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Dosimetric Comparison on inter-fraction variation between rigid needle and flexible catheter implant in interstitial HDR Brachytherapy

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ABSTRACT

***Background*:** Patient setup errors in External Beam Radiotherapy (EBRT) are minimized to a great extent, due to recent technological developments but in contrary brachytherapy received least attention in inter-fraction catheter movement and its impact in dose delivery. This article deals with inter-fraction interstitial catheter movement and its impact in dose delivery to the target. An attempt is made to study the dosimetric impact of this variation.

***Objectives*:** The objective of this study is to evaluate the inter-fraction variation in the position of implanted interstitial applicators and to assess the dosimetric impact in interstitial High Dose Rate (HDR) Brachytherapy and to estimate the variation between flexible and rigid needle implants.

Materials and Methods: 55 patients treated for carcinoma tongue, breast, buccal mucosa, cervix, floor of mouth and soft tissue sarcoma over a period of 2 years (December 2011 – May 2013) were considered. All the patients underwent CT scan on the next day of the implant and 3D planning was done either by Eclipse or Oncentra Master plan Treatment Planning System (TPS). Patients were treated by HDR brachytherapy remote after-loading units, either by Gamma Med iX plus or Microselectron. At the end of the last fraction, CT scan was repeated and re-planning done. The variation in position of the implanted applicators/catheters and its impact on dosimetric parameters were evaluated and analyzed.

Results: The range of positional displacement of the interstitial catheters ranges from - 4.5 mm to 6.8 mm. The maximum variation in prescribed dose to D90 of Clinical Target Volume was 10.88%.

***Conclusions*:** If the total duration of interstitial implant of HDR brachytherapy extends for more than a week from the day of imaging, it is recommended to do CT imaging and re-plan again. It is mandatory to suture the buttons of the implant to the skin. Edema and movement of organs (e.g., tongue) are the main cause for the positional variation of the catheters.

Key words: HDR, Brachytherapy, Interstitial implant, inter-fraction variation, dosimetric variation.

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1. INTRODUCTION

The worldwide incidence of squamous cell carcinoma of head and neck is more than 500,000 cases per year and the management of patients with head and neck cancer is complex (Ortega et al. 1995). The choice of treatment modality depends on the stage and site of disease. Brachytherapy plays an integral role in the management of head and neck cancers and has been described as the first form of conformal radiation (Jemal et al. 2003). Precise source placement enables very high doses within the tumor and sufficient dose at the margin between the tumor and normal tissue ensuring high tumor control. At the same time only small volumes of normal tissue is irradiated thus decreasing the normal tissue complications.

Brachytherapy involves the implantation of plastic catheters (applicators) into tumors. In 1904, Wickham and Derais used sharpened goose quills to perform intratumoral implantations (Dale et al. 1998). Abbe and Morton have reported anecdotal reports of cure for cancers in the head and neck with brachytherapy (Joslin et al. 2001; Eeva et al. 2011). In 1909, Minet described the first use of a radium tube placed in a catheter to treat prostate cancer (Nath et al. 1995). Traditionally treatment planning of brachytherapy was mainly based on radiographs and point dosimetry (Velmurugan et al. 2010). The dose distribution was related to the geometry of the catheters. With the newer three dimensional treatment planning together with CT imaging, it is possible to get a 3D based dose distribution with reconstruction of the tumor volume and the catheters (Rey et al. 2013).

Table 1
Patient characteristics

Characteristics	No of patients (%)
Age	
Mean	50.1
Standard Deviation	10.3
Median	48
Range	32-73
Gender	
Male	26 (47.27%)
Female	29 (52.72%)
Diagnosis	
Carcinoma Breast	13 (23.63%)
Carcinoma Buccal Mucosa	17 (30.91%)
Carcinoma Cervix	1 (1.82%)
Carcinoma Floor of Mouth	2 (3.64%)
Carcinoma Tongue	19 (34.55%)
Soft tissue sarcoma (multiple site)	3 (5.45%)
T stage*	
T1	6 (10.91%)
T2	20 (36.36%)
T3	29 (52.73%)
T4	0 (0%)
N stage*	
N0	42 (76.36%)
N1	10 (18.18%)
N2	3 (5.45%)
N3	0

* According to the 7th American Joint Commission on Cancer/Union for International Cancer Control Staging system.

