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Intraoperative implantation of a mesh of directional palladium sources (CivaSheet™): Dosimetry verification, clinical commissioning, dose specification, and preliminary experience

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Abstract

PURPOSE—To present the clinical commissioning of a novel ¹⁰³Pd directional brachytherapy device (CivaSheet™) for intraoperative radiation therapy.

METHODS AND MATERIALS—Clinical commissioning for the CivaSheet™ consisted of establishing: (i) source strength calibration capabilities, (ii) experimental verification of TG-43 dosimetry parameters, (iii) treatment planning system validation, and (iv) departmental practice for dose specification and source ordering. Experimental verification was performed in water with radiochromic film calibrated with a 37kVp x-ray beam. Percentage difference ([measurements – calculation] / calculation) and distance to agreement (difference between film-to-source distance and distance that minimized the percentage difference) were calculated. Nomogram values (in U/100 Gy) for all configuration (up to 20 × 20 sheets) were calculated for seed ordering. Clinical commissioning was used on patients enrolled in an ongoing IRB-approved protocol.

Results—A source calibration procedure was established and the treatment planning system was commissioned within standard clinical uncertainties. Percentage dose differences (distances to agreement) between measured and calculated doses were 8.6% (–0.12mm), 0.6% (–0.01mm), –6.4% (0.22mm), and –15.8% (0.72mm) at depths of 2.3mm, 5.1mm, 8.0mm, and 11.1mm respectively. All differences were within the experimental uncertainties. Nomogram values depended on sheet size and spatial extent. A value of 2.4U/100 Gy per CivaDot™ was found to satisfy most cases, ranging from 2.3 to 3.3U/100 Gy. Nomogram results depended on elongation of the treatment area with a higher variation observed for smaller treatment areas. Post-implantation dose evaluation was feasible.

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CONCLUSIONS—Commissioning and clinical deployment of CivaSheet™ was feasible using BrachyVision™ for post-operative dose evaluation. Experimental verification confirmed that the available TG-43 dosimetry parameters are accurate for clinical use.

Keywords

CivaSheet™; dosimetry; dose specification; nomogram

Introduction

Intraoperative radiation treatment of a tumor bed after surgical resection(1–9) is a widely performed procedure. These treatments can be conducted using various modalities including high dose-rate (HDR) temporary implants(10), low dose-rate (LDR) permanent implants (5), external electron beam (11), and more recently using electronic brachytherapy devices(12).

Recently, the CivaDot™ (CivaTech Oncology Inc., Durham, NC), a novel palladium source with a gold shield on one side has been introduced (13,14). The CivaSheet™ consists of multiple CivaDots™ arranged in regular rectangular patterns and embedded in a bioabsorbable polymer. The gold shield permits preferential dose delivery on one side of the device (where the target is located), sparing the normal tissue lying on the opposite side. No clinically used dose specification methodology has been reported for this source. A procedure for obtaining traceable source strength measurement of the CivaDot has been described (13), and a special CivaDot insert for a well chamber is available for user calibrations. Dosimetry of LDR sources with the AAPM TG-43 dose calculation formalism typically relies on societal consensus dosimetry data (15). TG-43 parameters have been calculated with Monte Carlo simulations (14), but AAPM consensus data are not yet available for the CivaDot™.

In this paper, we report our experience with the various physics aspects of commissioning this new device. The TG-43 dosimetry parameters were experimentally verified. While this is not commonly part of a commissioning process, we undertook this step because no independent validation of the published Monte Carlo data currently exists. Details of our dose specifications for this device are presented, which are the basis for dose prescription and seed ordering that we used clinically in our ongoing clinical trial, on which we have so far treated four patients. Finally, we discuss our experience with acceptance, implantation, and post-operative dosimetry of the CivaSheet™. To our knowledge, this is the first report of the clinical implementation of this new device and of experimental verification of its dosimetry parameters.

Methods

Commissioning of the treatment planning system

Source information for the CivaDot™ was entered in the BrachyVision treatment planning system (TPS) (Varian Medical Systems, Inc. of Palo Alto, CA). Source geometry was entered from published parameters (14), with rounding and interpolation necessary to fit the BrachyVision templates. Test plans were generated for a single source and for a 6×6 array

for sources. Doses calculated by BrachyVision to a set of representative points were compared to an independent implementation of the TG-43 2D formalism written in MATLAB (MathWorks, Inc, Natick, MA), using the same source specifications and dosimetry tables provided in Rivard et al. (14) without any modification. Feasibility of CivaSheet™ post-implant reconstruction was evaluated.

