Intracavitary Combined with CT-guided Interstitial Brachytherapy for Locally Advanced Uterine Cervical Cancer: Introduction of the Technique and a Case Presentation

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Interstitial brachytherapy/Cervical cancer/Radiotherapy/CT-guided brachytherapy/Intracavitary brachytherapy.

We report a new technique of brachytherapy consisting of intracavitary combined with computed tomography (CT)-guided interstitial brachytherapy for locally advanced cervical cancer. A Fletcher-Suit applicator and trocar point needles were used for performing high-dose rate brachytherapy under in-room CT guidance. First, a tandem and ovoids were implanted into the patient’s vagina and uterus by conventional brachytherapy method. Based on clinical examination and MRI/CT imaging, operating radiation oncologists decided the positions of insertion in the tumor and the depth of the needles from the upper surface of the ovoid. Insertion of the needle applicator was performed from the vaginal vault inside the ovoid within the tumor under CT guidance. In treatment planning, dwell positions and time adaptations within the tandem and ovoids were performed first for optimization based on the Manchester system, and then stepwise addition of dwell positions within the needle was continued. Finally, dwell positions and dwell weights were manually modified until dose-volume constraints were optimally matched. In our pilot case, the dose of D90 to high-risk clinical target volume was improved from 3.5 Gy to 6.1 Gy by using our hybrid method on the dose-volume histogram. D1cc of the rectum, bladder and sigmoid colon by our hybrid method was 4.8 Gy, 6.4 Gy and 3.5 Gy, respectively. This method consists of advanced image-guided brachytherapy that can be performed safely and accurately. This approach has the potential of increasing target coverage, treated volume, and total dose without increasing the dose to organs at risk.

INTRODUCTION

The combination of external beam radiotherapy (RT) and intracavitary brachytherapy (ICBT) is a standard treatment technique of RT for uterine cervical cancer, and concomitant chemotherapy is combined for locally advanced cases.1–5) ICBT plays an important role because the brachytherapy system allows a much higher dose to the cervix while sparing adjacent bladder and bowels. Local control rates of cervical cancer have been reported at 80–90% for early stages.6–8) However, those for advanced stages show a range of 67–75% and further improvement is needed.4,5,9) One of the reasons for local failure is inadequate dose coverage to bulky and/or irregular-shape tumors. In order to realize adequate dose coverage to cervical tumors, intracavitary combined with computed tomography (CT)-guided interstitial brachytherapy was developed at Gunma University. We introduce the new technique of hybrid-brachytherapy with a pilot case.

PATIENT

The patient was a 53-year-old woman with stage IIIB squamous cell carcinoma of the uterine cervix according to the International Federation of Gynecology and Obstetrics (FIGO) staging system.10) On image diagnosis, CT detected a bulky tumor at the uterine cervix with left hydronephrosis. MRI before treatment revealed a cervical mass measuring 60 × 58 × 70 mm3. The tumor extension reaching the pelvic side-wall before RT still existed at the time of brachytherapy (Fig. 1).

The patient was treated with a combination of external...
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beam RT and high-dose rate (HDR) brachytherapy. She did not receive concurrent chemotherapy because of renal dysfunction. External irradiation to the whole pelvis was performed with antero-posterior and postero-anterior parallel-opposed ports with a total dose of 30 Gy at 2 Gy per fraction, 5 times per week. This was followed by a central shielding pelvis field up to a total pelvis irradiation dose of 50 Gy at 2 Gy per fraction, 5 times per week. Along with the central shielding irradiation, she was given HDR brachytherapy by HDR-remote afterloading system (RALS) 5 times using an iridium-192 source. In the first three sessions, she received ICBT without interstitial brachytherapy administered once per week at fraction doses of 7.5, 7 and 7 Gy at Point A, with a total dose of 21.5 Gy. In the remaining two sessions, the hybrid method was used because the tumor showed poor response to radiotherapy. Written informed consent was obtained from the patient before this brachytherapy.

METHODS

In-Room CT Imaging

Brachytherapy was delivered in our unit, comprising HDR-RALS (microSelectron HDR; Nucletron, The Netherlands) coupled to a CT scanner and X-ray imager sharing a common couch. The couch rotates 230° at the CT-scanning position or 50° at the X-ray imaging position. During CT scanning, the gantry moves along rails on the floor while the table remains stationary. Applicators are implanted into the patient’s vagina and uterus on the couch, and all processes including application, imaging, and irradiation can be performed on the same couch using the in-room CT brachytherapy system.11,12

Brachytherapy application

A set of Fletcher-Suit Asian Pacific applicator (tandem and half-size ovoids) and trocar point needles (Nucletron) was used. This hybrid application was done without general anesthesia or spinal anesthesia. The tandem and ovoids were implanted into the vagina and uterus by the procedure of conventional brachytherapy. After implantation, CT scans were generated on the same couch at 3-mm slice thickness. Magnetic resonance images (MRI) were taken before brachytherapy and used as reference images of the tumor. Based on clinical examination and MRI/CT imaging, operating radiation oncologists decided the positions of insertion in the tumor and the depth of the needles from the upper surface of the ovoid.