Interstitial implant procedure involves using a metal needle or trocar, the skin is pierced at the planned entry site and coursed along in the tumor volume, exiting at the marked skin site at the other end of the target volume. Once in place, a nylon after-loading catheter is then adjusted such that the wider portion of the after-loading catheter encompasses the target volume. The trocar is then removed along its original pathway while holding the implanted catheter in place. A metal button along with a half-moon-shaped plastic button is then threaded over the *exposed ends of the catheter and crimped in placed over the skin entry sites*. Silk ties can then be sutured to the skin through the available holes in the button for further stabilization.

The exposed end of the catheter is then cut off leaving at least several centimetres distal to the metal button. These series of steps would then be repeated, resulting in a parallel distribution of catheters along the tumor volume (Figure 1). Depending upon the site, patient's co-morbidities and extent of implant, the procedure can be done under local or general anaesthesia. Since, brachytherapy treatment is delivered over many days the implanted catheters can move either due to oedema or movement of the implanted organ. The positional stability of the catheters and the resultant dosimetric variation over a period of time is studied and presented.

1.1. Objectives

The objective of the study is to quantify the variation in the position of implanted applicators during treatment and assess the dosimetric impact of this variation on Clinical Target Volume (CTV) in interstitial HDR brachytherapy.

2. MATERIALS AND METHODS

The remote after-loading HDR Brachytherapy treatment unit GammaMed plus iX plus (Varian Medical Systems, Palo Alto, CA) or Microselectron HDRV3 (Nucletron, BV) using single sealed Iridium 192 radioactive source was used. For treatment planning Eclipse (Varian Medical Systems, Palo Alto, CA) or Oncentra Master plan (Nucletron, BV) was used. Images for planning were acquired by CT Somatom spirit (Siemens). Fifty five patients were included in this study from December 2011 to May 2013 (Table 1). The patients were treated after evaluation according to the stage of the disease.

2.1. Treatment protocol

Patients were treated according to the institutional protocol (Table 2).

2.2. Interstitial Implant application

Saravanan et al.
Dosimetric Comparison on inter-fraction variation between rigid needle and flexible catheter implant in interstitial HDR Brachytherapy,
Medical Science, 2013, 3(9), 37-42,
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Table 2
Institutional Treatment protocol

Diagnosis	EBRT*	HDR **
Carcinoma Breast	200 c Gy x 20 fractions	250 c Gy x 6 fractions
Carcinoma Buccal Mucosa	200 c Gy x 25 fractions***	350 c Gy x 6 fractions
Carcinoma Cervix	200 c Gy x 25 fractions	400 c Gy x 5 fractions
Carcinoma Floor of Mouth	200 c Gy x 25 fractions ***	350 c Gy x 6 fractions
Soft tissue sarcoma	200 c Gy x 20 fractions	250 c Gy x 6 fractions
Carcinoma Tongue	200 c Gy x 25 fractions ***	350 c Gy x 6fractions

* Five fractions per week with one fraction per day.
** Two fractions per day with 6 hours gap between the two fractions.
*** With Spinal shield after 44 Gy.

Table 3
Institutional Treatment protocol

Type	No of patients (%)
Rigid Needle Implants	13 (23.64%)
Flexible Catheter Implants	42 (76.36%)
Number of Planes	
Single Plane	17 (30.91%)
Double Plane	34 (61.82%)
Triple Plane	4 (7.27%)

Under general anaesthesia, trocars and hollow needles were inserted as guide tubes in and around the tumor 1 cm apart in single or multiple planes through which plastic tubes were threaded. Theses tubes were then secured by buttons. Similarly for rigid needle implant, the sterilized needles with the appropriate length were selected. With the guidance of templates the needles were inserted into the tissue. The template helped to maintain a proper geometry of the needle placement. The needles were secured by stainless steel buttons. Table 3 gives the details of the interstitial implants.

