Intracavitary brachytherapy with additional Heyman capsules in the treatment of cervical cancer

Sophia Scharl (sophiascharl@yahoo.de)
Klinikum rechts der Isar der Technischen Universitat Munchen https://orcid.org/0000-0001-6849-6880
Christine Hugo
Clara-Bianca Weidenbächer
Holger Bronger
Christine Brambs
Marion Kiechle
Marcus R. Makowski
Stephanie E. Combs
Lars Schüttrumpf (Lars.Schuettrumpf@mri.tum.de)

Research Article

Keywords: Cervical cancer, brachytherapy, heyman capsules, tandem ring applicator

Posted Date: February 14th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1349261/v1

Abstract

Purpose

Brachytherapy is a mandatory component of primary radiochemotherapy in cervical cancer. The dose can be applied with a traditional intracavitary approach (IC alone) or with multiple catheter brachytherapy to optimize dose distribution in an individual concept. We therefore evaluated whether the utilization of a tandem-ring applicator plus additional intracavitary applicators (add IC) provides an advantage over the traditional IC alone approach as this method is less time consuming and less invasive compared to a combined intracavitary/interstitial brachytherapy.

Methods

23 procedures of intracavitary brachytherapy for cervical cancer with additional intracavitary applicators performed in 7 patients treated between 2016 and 2018 in our institution were included in this study. Plans were optimized for D90 HR-CTV with and without the utilization of the additional applicators and compared by statistical analysis.

Results

D90 for HR-CTV was 5.71Gy (± 1.17Gy) for fractions optimized with add IC approach and 5.29Gy (± 1.24Gy) for fractions without additional applicators ($p<0.01$). This translates to a calculated mean EQD2 HR-CTV D90 of 80.72Gy (± 8.34Gy) compared to 77.84Gy (± 8.49Gy) after external beam therapy and four fractions of brachytherapy for add IC and IC alone respectively ($p<0.01$). The predictive value of improved coverage of HR-CTV in the first fraction was high.

Conclusion

In a subgroup of cases, the addition of intracavitary heyman capsules can be an alternative to interstitial brachytherapy to improve the plan quality compared to standard IC alone brachytherapy. The benefit from the addition of applicators in the first fraction is predictive for the following fractions.

Introduction

Intracavitary brachytherapy is a mandatory component of primary radiochemotherapy in cervical cancer as it improves local control and subsequently overall survival [1–3]. Although brachytherapy is one of the oldest techniques in radiation oncology, the benefit is undoubted and no other modern radiation technique can offer the same precision of local high dose deposition and sparing of normal tissue. The technical improvements of percutaneous irradiation in intensity modulation (IMRT) and the more precise application by imaging (IGRT) nowadays allow better protection of organs at risk with smaller setup margins, but cannot compensate for the physical advantages of modern brachytherapy. In terms of overall survival, a hypofractionated percutaneous dose application (stereotactic body radiotherapy) appears to be equivalent to brachytherapy but results in high unacceptable toxicity rates [3, 4]. In recent

years numerous advances have been implemented in brachytherapy as well. Image-guided brachytherapy has provided improved results in terms of local control and reduced side-effects compared to the traditional point A dosimetry [5]. Contouring guidelines have been published by the GEC-ESTRO to standardize target volume definition [6, 7].

Even though image-based brachytherapy has enabled physicians to optimize their target volume and precisely locate the organs at risk, it has become clear that in patients with large primary tumors or unfavorable anatomy the desired target volume coverage is prevented by the short-comings of the intracavitary applicator [8][3]. To overcome this issue, combined intracavitary and interstitial brachytherapy applicators such as the tandem-ring Vienna applicator and the tandem-ovoid Utrecht applicator have been developed [9, 10]. In a further development, the Venezia applicator (Elekta, Sweden) was introduced, offering a template within the ring for the guidance of parallel and/or oblique interstitial needles for even more advanced tailoring of dose distribution. [11]. Other centers apply free-hand insertion of metal needles [8][3]. Interstitial brachytherapy consistently improved plan quality leading to higher target volume doses and better coverage while sparing surrounding organs at risk. While multiple catheter brachytherapy is being used by many centers others refrain from applying brachytherapy at all as it requires expensive equipment and trained physicians [2]. In general, accurate implantation of interstitial needles is difficult and time-consuming [8]. Subsequently, a large number of centers are currently not applying interstitial brachytherapy although brachytherapy is considered mandatory based on all cervical cancer treatment guidelines [1, 6, 12, 13]. Therefore, we intended to evaluate whether the utilization of additional intracavitary applicators (add IC) provides an advantage over the traditional tandem-ring applicator (IC alone) as it is a method that requires little additional time and experience compared to standard intracavitary brachytherapy. Therefore, it can be performed at any center carrying out intracavitary brachytherapy at the moment.

