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Indications And Rationale For High-Dose-Rate Interstitial Brachytherapy In The Management of Carcinoma Cervix and Other Gynaecologic Malignancies

Dr. George John[1],Dr. Hasib A.G[2],Mr. Sridhar C.H[3],Dr. M.S Athiyamaan[4],
Dr.Sandesh Rao[5],Dr. Sharaschandra Shankar[6],
Dr. Pavan Kumar Reddy[7], Dr.Priyanka Augustine[8]
(Department Of Radiation Oncology, Father Muller Medical College, Mangalore, Karnataka, India)[12345678]
Corresponding author: Dr. Hasib A.G[2]

Abstract
Objective:*To report indications, rationale and technique of high-dose-rate (HDR) interstitial brachytherapy in the treatment of cervical carcinoma and other gynaecologic malignancies.*
Materials and Methods:*Between 2014 and 2017, 45 patients (35 - cervical carcinoma, 8 –Ca vaginal vault, 1 – Ca cervical stump and 1 – Ca vagina) were treated with interstitial implant. Patient characteristics, implant technique, and indications were reported.*
Results:*All patients completed EBRT prior to brachytherapy and underwent an interstitial implant using a MUPIT applicator. Clinical and imaging findings prior to EBRT and brachytherapy were used to estimate tumour volume and number of needles required for implantation. 71% of patients received external beam RT to a dose of 50Gy in 25 fractions. 38 patients received concurrent cisplatin along with radiotherapy. ISBT dose ranged from 8Gy to 22.5Gy. The indications for interstitial brachytherapy for patients in our study are bulky parametrial disease (n = 27), extensive vaginal extension (n = 11), bulky primary disease (n= 10), recurrent disease post hysterectomy (n = 8), adjacent organ invasion (n = 7), presence of fistula (n = 4), obliteration of cervical os (n = 4), recurrent disease after pelvic RT (n = 2) and Carcinoma cervical stump (n = 1).*
Conclusion:*Interstitial implant can be a feasible treatment option in patients with gynaecologic malignancies who have limitations with standard intracavitary insertion. The case selection for interstitial brachytherapy should be done judiciously.*
Keywords: *Ca Cervix, HDR, Interstitial brachytherapy, Intracavitary brachytherapy, MUPIT*

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I. Introduction

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.As a means of radiation dose escalation to tumour with normal tissue sparing, brachytherapy is critical to the curative management of cervical cancer. When executed correctly and in conjunction with EBRT it results in improved survival rates [(1-4)]. The majority of patients with cervical cancer are able to be treated with intracavitary brachytherapy.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. Conventional intracavitary brachytherapy (ICBT) may not deliver adequate doses in cases of advanced cervical disease or in patients with distorted anatomy. Such cases are associated with a high incidence of local failure and complications[5].

The indications of interstitial brachytherapy for carcinoma cervix are for distorted anatomy or poor geometry, narrow vagina and obliterated fornices not allowing an ovoid, loss of endocervical canal not allowing a tandem placement, bulky primary disease, bulky parametrial disease which will require boost, extensive paravaginal or distal vaginal involvement, persistent or recurrent carcinoma cervix post-EBRT and post brachytherapy, carcinoma of the cervical stump, cut through hysterectomy or prior supracervical hysterectomy, presence of a fistula and/or adjacent organ invasion. The indications for carcinoma vagina and vulva are radical brachytherapy in early lesions (T1/N0), boost in addition to EBRT in large lesions (T2/3) and locally confined recurrent cases [(6)].The primary aim of this study is to present our institutions rationale, indications, techniques and method of application of interstitial brachytherapy for carcinoma cervix and other gynaecologic malignancies.

II. Materials And Methods

45 Patients received HDR- interstitial brachytherapy using MUPIT applicator under spinal/epidural anaesthesia from 2013 to 2017 using Ir-192 source (Nucletron).Pre-treatment evaluation consisted of physical and pelvic examination, complete blood tests, chest x-ray and 2D echo. Diagnostic Computerized tomography (CT) or MRI was done for patients before the procedure. Patients' medical records were retrospectively reviewed. Patient characteristics, details of treatment, including interstitial brachytherapy technique, indications and rationale of were reported.

