

HDR Interstitial Perineal Implant for Locally Advanced or Recurrent Uterine Cervix Cancer

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Purpose: To evaluate whether high-dose-rate (HDR) interstitial perineal implants can effectively eradicate residual tumor or recurrent tumor in uterine cervix cancer after complete radiation treatment.

Materials and Methods: This method of treatment was commenced in January 2002, and four advanced stage and four uterine cervix cancer (UCC) recurrences were admitted for this study. All untreated stage II bulky mass and IIIB patients received 50 Gy external beam radiotherapy (EBR) to the whole pelvis prior to the interstitial perineal implant. No EBR was given to recurrent UCC. Brachytherapy was delivered using Martinez Universal Perineal Interstitial Template (MUPIT) and ^{192}Ir HDR. This implant will only be done if residual disease on the parametria was bimanually palpable or was proven by CT scan or MRI. The dose of interstitial brachytherapy boost to the parametria was 17 to 30 Gy, and treatment days ranged from 42 to 64 days. Uterine recurrences were found on the uterine cervix and/or parametria. The dose delivered by this implant ranged from 6 to 16 Gy and encompassed either uterus or vaginal stump and both parametria. Total treatment days ranged from 1 to 2 days.

Results: This short-term study showed that almost all tumors were locally controlled when the study was closed (1 to 15 months). One distant metastasis was found. No significant morbidity has been identified until now.

Conclusion: HDR ^{192}Ir interstitial perineal implants were proven to be effective in eradicating tumor cells in advanced stage UCC and recurrent disease with no significant morbidity.

Key words: uterine cervix cancer, interstitial implant, residual disease, recurrence

INTRODUCTION

UTERINE CERVIX CANCER (UCC) ranked number one among other malignancies in Indonesia.¹ Treatment of choice for stage I to IIA is radical surgery. Radiotherapy was given only for irradiably resected lesions or those with positive lymph nodes and closed margin.

Multivariate analysis shows that tumor size, hemoglobin value, and pelvic and paraaortic lymphnode metastases are well correlated with 5-year survival and local control rates. Smaller tumor sizes give favorable treatment results.² Most failures after radiotherapy are local failures caused by inadequate brachytherapy. The

majority of our patients were admitted in stage IIIB or stage IIB with bulky tumor. Several publications have reported 5-year actuarial survival for stage III ranges from 35% to 50%.³⁻⁵

To improve this poor outcome, attempts have been made to modify the conventional method with interstitial perineal implants for advanced stage or recurrent diseases. Compared with conventional intracavitary treatment, this method can deliver the maximal dose to the parametria.

This treatment method has been administered since the early 1980s in many institutions. With the advance of technology, more good results have been reported.^{6,7}

MATERIALS AND METHODS

Brachytherapy was delivered using the modified intracavitary method and the Martinez Universal Perineal Interstitial Template (MUPIT) (Fig. 1). The template is placed against the perineum. This template

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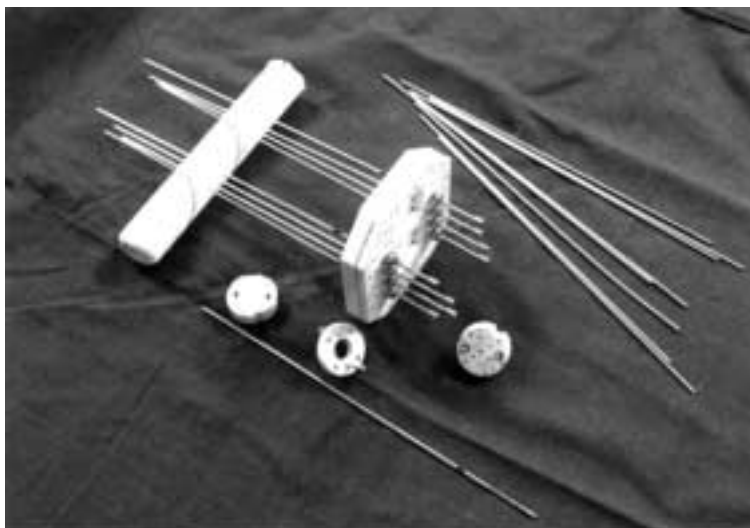


Fig. 1. Martinez Universal Perineal Interstitial Template (MUPIT) used in this study.

consists of two large holes to accommodate intracavitary and the rectal probes. The rectal hole is closed when the intracavitary obturator is in place. Smaller drilled holes are scattered uniformly around these holes. Hollow needles should be inserted through some of the holes initiated by the needles placed in the grooves of the probe. The small holes will keep all the needles in a parallel direction. The total number of needles and their distribution are based on the clinical target volume defined by physical examination and CT or MRI findings.