Dosimetry verification

Due to the lack of societal consensus dosimetry parameters for this new source, a preliminary independent dosimetric verification of the TG-43 parameters was performed. Sources were provided by the manufacturer and individually calibrated. Figure 1 shows the experimental setup consisting of the CivaDot™, plastic (PMMA) frame, and radiochromic film (Gafchromic™ model EBT3, Ashland Specialty Ingredients, Bridgewater, NJ) in a water bath. The source was taped by its membrane edges such that the active surface faced the film. The film was supported flat in the horizontal plane using a 0.8 mm-thick plastic sheet. Variable standoffs allowed the depth of water between the source and film to be accurately selected. Physical distances were adjusted by adding 0.125 mm for the half-thickness of the film and subtracting the offset between the source origin and the surface of the source holder. This resulted in source:film distances of 2.3 mm, 5.1 mm, 8.0 mm, and 11.1 mm. Fixed 13 mm-thick standoffs below the film holder allowed water as backscatter material.

Film calibration was performed using a Philips RT 100 orthovoltage unit (calibrated with an ADCL-calibrated ion chamber). Film was supported in air at the end of an 8 cm cone at 30 cm from the x-ray source. For the purpose of this validation, a 37 kVp energy setting was chosen as its mean energy most closely approximated the expected CivaDot™ photon emissions. Calibration films exposed to 0–9 Gy in 1 Gy steps were scanned 5 days following the final exposure along with the Pd films to minimize optical density growth artifacts using an Epson 11000XL scanner and FilmQA Pro software (Ashland Global Holdings Inc., Covington, KY) at 150 dpi (0.17 mm resolution). Measured results were compared to MATLAB-based dose calculations. The percentage agreement between experiment and calculation was defined as the mean difference ($[\text{measurement} - \text{calculation}] / \text{calculation}$) over all points within 2.5 mm of the center of the exposure. The distance to agreement (DTA) was calculated by subtracting from the source:film physical distance the distance necessary to minimize the difference between the measured and calculated dose.

For the purpose of clinical validation, agreement between measurement and calculation was considered acceptable if the DTA was below the expected uncertainty. Three uncertainty components were considered: source strength measurement, assumed to be 3% ($k=1$); film calibration, mainly uncertainty in calibration coefficient due to source energy spectrum changes with depth, estimated to be 15% ($k=1$) after accounting for the rapid change in response in the 30 kVp to 70 kVp range; and source:film distance, estimated to be 0.5 mm. Summing the three components in quadrature, the uncertainty as percentage dose uncertainty (distance uncertainty) was 40.3% (0.55 mm), 26.3% (0.62 mm), 21.7% (0.71 mm), and 19.6% (0.81 mm) at source:film distances of 2.3 mm, 5.1 mm, 8.0 mm, and 11.1 mm, respectively.

Dose specification

Doses from an ideal, flat distribution of all square and rectangular configurations of 2×2 to 20×20 (4 to 400) CivaDots™ of nominal source strengths of 1 U each were calculated in MATLAB™. The sheet area was defined as the area enclosed by the peripheral source centers (e.g., a CivaSheet™ of 6×6 CivaDots™ with a spacing of 0.8 cm would be associated with a sheet area of $4.0 \text{ cm} \times 4.0 \text{ cm}$), in accordance with our historical definition of area for intraoperative radiation therapy (IORT) devices. Also following institutional historical practice, the treatment depth (from the active side) for dose calculation was 5 mm from the source origin, which is centered within the gold shield (14). Dose at depths of 2 mm, 5 mm, and 7 mm were calculated. The reference dose for the nominal source strength of 1 U per CivaDot™ was defined such that the mean dose to the periphery of the sheet area at the 5 mm treatment depth was 90% of the reference dose.