Figure 1
Patient with flexible interstitial implant

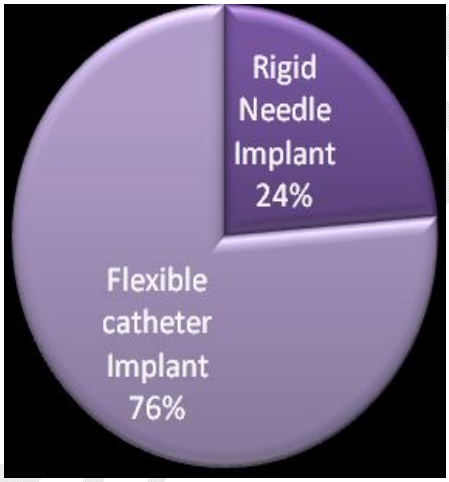

Figure 2
Distribution of rigid and Flexible implant

2.3. Imaging and planning

On the second day of implantation, the patients underwent CT scan of the involved region with a slice thickness of 1 mm. The applicator reconstruction was done and at the tip of all the applicators a reference point was inserted (Figure 2). The source dwell positions and step size were identified and accordingly the fine tuning of dose optimization was performed by changing the dwell time and dwell weightage for individual dwell positions. In most cases, dwell time was changed to reduce the hot spot or to remove the cold spot. Graphical optimization was never used. It was ensured that at least 90% of the CTV receives the prescribed dose. The dose distribution was generated by TPS using the AAPM TG-43 dose formalism (Eeva et al. 2011). Treatment was delivered using the HDR remote after-loading system. On the last fraction a repeat CT and re-planning was done and the catheters were removed.

For each patient planning was done on both Pre HDR and Post HDR images. Pre HDR and Post HDR images were fused and matched using a prominent anatomical land mark. The step size, dwell position and dwell time was maintained the same in both the plans and only the catheter position was updated in the post HDR brachytherapy plan. The tip of the catheters where the reference points were inserted gave the co-ordinates in x, y and z axis. The variation in the reference points between the two plans were estimated which gave the actual displacement in the catheter position in 3D axis. Using the Dose Volume Histogram (DVH) the dosimetric parameters were studied.

3. RESULTS

A total of 55 patients were treated between December 2011 to May 2013. 110 brachytherapy plans were generated. The demographic details of the patients included in the study are listed in Table 1. In three patients, brachytherapy was the sole modality of treatment. All other patients were treated with both external beam radiation and brachytherapy. Table 4 gives the details of the mean dose variation (%) to D90 of CTV. Rigid implant was used for patients with carcinoma breast and cervix (25.45%). For all the other patients flexible catheter implants were used (74.55%). Table 5 gives the variation in dose to the volume receiving 150% of the prescribed dose. For patients with carcinoma breast the displacement in catheter position is shown in Figure 3. For all the patients the catheter displacement and D90 dose to CTV is less than 3mm and 3% respectively. For patients with carcinoma buccal mucosa the catheter displacement for 35.29% of the patients was more than 5mm (Figure 4). In 29.41% of the patients D90 dose to CTV was more than 3%. For patients with carcinoma tongue the displacement in catheter position is shown in