Material And Methods

Patients

Twenty-three (23) procedures of intracavitary brachytherapy for cervical cancer with additional intracavitary applicators (add IC) performed in 7 patients treated between 2016 and 2018 in our institution were included in this study. In 6 patients with 21 procedures, two applicators were used, in one patient with 2 procedures only one additional applicator was used. Patients' characteristics are shown in table 1. Written informed consent in the use of scientific data was obtained by all patients. This study was approved by the Ethics Committee of the Technical University of Munich.

Brachytherapy applicators

Brachytherapy was performed under general anesthetic by a gynecological oncologist and radiation oncologist. The cervical canal was dilated by hegar pens (MEDICON eG, Germany). 1 to 2 Heyman Capsules (Varian Medical Systems, Palo Alto, CA, USA) were inserted into the uterus prior to the tandem

and ring. A traditional tandem-ring applicator (Titanium Vienna-style ring applicator, Varian Medical Systems, Palo Alto, CA, USA) was used. Three angles (30°, 45° and 60°) for ring and tandem and three different lengths (2 cm, 4 cm, 6 cm for the tandem) were available. The applicator was chosen by the treating physician depending on patients' anatomy.

Imaging and planning procedures

A pretreatment magnetic resonance imaging (MRI) or positron emission tomography (PET)-MRI was obtained not more than one week before the start of radiochemotherapy. At approximately 40 to 45 Gy prior to the first brachytherapy procedure, another MRI was performed (Fig. 1). MRIs and PET-MRIs were obtained at the radiology department or department of nuclear medicine of our institution.

A treatment planning computed tomography (CT) was carried out on the day of brachytherapy with brachytherapy applicators in position using a Somatom Emotion CT-scanner (Siemens, Germany) (Fig. 2). To facilitate contouring of organs at risk bladder and rectum were filled with 5ml of contrast medium (Telebrix Gastro, Guerbet, Germany) diluted in 115ml and 45 ml of sterilized water, respectively. The additional applicators were labeled with numbers and equipped with distinct radiopaque wires.

Pretreatment and pre-brachytherapy MRI were coregistered to the planning CT. High-risk clinical target volume (HR-CTV), intermediate-risk clinical target volume (IR-CTV), residual gross tumor volume (GTVres) and the organs at risk (OAR) were contoured according to GEC-ESTRO Guidelines [6, 7]. Treatment planning was carried out using Eclipse treatment planning software (version 13.0.33; Varian Medical Systems, Palo Alto, CA, USA). For each single brachytherapy fraction, two different plans were generated utilizing the tandem-ring applicator and the additional intracavitary applicators (add IC) or the tandem-ring applicator alone (IC alone). Planning aims and constraints are described in Table 2. Plans were optimized to reach the indicated dose coverage of HR-CTV D90 without exceeding the tolerance doses of organs at risk. If the intended dose of HR-CTV was reached, the plan was further optimized to improve D98 GTVres and D98 HR-CTV (in this order).

The theoretical equivalent dose in two Gray fractions (EQD2) for each brachytherapy fraction was calculated using the EQD2 model, with an α/β of 10 for tumor and α/β of 3 for normal tissue, taking in therefore to account previous external beam therapy of 50.4 Gy in 28 fractions and the dose of the corresponding brachytherapy fraction multiplied by four. This method of calculating EQD2 doses for each fraction separately was used since not every patient received brachytherapy with additional Heyman capsules in every fraction. Nevertheless, information on EQD2 doses is essential as it is the relevant quantity to estimate the benefit for local control [14].

The chosen dose constraints based on the EMBRACE II study [15].

