**Assessment of Daily Needle Applicator Displacement during High-Dose-Rate Interstitial Brachytherapy for Prostate Cancer using Daily CT Examinations**

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To improve treatment conformity for prostate cancer, we investigated daily applicator displacement during high-dose-rate interstitial brachytherapy (HDR-ISBT). Thirty patients treated with HDR-ISBT as monotherapy were examined. All patients received a treatment dosage of 49 Gy per 7 fractions over 4 days. For dose administration, we examined 376 flexible applicators (1128 points) using our unique ambulatory implant technique. Using CT images with a 3-mm slice thickness, we calculated the relative coordinates of the titanium markers and the tips of the applicators. We calculated the distance between the center of gravity of the markers and the tips of the catheters, and compared the distances measured on the day of implantation and the second, third, and fourth treatment days. The mean displacement distance for all applicators was 4.3 ± 3.4 mm, 4.6 ± 4.1 mm, and 5.8 ± 4.5 mm at 21, 45, and 69 hours after initial planning CT. We used a 15-mm margin for needle displacement and only 2 points of 2 patients (16 mm and 18 mm at 69 hours, 2/1128 = 0.2%) exceeded this range. Almost patients (87%) showed the largest displacement within the first 21 hours. The relative doses that covered 100% of CTV (D100(CTV)) values compared with the initial treatment plan were reduced to 0.96 ± 0.08, 0.96 ± 0.08 and 0.94 ± 0.1 at 21, 45 and 69 hours. However, the relative D90(CTV) values kept acceptable levels (1.01 ± 0.02, 1.01 ± 0.03 and 1.01 ± 0.03). Cranial margin of 15 mm seems to be effective to keep D90(CTV) level if we do not do corrective action.

**INTRODUCTION**

High-dose-rate interstitial brachytherapy (HDR-ISBT) in combination with external beam radiotherapy (EBRT) is one of the standard therapies for localized prostate cancer. Some institutions have reported promising results with HDR-ISBT as monotherapy (HDR-ISBTM) with or without hormone therapy. Although many of these reports limited the indications to relatively low-risk patients, Yoshioka et al. treated high-risk patients and reported good outcomes using HDR-ISBTM. They attributed this favorable result to adequate tumor coverage resulting from the implantation of HDR-ISBT needles in and around the extracapsular region and bladder pouch.

Based on this earlier report, we commenced HDR-ISBTM with or without hormone therapy in 2003. We initiated several new innovative approaches to expand the indications for HDR-ISBTM. As a first step, we changed the non-removable template with a metallic needle to a removable template with a flexible tube, which enabled our patients to walk during the treatment period. In addition, improved dose distribution resulted in less toxicity, i.e., only 1 of 23 patients (4%) had acute Grade 2 rectal toxicity and no patient suffered Grade 3 or higher toxicity.

Needle applicator displacement is a major problem in HDR-ISBT in multifractionated treatments, and this problem is more critical in HDR-ISBT than in boost therapy because there is no supplementation by EBRT; hence, we...
investigated the displacement along the needle vector by utilizing CT images more precisely. The median displacement for all 776 applicators was 7 mm (range: −14–24 mm) 3 days after planning CT. Based on these results, we decided to initiate daily CT examinations to correct the dwell position of each applicator. In addition, to reduce the workload, we calculated the displacement along the CT axis only because precise calculation is time-consuming and simple methods have been able to produce a similar precise displacement analysis in previous reports. We calculated the difference between the needle vector method and CT axis method for 20 patients and 11 of 249 applicators (4%) showed more than 3 mm difference (data not shown). We considered that it was permissible.

MATERIALS AND METHODS

Patient characteristics

Between May 2007 and December 2008, 30 patients at the National Hospital Organization Osaka National Hospital were treated with HDR-ISBTM using our ambulatory technique. The median age of the patients was 71 years (range: 52–77 years). All patients had histologically proven adenocarcinoma. Gleason scores (GS) were < 7 for 10 patients, 7 for 14 patients, and > 7 for 6 patients. Based on the UICC classification of 2002, 9 patients were classified as T1, 16 as T2, and 5 as T3. The median pretreatment PSA level was 9.8 ng/ml (range: 3.2–148.9 ng/ml). Using the Seattle risk group classification, 4 patients were classified as low risk, 9 patients as intermediate risk, and 13 patients as high risk.