A table for source ordering was generated providing the source strength per unit dose (in U/100 Gy) for each configuration; a table with the unit dose per source strength (in Gy/U) was also generated for use in the operating room to calculate the expected dose given the final implanted sheet size. The A80%, A100%, and A120% (percent of the sheet area at depth receiving 80%, 100%, and 120% respectively of the reference dose) were calculated. Mean, minimum, and maximum doses as a percentage of the reference dose within the sheet area at all depths under consideration were calculated for all configurations. Doses on the shielded side of the CivaSheet™ were also investigated for all dimensions at distances of 2, 5, and 7 mm from the CivaDots.

Source calibration

Using the calibration procedure detailed in *Aima et al.*(13) a CivaDot™ calibrated by an Accredited Dosimetry Calibration Laboratory was obtained in order to calibrate a reentrant well-type air ionization chamber (model HDR 1000 Plus by Standard Imaging, Inc. of Middleton, WI) with a special holder supporting the CivaDot™. Feasibility and discrepancies observed between measurements and calibration certificates for clinical cases were reported.

Clinical deployment

Finally, we report our physics experience with the first clinical cases at our institution using the CivaSheet™, which was performed within an IRB-approved protocol. Further information about this clinical trial is publicly available on [ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/NCT02902107?term=civasheet&rank=3)¹. Seeds calibration, sheet implantation, and post-operative dose evaluation are discussed. Detailed clinical descriptions are not presented and will be reported in the future once increased patient accrual and follow up information is available.

¹<https://clinicaltrials.gov/ct2/show/NCT02902107?term=civasheet&rank=3>

Results

Commissioning of the treatment planning system

Characterization in BrachyVision™ of the CivaDot™ dose distribution with the brachytherapy dosimetry parameters was feasible. For the 6×6 configuration, 55 points distributed on the hot side of the source, at a distance (mean $\pm$ 1 standard deviation) from the plane of the CivaSheet™ of 8.56 ± 5.70 mm, with distance from the closest CivaDot™ of 10.14 ± 7.29 mm, presented a discrepancy in dose between BrachyVision and the independent MATLAB™ calculation of $0.1 \pm 0.56\%$ (1.21% maximum, -1.24% minimum), and a DTA of 0.03 ± 0.03 mm (0.18 mm maximum, 0.00 mm minimum). Three points, positioned in the plane of the CivaSheet™ (where the dose gradient is greatest) with distance from the lateral edge of the CivaSheet™ of 5 mm, 10 mm, and 30 mm, presented a discrepancy in dose between BrachyVision™ and independent MATLAB™ calculation of 9.1%, 10.3%, and 10.7% and DTAs of -0.04 mm, -0.13 mm, and -0.61 mm. For the single CivaDot™ configuration, 16 points (with one located on the shielded side of the source) at a distance from the CivaDot™ of 11.10 ± 10.57 mm presented a discrepancy in dose between BrachyVision™ and the independent MATLAB™ calculation of $-0.5 \pm 0.4\%$, and a DTA of 0.04 ± 0.09 mm.

Dosimetry verification

Calculated irradiation times varied from 1 to 10 days depending on depth. Percentage difference (and DTA) were 8.6% (-0.12 mm), 0.6% (-0.01 mm), -6.4% (0.22 mm) and -15.8% (0.73 mm) at source:film distances of 2.3 mm, 5.1 mm, 8.0 mm, and 11.1 mm. All differences were within the experimental uncertainty. Dose profiles from measurements and TG-43 calculation are shown in Figure 2. All DTAs were deemed clinically acceptable.

Dose specification

The calculated nomogram for selection of source strength based on desired prescription dose and expected CivaSheet™ size is shown in Figure 3. Also, the nomogram for the determination, in the operating room, of the expected dose given the source strength and the actual sheet size used is shown in Figure 3. Minimum, mean, and maximum doses within the sheet area, as percentages of the reference dose (defined at 5 mm depth) are presented (Figure 4). The A80%, A100%, and A120% are also reported (Figure 5).

For all sheet configurations, mean doses on the shielded side of the sheet expressed as percent of the reference dose (at a depth of 5mm on the active side) were $< 22\%$ of at 2 mm, $< 11\%$ at 5 mm and $< 8\%$ at 7 mm distances. For all depths, the highest dose on the shielded side was on the outside border (as defined by the peripheral CivaDot™ centers) where radiation scatter was greatest.

