Interstial Brachytherapy Using Virtual Planning and Doppler Transrectal Ultrasonography Guidance for Internal Iliac Lymph Node Metastasis

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To expand the indications for high-dose-rate interstitial brachytherapy (HDR-ISBT) for deep-seated pelvic tumors, we investigated the usefulness of Doppler transrectal ultrasonography (TRUS) guidance and virtual planning. The patient was a 36-year-old female. She had right internal iliac lymph node oligometastasis of vaginal cancer 12 months after radical radiotherapy. The tumor could not be found by gray-scale TRUS and physical examination. Virtual planning was performed using computed tomography with template and vaginal cylinder insertion. We uploaded the images to our treatment planning software and reconstructed the contours of the clinical target volume (CTV) and right internal iliac vessel. Virtual needle applicators were plotted using the template holes for virtual planning. At the time of implantation, Doppler TRUS was used to prevent vessel injury by needle applicators. Applicators were implanted in accordance with virtual planning and Doppler TRUS could detect the right iliac vessel. The percentage of CTV covered by the prescribed dose was 99.8%. The minimum dose received by the maximally irradiated 0.1-cc volume for the right internal iliac vessel was 95% prescribed dose. Complete response was achieved, however, radiological findings showed marginal recurrence at 15 months after HDR-ISBT. Post-radiation neuropathy occurred as a late complication four months after treatment; however, the pain was well controlled by medication. We consider that virtual planning and Doppler TRUS are effective methods in cases where it is difficult to detect the tumor by physical examination and gray-scale TRUS, thereby expanding the indications for ISBT.

INTRODUCTION

Interstitial brachytherapy (ISBT) for pelvic malignancy is a useful method with potential for use as a curative treatment modality. However, deep-seated tumors such as those in internal iliac lymph nodes are not good candidates for ISBT because of the difficulty in inspecting and palpating such tumors. Recently, transrectal ultrasonography (TRUS) has been incorporated into ISBT, thereby enabling us to treat deep-seated tumors. However, it is sometimes difficult to visualize deep-seated tumors by TRUS because bowel contents may degrade the image quality.

We present a case report in which these obstacles were overcome. First, Doppler TRUS could detect the tumor at implantation when the tumor could not be visualized via gray-scale TRUS before implantation. Then, virtual planning enabled us to identify the relationship between the tumor locations and implantation points in template holes. These devices assisted in precise implantation of needle applicators without any major complications.
MATERIALS AND METHODS

Patient characteristics

The patient was a 36-year-old female. She had a vaginal cancer categorized as cT3N1M0 using UICC classification of 2009. The right internal iliac lymph node was swollen. A biopsy of the primary lesion was performed and histological findings confirmed squamous cell carcinoma. She received combined external beam radiotherapy (EBRT) and high-dose-rate (HDR) ISBT with concurrent chemotherapy (nedaplatin) from January to February 2009. EBRT was performed at Kaizuka City Hospital and the treatment doses were 30 Gy in 15 fractions for the whole pelvis, 20 Gy in 10 fractions for center-shielded EBRT, and 10 Gy in 5 fractions for right internal iliac lymph node metastasis. HDR-ISBT was administered to the primary site (30 Gy in 5 fractions).

The primary tumor was controlled until this point; however, the right internal iliac lymph node metastasis showed regrowth 12 months after the first treatment. She complained of right hip and leg pain. The recurrent node had a maximum diameter of 16 mm and positron emission tomography (PET) showed positive uptake. The tumor marker (SCC) value was elevated to 1.6 despite the nadir value being 0.8 after the first therapy.

Virtual planning

Preplanning was performed after template insertion with a vaginal cylinder. We used a modified acryl template used for the prostate (Taisei medical, Osaka, Japan), with a custom-made vaginal cylinder and button stopper (Fig. 1). Because cylinder is positioned in a direction perpendicular to the template, applicators could be implanted parallel to the template holes.

We obtained computed tomography (CT) images and uploaded these images to our treatment planning software (Oncentra® Brachy; Nucletron B.V., Veenendaal, The Netherlands). We reconstructed the contours of the gross tumor volume as the clinical target volume (CTV), the vessel near the tumor as the organ at risk, and the pelvic bone (Fig. 2a). We also obtained the contour of the template and vaginal cylinder.