Previously untreated stage IIB with bulky mass or IIIB patients with extensive parametrial involvement and recurrent patients after completing treatment with external radiotherapy were planned to have intracavitary tandem combined with interstitial implant, instead of combination intracavitary and ovoids. Recurrent patients who had prior hysterectomy with the impossibility to insert the tandem due to the absence of the uterus were treated by interstitial implant only. External beam radiotherapy (EBR) of 50 Gy was administered to previously untreated patients only. Interstitial brachytherapy was followed using ^{192}Ir high-dose-rate (HDR) to encompass the uterine cervix and both parametria with a dose of 4 Gy per fraction for four fractions for standard methods. There were dose differences for some patients adjusted for local conditions, large tumors, and complications arising after EBR. The dose distribution is shown in Fig. 2.

The applicator needles were implanted to the patient in gynecologic position under spinal or epidural anesthesia. No anesthesia is required to withdraw the template and the applicators. To avoid needle penetration

to the rectum, it is advisable to work with one finger in the rectum against the anterior rectal wall. The rectal cavity must be cleaned from fecal masses before the implantation. A low-fiber diet is applied to suppress excessive fecal formation. Infusion of physiologic salt and glucose during this procedure until completion of the treatment is mandatory in order to prevent dehydration.

Since this is a pilot project study, not all stage IIB patients with bulky mass and IIIB patients were treated by this method. No special criteria were applied to select the patients. Staging of the tumor (FIGO) was established by gynecologists together with radiation oncologists. Examinations to exclude distant metastases were performed as was done to other patients.

Interstitial perineal implants not initiated by EBR were done on five recurrent patients. The total dose given was 6-16 Gy, delivered in 2-4 fractions.

The local control criteria and complications were based on the WHO classification. All patients were evaluated by gynecologic oncologists after completion of the treatment and during follow-up until the study was closed.

To avoid local complications, we kept the maximal doses to bladder and rectum to 4 Gy and 6 Gy per implantation, respectively.

RESULTS

Since this treatment method was commenced only one year ago, only local control rate, acute complications, and short-term follow-up could be analyzed.

All untreated stage IIB with bulky mass (2 patients)

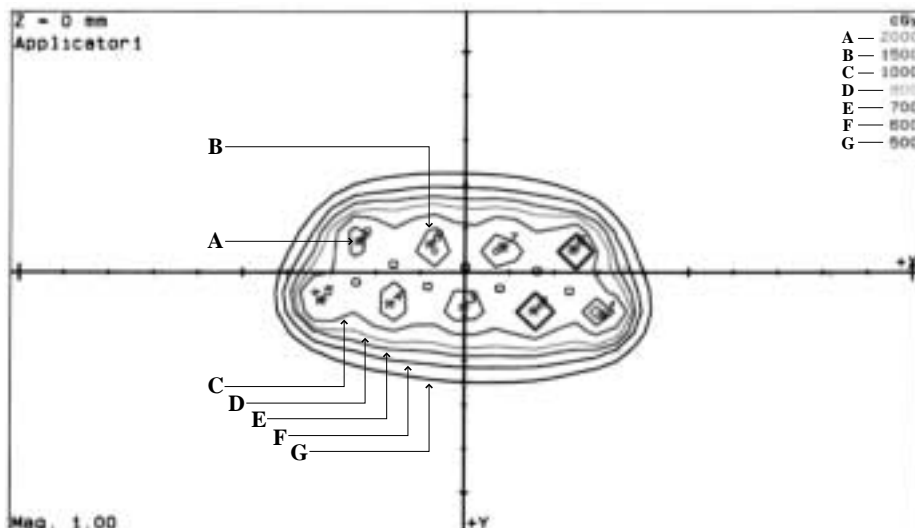


Fig. 2. Dose distribution produced by radioactive configuration covering both parametria. A: center of applied needles, B: around the needles.

