



# Brachy in Tricky Situations: A Trans Perineal Interstitial Implant in a Case of Carcinoma Cervix Co-occurring with Uterine Didelphys

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**Abstract:** A 43 year old lady with a uterine anomaly was diagnosed to have FIGO stage II B -HPV associated poorly differentiated cervix adenocarcinoma. She has a bicornuate unicolis uterus -class U3b, subclass C0, subclass V0 as per ESHRE/ESGE classification system of female genital anomalies. Post 50 Gy of chemo radiotherapy to the pelvis, her peculiar anatomical configuration posed a challenge for delivering HDR brachytherapy boost. We decided to proceed with a transperineal interstitial implant & achieved a total EqD2 of 80 Gy to HRCTV. The target coverage was achieved with 11 needles held up by Syed Neblett template guided by transrectal ultrasound [TRUS]. Interstitial implant using TRUS is a safe technique in a resource limited setting allowing an image guided approach for brachytherapy. Patient is on follow up since 2 years with no evidence of disease.

**Keywords:** uterine diadelphys, transperineal interstitial implant, brachytherapy, cervix cancer, uterine malformation

## PURPOSE

The purpose of this study is to describe an approach to use the clinical application of transperineal interstitial technique in locally advanced cervical cancer accompanied with uterine malformation.

## CASE PRESENTATION

A 43 year old premenopausal female was previously diagnosed at an infertility clinic to have a bicornuate unicolis uterus. In April 2023, she presented with a history of menorrhagia for 2 months and was diagnosed with FIGO stage II B cervical carcinoma. Biopsy revealed HPV associated poorly differentiated carcinoma favoring adenocarcinoma. Risk factors such as promiscuity or nicotine abuse were negated by the patient. Her uterine abnormality was described as bicornuate unicolis class U3b subclass C0 subclass V0 as per the ESHRE/ESGE classification system of female genital anomalies (Fig 1). She received external beam radiotherapy [EBRT] using 15 MV photons by image-guided radiotherapy [IGRT] technique, 50 Gy in 25 fractions to the pelvis completing in 2023 along with 5 cycles of weekly cisplatin. Post pelvic radiotherapy, she had grade 2 enteritis and fatigue, and both were managed conservatively. She was assessed for brachytherapy boost after the completion of EBRT. Her intracavitary assessment findings were as follows- minimal residual growth involving both lips of the cervix near the external os. Fornices & vaginal walls were not involved. There was residual induration in the bilateral parametrium up to the medial third. Her cervix was

stenosed and the external os was not sound able. An MRI pelvis was done to evaluate her clinical response. T2-weighted images showed diffuse hypointense cervix with ill-defined STIR hyper intense thickening of the lower anterior lip of cervix and right lateral wall of upper vagina, measuring 22 x 21 x 13 mm, with bilateral parametrial fat stranding. There was discrepancy in the vaginal findings between the clinical examination & MRI with concordance in the rest of the findings and this may be due to the absence of vaginal opacification.

### **BRACHYTHERAPY PROCEDURE**

Since routine intracavitary application was not possible, we proceeded with an interstitial implant using a transperineal approach with Syed Neblett template & 11 stainless steel [length -20 mm] needles (Fig. 2 and 3). Positions of needles were confirmed by transrectal ultrasound (TRUS) [A trans-rectal bi-planar probe (BK Medical Flex Focus 800, probe No. 8848)] set at a frequency of 9 Hz & an additional C-arm. Dual technique was used where TRUS aided in adequate coverage of the residual tumor & and C-arm helped to avoid crowding of needle tips in this difficult anatomy. The patient was shifted to the brachytherapy department and CT simulation was done using 2.5 mm slice thickness on our Philips Big Bore CT simulator. 20 cc of bladder contrast was given for better bladder delineation. A rectal tube was inserted and kept in situ till completion of the procedure. She was planned for a total dose of 21 Gy in 3 fractions, 700 c Gy per fraction with a minimum of 6 hours between fractions by iridium-192 High Dose Rate (HDR) remote after-loading technique after digitalization and optimization using CT based computerized treatment planning system (BRACHY VISION, ECLIPSE version 15.6).