Statistical evaluation

Continuous data were expressed as means ± standard deviation (SD). Comparisons were made by two-sided paired t-test for dependent variables and unpaired t-test was used for independent samples. A p-

value of 0.05 was defined as the threshold for statistical significance within a confidence interval of 95%. All calculations and figures were done with the software packages SPSS 23 (IBM, USA).

Results

HR-CTV

D90 HR-CTV was 5.71 Gy (± 1.17 Gy) for fractions optimized with add IC approach and 5.29 Gy (± 1.24 Gy) for fractions with IC alone ($p < 0.01$). The mean improvement achieved by applying additional applicators was 0.42 Gy (± 0.49 Gy). In 7 fractions an improvement of more than 0.5 Gy and in 10 fractions an improvement of 0.2–0.5 Gy per fraction was achieved. In 6 fractions no benefit through the addition of applicators was reached. D98 HR-CTV was 4.49 Gy (± 1.07 Gy) for fractions with add IC approach and 4.10 Gy (± 1.20 Gy) for fractions with IC alone. This translates into a mean of calculated EQD2 HR-CTV D90 of 80.72 Gy (± 8.34 Gy) compared to 77.84 Gy (± 8.49 Gy) with or without additional applicators respectively ($p < 0.01$). Patients with a benefit of 0.5 Gy in the first fraction D90 HR-CTV was 77.65 Gy (± 9.66 Gy) without compared to 83.18 Gy (± 8.93 Gy) with the additional applicators.

V100% HR-CTV was 74.14% (± 14.75%) and 70.98% (± 14.72%) for patients with and without additional applicators, respectively ($p < 0.01$).

GTVres

D98 and D90 GTVres were 7.09 Gy (± 2.34 Gy) and 8.84 Gy (± 2.59 Gy) for fractions with add IC and 6.53 Gy (± 2.69 Gy) and 7.72 Gy (± 2.86 Gy) for fractions with IC alone, respectively ($p < 0.01$). EQD2 for D98 GTVres was 92.53 Gy (± 17.94 Gy) and 88.66 Gy (± 19.15 Gy) for add IC and IC alone, respectively ($p < 0.01$). Patients with a benefit of 0.5 Gy in the first fraction D98 GTVres was 80.11 Gy (± 17.97 Gy) without compared to 85.89 Gy (± 13.94 Gy) with the additional applicators. Further mean values are described in Table 3.

Organs at risk

The organ at risk limiting dose escalation in the majority of cases was the bladder with mean doses of 5.50 Gy (± 0.41 Gy) and 5.65 Gy (± 0.35 Gy) for fractions with add IC and IC alone ($p = 0.02$). There were no significant differences in mean doses of the remaining organs at risk (Table 4).

Feasibility

The insertion of additional Heyman capsules did not require additional training.

Fractions with improved coverage of D90 HR-CTV

The predictive value of an improved coverage of HR-CTV in the first fraction was high. For patients with an improvement of more than 0.5 Gy in the first fraction, the mean improvement in the remaining fractions was 0.63 Gy (± 0.52Gy), whereas it was 0.07 Gy (± 0.16 Gy) for patients without any dosimetric

improvement with additional applicators. The mean improvement for the subsequent fractions in patients with an improvement of 0.2-0.5Gy in the first fraction was 0.30 Gy (± 0.13Gy).

The inital GTV in the 3 patients that showed a clear improvement through the addition of heyman capsules was slightly larger, particularly in cranio-caudal extension compared to the other patients (7.13 cm ± 3.78 cm vs 5.58 cm ± 2.71 cm). The difference was not statistically significant (p = 0.58). When only one heyman capsule was used (2 fractions in one patient), no improved dose coverage was observed.

Discussion

We performed an analysis inserting one or two heyman capsules into the uterus in addition to a tandem-ring applicator when conducting an intracavitary brachytherapy in patients with cervical cancer. We observed a mean improvement of 0.42 Gy per fraction leading to a calculated mean EQD2 of 80.72 Gy compared to 77.84 Gy for D90 HR-CTV and 92.53 Gy compared to 88.66 Gy for D98 GTVres. In 3 of the 7 analyzed patients the benefit from the addition of heyman capsules seemed to be greater compared to the others, whereas in 3 patients no improvement was observed. At the same time, the insertion of additional Heyman capsules did not require additional training.