Clinical deployment

Seven patients have been consented for CivaSheet™ implantation. In four patients the CivaSheet™ was implanted as originally planned, one case was converted to our standard HDR ^{192}Ir BT technique in the OR due to concerns about possible fixation of the CivaSheet™ to the surgical site, one case was deemed to no longer warrant radiotherapy

based on intraoperative assessment, and one case was canceled ahead of the surgery due to change in the patient's medical condition (no calibration was performed). The CivaSheets™ were obtained under sterile conditions and the sheet was cut to size to deliver 100 Gy to the area at risk. The sheet was then sutured in place using monofilament polypropylene (Prolene®) sutures such that all the CivaDots™ were in close contact with the target tissue. Calibrations performed by a board-certified medical physicist on 48 non-sterile CivaDots™ from six orders resulted in $-0.8 \pm 1.1\%$ discrepancies between measured source strengths and the manufacturer reported source strengths. Post implantation CT scans were performed between 3 and 7 days after implantation with 1-mm slice thickness with the smallest field-of-view permitting visualization of the sources and the relevant organs-at-risk. Identification of the CivaDots™ for post-operative treatment planning was feasible and was confirmed by three board-certified medical physicists. Manual angular orientation of each source based on the relative position of adjacent sources proved feasible but time consuming. Dose distributions from BrachyVision™ for a clinical case are shown in Figure 6.

Discussion

The CivaSheet™ is a device consisting of shielded ^{103}Pd sources called CivaDots™, and has the unique feature of preferentially delivering radiation to one side of the sheet while sparing normal tissue dose on the other side. The CivaSheet™ has much promise for intra-operative brachytherapy due to potential for sparing uninvolved organs. Compared to HDR IORT, which is standard practice in our institution, the CivaSheet™ does not require the initial investment of a shielded operating room and an HDR ^{192}Ir remote afterloader. Moreover, the visibility of the CivaSheet™ in post-implantation evaluation scans can be useful to analyze the adequacy of CivaSheet™ placement and potential for further re-irradiation of the surgical site or neighboring anatomy. This device has been described before in two non-clinical publications: a description of the calibration procedure for the CivaSheet™ source, the CivaDot™ (13) and a Monte Carlo simulation study establishing the dosimetry parameters necessary to perform TG-43 dose calculations (14). To our knowledge, this is the first description of the commissioning of the CivaSheet™ as applied to clinical practice. Due to the novel design of this device, clinical commissioning required addressing multiple aspects exceeding the typical scope of source commissioning: source calibration, TPS commissioning, dosimetry verification, and dose specification.

No custom treatment pre-plan is typically performed at our center prior to the surgical procedure for permanent LDR IORT cases, as area and positioning of the radioactive mesh based on clinical judgment can change drastically from pre-operative assessment. Dose calculation is still central to these cases: dose specification and nomograms for seed ordering are derived from these dose calculations, as are custom post-implantation dosimetric verification plans. Typically, dose calculation is performed according to the TG-43 formalism (15), which assumes a uniform water medium. While new dose calculation models have recently become available that account for material inhomogeneities (16), dose relationships are historically based on TG-43 calculations. Therefore, TG-43 calculation of dose from a new source is central to clinical commissioning. Consensus dosimetry parameters for a brachytherapy source are drawn from measurements and Monte Carlo simulation studies (17). Dosimetry parameters are not typically verified by the clinical

medical physicist in the commissioning process. Due to the recent availability of the CivaSheet™, consensus data do not yet exist and the dosimetry parameters (based on Monte Carlo simulations) are from a single investigation (14). Therefore, independent verification was pursued at our institution for the dosimetric validation of this device.

Large percentage differences between the measured and calculated doses for a brachytherapy source are expected due to the sharp dose gradients (amplified by the shielding built into the CivaSheet™), detector positioning uncertainties, and the difficulty in film calibration for the expected source energy spectrum. For this reason, we opted for an analysis focusing on DTA between the measured and calculated dose. We found DTAs within our acceptability criteria for all our measured results. This is to our knowledge the first independent dosimetric verification for this device. Our experiments were sufficient to ascertain the clinical suitability of the published brachytherapy dosimetry parameters (14). These data were formatted for our use in BrachyVision and independent secondary calculations were performed to confirm the accuracy of the TPS calculations. Further investigation is necessary to reach the evidence needed to contribute to consensus data. In particular, a limitation of this clinical investigation lies in the use of a film calibration procedure that did not account for changes in energy spectrum over the examined depths.