Table 1. Characteristics of patients

No.	Age (yrs)	Stage (FIGO)	Treatment	Results	Treatment time (days)	Notes
1.	65	IIIA-B	EBR: 25 fr × 2 Gy BT: 3 × 10 Gy	CR	64	
2.	59	IIB bulky mass	EBR: 25 fr × 2 Gy BT: 2 × 8.5 Gy	CR	53	
3.	42	IIIB	EBR: 25 fr × 2 Gy BT: 2 × 2 fr × 5 Gy	CR	46	TAH CRF
4.	24	IIB bulky mass	EBR: 25 fr × 2 Gy BT: 2 × 8.5 Gy	PR	42	Liver metastases
5.	53	Recurrence	BT: 1 × 2 fr × 6.2 Gy	PR	1	3 months after 1st treatment
6.	45	Recurrence	BT: 4 × 2 fr × 3 Gy	CR	4	7 months after 1st treatment Chemo
7.	49	Recurrence	BT: 2 × 2 fr × 4 Gy	CR	2	12 months after 1st treatment
8.	53	Recurrence	BT: 2 × 2 fr × 4 Gy	CR	2	6 months after 1st treatment
9.	48	Recurrence	EBR: 25 fr × 2 Gy BT: 2 × 2 fr × 4 Gy	CR	53	11 years after 1st treatment

EBR, external beam radiotherapy; BT, brachytherapy, interstitial perineal implant; Fr, fractions; CR, complete response; PR, partial response; TAH, total abdominal hysterectomy; CRF, chronic renal failure.

and IIIB UCC patients (2 patients) received 50 Gy EBR followed by interstitial implant with doses ranging from 17 to 30 Gy in 2-4 fractions. Until the end of the study local tumor control was demonstrated by almost all of the patients. Only one patient experienced local response. Later liver metastases were found in this patient. Total treatment days of these patients ranged from 42 to 64

days. Admitted locally recurrent UCC patients were diagnosed 3 to 12 months after the last treatment. These patients underwent interstitial perineal implant only. All but one of these patients demonstrated complete response of the local recurrence.

Total treatment days for combined treatment ranged from 42 to 64 days. It seems that there was no direct

correlation between this and clinical outcome.

No severe acute local complications were found.

Characteristics and results of the treatment are shown in Table 1.

DISCUSSION

Unlike to many reports,^{8,9} Meder *et al.* stated that no potential benefit has been shown by this treatment method.¹⁰ This short-term study showed not only prospective results but also considered the treatment more efficient than any other method. Combination chemoradiotherapy is limited to those who can purchase chemotherapy. In the last decade various types of chemotherapy were introduced to our market but only a small percentage of UCC patients in Indonesia can afford this combined method.

EBR was given to previously untreated patients, except one recurrent patient who underwent this treatment more than 11 years ago. The aim of EBR is to reduce primary tumor size and to eradicate lymph node metastases if they occur.

Of 16 existing radiotherapy centers in this country of more than 200 millions, some have been equipped with HDR ¹⁹²Ir brachytherapy machines. By these machines a high number of stage IIIB and recurrent UCC patients are expected to be optimally treated by either conventional or interstitial implants.

Problems encountered by many radiotherapy centers are shortage of human resources, in particular medical physicists. It is generally accepted that HDR source machines require experienced experts to have optimal treatment results with minimal complications on healthy tissue adjacent to the tumor site. Otherwise low-dose-rate (LDR) source machines should be used with their consequences. Patients treated by LDR need hospitalization. In his study Gupta found that the complication rate of LDR interstitial implants was low and operator independent.¹¹

The long treatment in these patients actually could be shortened by carrying out the implantation during the delivery of EBR, instead of giving it one week after completion of EBR as previously done. Although no clinical correlation between treatment result and shortened treatment days was noted, financial benefit was achieved for the patients who live far away from the radiotherapy center.

CONCLUSION

Many authors have reported the poor outcome of stage IIIB patients or recurrent UCC treated by conventional

combination EBR and brachytherapy. Short evaluation of these patients treated by interstitial HDR ¹⁹²Ir implant (with or without EBR) shows promising treatment results. Local control was noted in the majority of patients, and local complications could be well tolerated. Further evaluation of these patients and better selection is required.

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