Multiple studies have demonstrated the necessity to perform brachytherapy in patients treated by primary radio-chemotherapy for cervical cancer [1, 2]. The relationship between the applied dose and local control as well as patient survival are well understood [15, 16]. Particularly in patients with large primary tumors, doses exceeding 85 Gy for HR-CTV are essential.

In our cohort, the estimated overall benefit in local control according to Tanderup et al. would be around 2% for FIGO stage II patients but rises to approximately 5–8% for FIGO stages III and IV [14]. Taking into account only patients that benefitted from the additional applicators the estimated improvement in local control is 5–10% for stages II-IV. In other patients no benefit through additional applicators was achieved. Compared to combined intracavitary/interstitial brachytherapy with reported cumulative EQD2 D90 HR-CTV of approximately 87–90 Gy and increases of 5–10 Gy our approach is showing a considerably smaller improvement [8, 11, 17, 18]. The implementation, however, is easier and viable in any department that regularly performs intracavitary brachytherapy with a tandem-ring applicator. The Method utilized in our institution is an adapted version of the heyman packing method which demonstrated excellent results in patient populations treated by primary radiotherapy for endometrial cancer due to comorbidities [19, 20]. In comparison to the technique applied for endometrial cancer, we used only two capsules in addition to the traditional tandem-ring applicator as only the cervix and the initial tumor extension need to be covered by an adequate dose [19, 20].

The characteristics of patients that potentially benefit from this concept are yet to define. Since the benefit was relatively consistent over fractions, certain primary tumor and their spatial situations to the organs at risk are likely to be predictors for an advantage from this concept. In fractions with only one heyman capsule, no profit was observed. Therefore, we recommend the usage of two heyman capsules. The planning time and the time needed to place the applicators, on the other hand, increases when

additional applicators are used. Furthermore, the exact position of the heyman capsules is difficult to control beforehand as the tube of the heyman capsules that are positioned into the cervix is flexible. Therefore, potential advantages in dose coverage should be weighed against the increased expenditure. Since patients that did not benefit from the procedure in the first fraction did not seem to benefit in further fractions, it seems reasonable to test the addition of applicators in the first fraction and decide whether to continue thereafter. Subsequent slipping of the Heyman capsules is unlikely as they are fixed together with the tandem-ring applicator by using a tamponade.

The limitations of this study are the small patient and fraction numbers. These impede conclusions on the characteristics of patients that potentially benefit from this procedure.

Conclusion

The therapeutic potential of brachytherapy in the curative treatment of cervical carcinoma should be fully exploited. The addition of heyman capsules to intracavitary brachytherapy can be an alternative for centers to interstitial brachytherapy as it is less invasive and implementation is easier. The first practical applications of this method already give an idea of the potential overall success. The treatment of patients with cervical carcinoma should be carried out in a certified center where all treatment modalities are available.

Declarations

Funding: Not applicable

Competing interests: The authors declare that they have no competing interests.

Authors' contributions: SS, LS collected data und statistically analyzed dose distribution to target volumes and organs at risk. CH performed treatment planning. SS wrote the manuscript with the help of LS and SC. SS, CBW, HB and LS carried out the initial clinical treatment of the patients. All authors read and approved the final manuscript.

Ethics approval: Ethical approval was obtained for the acquisition and analysis of patient data. (Ethics committee of the medical faculty of the technical university of Munich. 142/19 S-SR). Informed consent in the use of scientific data was obtained by all patients

Consent to participate: Not applicable.

Consent to publish: Not applicable.

Availability of data and materials: The datasets generated and/or analyzed during the current study are not publicly available due to privacy regulations in the ethics approval but are available from the corresponding author on reasonable request.

