# High-Dose-Rate Interstitial Brachytherapy in the Management of Carcinoma of the Uterine Cervix and Other Gynecologic Malignancies

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***Objective:*** *To report technique and experience of high-dose-rate (HDR) interstitial brachytherapy in the treatment of cervical carcinoma and other gynecologic malignancies.*
***Material and Method:*** *Between April 2003 and October 2004, ten patients (7-cervical carcinoma, 3-vaginal stump carcinoma) were treated with interstitial implant. Indications for implant include previous hysterectomy and previous pelvic radiation. Patient characteristics, implant technique, and initial outcomes were reported.*
***Results:*** *Transperineal interstitial implant was performed using fluoroscopy-guided technique. Brachytherapy dose/fraction ranged from 500-750 cGy for 1 to 6 fractions. Combined external beam radiation was given in 8 patients. After 5-21 months follow-up, all the patients were alive. Local control was achieved in 9 patients. One patient had persistent disease at the implant site. No acute complication from the procedure or serious late complication was observed.*
***Conclusion:*** *Interstitial implant can be a treatment option in patients with gynecologic malignancies who have limitations with standard intracavitary insertion. This technique is feasible, providing good local control without serious complications. However, long term follow-up is needed.*

***Keywords:*** *Interstitial implant, Brachytherapy, Cervical carcinoma, Gynecologic malignancies*

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Cancer of the uterine cervix is the most common cancer in Thai women[1]. Management of early-staged diseases can be done either by surgery or radiation therapy, while radiation therapy is the primary treatment in locally advanced diseases. Radiotherapy techniques used in the curative treatment of cervical cancer, in most circumstances, include external beam radiation (EBRT) and intracavitary brachytherapy (ICBT) by insertion of the uterine tandem and vaginal ovoids (colpostats). However, a "proper" ICBT placement requires a good geometry, including a patent cervical os and adequate space in the vagina, which may not be possible in some patients.

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Interstitial implantation is a brachytherapy technique performed by inserting radiation sources into the needles or catheters placed directly into the tumor. It has been used to overcome limitations of ICBT. Theoretically, interstitial implantation should be used in which circumstances that the dose distribution from standard ICBT does not adequately encompass the tumor. At Ramathibodi Hospital, interstitial implant was performed in the patients who could not undergo proper ICBT, including those with poor vaginal anatomy, obliteration of the cervical os, previous hysterectomy, and prior pelvic radiation. The present study presents the authors' technique and experience of high-dose-rate (HDR) interstitial brachytherapy for the treatment of cervical carcinoma and other gynecologic malignancies.

## Material and Method

Since HDR Iridium-192 brachytherapy machine (microSelectron, Nucletron) was available in 1999, there were 10 patients (age 47-87) treated with interstitial implantation for their gynecologic malignancies from April 2003 to October 2004. Seven patients had cervical carcinoma, 3 had carcinoma of the vaginal stump after previous hysterectomy. Patient characteristics and indications for interstitial implant are shown in Table 1. Pretreatment evaluation consisted of physical and pelvic examination, complete blood counts and chemistries, chest x-ray, IVP, and cysto-proctoscopy. Computerized tomography (CT) scan of the abdomen and pelvis was done in 7 patients. Biopsy confirmation of invasive carcinoma was obtained in all cases. Patients' medical records were retrospectively reviewed. Patient characteristics, details of treatment, including interstitial brachytherapy technique and implant parameters, treatment complications, and initial outcomes were reported.

## Results

Pelvic examination, CT scan, and, in some cases, transvaginal ultrasound were used to determine tumor extension and the target volume. Transperineal interstitial implant was performed using fluoroscopy-guided technique[2] under local, spinal, or epidural anesthesia. While the patient was in the lithotomy position, a foley catheter was inserted into the urinary bladder. Whenever possible, surgical clip markers were placed at the cervix or tumor margins at the vagina. The Martinez Universal Perineal Interstitial Template (MUPIT) was used in 8 cases with the vaginal obturator inserted into the vagina. Needle positions were selected to adequately encompass the tumor, normally 1-1.5 cm apart from each other. Hollow needles (12-20 cm long) were inserted through the perineal skin, into the paravaginal and/or parametrial tissues under fluoroscopy guidance helped to confirm the depth of the needle insertion and to ensure parallelism of the needles. Tips of the needles usually extended about 2-4 cm superior to the cervical os when treating the cervical tumor or about 1-2 cm beyond superior extent of the vaginal tumor or the vaginal vault. After needle insertion was completed, rectal examination was performed to make sure that no needle was present in