The CT-guided insertion of the needle applicator was performed along the inside of the half-size ovoid into the tumor (Fig. 2). After tumor location and needle position were confirmed, anterior and posterior vaginal packing was done in a manner similar to the non-interstitial procedure. CT scans were generated again and used for treatment planning. Then, X-ray images were also taken in the same position while rotating the couch. After completion of irradiation, the applicator was removed in the order of tandem and ovoids, followed by the needles.

Treatment Planning

The applicator geometry was digitized, reconstructed and registered to the X-ray and CT images. Image registration was performed with the evaluation module of the PLATO Brachytherapy Planning System v14.3.6 (Nucletron).

The current brachytherapy planning process starts with a conventional pattern for tandem and ovoids planning based on the Manchester system. Point A was defined on the X-ray as being 2 cm superior to the external os, and 2 cm lateral from the axis of the intrauterine tandem. At first, the dose of point A at the opposite side of needle placement was normalized to 6 Gy. A dwell position and time adaptation were established first to optimize the initial standard dose distribution, and then continued with 2.5-mm stepwise additions as dwell positions within the needle. Dose distribution by the resulting treatment plan was confirmed on CT images for the high-risk clinical target volume (HRCTV), which is

Fig. 1. MRI images before treatment and after 30 Gy.

Fig. 2. X-ray photographs of needle placement after implantation of a tandem and ovoids.
defined as the parameter of ICBT in the GYN GEC ESTRO recommendation and for organs at risks (OARs) such as bladder, rectum and sigmoid colon.\textsuperscript{13,14} HRCTV, which is a major risk for local recurrence because of residual macroscopic disease, is defined as the whole cervix and the presumed extracervical tumor extension at the time of brachytherapy. Certain dose coverage values can be defined to describe the specific shape of such a dose-volume histogram (DVH), e.g. D100 and D90, defining the minimum dose delivered to 100 and 90% of the volume of interest, respectively. The OARs were contoured using the external wall contours. Cumulative DVHs were calculated for delineated organs of bladder, rectum and sigmoid colon, and the following parameters were reported: absolute volume and minimum dose to the most irradiated 0.1, 1, 2 cm\textsuperscript{3} (D0.1 cc, D1 cc, D2 cc, respectively).\textsuperscript{13,14}

Dwell positions and dwell weights in the tandem, ovoids and needles were manually modified until the dose distribution was optimally matched to cover HRCTV with a 6-Gy isodose line as much as possible. This planning was com-
pared with conventional ICBT planning without interstitial needle by using DVH parameters for HRCTV and OARs. In conventional ICBT planning, the same source arrangement and irradiation conditions are used, and the dose distribution was based on the Manchester system. The prescribed dose was generated by the PLATO treatment planning system (TPS) with a dose of 6 Gy normalized to point A.

**RESULTS**

*Dose distribution and dose volume histogram*

Figures 3 and 4 show dose distributions and DVHs by our hybrid method and conventional ICBT. D90 to HRCTV by this hybrid method and conventional ICBT were 6.1 Gy and 3.5 Gy, respectively. D1cc of the rectum, bladder and sigmoid colon by this hybrid method were 4.8 Gy, 6.4 Gy and 3.5 Gy, respectively, whereas they were 5.7 Gy, 6.3 Gy and 3.4 Gy by conventional brachytherapy (Table 1, Fig. 4).

**Table 1.** Dose of HRCTV, Rectum, Bladder and Sigmoid Colon.

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<tr>
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<th>Conventional brachytherapy</th>
<th>Our hybrid-brachytherapy</th>
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<tbody>
<tr>
<td>HRCTV D100</td>
<td>1.9 Gy</td>
<td>3.4 Gy</td>
</tr>
<tr>
<td>D90</td>
<td>3.5 Gy</td>
<td>6.1 Gy</td>
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<tr>
<td>Rectum D0.1cc</td>
<td>5.8 Gy</td>
<td>6.7 Gy</td>
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<tr>
<td>D1cc</td>
<td>4.8 Gy</td>
<td>5.7 Gy</td>
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<tr>
<td>D2cc</td>
<td>4.4 Gy</td>
<td>5.2 Gy</td>
</tr>
<tr>
<td>Bladder D0.1cc</td>
<td>8.0 Gy</td>
<td>8.0 Gy</td>
</tr>
<tr>
<td>D1cc</td>
<td>6.4 Gy</td>
<td>6.3 Gy</td>
</tr>
<tr>
<td>D2cc</td>
<td>5.8 Gy</td>
<td>5.8 Gy</td>
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<tr>
<td>Sigmoid colon</td>
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<tr>
<td>D0.1cc</td>
<td>4.5 Gy</td>
<td>4.3 Gy</td>
</tr>
<tr>
<td>D1cc</td>
<td>3.5 Gy</td>
<td>3.4 Gy</td>
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<tr>
<td>D2cc</td>
<td>3.2 Gy</td>
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_Treatment Outcome_