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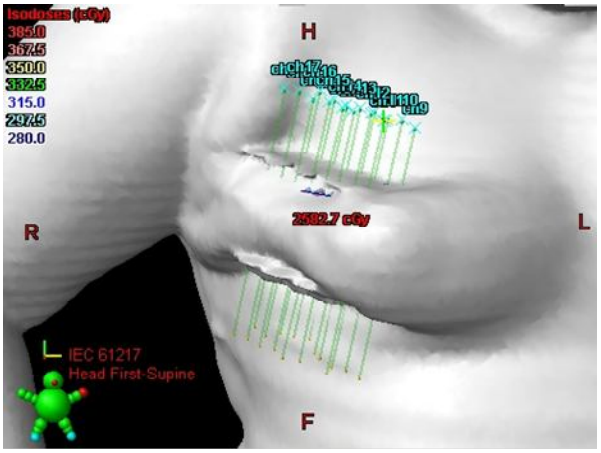

Figure 2a
Reconstructed rigid needle implant with reference points

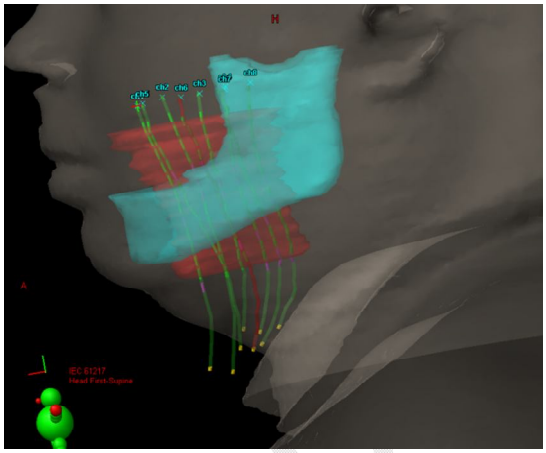

Figure 2b
Reconstructed flexible implant with reference points

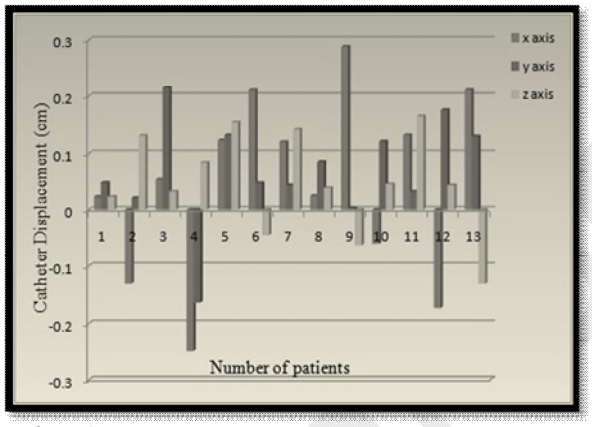

Figure 3
Catheter displacement for Carcinoma Breast

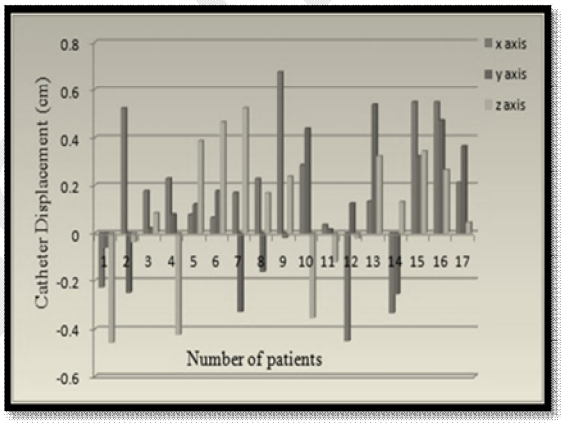

Figure 4
Catheter displacement for Carcinoma Buccal mucosa

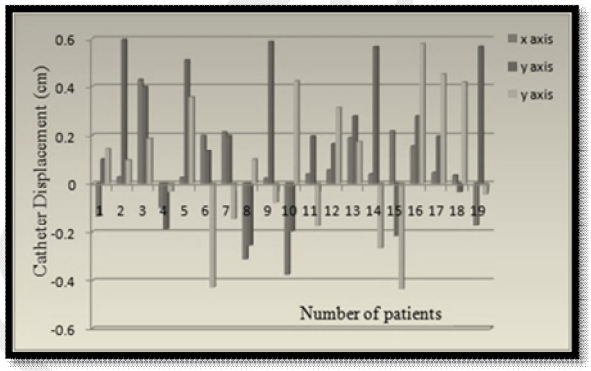

Figure 5
Catheter displacement for Carcinoma Tongue

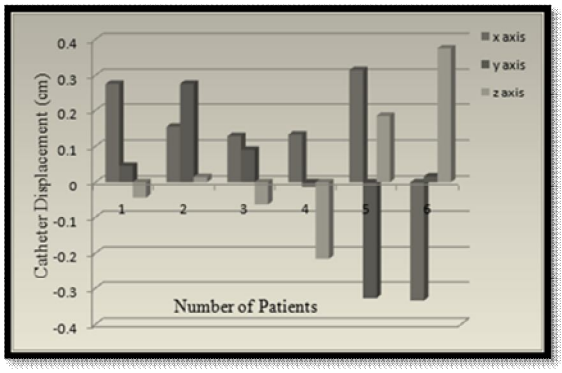

Figure 6
Catheter displacement for soft tissue sarcoma (1-3), carcinoma floor of mouth (4,5) and carcinoma cervix(6)

Figure 5. The catheter displacement for 42.11% of patients was more than 5mm. As per DVH in 26.32% of the patients D90 dose to CTV was more than 3%. Figure 6 shows the catheter displacement in patients with soft tissue sarcoma (3 patients), carcinoma floor of mouth (2 patients) and carcinoma cervix (1 patient). In Figure 7 the maximum dosimetric variation (D90) to CTV is shown with respect to the time interval in days between the Pre HDR and Post HDR plans. In 15 patients the