Dose specification depends on many clinical considerations, such as definition of reference dose, calculation geometry, reference depth, and actual desired dose. For IORT LDR devices, dose specification is directly tied into source ordering decisions, which occur many days before implantation. We presented in this work our nomogram, based on our clinical protocol of prescribing dose to 5 mm depth from the source origin (approximately 4.4 mm in tissue from the surface of the source), with reference dose such that 90% coverage is on average achieved at the periphery of the treatment area. Other clinics may choose a different depth, or define the reference dose differently. We opted for a definition consistent with our historical practice, where the physical size of the source was not considered. We found that values of 2.3–2.4 U per CivaDot™ per 100 Gy reference dose are appropriate for square CivaSheet™ of 6×6 sources or larger. This value is in line with the value of 2.6 U per CivaDot™ per 120 Gy (2.2 U per CivaDot per 100 Gy) suggested by Rivard (14). We found that higher source strengths are needed for non-square geometries and for smaller CivaSheets™. It is therefore important to estimate the expected size and dimensions of the treatment area before surgery. The nomogram we presented has been used clinically for seed ordering and in the operating room to present an estimate of the discrepancy resulting from differences between the expected and the actual implant geometry. Our preliminary clinical results show doses in agreement with the specified dose. Implantation of the CivaSheet™ did not result in crumpling, and reconstruction on CT images was feasible. BrachyVision commissioning was described, and post-implantation evaluations were feasible, although time consuming. Similar results were described for the VariSeed TPS commissioning and use (14).

The clinical success of the CivaSheet™ will need to be evaluated based on patient outcomes. This will be reported in the future as protocol accrual and follow-up increases.

Conclusion

The CivaSheet™ brachytherapy dosimetry parameters were experimentally verified with good agreement to the reference simulation results. Commissioning and clinical deployment of CivaSheet™ was feasible using the BrachyVision TPS for post-operative dose evaluation. We presented a system for dose specification to permit planning of the radiation dose, and evaluation in the operating room of the expected dose given the actual implantation geometry.

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Abbreviations

CT	Computed tomography
DTA	Distance-to-agreement
HDR	High dose-rate
IORT	Intra-operative radiation therapy
LDR	Low dose-rate
TPS	Treatment planning system

Fig. 1.

Experimental setup for the dosimetry verification. The CivaDot and the radiochromic film were separated by plastic standoffs of four different sizes, to ensure precise separation between source and detector². The entire experimental setup was submerged in water. Only the bottom of the tank is shown in the schematic. Figure not to scale.

²Source:film distance = variable standoff distance (measured) – distance between back of CivaDot and source holder (0.66 mm, measured) – distance between shield and back-of-source (0.063 mm) + half thickness of film (0.125 mm)

Fig. 2.

Plots of the measures and calculated doses along two orthogonal (horizontal and vertical) axes on the film plane. “TG-43 corrected” displays the TG-43 calculation performed with the distance between the source and film plane adjusted by the distance-to-agreement value found for each configuration³.

³This corrected calculation was performed by adding the distance-to-agreement to the source:film distance, recalculating the new point:source distance for each calculation point (using trigonometric relationship between the source:film distance and point to central axis distance, and obtaining the TG43 value at those points.