### **BRACHYTHERAPY PLANNING PARAMETERS**

OARS (organs at risk) & HR CTV (High Risk Volume), IRCTV (Intermediate Risk Volume) were contoured as per IBS [Indian Brachytherapy Society] & GEC ESTRO guidelines (Fig. 4). These guidelines provide recommendations for CT-based contouring in image-guided adaptive brachytherapy for cervical cancer for various clinical radiological environments [13]. We have used CT and TRUS combination at the time of brachytherapy boost to help in contouring although MRI based brachytherapy is still considered as gold standard. The volume of HRCTV was 59.8cc. HRCTV coverage was adequate with D90 (dose to 90% volume) achieving 101%, total radiotherapy dose EQD2 to tumor [EBRT+BT] was 80.4Gy with D2cc of bladder, rectum, & sigmoid as 4.6Gy, 4.6Gy & 1.58Gy respectively. In terms of acute complications, local site pain and minimal vaginal bleeding, not requiring any vaginal packing, were experienced.

### **FOLLOW UP**

On a 3-month follow-up, PET-CT was done for response assessment. There was a metabolically complete response. She underwent PET-MRI subsequently the next year and no clinically significant uptake was present. The patient is on regular follow-up & is clinically disease free for 2 years.

## DISCUSSION

According to the George Institute of Global Health, in India, cervix cancer is the second leading cause of death among women with age-standardized incidence and mortality rates of 22 and 12.4 per 100,000 women per year. The co-occurrence of uterine abnormalities with cervical cancer is extremely rare and to date, almost exclusively case reports are available in the literature [2-5]. Didelphic uteri account for approximately ~8% (range 5-11%) of Müllerian duct anomalies. Deficiencies in the merging process of the paramesonephric ducts (Müllerian ducts) occur between the 12th and 16th week of pregnancy as part of embryogenesis & lead to anomalies of the uterus, cervix, fallopian tubes, and proximal vagina [9,10]. An estimated 5% of all cervical cancer patients may have undetected various degrees of malformations, and these patients could receive improper dose distributions attributable to non-recognition of peculiar anatomical configurations.

In recent years, three-dimensional (3D) ICBT {intracavitary brachytherapy} based & IC/IS hybrid based brachytherapy & IG-ISBT {Image Guided - Interstitial Brachytherapy} using magnetic resonance or computed tomography (CT) imaging facilitates the individualization of treatment in carcinoma cervix [12,13].

However, for uterine anomalies, there are no standard recommendations in terms of the delivery of radiotherapy. The presence of two uterine bodies with a single cervix poses a serious challenge. Many forms of brachytherapy techniques have been reported with customized applicators, two tandems in the two uterine canals [6]; vaginal mold and catheter alternately in each uterine canal have also been used as customized brachytherapy applicator [11]. Fabian et al. used MRI-guided Hybrid intracavitary/interstitial applicators to improve tumor coverage in a bicornuate uterus [12].

According to the ESHRE/ESGE classification method, the Rotte-Y tandem is suitable for cases of mediastinal uterus; conventional treatments are applicable for cases of uniangular uterus. In scenarios where the residual lesion is extensive or there are uterine abnormalities, interstitial treatment may be combined.

A comparison can thus be drawn between the different brachytherapy modalities used in the management of uterine anomalies. We can use a double tandem + double ovoid (DT+DO) application which has the advantage of being a relatively simple applicator, non-invasive but we may need to dilate the cervix for accommodation of both tandems, and the delivery of treatment is phased. The 2nd modality is a Y-shaped tandem with double ovoids (Y+DO) which are again relatively simple to operate & noninvasive, but require a special Y-shaped applicator which may not be readily available at many institutions. The 3rd modality is the interstitial implant (ISBT). It is invasive, skill dependent, requires expertise & difficult to operate but can confer advantages of flexible treatment planning and is 3D printable, and most importantly can be used in cases where it cervix is stenosed as it was in this case. The implementation of 3D brachytherapy technology and the availability of various applicator types provide more treatment options for patients with reproductive tract malformations. However, due to the diversity of uterine deformities, the range of applicators currently in use is limited.

