

Conclusion

In this study, a novel rectal applicator for contact radiotherapy was designed, showing that it is possible to use commonly available ^{192}Ir HDR sources and afterloaders to obtain dose distributions that are similar to the ones delivered by 50 kV CXRT devices. The use of multiple channels increases the degrees of freedom available for the TPS, potentially allowing the delivery of a personalized dose distribution for the treatment of tumors with different shapes.

Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.brachy.2018.07.012.

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