References

1. Holschneider CH, Petereit DG, Chu C, Hsu I-C, Ioffe YJ, Klopp AH et al (2019) Brachytherapy: A critical component of primary radiation therapy for cervical cancer: From the Society of Gynecologic Oncology (SGO) and the American Brachytherapy Society (ABS). Brachytherapy 18:123–132. doi:10.1016/j.brachy.2018.11.009
2. Mayadev J, Klapheke A, Yashar C, Hsu I-C, Kamrava M, Mundt AJ et al (2018) Underutilization of brachytherapy and disparities in survival for patients with cervical cancer in California. Gynecol Oncol 150:73–78. doi:10.1016/j.ygyno.2018.04.563
3. O'Donnell B, Shiao JC, Pezzi TA, Waheed N, Sharma S, Bonnen MD, Ludwig MS (2018) Stereotactic Body Radiation Therapy, Intensity-Modulated Radiation Therapy, and Brachytherapy Boost Modalities in Invasive Cervical Cancer: A Study of the National Cancer Data Base. Int J Gynecol Cancer 28:563–574. doi:10.1097/IGC.0000000000001200
4. Albuquerque K, Tumati V, Lea J, Ahn C, Richardson D, Miller D, Timmerman R (2020) A Phase II Trial of Stereotactic Ablative Radiation Therapy as a Boost for Locally Advanced Cervical Cancer. Int J Radiation Oncology*Biology*Physics 106:464–471. doi:10.1016/j.ijrobp.2019.10.042
5. Harkenrider MM, Alite F, Silva SR, Small W (2015) Image-Based Brachytherapy for the Treatment of Cervical Cancer. Int J Radiat Oncol Biol Phys 92:921–934. doi:10.1016/j.ijrobp.2015.03.010
6. Haie-Meder C, Pötter R, van Limbergen E, Briot E, de Brabandere M, Dimopoulos J et al (2005) Recommendations from Gynaecological (GYN) GEC-ESTRO Working Group (I): Concepts and terms in 3D image based 3D treatment planning in cervix cancer brachytherapy with emphasis on MRI assessment of GTV and CTV. Radiother Oncol 74:235–245. doi:10.1016/j.radonc.2004.12.015
7. Pötter R, Haie-Meder C, van Limbergen E, Barillot I, de Brabandere M, Dimopoulos J et al (2006) Recommendations from gynaecological (GYN) GEC ESTRO working group (II): Concepts and terms in 3D image-based treatment planning in cervix cancer brachytherapy-3D dose volume parameters and aspects of 3D image-based anatomy, radiation physics, radiobiology. Radiother Oncol 78:67–77. doi:10.1016/j.radonc.2005.11.014
8. Liu Z-S, Guo J, Zhao Y-Z, Lin X, Zhang B-Y, Zhang C et al (2017) Computed Tomography-Guided Interstitial Brachytherapy for Locally Advanced Cervical Cancer: Introduction of the Technique and a Comparison of Dosimetry With Conventional Intracavitary Brachytherapy. Int J Gynecol Cancer 27:768–775. doi:10.1097/IGC.0000000000000929
9. Kirisits C, Lang S, Dimopoulos J, Berger D, Georg D, Pötter R (2006) The Vienna applicator for combined intracavitary and interstitial brachytherapy of cervical cancer: Design, application, treatment planning, and dosimetric results. Int J Radiat Oncol Biol Phys 65:624–630. doi:10.1016/j.ijrobp.2006.01.036
10. Nomden CN, de Leeuw AAC, Moerland MA, Roesink JM, Tersteeg RJHA, Jürgenliemk-Schulz IM (2012) Clinical use of the Utrecht applicator for combined intracavitary/interstitial brachytherapy treatment in locally advanced cervical cancer. Int J Radiat Oncol Biol Phys 82:1424–1430. doi:10.1016/j.ijrobp.2011.04.044