2.1Treatment Protocol: All patients completed EBRT prior to brachytherapy and underwent a interstitial implant using a MUPIT applicator (Figure 1).

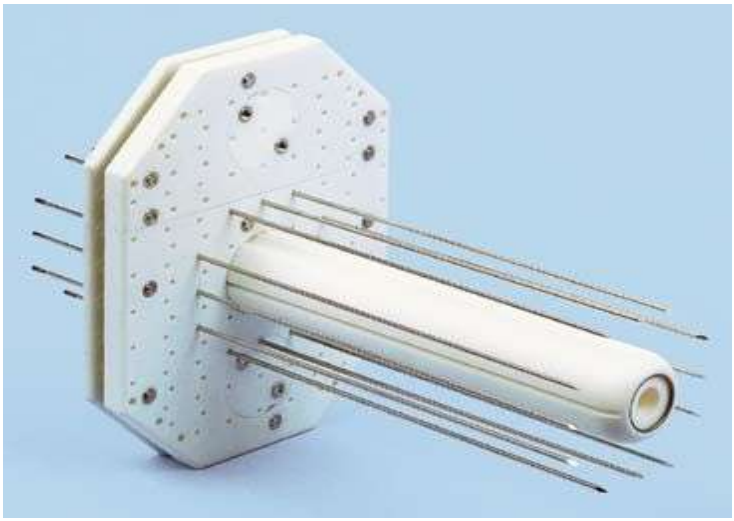

Fig.1:MUPIT applicator

Clinical and imaging findings prior to EBRT and brachytherapy were used to estimate tumour volume and number of needles required for implantation. While under spinal or epidural anaesthesia, a pelvic examination was performed to evaluate extent of disease. A foleys catheterwas placed in the bladder and the balloon was filled with 7 ml of contrast. Bladder filling was done with normal saline till bladder is visualised in USG and foley's catheter is clamped. The uterine sounding is done to assess the uterine length. The uterine tandem is placed to the uterine cavity (if uterus is intact). The vaginal length is determined and the vaginal obturator is inserted over tandem until its tip abuts the cervical os. Base plate is fixed to obturator with screws and to perineum by stitches at 4 corners. A guide needle is inserted 3–4 cm beyond the clinically palpable disease, starting with the needles near the rectum, with one finger inside the rectum to avoid rectal perforation. The rest of the needles are inserted around the vaginal cylinders up to the pre-set depth. The number and position of the needles are according to the extent of the disease. All the needle insertions are done under Trans abdominal USG guidance and position is checked. The cover plate is placed over the template to prevent the needles from displacement.