Source Strength (U) per 100 Gy		Number of CivaDots in x direction																		
		2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Number of CivaDots in y direction	2	3.30	3.05	2.92	2.85	2.80	2.76	2.73	2.71	2.70	2.69	2.67	2.67	2.66	2.65	2.65	2.64	2.64	2.63	2.63
	3	3.05	2.83	2.73	2.67	2.62	2.59	2.56	2.54	2.53	2.51	2.50	2.49	2.49	2.48	2.47	2.47	2.46	2.46	2.45
	4	2.92	2.73	2.64	2.59	2.55	2.52	2.50	2.48	2.47	2.46	2.45	2.44	2.43	2.42	2.42	2.41	2.41	2.40	2.40
	5	2.85	2.67	2.59	2.54	2.51	2.49	2.47	2.45	2.44	2.43	2.42	2.41	2.40	2.40	2.39	2.39	2.38	2.38	2.37
	6	2.80	2.62	2.55	2.51	2.48	2.46	2.45	2.43	2.42	2.41	2.40	2.40	2.39	2.38	2.38	2.37	2.37	2.36	2.36
	7	2.76	2.59	2.52	2.49	2.46	2.45	2.43	2.42	2.41	2.40	2.39	2.39	2.38	2.37	2.37	2.37	2.36	2.36	2.35
	8	2.73	2.56	2.50	2.47	2.45	2.43	2.42	2.41	2.40	2.39	2.38	2.38	2.37	2.37	2.36	2.36	2.36	2.35	2.35
	9	2.71	2.54	2.48	2.45	2.43	2.42	2.41	2.40	2.39	2.38	2.38	2.37	2.37	2.36	2.36	2.36	2.35	2.35	2.35
	10	2.70	2.53	2.47	2.44	2.42	2.41	2.40	2.39	2.38	2.38	2.37	2.37	2.36	2.36	2.36	2.35	2.35	2.35	2.34
	11	2.69	2.51	2.46	2.43	2.41	2.40	2.39	2.38	2.38	2.37	2.37	2.36	2.36	2.35	2.35	2.35	2.35	2.34	2.34
	12	2.67	2.50	2.45	2.42	2.40	2.39	2.38	2.38	2.37	2.37	2.36	2.36	2.35	2.35	2.35	2.35	2.34	2.34	2.34
	13	2.67	2.49	2.44	2.41	2.40	2.39	2.38	2.37	2.37	2.36	2.36	2.35	2.35	2.35	2.35	2.34	2.34	2.34	2.34
	14	2.66	2.49	2.43	2.40	2.39	2.38	2.37	2.37	2.36	2.36	2.35	2.35	2.35	2.35	2.34	2.34	2.34	2.34	2.33
	15	2.65	2.48	2.42	2.40	2.38	2.37	2.37	2.36	2.36	2.35	2.35	2.35	2.35	2.35	2.34	2.34	2.34	2.33	2.33
	16	2.65	2.47	2.42	2.39	2.38	2.37	2.36	2.36	2.36	2.35	2.35	2.35	2.34	2.34	2.34	2.34	2.33	2.33	2.33
	17	2.64	2.47	2.41	2.39	2.37	2.37	2.36	2.36	2.35	2.35	2.35	2.34	2.34	2.34	2.34	2.33	2.33	2.33	2.33
	18	2.64	2.46	2.41	2.38	2.37	2.36	2.36	2.35	2.35	2.35	2.34	2.34	2.34	2.34	2.33	2.33	2.33	2.33	2.33
	19	2.63	2.46	2.40	2.38	2.36	2.36	2.35	2.35	2.35	2.34	2.34	2.34	2.34	2.33	2.33	2.33	2.33	2.33	2.32
	20	2.63	2.45	2.40	2.37	2.36	2.35	2.35	2.35	2.34	2.34	2.34	2.34	2.33	2.33	2.33	2.33	2.32	2.32	2.32