Most of these case reports have used 2D ICR based techniques where dose prescription was to point A, however, in 2005, the Groupe Européen de Curietherapie-European Society for Radiotherapy & Oncology (GEC ESTRO) and the American

Brachytherapy Society (ABS) recommended using 3D-ICBT for the treatment of advanced cervical cancer. The DVH parameters of HR-CTV- D90 and D1cc, D2cc of rectum, bladder, and other concepts were adopted [7]. Gao et al. retrospectively analyzed the dose volume histograms of 2D-ICBT & found that, compared with 3D-ICBT, the cervical dose coverage rate was not satisfactory, and the coverage rate was negatively correlated with the cervical shape and size [8].

In the recent past, there has been a shift to 3D-based brachytherapy planning where 3D-based IC & IC/IS approaches have been attempted in uterine malformations. Platta et al have used CT-based planning [13] whereas Fabian et al. have used an MRI-based brachytherapy approach. We too have adopted the 3D-based IBS-GEC ESTRO guidelines [14] for planning in our pure interstitial brachytherapy technique and have been able to achieve the tolerance doses satisfactorily.

To the best of our knowledge, this is the *first case* of uterine diadelphys that has been treated with transperineal interstitial brachytherapy implant reported in the literature. This is also one of the few uterine malformation cases to have used 3D-based brachytherapy planning.

## **CONCLUSION**

Herein, we report the first documented case of image-guided interstitial brachytherapy in a patient with bicornuate unicollis uterus and locally advanced cervical carcinoma. In the absence of any clinical guidelines for such rare cases, brachytherapy can be challenging but interstitial implants can be a very safe & feasible approach. 3D brachytherapy planning should be adopted as it refines the dose delivery, especially in such challenging situations.

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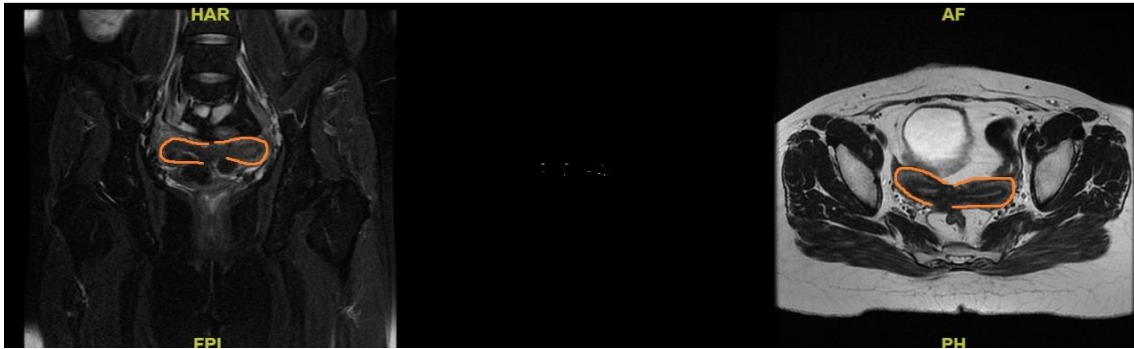
## **Conflict of Interest**