duration between the two plans was 5 days, in 10 patients it was 6 days. In 5 patients the time interval was 7 days and in 8 patients it was 8 days. 5 patients (9.09%) had 9 days and 2 patients (3.67%) had 10 days interval between the plans. The variation in intervals between plans was because of treatment protocol, holidays and machine down time.

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Table 4

Dosimetric Variation in percentage to D90 of CTV

Type of Tumor	Mean Value + 1 Standard Deviation
Carcinoma Breast	0.423 ± 1.72 (13 patients)
Carcinoma Buccal Mucosa	1.16 ± 3.88 (17 patients)
Carcinoma Tongue	1.22 ± 2.71 (19 patients)
Soft Tissue Sarcoma	1.53 ± 4.66 (3 patients)
Carcinoma Floor of Mouth	4.6 ± 5.37 (2 patients)
Carcinoma Cervix (MUPIT)	5.72 (1 patient)

D90 - Dose received by at least 90% of the volume.

Table 5

Dosimetric variation to Volume receiving 150% of dose

Type of Tumor	Variation in Volume receiving more than 150% of dose	
Carcinoma Breast	1.8 cm^3	(1.76%)
Carcinoma Buccal Mucosa	-6.42 cm^3	(-2.14%)
Carcinoma Tongue	1.04 cm^3	(7.91%)
Soft Tissue Sarcoma	1.3 cm^3	(2.31%)
Carcinoma Floor of Mouth	2.8 cm^3	(2.85%)
Carcinoma Cervix (MUPIT)	1.2 cm^3	(1.35%)