![Fig. 1.](image1) Template and vaginal cylinder. We used an acryl template (Taisei medical, Osaka, Japan), used for the prostate. The vaginal cylinder (light blue) was made of silicone and fixed to the template by a red button.

![Fig. 2a.](image2) CT images uploaded to the treatment planning software. The contours of the gross tumor volume as clinical target volume (purple), right internal iliac vessel (red) as organ at risk, and pelvic bone (white) are reconstructed from the CT images. The contour of the template (green) and vaginal cylinder (light blue) is also reconstructed. Virtual applicators are also plotted (blue).

![Fig. 2b.](image3) Virtual dose distribution curve. Fifty to 200% prescribed doses are shown (blue solid line = 50%, white dotted line = 100%, orange solid line = 150%, and white solid line = 200%). The clinical target volume (red) could be covered by the isodose curve of the prescribed doses (white dotted line) without excessive doses to the right internal iliac vessel (black dotted line).
Next, we plotted template holes as applicator points on both edges of the perineal skin side (cranial side) and the opposite side (caudal side). After plotting, Oncentra® Brachy indicated the applicator points by showing the expected coordinates of these points. Using this function, we plotted the virtual applicator points in the patient’s body. We selected the most suitable template holes for implantation and plotted each of the apex points of the applicators as if they were actual implantation points.

Finally, we performed treatment planning. We selected adequate dwell positions and plotted an isodose curve to deliver the prescribed doses for CTV without excessive doses to the vessel near the tumor (Fig. 2b).

**Applicator implantation**

Applicator implantation was performed in the operating

![Fig. 3a. Transrectal ultrasonography showing the tumor lesion as a low echoic area (arrows).](image)

![Fig. 3b. Transrectal ultrasonography showing the applicators into or around the tumor as high echoic areas (arrow heads). The color Doppler function shows two vessel flows near the tumor.](image)

![Fig. 3c. Transrectal ultrasonography after implantation. A three-plane implant was performed.](image)

![Fig. 4. Actual dose distribution curve. Fifty to 200% prescribed doses are shown (outer green solid line = 50%, outer yellow solid line = 70%, light blue solid line = 80%, blue solid line = 90%, white dotted line = 100%, white solid line = 120%, pink solid line = 130%, inner green solid line = 150%, and inner yellow solid line = 200%). The clinical target volume (red line) is well covered by the isodose curve of the prescribed doses. The minimum dose received by the maximally irradiated 0.1-cc volume and the maximum dose for the right internal iliac vessel (black dotted line) was 5.7 Gy and 7.3 Gy, respectively.](image)
Virtual Planning and Doppler Ultrasonography

The implantation was monitored by TRUS with a color Doppler function (Prosound α-7®; ALOKA Co. Ltd., Tokyo, Japan). We inserted the template–cylinder complex the same way as for preplanning.

First, we carefully implanted a flexible needle applicator (ProGuide Sharp Needle®; Nucletron B.V., Veenendaal, The Netherlands). We monitored the applicator point by TRUS. We moved the TRUS probe cranially and monitored the expected applicator position before the actual applicator tip reached the position to prevent large vessel injury. Large vessels were clearly observed using the color Doppler function. We also monitored the expected applicator implantation point to acquire the tumor image. At the calculated depth from the perineal skin where the applicator would reach the tumor lesion, we found a low echoic area (Fig. 3a). We also visualized the vessel near the tumor using the color Doppler function. This finding seemed consistent with the CT/magnetic resonance imaging (MRI) findings before implantation, and hence, we surmised that the low echoic area must be a recurrent tumor.

Next, we pushed the applicator deeply and stopped when we felt hard resistance; the length of the inserted applicator at this time was the same as the distance between the perineal skin and pelvic bone measured at the time of virtual planning. On the basis of these findings, we were convinced that our virtual planning was very effective in terms of a successful first needle applicator implantation. Using the same procedure, we implanted a total of 10 applicators with color Doppler guidance (Fig. 3b, c).

After implantation, we extracted the template–cylinder complex and only the applicators were rested on the patient’s perineal skin. For treatment planning, CT and MRI were performed. CT-based planning was performed using MRI as a reference to contour CTV. The CTV was delineated with the assistance of axial T2-weighted MR images. We determined dwell positions of the treatment source to cover the CTV and used an additional 15-mm cranial margin for needle displacement except when the applicator tip was stopped by the pelvic bone before an extra implantation of 15 mm.