11. Walter F, Maihöfer C, Schüttrumpf L, Well J, Burges A, Ertl-Wagner B et al (2018) Combined intracavitary and interstitial brachytherapy of cervical cancer using the novel hybrid applicator Venezia: Clinical feasibility and initial results. Brachytherapy 17:775–781. doi:10.1016/j.brachy.2018.05.009
12. National Comprehensive Cancer Network (2020) NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)- Cervical cancer. https://www.nccn.org/professionals/physician_gls/pdf/cervical.pdf. Accessed 1
13. Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Krebshilfe D (2020) AWMF): S3-Leitlinie Diagnostik, Therapie und Nachsorge der Patientin mit Zervixkarzinom. http://leitlinienprogramm-onkologie.de/Leitlinien.7.0.html. Accessed 1
14. Tanderup K, Fokdal LU, Sturdza A, Haie-Meder C, Mazeron R, van Limbergen E et al (2016) Effect of tumor dose, volume and overall treatment time on local control after radiochemotherapy including MRI guided brachytherapy of locally advanced cervical cancer. Radiother Oncol 120:441–446. doi:10.1016/j.radonc.2016.05.014
15. Pötter R, Tanderup K, Kirisits C, de Leeuw A, Kirchheiner K, Nout R et al (2018) The EMBRACE II study: The outcome and prospect of two decades of evolution within the GEC-ESTRO GYN working group and the EMBRACE studies. Clin Transl Radiat Oncol 9:48–60. doi:10.1016/j.ctro.2018.01.001
16. Sturdza A, Pötter R, Fokdal LU, Haie-Meder C, Tan LT, Mazeron R et al (2016) Image guided brachytherapy in locally advanced cervical cancer: Improved pelvic control and survival in RetroEMBRACE, a multicenter cohort study. Radiother Oncol 120:428–433. doi:10.1016/j.radonc.2016.03.011
17. Wang C, Raince J, Swamy U, Park S-J, Zaide L, Mesko S et al (2018) Clinical outcomes using image-guided interstitial brachytherapy for definitive cervical cancer patients with high-risk clinical target volumes greater than 30 cc. Brachytherapy 17:392–398. doi:10.1016/j.brachy.2017.10.004
18. Otter S, Coates A, Franklin A, Cunningham M, Stewart A (2018) Improving dose delivery by adding interstitial catheters to fixed geometry applicators in high-dose-rate brachytherapy for cervical cancer. Brachytherapy 17:580–586. doi:10.1016/j.brachy.2018.01.003
19. van der Steen-Banasik E (2014) Primary brachytherapy as a radical treatment for endometrial carcinoma. J Contemp Brachytherapy 6:106–112. doi:10.5114/jcb.2014.42028
20. Weitmann HD, Pötter R, Waldhäusl C, Nechvile E, Kirisits C, Knocke TH (2005) Pilot study in the treatment of endometrial carcinoma with 3D image-based high-dose-rate brachytherapy using modified Heyman packing: Clinical experience and dose-volume histogram analysis. Int J Radiat Oncol Biol Phys 62:468–478. doi:10.1016/j.ijrobp.2004.10.013

Tables

Mean Age (years)	53±5.2
Histology	
Squamous cell cancer	7 (100%)
Grading	
G1	0
G2	3 (43%)
G3	4 (57%)
Tumor stage	
T	1 (14%)
T1b2	
T2a	1 (14%)
T2b	4 (57%)
T3	0
T4	1 (14%)
N	
N0	2 (29%)
N1	5 (71%)
M	
M0	7 (100%)
Size of primary tumor pretreatment MRI (cm)	
craniocaudal	6.8 ± 3.0
anteroposterior	5.7 ± 0.8
lateral	6.4 ± 1.5
Size of primary tumor planning MRI (cm)	
craniocaudal	2.0 ± 2.1
anteroposterior	2.2 ± 1.3
lateral	3.3 ± 1.4

Table 1: Patients'characteristics

	EQ D2	Dose per fraction
Planning aims		
D90 HR-CTV	>85 Gy	6.5 Gy
D 98 GTVres	>90 Gy	7.1 Gy
D98 HR-CTV	>75 Gy	5.1 Gy
Constraints (D2cm³)		
Bladder	<90 Gy	5.8 Gy
Rectum	<75 Gy	4.4 Gy
Sigmoid	<75 Gy	4.4 Gy
Bowel	<70 Gy	3.9 Gy