Applicator implantation

Applicator implantation was performed in a lithotomy position under lumbar anesthesia with continuous epidural anesthesia. The implantation was monitored by transrectal ultrasonography (SSD-1000® and ProSound Alpha 7®, ALOKA, Tokyo, Japan). We used flexible tubes (ProGuide Sharp Needle® Nucletron, Veenendaal, The Netherlands) for all patients. We implanted 11–15 applicators (total 376 applicators). The template had holes at 5-mm intervals in each direction. Before applicator implantation, 3 titanium seed markers were implanted in the prostatic apex and near the medial end of the bilateral SV. We also inserted urinary balloon catheters before implantation.

The ambulatory flexible tube technique was used, as described in our previous report. A new template was installed (Taisei Medical, Osaka, Japan), which could be removed after the implantation of flexible tubes. Flexible tubes were sutured tightly to the perineal skin to prevent displacement.

Treatment

The patients were treated with HDR-ISBTM. A dosage of 49 Gy per 7 fractions over 4 days was administered to the planning target volume (PTV). Treatment was controlled using microSelectron-HDR® (Nucletron, Veenendaal, The Netherlands) by computer optimization (PLATO®, version 14.2, Nucletron, Veenendaal, The Netherlands) with manual modification. The treatment plan was based on CT images (Xvision TM/SP, Toshiba Medical Systems Corporation, Tochigi, Japan). CT scans were obtained with a section thickness of 3 mm and pitch of 3 mm. We injected contrast medium with saline into each patient’s bladder and povidone iodine gel into the rectum prior to obtaining CT images. MRI images were used because no metallic material was employed in this technique. Immediately after undergoing CT, the patients underwent MRI. T2-weighted images were helpful mainly for determining the contours of the clinical target volume (CTV) and OARs. The CTV was the prostate; the medial portions of SV were also included for intermediate and high-risk patients, as scored by the Seattle classification. We defined the planned target volume as being equivalent to the anteroposterior, lateral, and caudal sides of the CTV. On the cranial side, we defined a treatment margin of approximately 15 mm to avoid producing a cold spot by applicator displacement. This treatment margin was supported not only by source dwell positions but also by manual modification after computer optimization.

Applicator displacement

To measure the flexible needle applicator displacement between fractions, we took CT images at approximately 21 hours, 45 hours, and 69 hours after initial planning CT, which was performed within 1 hour of implantation. We took CT images after the second, fourth, and sixth fractions of the treatment.

We loaded CT images in PLATO and obtained the relative coordinates of the 3 titanium markers and needle applicators. The tips of the needle applicators were identified by locating the end of the air column in each needle on the CT image. This calculation method was similar to the method used by Kim Y. et al. The air column in a needle appears as a black dot on the axial CT image and seems smaller than expected on the CT image containing the tip of a needle because the reconstruction volumes for that CT slice do not fully contain the tip of the needle. To estimate the difference, we added 1 mm to or subtracted 1 mm from the coordinate depending on the size of the black dot. We used the center of gravity of the 3 markers as a reference. We omitted the marker if we found the marker migration of more than 1 CT slice (> 3 mm). Five of 90 markers (6%) were migrated more than 3 mm during treatment (data not shown) and the other two markers were used for this study. We calculated the distance between the tip of the needle and the center of gravity (Fig. 1). A positive value indicated that the needle displaced caudally, and a negative value indicated that the needle displacement cranially.

After calculation, we altered the treatment plan based on...
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the displacement distance. We changed the value of each needle applicator length to the value of initial length plus or minus the displacement value. This moved dwell positions of the treatment source parallel to the needle applicator in order to treat the same position as that on the implanted day. Displacement of less than or equal to 3 mm was disregarded because the section thickness of the CT image was 3 mm. This adjustment was possible because we implanted the applicators deeper than the CTV. Correction was performed for the third, fifth, and seventh fractions only because we performed CT imaging and evaluation of the displacement after the second, fourth, and sixth fractions. The time between CT imaging and next treatment was 6–7 hours.

**Analysis**

Dose–volume analysis was performed using a dose–volume histogram (DVH) and the doses that covered 90% and 100% of CTV (D90(CTV) and D100(CTV)) were calculated. We used CT data obtained on the day of implantation for DVH calculation because CTV obtained on that day was determined by CT and MRI, whereas CT data obtained on the other days was determined by only CT without MRI. And so, we used CT on the other days only for measuring displacement distance in this analysis and input these data into the CT taken on the day of implantation.

