Role and benefits of intraoperative ultrasound guidance in intracavitary brachytherapy for cervical cancer

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Purpose

Cervical cancer is a major world health problem and it is the fourth most common cancer in women worldwide, with 85% of cases occurring in developing countries, where cervical cancer is a leading cause of cancer death in women [1-3]. The standard treatment for locally advanced cervical cancer (stages IB2 to IVA) is external beam radiation therapy with concurrent chemotherapy followed by brachytherapy (NCCN). Intracavitary brachytherapy facilitates a high radiation dose to cervical cancer with relative sparing of normal tissues and is an integral component of definitive radiation for this disease [4]. In intracavitary brachytherapy, an applicator (a uterine tandem and vaginal ovoids or a ring) is placed in the uterine cavity and vaginal fornices under sedation or anesthesia through the cervical os; this is often done "blindly" by advancing the tandem until sensing the uterine fundus. Intraoperative complications of brachytherapy include vaginal lacerations, penetration of the tandem into the uterine wall and perforation of the uterus and other pelvic organs with the applicator [5]. Proper placement is critical to the success of brachytherapy: inadequate geometry has been correlated with significantly impaired local control and operative complications if unrecognized can result in inappropriately high radiation doses to organs at risk [4]. Applicator placement can be technically challenging and one technique for real time verification of tandem position is intraoperative ultrasonography. Data suggest that the routine use of intraoperative ultrasonography facilitates ideal tandem placement and decreases the risk of uterine perforation, thereby diminishing an underappreciated source of toxicity while optimizing disease control [4].

In this study, we aimed to describe the role and benefits of intraoperative ultrasound guidance in intracavitary brachytherapy in an attempt to minimize the risk of complications.
Methods and materials

The clinical and radiologic data of 142 patients who received tandem-based intracavitary brachytherapy after external beam pelvic radiotherapy at the Acibadem Adana Hospital between January 2010 and June 2015 were retrospectively reviewed. Within our hospital, cervical cancer patients are generally treated with external beam pelvic radiotherapy (45-50.4 Gy) followed by high dose rate tandem-based intracavitary brachytherapy with curative intent. The whole brachytherapy procedures were performed in a brachytherapy suite with dedicated and specialized staff, including registered nurses and physicists, together with the attending radiation oncologist and radiologist. In addition, members of the anesthesia staff were available to assist as needed in the brachytherapy suite. The procedures were performed under sedation using 3 to 5 mg midazolam followed by 50 mcg fentanyl and 50 mg ketamine intravenously if needed added doses of ketamine were used, and the applicator were placed in the lithotomy position. Ultrasound guidance was carried out in cooperation with a diagnostic radiologist.

Pre-operative evaluation under anesthesia in our department includes a diagnostic ultrasound to examine uterus, endometrial rim and as well as residual primary tumor and a pelvic examination for identification of the cervical os. A Foley catheter was inserted into the bladder followed by retrograde instillation of 250-300 mL of normal saline into the bladder for better visualization. A diagnostic radiologist proceeds with real-time transabdominal ultrasound imaging. Scans were performed in the sagittal and axial planes, and the length of the endometrial cavity, length of the cervical canal, echo characteristics of the endometrium (hyperechoic or hypoechoic, polyps, myoma, fluid), cervico-uterine angle, uterine anteversion, retroversion and deviation were determined. A Siemens Acuson S2000 portable ultrasound machine was used, with a curved 6.0-MHz ultrasound transducer (Siemens, CA, USA). The cervix was grasped with tenaculum for some patients. The Fletcher-Suit applicator set was used, tandem angle and length are selected based upon the uterine angle and size under ultrasound guidance. The tandem was inserted into the uterine cavity, and optimal position was confirmed using ultrasound imaging in sagittal and axial planes. A sagittal view of the uterus was maintained to assess the suitability of tandem length and angle. Axial view of the uterus was also performed to verify that the tandem was at the midline within the endometrial cavity and not too advanced. Vaginal ovoids were then placed using the maximum possible diameter, the geometry was confirmed before fixation by vaginal packing using radiopaque lubricated gauze to displace the bladder anteriorly and rectum posteriorly. Following the packing, the applicators were controlled for the last time and the ultrasonography was terminated. All patients underwent CT based conformal treatment planning for the delivery of intracavitary brachytherapy.
Results

Between January 2010 and June 2015, 412 insertions for intracavitary brachytherapy was performed under ultrasound guidance in 113 consecutive patients with cervical cancer. Previously, application for 29 patients was done without ultrasound guidance and 2 patients had uterine perforations (6.9%). The patients were treated with 3D conformal brachytherapy and CT imaging was used for treatment planning. After detecting uterine perforations with planning tomography, we decided to perform ultrasound guidance for applicator insertions. Only one of 113 patients after ultrasound guidance had uterine perforation (0.9%). The perforation sites for the patients without ultrasound guidance was anterior and posterior uterine wall, but for the procedure with ultrasound guidance the perforation site was uterine fundus due to a too advanced tandem.

A preliminary pelvic ultrasonography was performed before application at the first fraction in the operative room to assess the uterus (anteversion, retroversion, deviation, myoma et cetera). The tandem curvature was selected based upon the uterine flexion before insertion (Figure 1). The central placement of tandem was confirmed with axial sweeps and length, angle and relation with anterior, posterior and superior walls were confirmed with sagittal sweeps (Figure 2). For optimal positioning, tandem was tracked during procedure with real-time ultrasound guidance. Tandem was repositioned according to the ultrasound visualization, i.e. if short or too advanced, impinging against anterior or posterior myometrium (Figure 3).