Reference Dose (Gy/U)		Number of CivaDots in x direction																		
		2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Number of CivaDots in y direction	2	30.3	32.8	34.2	35.1	35.8	36.2	36.6	36.8	37.1	37.2	37.4	37.5	37.6	37.7	37.8	37.9	37.9	38.0	38.0
	3	32.8	35.3	36.6	37.5	38.1	38.6	39.0	39.3	39.6	39.8	39.9	40.1	40.2	40.3	40.4	40.5	40.6	40.7	40.7
	4	34.2	36.6	37.8	38.6	39.2	39.6	40.0	40.3	40.5	40.7	40.9	41.0	41.2	41.3	41.4	41.5	41.6	41.6	41.7
	5	35.1	37.5	38.6	39.3	39.8	40.2	40.5	40.8	41.0	41.2	41.3	41.5	41.6	41.7	41.8	41.9	42.0	42.1	42.1
	6	35.8	38.1	39.2	39.8	40.3	40.6	40.9	41.1	41.3	41.5	41.6	41.7	41.9	42.0	42.1	42.1	42.2	42.3	42.3
	7	36.2	38.6	39.6	40.2	40.6	40.9	41.1	41.3	41.5	41.7	41.8	41.9	42.0	42.1	42.2	42.3	42.3	42.4	42.5
	8	36.6	39.0	40.0	40.5	40.9	41.1	41.3	41.5	41.7	41.8	41.9	42.0	42.1	42.2	42.3	42.4	42.4	42.5	42.6
	9	36.8	39.3	40.3	40.8	41.1	41.3	41.5	41.7	41.8	41.9	42.0	42.1	42.2	42.3	42.4	42.5	42.5	42.6	42.6
	10	37.1	39.6	40.5	41.0	41.3	41.5	41.7	41.8	41.9	42.1	42.2	42.2	42.3	42.4	42.5	42.5	42.6	42.6	42.7
	11	37.2	39.8	40.7	41.2	41.5	41.7	41.8	41.9	42.1	42.2	42.2	42.3	42.4	42.5	42.5	42.6	42.6	42.7	42.7
	12	37.4	39.9	40.9	41.3	41.6	41.8	41.9	42.0	42.2	42.2	42.3	42.4	42.5	42.5	42.6	42.6	42.7	42.7	42.8
	13	37.5	40.1	41.0	41.5	41.7	41.9	42.0	42.1	42.2	42.3	42.4	42.5	42.5	42.6	42.6	42.7	42.7	42.8	42.8
	14	37.6	40.2	41.2	41.6	41.9	42.0	42.1	42.2	42.3	42.4	42.5	42.5	42.6	42.6	42.7	42.7	42.8	42.8	42.9
	15	37.7	40.3	41.3	41.7	42.0	42.1	42.2	42.3	42.4	42.5	42.5	42.6	42.6	42.7	42.7	42.8	42.8	42.9	42.9
	16	37.8	40.4	41.4	41.8	42.1	42.2	42.3	42.4	42.5	42.5	42.6	42.6	42.7	42.7	42.8	42.8	42.9	42.9	42.9
	17	37.9	40.5	41.5	41.9	42.1	42.3	42.4	42.5	42.5	42.6	42.6	42.7	42.7	42.8	42.8	42.9	42.9	42.9	43.0
	18	37.9	40.6	41.6	42.0	42.2	42.3	42.4	42.5	42.6	42.6	42.7	42.7	42.8	42.8	42.9	42.9	42.9	43.0	43.0
	19	38.0	40.7	41.6	42.1	42.3	42.4	42.5	42.6	42.6	42.7	42.7	42.8	42.8	42.9	42.9	42.9	43.0	43.0	43.0
	20	38.0	40.7	41.7	42.1	42.3	42.5	42.6	42.6	42.7	42.7	42.8	42.8	42.9	42.9	42.9	43.0	43.0	43.0	43.0

Fig. 3.

Top: Nomogram indicating the source strength (U) per CivaDot™ to be ordered in order to obtain a reference dose of 100 Gy according to our dose specification. Bottom: Nomogram indicated the expected reference dose given the available source strength (U) per CivaDot™ and the desired size.

Fig. 4.

Minimum, mean, and maximum dose in the sheet area at 5 mm depth as a function of the sheet area. The scale of the dose axis is different for each panel to improve readability. Small CivaSheets™ deliver less dose for the same reference dose than larger CivaSheet™, with the effect being more pronounced for CivaSheets™ having rectangular shapes with large elongations.

Fig. 5.

Percentage of the sheet area, at 5 mm depth, receiving 80%, 100%, and 120% of the reference dose. The scale of the dose axis is different for each panel to improve readability. Small CivaSheets™ (and CivaSheets™ with large elongations) may result in less than 60% of the sheet area receiving the reference dose at 5 mm depth.

Fig. 6.

Examples of isodose lines (100%, 60%, and 30% of prescription dose) in 3 clinical colorectal cases implanting pre-sacral and pelvic sidewall areas. Implantation remained planar after surgery, and CivaSheet™ reconstruction was possible. Sparing of tissue on the shielded side of the CivaSheet™ results in < 30% of the dose impacting normal organs.