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

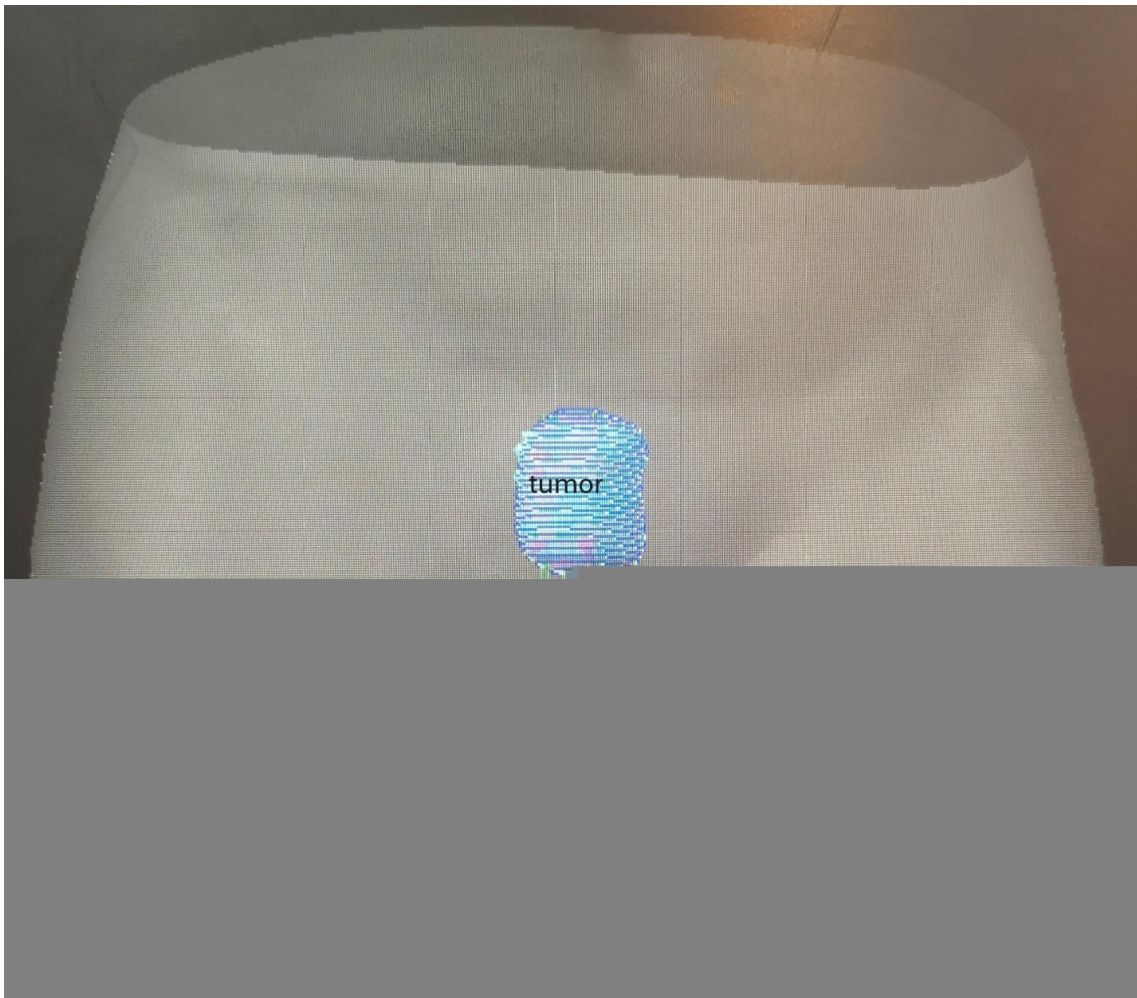
## **REFERENCES**

1. Chan YY, Jayaprakasan K, Zamora J, et al. The prevalence of congenital uterine anomalies in unselected and high-risk populations: a systematic review. Hum Reprod Update. 2011; 17:761-771. doi: 10.1093/humupd/dmr028.
2. Lei C, Huang M, Li N et al: Intensity-modulated radiotherapy combined with intracavitary brachytherapy for locally advanced cervical cancer with uterus didelphys. Gynecol Oncol Rep. 2021 Feb 8; 36:100724. doi: 10.1016/j.gore.2021.100724. PMID: 33718560; PMCID: PMC7909386.