**Table 1.** Patient characteristics and indications for interstitial implant

| Pt # | Age | Diagnosis | Stage | Patho | Implant site | Implant indication |
|---|---|---|---|---|---|---|
| 1. | 56 | CA cervix | IIIB | Sq CCA | Cervix | Previous subtotal hysterectomy |
| 2. | 49 | CA cervix | IIIB | Sq CCA | Cervix | Underwent subtotal hysterectomy from outside hospital |
| 3. | 50 | CA cervix (new primary) | IIB | Sq CCA | Cervix | Received radical RT from previous CA cervix 10 years ago |
| 4. | 55 | CA cervix | IIIB | Sq CCA | Cervix | Recurrence 3 years after radical RT |
| 5. | 47 | CA vagina | II | Small cell CA | Vagina | Received radical RT from previous CA cervix 5 years ago |
| 6. | 70 | CA vaginal stump | I | Sq CCA | Vaginal stump | Previous TAH |
| 7. | 47 | CA cervix | IB | Sq CCA | Vaginal stump | Vaginal stump recurrent after radical RT & TAH |
| 8. | 82 | CA ovary | - | AdenoCA | Vaginal stump | Vaginal stump recurrent after TAH |
| 9. | 61 | CA vaginal stump | I | Sq CCA | Vaginal stump | Previous TAH |
| 10. | 87 | CA vulva ($2^{nd}$ primary) | - | Sq CCA | Vulva, vagina | Received radical RT from previous CA cervix 14 years ago |

Pt # = patient number, CA = carcinoma, Sq CCA = squamous cell carcinoma, TAH = total abdominal hysterectomy, RT = radiation therapy

the rectum. Two semi-orthogonal radiographs were obtained for confirmation of the needle positions and for dosimetric calculation. Radiation dose distribution was calculated using the PLATO Brachytherapy Planning System and was adjusted to achieve optimal tumor coverage with maximal dose uniformity and acceptable bladder and rectal doses. Implant needles were then connected to the HDR brachytherapy machine with the transfer cables (Fig. 1). The radiation was delivered with the 10-Curie Iridium-192 source in the shielded brachytherapy room using remote-controlled afterloading technique.

The HDR dose/fraction of 500 to 750 cGy, prescribed at the first isodose line that contiguously included all of the needles (normally at 5 mm from the needles), was used. The treatment time ranged from 3 to 14 minutes. Nine patients were treated with 1 fraction/day, once a week, to the total of 1-4 fractions. Patient number 5 was treated with 6 fractions of 500 cGy, administered twice a day (b.i.d), with an interval of at least 6 hours between fractions, to the total dose of 30 Gy in 3 consecutive days. Details of treatment and implant parameters are shown in Table 2. When the treatment was completed, implant needles and the template were removed without difficulty. Bleeding was stopped by applying pressure onto the needle sites. No acute complication, such as bleeding or infection, was observed.

Combined EBRT (dose 10-60 Gy) to the pelvis was given before implant in 8 patients. Five patients received cisplatin chemotherapy concurrently with external radiation. One patient had mild degree of diarrhea, and 2 had moist desquamation as a consequence of EBRT.