Treatment planning was performed using the PLATO® planning system (version 14.2; Nucletron B.V., Veenendaal, The Netherlands) and Oncentra® Brachy with manual modification. We used microSelectron-HDR® (Nucletron B.V., Veenendaal, The Netherlands) with a 192Ir source for treatment.

RESULTS AND DISCUSSION

CT and MRI revealed that the applicators displaced slightly laterally compared with virtual planning. However, we could deliver the prescribed doses to CTV after computer optimization with manual modification (Fig. 4). The right internal iliac vessel near CTV could not be visualized by CT; however, MRI could detect the vessel and was useful for planning (Fig. 5). We administered 48 Gy in 8 fractions as the prescribed dose, in accordance with our protocol. The percentage of CTV covered by the prescribed dose (V100) was 99.8%. The minimum dose received by the maximally irradiated 0.1-cc volume and the maximum dose for the right internal iliac vessel was 5.7 Gy (95% prescribed dose) and 7.3 Gy (122% prescribed dose), respectively.

Treatment was completed without any difficulty. The patient complained of additional perineal and right lower leg pain because of the implant. This pain was controlled by epidural anesthesia and non-steroidal anti-inflammatory drug. After treatment was completed, the pain was reduced; however, the pain caused by the tumor and/or implant continued.

The tumor marker value decreased from 1.6 to 0.6 at three months after ISBT. PET showed complete response at 11 months after ISBT. However, radiological findings showed marginal recurrence at 15 months after ISBT. Post-radiation neuropathy occurred as a late complication four months after treatment and the patient of complained of increased right leg pain. She was admitted for pain control and was prescribed fentanyl (2.1 mg; Durotep® Patch).

Deep-seated pelvic tumors are a challenge for adequate implantation, even with image guidance. Although TRUS is often used for gynecological ISBT, it was rarely indicated for deep-seated pelvic tumors like the present case. Usually implantation is performed in centrally located regions such as the uterus, vagina, or cervical stump, and pelvic sidewall and lymph node lesions are not suitable for implantation. One of the reasons for this is because detecting tumor lesions by TRUS and physical examination is difficult, especially in the case of lymph node metastasis.

Heneghan JP et al. demonstrated that color flow imaging and pulsed Doppler imaging provide additional useful infor-
mation to gray-scale TRUS in staging primary rectal cancer. However, there are few reports for gynecological cancer. We have applied Doppler TRUS, which clearly visualized the vessel near the tumor. Doppler TRUS was very useful not only for detecting the tumor but also for avoiding vessel injury by virtue of precise implantation guidance. We consider that Doppler TRUS guidance has potential for use in ISBT, especially for tumors near large vessels.

Another important aspect in the treatment of our patient was virtual planning. Virtual planning for pelvic tumors has been reported by Eisburch et al. who used custom-made plastic templates attached to the perineum through which a cylindrical plastic vaginal obturator was inserted. They then loaded the entire set of CT images into the treatment planning system. CTV, organs at risk, and the vaginal cylinder were contoured on each axial CT slice and displayed as three-dimensional structures. The authors provided a "cylinder’s eye view," which is the view of the anatomy as seen from the external end of the vaginal cylinder looking down the long axis of the cylinder. The implantation points were decided on the basis of the cylinder’s eye view. Because applicators were implanted parallel to the cylinder, cylinder’s eye view is very useful for the physician to select adequate implantation points. They decided the optimal angles for unimpeded view of the tumor and adequate needle depth to cover the tumor. They achieved a good local control rate (55%).

However, there is a shortcoming in this report of Eisburch et al. They did not perform MRI. We performed MRI-assisted image-based treatment for previously gynecological ISBT. Because the usage of a removable template, we could achieve MRI-assisted image-based treatment and it will leads to good treatment conformity. The dose–volume histogram findings were satisfactory. V100 was 99.8% and the CTV was almost covered by the prescribed doses. However, unfortunately, marginal recurrence was occurred at 15 months after ISBT. No consensus was achieved about the dose–volume relationship for the organs at risk, especially, in the case of reirradiation. This aspect will be deliberated upon in further studies.

We consider that virtual planning and Doppler TRUS have a possibility to become an effective method in cases where it is difficult to detect the tumor by physical examination and gray-scale TRUS, thereby expanding the indications for ISBT.

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