Table 2: Planning aims and Constraints

	With Heyman capsules	Without Heyman capsules	p
Target volume (Gy per fraction / V100 in percent of volume)			
HR-CTV	2.95±0.64	2.79±0.84	
D100 HR-CTV			0.13
D98 HR-CTV	4.49±1.07	4.10±1.20	0.01*
D90 HR-CTV	5.71±1.17	5.29±1.24	<0.01*
D50 HR-CTV	9.53±1.79	8.91±1.49	<0.01*
V100 HR-CTV	74.14±14.75	70.98±14.72	<0.01*
IR-CTV	2.11±0.84	2.09±0.91	
D100 IR-CTV			0.75
D98 IR-CTV	2.91±1.10	2.82±1.20	0.26
D90 IR-CTV	4.00±1.16	3.92±1.61	0.67
GTVres			
D 100 GTVres	5.82±2.23	5.51±2.47	0.04*
D 98 GTVres	7.09±2.34	6.53±2.69	<0.01*
D 90 GTVres	8.48±2.59	7.72±2.86	<0.01*
Target volume (EQD2)			
D 98 HR-CTV	72.44±6.73	70.11±7.14	0.01*
D 90 HR-CTV	80.72±8.34	77.84±8.49	<0.01*
D 98 GTVres	92.53±17.94	88.66±19.15	<0.01*

Table 3: Doses of HR-CTV, IR-CTV and GTVres for plans with and wihtout additional applicators. Significant differences are labelled by *

	With Heyman capsules	Without Heyman capsules	p
Organs at risk (D2cm³)			
Bladder	5.50±0.41	5.65±0.35	0.02*
Rectum	3.79±0.66	3.72±0.68	0.45
Sigmoid	2.87±1.07	2.79±1.08	0.06
Bowel	2.40±1.05	2.32±1.09	0.43
Organs at risk (D2cm³)			
Bladder	7.22±0.90	7.37±0.80	0.36
Rectum	4.98±1.18	5.10±1.06	0.55
Sigmoid	3.88±1.64	3.77±1.59	0.25
Bowel	3.30±1.72	3.34±1.72	0.78

Table 4: Doses of organs at risk. Significant differences are labelled by *

Figures

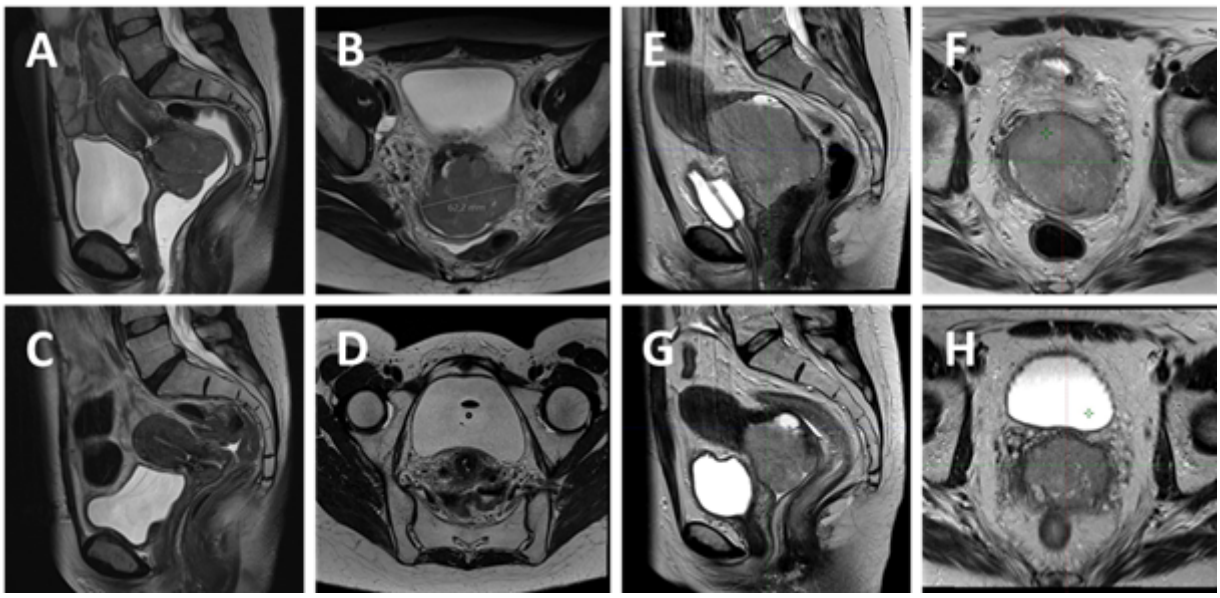

Figure 1

An example of a fast-responding tumor before starting percutaneous radiotherapy (A and B) and after 40 Gy were applied (C and D). An example of a slow-responding tumor before starting percutaneous radiotherapy (E and F) and after 40 Gy have been applied (G and H).