The applicators were removed if perforation was detected and patients were treated conservatively. The patients were monitored for at least 24 hours and evaluated with pelvic ultrasound for free fluid or hematoma or any other complications.

All patients underwent treatment planning tomography and applicator suitability and complications like perforation were evaluated with tomography. All planning tomographies were retrospectively reviewed by the radiologist for the optimal tandem placement as well as the uterine characteristics for the study. Of the 142 patients, 132 (93%) had anteverted and 10 (7%) had retroverted uterus (Figure 4). The tandem length was short in two (1.4%) patients, long in four (2.8%) patients and was in myometrium in three (2.1%) patients before ultrasound guidance (Figure 5). The uterus was laterally deviated in 76 (53.5%) patients. No other major complications were seen in our patients.
**Fig. 1:** USG images demonstrating tandem (white arrowheads) selection according to uterine anteversion angle in different patients. Tandem angles are 15°(A) and 45°(B).

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Fig. 2: USG images demonstrating the tandem (white arrowheads) impinging against posterior uterine wall (A), repositioned tandem to the endometrial cavity (white arrow) (B), the tandem impinging against lateral uterine wall (C) and repositioned tandem to the endometrial cavity (curved arrow) (D) corrected by real time USG guidance.

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**Fig. 3:** USG images demonstrating a suboptimal placement of the tandem (white arrowheads) which was short (A) and repositioned tandem to the optimal location (B) corrected by real time USG guidance.

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Fig. 4: Sagittal CT images after brachytherapy confirming appropriate tandem (white arrowhead) placements according to anteversion (A) and retroversion (B) of uterus.

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Fig. 5: MRG images demonstrating suboptimal tandem (white arrowheads) placement in patients before USG guidance; short tandem (A), too advanced tandem (B) and tandem in myometrium (C). B, bladder. U, uterus.

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Conclusion

In this study, we have presented that routine ultrasound guidance during intracavitary brachytherapy for cervical cancer patients may result in appropriate insertion and very low rates of uterine perforation. Previous studies have shown perforation rates ranging from 1.4 to 13.7% [4-9]. Before ultrasound guidance in our patients, our perforation rate was 6.9%, but after ultrasound guidance perforation was detected only in one patient (0.9%). Since perforation may lead to direct trauma to the surrounding organs, such as bladder and intestine, and increases radiation dose to organs at risk, it is important to lower perforation rates. Although we have seen perforation in three patients, there were no bowel or bladder perforation.

The uterine perforation typically occurs in the posterior cervix but it may also occur at the fundus; therefore, a proper understanding of the uterine size, position, and flexion (e.g. anteversion, retroflexion) may be helpful in avoiding such occurrences [10].

In a large series by Schaner et al there were 5 perforations and 3 of them were lateral perforations [4]. Upon review of the ultrasound images, it became evident that although sagittal ultrasound imaging indicated adequate tandem placement, insufficient axial imaging was obtained and effective utilization of ultrasound requires at least 2 axial views, one at the cervix and one at the uterine fundus. When a perforation was diagnosed in our patients on planning CT imaging, the applicators were removed and the patients were treated conservatively. The patients were monitored for a minimum of 24 hours and administered prophylactic antibiotics.

In previous studies, it has been demonstrated that appropriate intracavitary insertions improve pelvic control, survival and decrease toxicity among patients with locally advanced cervical cancer [11, 12]. In our study, the effects of optimal application on local control, survival rates and late complications have not been examined. When brachytherapy applicators are appropriately placed, relatively high paracentral doses can be delivered that yield a high rate of central disease control with an acceptable rate of complications [12]. Several reports have described the use of ultrasound guidance in especially complex applicator placements [13]. Corn et al. used ultrasound in challenging cases such as cervical os stenosis, fibrosis, indeterminate orientation of the endometrial cavity axis, or previous perforation [14]. Mayr et al. demonstrated that the use of ultrasound-guided uterine anteversion for brachytherapy implant placement was feasible and resulted in acceptable outcome and complication rates in a population otherwise difficult to manage and at high risk for uterine perforation [15]. In our study, 7% of patients had retroverted uterus and in 53.5% of patients the uterus was laterally deviated to right
or left which also makes the insertion difficult and in these patients ultrasound guidance also helped to guide the tandem appropriately.

Portable transabdominal ultrasound machine is readily available at our radiation oncology department, and it provides easy, safe, fast, inexpensive and real time guidance during brachytherapy applications. Applicator placement have been traditionally done "blindly" without ultrasound guidance and suboptimal placement can occur without awareness. When a perforation is discovered on planning CT, the applicators must be removed and a second procedure is scheduled, this process is time consuming and expensive and may result in a treatment delay, which is known to compromise local control [13]. The incorporation of ultrasound guidance in intracavitary brachytherapy in a previous study did not lengthen the time to complete the procedure and it decreased the average overall insertion time [8].

In conclusion, the implementation of routine ultrasound guidance resulted in decreased rates of perforations and increased rates of accurate applicator placement. Ultrasound imaging provided safe, cost-effective and real-time guidance. Also it is important for radiologists to be familiar with the appropriate positioning of applicator as well as any potential complications.