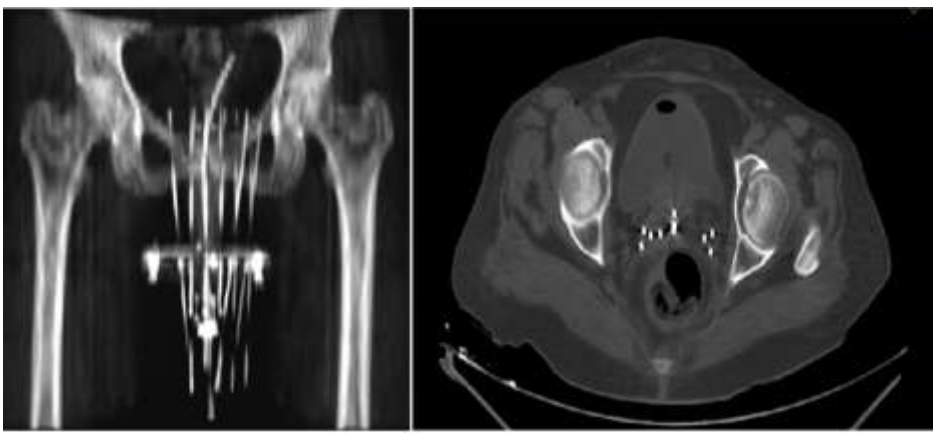

Fig.2 :Planning CT scan of a patient

Planning CT scan is done after the procedure. Tumour CTV and organs at risk are contoured.The dose was prescribed to the CTV such that at minimum 90% of the CTV (D90) received the prescription dose and with acceptable OARs doses (figure 3). The goal was to achieve a total D90 of 80 - 85 Gy to the CTV with a total dose to 2 cc (D2cc) of the rectum and sigmoid less than 75 Gy and bladder less than 90 Gy.

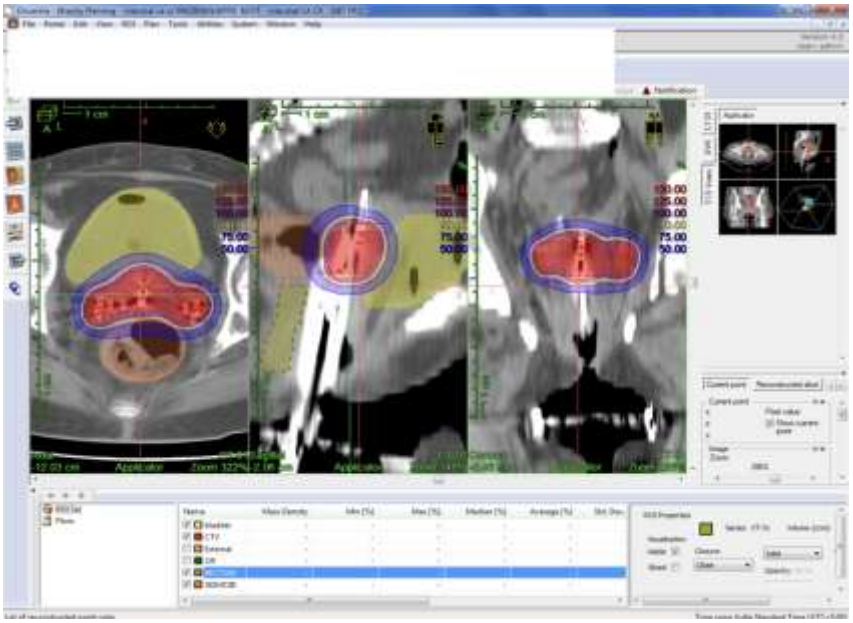

Fig. 3 :ISBT isodose curves

2.2Postimplant Care: Intravenous antibiotics, hydration, parenteral nutrition, and analgesia are to be maintained properly throughout during the treatment. A sterile gauze soaked in betadine is placed between the template and the skin to ensure that the template does not hurt the patient. Bowel sounds have to be assessed daily and should watch out for any haematuria.

III. Results

45 patients were treated with interstitial brachytherapy in the Department of Radiotherapy, Father Muller Medical College, Mangalore between 2014 to 2017. The median age of patients was 48 years. Patient characteristics are given in Table 1. Majority of patients were diagnosed with squamous cell carcinoma. 35 patients had carcinoma cervix, 8 patients had carcinoma vaginal vault, 1 patient had carcinoma cervical stump and 1 patient had carcinoma vagina. All patients received External Beam Radiotherapy prior to interstitial brachytherapy. 71% of patients received external beam RT to a dose of 50Gy in 25 fractions. 38 patients received concurrent cisplatin along with radiotherapy. ISBT dose ranged from8Gy to 22.5Gy.The indications for interstitial brachytherapy (Table 2) for patients in our study are bulky parametrial disease (n = 27), extensive vaginal extension (n = 11), bulky primary disease (n= 10), recurrent disease post hysterectomy (n = 8), adjacent organ invasion (n = 7), presence of fistula (n = 4), obliteration of cervical os (n = 4), recurrent disease after pelvic RT (n = 2) and Carcinoma cervical stump (n = 1).