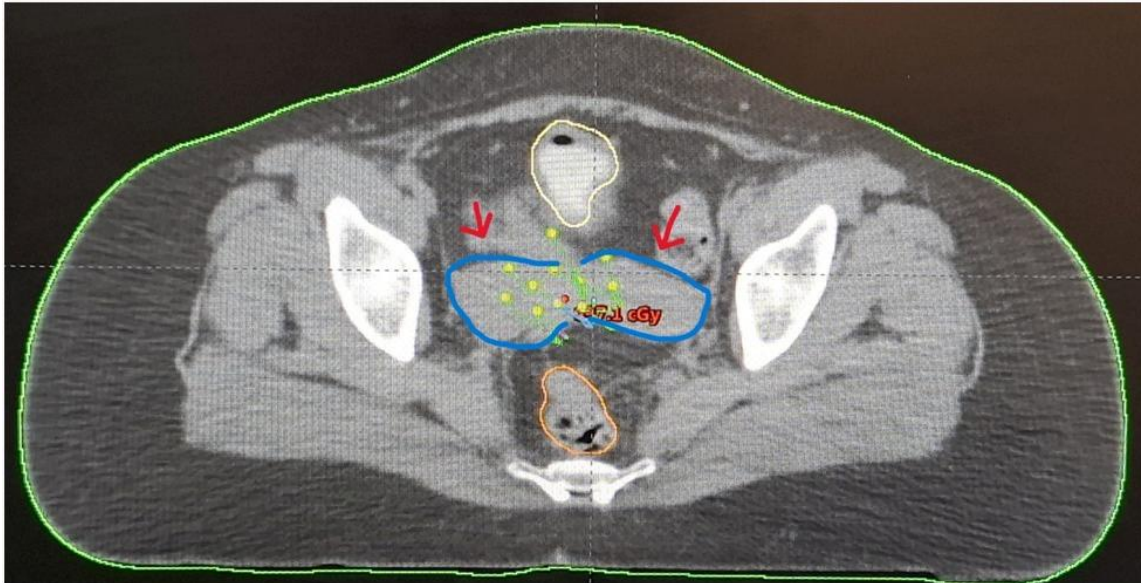
3. Matylevich OP, Schmeler KM, Gemer O, et al: High-grade cervical dysplasia in a woman with uterine didelphys: A case report. *Gynecol Oncol Rep.* 2022 Jun 17; 42:101027. doi: 10.1016/j.gore.2022.101027. PMID: 35754559; PMCID: PMC9218199.
4. Krückel A, Saatz M, Behrens AS, et al: Uterus didelphys and cervical cancer: A case report. *Gynecol Oncol Rep.* 2024 Sep 13; 55:101503. doi: 10.1016/j.gore.2024.101503. PMID: 39308900; PMCID: PMC11415808.
5. Kaneyasu, Yuko & Koh, Iemasa & Fujiwara et al (2019). Concurrent chemo radiotherapy for locally advanced squamous cell carcinoma of the cervix in a uterus didelphys with vaginal septum. *Journal of Contemporary Brachytherapy.* 11. 10.5114/jcb.2019.84506.
6. Ding L, Zheng Z, Cao Y, et al (2024) Case report: Cervical brachytherapy technique for locally advanced cervical cancer in a patient with complete bicorporeal uterus. *Front. Oncol.* 14:1361562. doi: 10.3389/fonc.2024.1361562
7. Pötter R, Haie-Meder C, Van Limbergen E, et al; GEC ESTRO Working Group. 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, and radiobiology. *Radiother Oncol.* 2006 Jan; 78(1):67-77. doi: 10.1016/j.radonc.2005.11.014. Epub 2006 Jan 5. PMID: 16403584.
8. Gao M, Albuquerque K, Chi A, et al: 3D CT-based volumetric dose assessment of 2D plans using GEC-ESTRO guidelines for cervical cancer brachytherapy. *Brachytherapy.* 2010 Jan-Mar; 9(1):55-60. doi: 10.1016/j.brachy.2009.05.004. Epub 2009 Oct 22. PMID: 19853536.
9. Passos IMPE, Britto RL. Diagnosis and treatment of müllerian malformations. *Taiwan J Obstet Gynecol.* 2020 Mar;59(2):183-188. doi: 10.1016/j.tjog.2020.01.003. PMID: 32127135.
10. Kiblboeck S, Oppelt P et al. Can Classifications Adequately Represent Genital Malformations? : EVA Study (E SHRE/ESGE | V CUAM | A FS) - A Prospective Multicenter Study to Evaluate the Current Female Genital Malformation Classifications. *Geburtshilfe Frauenheilkd.* 2023 Mar 29; 83(7):827-834. doi: 10.1055/a-2043-9982. PMID: 37564897
11. Cordoba A, Escande A, Comte P, et al. Locally advanced adenocarcinoma of the cervix on uterus didelphys: a case report. *Journal of Contemporary Brachytherapy.* 2017; 9(1):71-76. doi:10.5114/jcb.2017.65640.
12. Fabian D, LaRocco A, Olsen M, Quick A. Treatment of locally advanced cervical cancer in a patient with a bicornuate uterus with MRI-guided intracavitary/interstitial brachytherapy. *Journal of Contemporary Brachytherapy.* 2019;11(3):285-291. doi:10.5114/jcb.2019.85738.
13. Platta C, Wallace C, Gondi V, et al. Case report. Cervical brachytherapy technique for locally advanced carcinoma of the cervix in a patient with a septate uterus. *Journal of Contemporary Brachytherapy.* 2014;6(1):76-81. doi:10.5114/jcb.2014.40768.