At 12 months after treatment, the tumor in the left parametrium had disappeared almost completely according to pelvic MRI findings. Serum levels of squamous cell carcinoma antigen and cytokeratin fragment 21-1 were reduced to 1.1 ng/ml and 3.3 ng/ml from 2.6 ng/ml and 7.6 ng/ml, respectively. No recurrent lesions and distant metastases were detected at 18 months after the treatment, and she did not experience grade 2 or higher late morbidity.

**DISCUSSION**

When bulky and/or irregular-shape cervical cancer is treated with brachytherapy, using increments of the prescribed dose at the reference point is one of the approaches. However, such increments may result in increasing doses to surrounding normal tissues including the bladder, rectum, and small intestine. In recent years, Japanese researchers reported the correlation of rectal bleeding with the dose-volume parameter of rectum in patients with cervical cancer.15,16) Isohashi et al. reported that the mean biologically equivalent dose in 2-Gy fraction (EQD2) of rectum D1cc for patients with and without rectal bleeding was 76 Gy and 98 Gy, respectively, and there was a significant greater rectal bleeding risk for the high EQD2 group ($\geq 82$ Gy of D1cc rectum).15 In the current case, EQD2 of rectum D1cc was 79.9 Gy, which was calculated as the linear quadratic model for incomplete sublethal damage repair. If the dose prescription at point A could be increased by conventional ICBT until the dose of D90 for HRCTV reached 6 Gy, D1cc of the rectum would increase from 4.8 Gy to 8.2 Gy, and EQD2 of rectum D1cc would increase to 96.8 Gy. This method was able to increase the HRCTV dose while keeping the rectum dose at tolerable levels even in the case of bulky and/or irregular-shape cervical cancer. In the present case, primary tumor was well controlled without severe toxicities. However, further follow-up will be needed to confirm long-term efficacy and toxicities.

Historically, interstitial brachytherapy was performed with free hand-placement, and ultrasound-guided, CT-guided and template-guided needles for locally advanced tumor.17–21) To date, transperineal template techniques were the most commonly used methods for interstitial treatment in such cases. However, these techniques have difficulties in achieving accurate positioning of the implant and good parallelism of the needles. In addition, using these methods, the applicators have to be left in place for a few days after implantation. On the other hand, a major part of the procedure in the current hybrid method is derived from conventional brachytherapy. In-room CT-guided insertion of the interstitial needle could be performed after implantation of the Fletcher-Suit applicator. Furthermore, because this insertion is done for each brachytherapy session, the applicators do not need to be left in place. Therefore, this hybrid method is a non-complicated technique and is safe for patients compared with previous methods.

Considering the risk of perforation of the sigmoid colon or intestine, accurate positioning of the needle in interstitial brachytherapy is very important. Several researchers have reported achieving accurate positioning and avoiding perforation by several methods.17–21 With the present hybrid method, CT-guided insertion is performed after implantation of tandem and ovoid applicators. In addition, an in-room CT system is used for the current method. This system enabled implantation of the applicator, CT-guided placement of the needle and irradiation by RALS to be performed on the same couch. Movement of the applicator and needle can be min-
imized during implantation, planning and irradiation. Because of the CT-guided insertion and in-room system, accurate positioning and safe insertion can be achieved with this hybrid method.

Dimopoulos et al. and Kirisits et al. reported a similar technique of intracavitary and interstitial brachytherapy that uses a modified tandem-ring applicator for cervical cancer at Vienna University.22,23 In their method, needles are inserted through holes in the tandem-ring applicator. As it is limited to moderate lateral expansion of the HRCTV, for cases with involvement up to the pelvic wall, additional interstitial needles are required. Their method was also accurate and safe, based on an MRI-guided approach. However, the Vienna ring applicator is not commercially available, and in Japan the most common type of applicator is the Fletcher-Suit Asian Pacific applicator. In our hybrid method, similar to the Vienna ring applicator, needles can be placed in the tumor located at the posterior parametrium with high flexibility. The current technique of brachytherapy should be further investigated to confirm its safety and efficacy.

REFERENCES


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