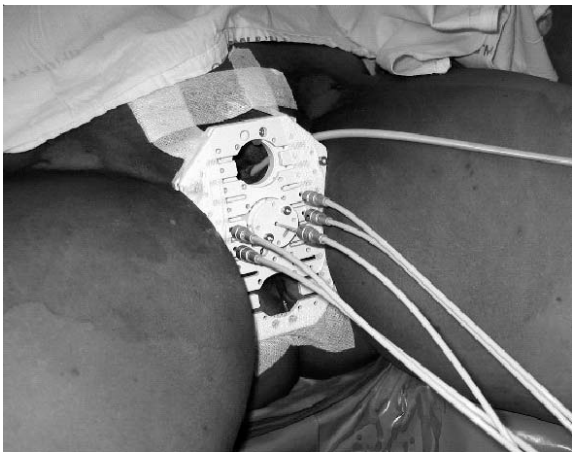

**Fig 1.** Martinez Universal Perineal Interstitial Template (MUPIT) with implant needles connected to transfer cables

After treatment completion, the patients were followed regularly by both a radiation oncologist and gynecologic oncologist. With the follow-up time of 5-21 months (median 9.5 months) after radiation therapy was completed, all patients were alive, 9 had local disease controlled. One patient (patient #10) had persistent disease at the vulva and lower vagina. One patient with small cell carcinoma of the vagina (patient #5) developed brain metastasis 4 months after the implant.

Radiation proctitis occurred in 3 patients which subsided after supportive treatment. All of them previously received radical radiation for their cervical cancer before this treatment. Vaginal adhesion was observed in 5 patients. No patient developed cystitis, fistula, or other serious complications.

**Table 2.** Details of treatment and implant parameters

| Pt # | EBRT (Gy) | Template | # of needles | HDR dose/F (cGy) | Presc. point | F # | Treatment delivery |
|---|---|---|---|---|---|---|---|
| 1. | 59.20 | MUPIT | 7 | 600 | 0.5 cm | 1 | Single fraction |
| 2. | 50.40 | MUPIT | 7 | 650 | 0.5 cm | 3 | 1 F/d, once a week |
| 3. | 40.00 | MUPIT | 10 | 600 | 0.5 cm | 3 | 1 F/d, once a week |
| 4. | 10.00 | MUPIT | 7 | 750 | 0.5 cm | 3 | 1 F/d, once a week |
| 5. | - | No | 5 | 500 | 0.5 cm | 6 | 2 F/d, 6F in 3d |
| 6. | 60.40 | MUPIT | 3 | 600 | 1.0 cm | 2 | 1 F/d, once a week |
| 7. | - | MUPIT | 10 | 700 | 0.5 cm | 4 | 1 F/d, once a week |
| 8. | 50.40 | MUPIT | 6 | 600 | 0.5 cm | 3 | 1 F/d, once a week |
| 9. | 50.40 | No | 4 | 600 | 0.5 cm | 3 | 1 F/d, once a week |
| 10. | 39.60 | MUPIT | 8 | 600 | 0.5 cm | 2 | 1 F/d, once a week |

Pt # = patient number, EBRT = external beam radiation, Gy = Gray, F = fraction, d = day, MUPIT = Martinez Universal Perineal Interstitial Template

## Discussion

Brachytherapy is an essential component of curative radiotherapy for cervical cancer. This is traditionally done by intracavitary insertion of the uterine tandem and colpostats. Reported local control rates after ICBT were 88-92% for stage I, 66-88% for stage II, 48-63% for stage III, and 13-28% for stage IV[3-5]. These outcomes illustrate that the more advanced the disease is, the more difficult it is to control. Failure to achieve local control has a major impact on the patients' survival and quality of life. Standard ICBT requires a good geometry to accommodate the uterine tandem and colpostats to produce an optimal pear-shaped dose distribution. ICBT gives high central dose but relatively low dose to the periphery. Additionally, the dose distribution from ICBT is symmetrical while there is no "symmetrical tumor" in clinical practice. Interstitial implant is an alternative method that has been used to overcome these limitations of ICBT. Indications for interstitial implant are summarized in Table 3.

Results of low-dose-rate interstitial brachytherapy in primary or recurrent cervical cancer from many retrospective series have shown a wide range of local control (22-100%), survival, and treatment complication[6-18]. However, there are very few data regarding HDR interstitial implant[19,20]. Although none of them is a prospective study, local control rates are somewhat better than expected for these selected poor prognostic patients. Patients with recurrent disease after radical radiotherapy have relatively few treatment options. Reirradiation by interstitial implant has been used to treat these patients but it was associated with poorer outcomes and higher morbidities. The reported incidence of major treatment-related toxicities ranged from 3-38%[6-20].