After completion of brachytherapy, patients were seen at onemonth follow-up by the treating Radiation Oncologist for first 6 months, then every3 months for the first 2 years, every 6 months for 3 to 5 years, andthen yearly thereafter.

Table 1: Patient Characteristics

Total no. of patients	**45**
Median age	48 yrs
Histology:	
SCC	43
Adenocarcinoma	2
Ca Cervix	
Stage:	
IIB	4
IIIA	1
IIIB	27
IVA	3
Ca vaginal vault/Ca cervical stump	9
Ca vagina	1
EBRT:	
50Gy/25#	32
46Gy/23#	12
50.4Gy/28#	1
Concurrent Chemotherapy:	
Cisplatin	38
Cisplatin + Paclitaxel	3
Carboplatin	1
None	3

Table 2 : Indications for Interstitial Brachytherapy in the study

Indications	**Number of patients**
Bulky parametrial disease	27
Extensive vaginal extension	11
Bulky primary disease	10
Recurrent disease post hysterectomy	8
Adjacent organ invasion	7
Presence of fistula	4
Obliteration of cervical os	4
Recurrent disease after pelvic RT	2
Carcinoma cervical stump	1

IV. Discussion

Brachytherapy forms an essential component of radiotherapy in the curative management of 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. [(7-9)]These outcomes indicate that as the stage of the disease increases the difficulty to achieve local control increases proportionally. Failure to achieve local control has a major impact on the survival and quality of life of the patient.Standard ICBT requires adequate geometrical space to accommodate the uterine tandem and colpostats in order 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 tumour" in clinical practice. Interstitial implant is an alternative method that can be tailored to overcome these limitations of ICBT. The common indications for interstitial implant are summarized in Table 2.

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%), improved survival, and manageable treatment complications[(10-24)]. Althoughnone of those studies were conducted on a prospective basis, local control ratesare somewhat better than expected for these selectedpatients with poor prognostic factors.
Patients with recurrentdisease after radical radiotherapy have relatively fewtreatment options. Reirradiation by interstitial implanthas been used to treat these patients although it is associatedwith poorer outcomes and higher morbidities.The reported incidence of major treatment-relatedtoxicities ranged from 3-38%[(10-24)].

The possible disadvantages of interstitial brachytherapy include that it is invasive, resource intensive, technically challenging, and can be ideally performed only in women who have a good performance status[(25,26)]. It is also time-consuming, requiring significant effort compared to conventional ICBT. Studies have

made comparisons between brachytherapy and few of the probable options for the alternatives such as EBRT boost using intensity modulated radiotherapy (IMRT), image-guided radiotherapy, volumetric modulated arc therapy, and stereotactic body radiotherapy[27-29]. In one such study, volumes receiving 60 Gy (EQD2) were approximately twice as large for IMRT compared with brachytherapy, and the high central tumour dose was lower than that achieved by brachytherapy[30].As prior trials that compared brachytherapy and EBRT boost evidently pointed that brachytherapy was superior with respect to survival, these trials were mostly confined to the patients who have denied brachytherapy or who were deemed unfit for brachytherapy such as those with a bicornuate uterus and those patients with recurrence.

These studies concluded that brachytherapy should be considered as the treatment of choice, but alternatives can be tried if there are constraints to brachytherapy with acceptabletoxicities and comparable results.

Future directions for the improvement include the use ofa pretreatment MRI to accurately determine the extent of tumour and the use of CT to facilitate properneedle insertion per operatively and the introduction of MRI compatible interstitial implants to facilitate MRI based planning.

V. Conclusion

Performing interstitial brachytherapy using implants such as MUPIT requires skill and expertise. However, the case selection for interstitial brachytherapy should be done judiciously. HDR interstitial brachytherapy can be considered for women with advanced primary or locally recurrent cervical carcinoma, in patients who require a parametrial boost or in other gynaecologic malignancies, whose tumour cannot be adequately encompassed by a standard intracavitary insertion.

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