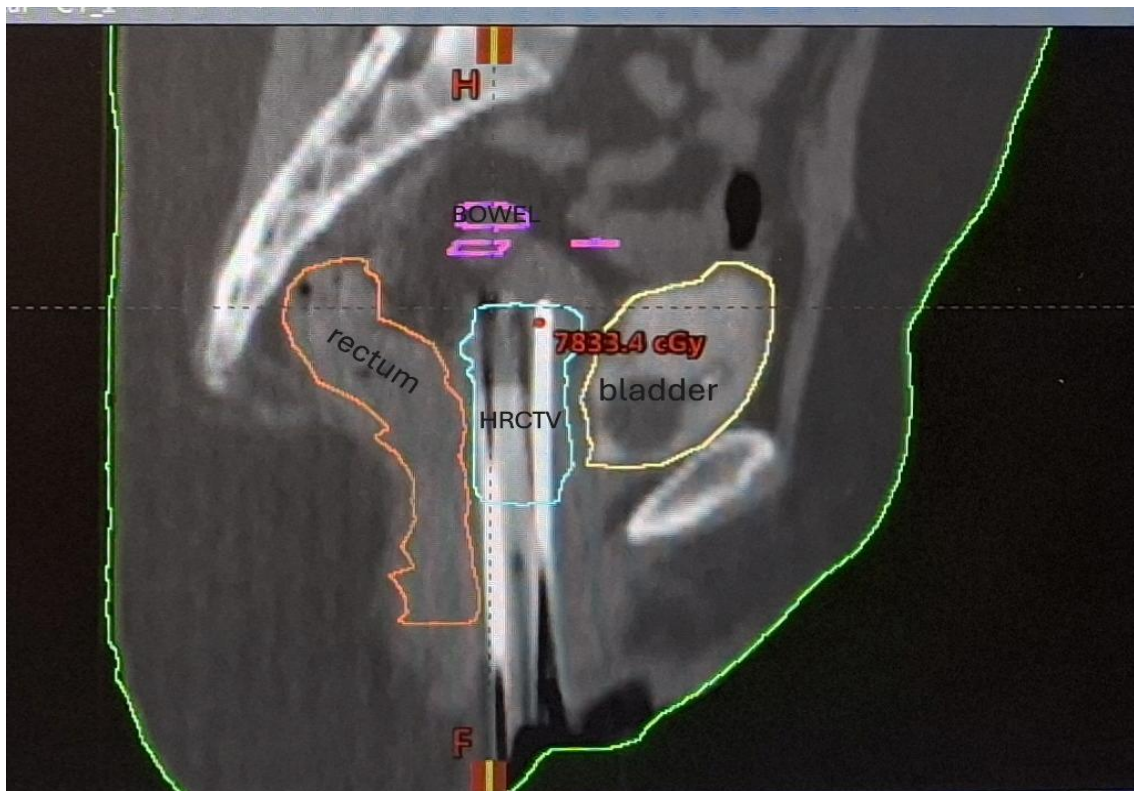
**Fig 1:** MRI axial & coronal images of pelvis showing bicornuate uterus with orange outlines lining the uterine bodies



**Fig 2:** Schematic diagram of a three-dimensional image reconstruction of the 11-channel applicator. 3D visualization of digitized interstitial needles (green) placed into the tumor (blue) for brachytherapy planning.



**Fig 3:** axial CT images cranial part of the interstitial application with tips of digitized needles visible [yellow dots] and two uterine corpus at the level of lower uterine segment as indicated by red arrows.



**Fig 4:** sagittal CT image of pelvis showing the GEC ESTRO based contours of sections of OARS [including rectum, bladder & bowel] and target volume HRCTV