**Table 3.** Summarized indications for interstitial implant

| |
|---|
| Primary disease |
| • Extensive parametrial extension |
| • Extensive vaginal extension (> 5 mm thickness) |
| • Narrow or distorted vagina (can not accommodate ovoids) |
| • Inability to insert uterine tandem |
| - obliteration of the cervical os |
| - previous hysterectomy |
| • Persistent disease after conventional radiation |
| Recurrent disease |
| • Prior pelvic radiotherapy |
| • Previous hysterectomy |

From the authors' experience, interstitial brachytherapy is technically feasible. However, the procedure is more invasive and the technique is more complicated. So it is time-consuming, requiring significant amounts of equipment, technical skill, and effort compared to conventional ICBT. In the present study, no acute complication from the procedure was observed. Preliminary results have shown that this technique can provide local control in 9 of 10 patients without serious late complication. But before any conclusion, more patients and longer follow up is needed. Future directions for improvement include a use of pretreatment MRI to more accurately determine tumor extension, the use of CT-guidance to facilitate proper needle insertion, and CT-based treatment planning to evaluate the actual dose distribution and allow proper dose modification.

## Conclusion

HDR interstitial brachtherapy is another treatment option for women with advanced primary or locally recurrent cervical carcinoma or other gynecologic malignancies, whose tumor cannot be adequately encompassed by a standard intracavitary insertion. This technique is feasible, providing good local control without serious complication. However, more patient numbers and longer follow up is needed.

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## การรักษาผู้ป่วยมะเร็งปากมดลูก และอวัยวะสืบพันธุ์สตรี โดยการฝังแร่ แบบ high dose rate

**ชมพร สีตะธนี, วิรัตน์ ไพรัชเวทย์, ลดาวัลย์ นาควงษ์, พุฒิพรรณ พัวทวีพงศ์**

***วัตถุประสงค์:*** *เพื่อรายงานวิธีการและศึกษาผลการรักษาผู้ป่วยมะเร็งปากมดลูกและอวัยวะสืบพันธุ์สตรี โดยการฝังแร่ แบบ high dose rate*

***วัสดุและวิธีการ:*** *ทำการรวบรวมและศึกษาข้อมูลย้อนหลังของผู้ป่วยมะเร็งปากมดลูกและอวัยวะสืบพันธุ์สตรี 10 ราย ที่ได้รับการรักษาโดยการฝังแร่แบบ high dose rate ที่โรงพยาบาลรามาธิบดี ตั้งแต่ เดือนเมษายน พ.ศ. 2546 ถึง เดือนตุลาคม พ.ศ. 2547 โดย ผู้ป่วยเหล่านี้เป็นผู้ที่มีข้อจำกัดในการใส่แร่แบบมาตรฐาน ได้แก่ผู้ป่วยที่ผ่านการผ่าตัดมดลูก หรือ เคยได้รับการฉายรังสี บริเวณอุ้งเชิงกรานมาก่อน*

***ผลการศึกษา:*** *วิธีการฝังแร่ทำโดยการเสียบเข็มผ่านทางผิวหนังบริเวณ perineum โดยใช้เครื่องเอกซเรย์ fluoroscopy เป็นตัวช่วย ปริมาณรังสีที่ใช้ อยู่ในช่วง 500-700 cGy ต่อครั้ง ทั้งหมด 1-6 ครั้ง ผู้ป่วย 8 ราย ได้รับการฉายรังสีจากภายนอกร่วมด้วย ภายหลังการติดตามผลการรักษาเป็นเวลา 5-21 เดือน ไม่พบผู้ป่วยเสียชีวิต สามารถควบคุมโรคเฉพาะที่ได้ในผู้ป่วย 9 ราย โดยผู้ป่วย 1 รายยังคงมีมะเร็งเหลืออยู่ในตำแหน่งที่ทำการฝังแร่ ไม่พบผลข้างเคียงระยะเฉียบพลันหรือผลข้างเคียงระยะยาวที่รุนแรงจากการรักษานี้*

***สรุป:*** *การฝังแร่แบบ high dose rate สามารถใช้รักษาผู้ป่วยมะเร็งปากมดลูกและอวัยวะสืบพันธุ์สตรี ที่มีข้อจำกัดในการใส่แร่แบบมาตรฐาน โดยสามารถควบคุมโรคเฉพาะที่ได้ดี และไม่พบผลข้างเคียงที่รุนแรงจากการรักษา อย่างไรก็ตามจะต้องติดตามผลการรักษาในระยะยาวต่อไป*