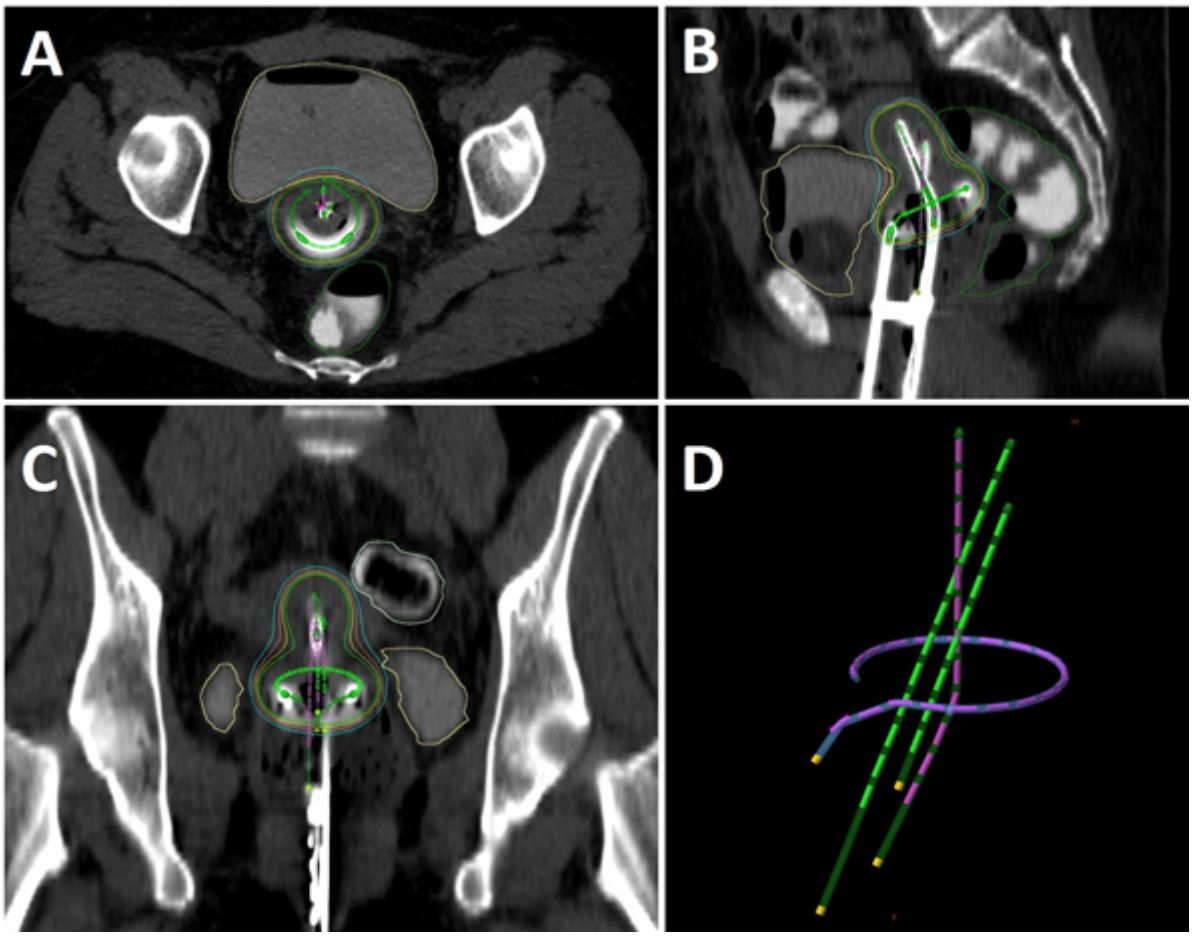

Figure 2

Axial (A), sagittal (B) and coronal (C) views of planning-CT with tandem-ring applicator and two additional intracavitary applicators. Three-dimensional reconstruction of the tandem-ring applicator (purple) and additional applicators (green) (D).