Statistical calculations were performed using StatView and results of daily displacements were compared. *p*-values were obtained for multiple comparisons using the t-test. A value of *p* < 0.05 was considered statistically significant.

**RESULTS**

The mean displacement distance for all applicators was $4.3 \pm 3.4$ mm (range: −9–15 mm), $4.6 \pm 4.1$ mm (range: −8–18 mm) at 21, 45, and 69 hours, respectively (Fig. 2). A statistically significant difference was observed between all treatment periods. The *p*-value was 0.009 between 21 and 45 hours and the *p*-values between every other period were < 0.0001.

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Absolute values of the mean displacement distance for 30 patients were $4.3 \pm 2.5$ mm (range: 0.3–10 mm), $4.9 \pm 2.8$ mm (range: 0.2–9.9 mm) and $6.0 \pm 3.3$ mm (range: 0.2–12.9 mm) for 21, 45, and 69 hours, respectively. The $p$-value was 0.06 between 21 and 45 hours and the $p$-values between every other period were $< 0.001$.

The time dependency of the displacement was also investigated. We divided displacements into 4 patterns depending on the extent of daily change in the displacement. A mean displacement of less than 3 mm in all treatment durations was observed in 6 of 30 patients (20%; no change type). Twenty of 30 patients (67%; 21 hours type) showed the largest displacement within the first 21 hours. Two patients (7%; 45 hours type) showed the largest displacement between 21 and 45 hours and 2 patients (7%; 69 hours type) showed the largest displacement between 45 and 69 hours (Fig. 3). Therefore, most of the displacement occurred within the first 21 hours and it gradually increased until at least 69 hours.

The DVH values with or without corrective action were investigated. D90(CTV) with or without corrective action is shown in (Fig. 4a). The relative D90(CTV) values compared with the initial treatment plan were $1.01 \pm 0.02$, $1.01 \pm 0.03$ and $1.01 \pm 0.03$ at 21, 45 and 69 hours. The relative D90(CTV) values with corrective action were $1.01 \pm 0.01$, $1.01 \pm 0.01$ and $1.01 \pm 0.01$ at 21, 45 and 69 hours. No significant difference was observed between both values.

D100(CTV) with or without corrective action is shown in (Fig. 4b). The relative D100(CTV) values compared with the initial treatment plan were $0.96 \pm 0.08$, $0.96 \pm 0.08$ and $0.94 \pm 0.1$ at 21, 45 and 69 hours. The relative D100(CTV) values with corrective action were $1.01 \pm 0.06$, $0.99 \pm 0.02$ and $0.99 \pm 0.03$ at 21, 45 and 69 hours. Significant difference was observed between both values ($p = 0.004, 0.003$ and 0.001 for 21, 45 and 69 hours).

**DISCUSSION**

HDR-ISBT has an advantage of high dose conformity and our study has attempted to prove the effectiveness of HDR-ISBT. However, needle applicator displacement is still a major problem in multifractionated treatments. In a previous study, we had investigated this problem using a CT method and our results showed a median displacement of 7 mm for 776 applicators (64 patients) after 3 days during prostate HDR-ISBT. However, it was time-consuming method (60–120 minutes) and it seems to be difficult for clinical use. In this study, we changed our calculation method from a time-consuming three-axis method to a simple one-axis method and undertook daily CT examinations. And our preceding experiment showed that only 11 of 249 patients (4%) showed more than 3 mm difference between two methods (data not shown). One-axis method was done about 20 minutes and it was considered better. The mean result for the current study was 6.2 mm after 69 hours and this was almost...
the same as our first report.

There are some earlier studies regarding needle displacement using the following 2 methods: fluoroscopy and CT. Although the fluoroscopic method\(^2,22\) begins earlier, displacement may be misread because pelvic flexion and rotation can significantly magnify the distance of catheter movement on an X-ray film. In addition, it can be difficult to verify whether the movement was a result of catheter or prostate movement during the fluoroscopic method. Therefore, the CT method could possibly be a superior method for correction of needle displacement.\(^{11-18}\)

Using the CT method, Hoskin \textit{et al.} reported that the mean interfraction catheter movement was 11.5 mm (range: 0–42 mm)\(^{11}\) and Kim \textit{et al.} reported a mean interfraction catheter movement of 5.5 mm (range: −3.8–8 mm) using a non-ambulatory technique.\(^{13}\) Compared with these reports, our results seem to lie within an acceptable range. Therefore, we can conclude that our ambulatory technique produced similar results to the non-ambulatory technique.