4. DISCUSSION

Feng Xu et al evaluated interfractional and intrafractional setup error in external beam radiotherapy using cone beam computed tomography as per their result a total of 1934 CBCT scans were performed on 51 patients, the setup errors were ≤ 2mm on all axes (Fen et al. 2008). Similarly, Slow et al (2011) has estimated interfraction prostate motion during intensity modulated radiotherapy for prostate cancer of 157 patients with prostate cancer the mean setup errors 21mm, whereas in interstitial HDR Brachytherapy we have estimated that the catheter positional variation is > 6mm for few cases which was not taken into account seriously. Velumurugan et.al evaluated MUPIT implantation in patients with carcinoma cervix. In their study they recommended to repeat CT and re-plan before each fraction (Velmurugan et al. 2010). In our study imaging and planning was done before the first fraction. This plan was used for treatment delivery. At the end of the last fraction imaging and re-planning was done again and this plan was used only for analysis. Velumurugan et al. (2010) observed that the CTV mean dose varies from +9.8% to -13.3%. Out of 10 patients the mean dose was more than the prescribed dose in seven patients and less in three patients. The maximum variation to CTV dose was estimated to be around 13%. In majority of the cases the variation was around 1%. However in their study the physical movement of the needles was not estimated. Similarly Rey et al. (2013) in their study estimated the d1(day 1) plan on the d2 (day 2) and d3 (day 3). CT and re-plan was done before each treatment, with updated catheter positions the treatment was delivered. The mean CTV D90 was reduced from 93.4% on D1 to 89.3% on D2 and to 87.7% on D3. Re-planning on D2 and D3 compensated for catheter movement. They have also not estimated the positional variation of catheters. In our study we have estimated the positional variation of catheters and its dosimetric implant and we have also extended the study to different sites of implants and given the comparison. Similarly we have also given the comparison between rigid and flexible implants. As per International Commission on Radiation Units and Measurements (ICRU 58) the dosimetric variation should be limited to 3% of D90 to CTV. As per our results it has been identified that for carcinoma tongue the variation in catheter dislocation is relatively more when compared to other sites because of the movement of the organ. Hence, dosimetric variation is more for implants of carcinoma tongue. Our data also shows those rigid needle implants are more stable compared to flexible implant with less dosimetric variation for the former. The method that has been adopted to restrict the catheter movement is by pasting a micro pore at the edge of the buttons as shown in Figure 8. This micro pore flags not only act as a label to identify the channel number but also helps in arresting the button and catheter movement. This method has given a significant response in reducing the inter-fraction variation in flexible catheter movement.

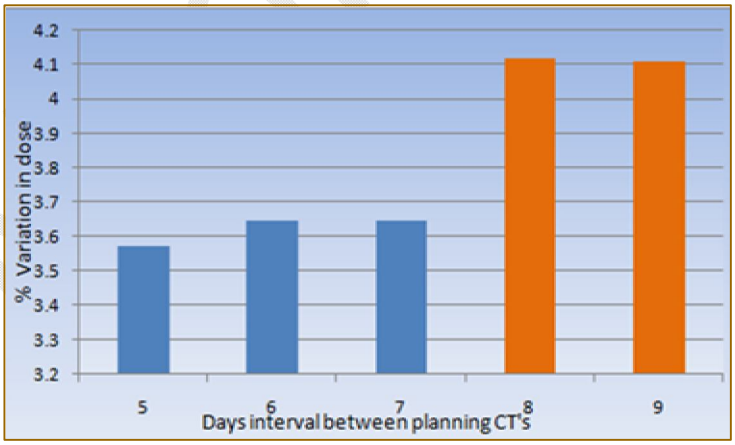

Figure 7

Dosimetric variation with time

Figure 8

Patient with Micro pore flags for reducing the catheter movement

Saravanan et al.
Dosimetric Comparison on inter-fraction variation between rigid needle and flexible catheter implant in interstitial HDR Brachytherapy,
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4. CONCLUSION

Inter-fraction error is reported frequently in HDR-brachytherapy. Rigid needle implants are dosimetrically superior to flexible implants. Suturing of the buttons in flexible implant is not a solution for arresting the catheter movement, since, it immobilizes the button alone and catheter movement is still possible. Adequate care should be taken while connecting the catheters to the HDR brachytherapy unit with transfer tubes to prevent physical displacement of the catheters. With increase in duration of treatment, the inter-fraction error increases and it is recommended to repeat CT and re-plan on the fifth day from the day of implant.

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Medical Science

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