Mullokandov \textit{et al.} reported that needle displacement occurs in a time-dependent fashion (2 mm before the second fraction, 8 mm before the third fraction, and 10 mm before the fourth fraction).\(^{12}\) Simnor \textit{et al.} reported that the mean interfraction catheter movement relative to the prostate is 7.9 mm for the second fraction (about 21 hours after first fraction imaging) and 3.9 mm for the third fraction (about 28 hours after first fraction imaging).\(^{15}\) More than 70% of all catheters had moved 5 mm or more at fraction 2 and more than 35% at fraction 3. From these results, almost displacement was seen within first 24 hours, which concurred with our results. The mean catheter movement relative to the prostate was 4.3 mm for about 21 hours, 4.6 mm for about 45 hours, and 5.8 mm for about 69 hours. Twenty of 30 patients (67%) showed the largest displacement within the first 21 hours. Two patients (7%) showed the largest displacement between 21 to 45 hours, and 2 patients (7%) between 45 and 69 hours. Therefore, most of the displacement occurred within the first 24 hours and it gradually increased until at least 69 hours.

Hoskin \textit{et al.} identified 3 possible causes for applicator displacement during prostate brachytherapy.\(^{13}\) The first cause was template movement, the second internal prostate movement, and the third tissue edema between the prostate apex and the perineum. Kim \textit{et al.} also reported similar possible causes for displacement as follows: 1) CT slice thickness (reading error of the applicator tip), 2) CT slice thickness (reading error of the marker seeds), 3) migration of the marker seeds, 4) organ and patient movement, 5) error generated from the slanting angle of the catheters, and 6) observer error.\(^{13}\) In regard to CT slice thickness, we used thickness of 3 mm and pitch of 3 mm. Kim \textit{et al.} reported that thickness of 3 mm appeared to be a good compromise showing an acceptable average dose uncertainty of 1% without unduly increasing the number of slices.\(^{21}\)

To resolve these problems, corrective action for the treatment position of the applicator should be implemented. In prostate brachytherapy, many authors have reported an improvement in DVHs\(^{11,12,15-18}\) using corrective action. Simnor \textit{et al.} took CT images before every treatment session and performed the one of following types of corrective action: 1) shifting the dwell positions distally relative to the extent of catheter displacement or 2) physical re-advancement of the catheter\(^{15}\) when the displacement value was more than 5 mm. They improved the D90% value from −27.7 ± 22.8% (without correction) to −5.32 ± 6.6% (with correction). Their correction method was similar to ours and it implies similar effort on this study. In this study, the relative D100(CTV) values compared with the initial treatment plan reduced to 0.96 ± 0.08, 0.96 ± 0.08 and 0.94 ± 0.1 at 21, 45 and 69 hours. Corrective action improved these values to adequate levels (1.01 ± 0.06, 0.99 ± 0.02 and 0.99 ± 0.03 at 21, 45 and 69 hours). However, D90(CTV) values did not reduce (1.01 ± 0.02, 1.01 ± 0.03 and 1.01 ± 0.03 at 21, 45 and 69 hours) and keep acceptable level. We considered that 15 mm of cranial margin was effective to keep stable level for D90(CTV) without corrective action. We also considered that corrective action will reduce the length of cranial margin.

Additional CT scanning and corrective actions for all treatment fractions could improve treatment conformity even further. However, there will be an opposing view to this ideal conformal brachytherapy system. It may be difficult to take CT twice a day for all brachytherapy patients because of manpower constraint for many institutes. In this study, almost patients (87%; 20% for no change type and 67% for 21 hours type) showed the largest displacement within the first 21 hours. And so, we recommend that CT scanning and corrective action should be performed at 21 hours after initial planning CT if we can help but reduce the frequency of CT scanning. Further investigation is needed, including DVH calculation with a longer follow-up period, to confirm the improvement of clinical outcomes.

In summary, our investigation into needle applicator displacement using daily CT examination showed that majority of the displacement occurred within the first 21 hours after initial CT imaging and gradually increased until at least 69 hours. Cranial margin of 15 mm seems to be necessary if we do not do corrective action. With corrective action, we will reduce the cranial margin and expect that the clinical result using our ambulatory technique will improve.

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