J Gynecol Oncol. 2018 May;29(3):e42
https://doi.org/10.3802/jgo.2018.29.e42
pISSN 2005-0380·eISSN 2005-0399

JOURNAL OF GYNECOLOGIC ONCOLOGY

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Outpatient cervical brachytherapy in the setting of ongoing antiplatelet therapy or oral anticoagulation

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Received: Dec 28, 2017
Revised: Jan 30, 2018
Accepted: Feb 7, 2018

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Conflict of Interest
No potential conflict of interest relevant to this article was reported.

Author Contributions
Conceptualization: V.V.; Data curation: V.V.; Formal analysis: V.V., M.S.A., T.M.G.; Investigation: V.V., M.S.A., T.M.G.; Methodology: V.V., M.S.A., T.M.G.; Project administration: V.V.; Resources: V.V., M.S.A., T.M.G.; Software: V.V., M.S.A., T.M.G.; Supervision: V.V., M.S.A., T.M.G.; Validation: V.V., M.S.A., T.M.G.; Visualization: V.V., M.S.A., T.M.G.; Writing - original draft: V.V., M.S.A., T.M.G.; Writing - review & editing: V.V., M.S.A., T.M.G.

Outpatient cervical brachytherapy in the setting of ongoing antiplatelet therapy or oral anticoagulation high-dose-rate intracavitary brachytherapy is essential to the contemporary non-surgical management of the International Federation of Gynecology and Obstetrics (FIGO) stage IA–IVB cervical cancer treated with curative intent [1]. While institutional protocols vary, the placement of an intracavitary cervical implant (tandem and ovoids or tandem and ring) is usually performed on the outpatient basis, and a total of 3 to 6 brachytherapy procedures are commonly prescribed. In order to facilitate office-based implants, practitioners often precede cervical brachytherapy by temporary insertion of a cervical sleeve [2]. This device is inserted into and sutured to the cervix, and it is also known as a disposable indwelling intrauterine tube or a cervical stent [3]. Various modifications of cervical brachytherapy sleeves are commercially available, designed to be either open at the cephalad extent or to be closed-end. We have noted that presence of a closed-end, adequately positioned cervical sleeve at the time of insertion of an intrauterine tandem minimizes the amount of required manipulation of the uterus by the brachytherapist, leading to less procedural discomfort, decreasing the need for analgesia, providing shorter appointments, and overall improved patient satisfaction.

The successful outpatient placement of a cervical brachytherapy apparatus requires meticulous attention to procedural protocols and patient-specific details. In particular, ongoing anticoagulation or antiplatelet therapy poses a challenge since it increases the risk of procedure-related hemorrhage [4] and the use of these agents is increasingly more common in patients. Current cervical intracavitary brachytherapy guidelines call for the temporary cessation of all anticoagulation and antiplatelet medications for the duration of brachytherapy [5]. Unfortunately, difficult clinical scenarios exist when stopping anticoagulation or antiplatelet agents for brachytherapy is either too risky or highly impractical. In our practice, we have recently performed 14 consecutive outpatient intracavitary implants for 4 women with malignancies of the intact cervix who were simultaneously receiving combination antiplatelet therapy or oral anticoagulation. We postulated that intracavitary brachytherapy facilitated by the insertion of a closed-end cervical sleeve would result in a very low risk of procedure-related bleeding despite anti-clotting medications.

The Institutional Review Board approved this retrospective study (approval number: 2017-253). Patients were treated between 2016 and 2017. The median age was 51 years. Three women had primary cervical carcinomas of FIGO stages IB1 or IB2, and 1 was treated for medically inoperable uterine serous carcinoma involving the cervix and a vaginal fornix.

Prior to brachytherapy, all 4 received external beam radiotherapy to a total dose of 44–50.4 gray (Gy) in 22–28 fractions. In 3 of 4 cases, cisplatin chemotherapy was also administered for a total of 5 or 6 weekly cycles. Brachytherapy planning was complicated in these for the following reasons. Two out of 4 women had suffered a recent myocardial infarction requiring coronary angioplasty, insertion of drug-eluting coronary stents and long-term antiplatelet therapy using acetylsalicylic acid 81 mg by mouth (PO) once a day (q.d.) combined with ticagrelor 90 mg PO twice a day (b.i.d.) in 1 case and with clopidogrel 75 mg PO q.d. in another. For both of these patients, temporary stoppage of antiplatelet therapy for brachytherapy was deemed high-risk for arterial thrombosis by the managing cardiologists. Another patient was receiving rivaroxaban 20 mg PO q.d. for a concurrent diagnosis of lower extremity deep venous thrombosis and the fourth woman was on apixaban 5 mg PO q.d. for long-standing atrial fibrillation. Brief cessation of oral anticoagulation likely carried the acceptable risk for thromboembolic events for the latter 2 women, with or without the use of heparin bridging [4]. However, it was decided by the Multidisciplinary Gynecologic Oncology Team that change to the medication regimen was highly impractical due to these patients' personal history of noncompliance with physicians' recommendations.

Therefore, all 4 women described here received cervical brachytherapy during ongoing anticoagulation or antiplatelet therapy. All procedures were similar and followed the institutional guidelines. First, with the aid of monitored anesthesia care in the operating room, an examination was performed and closed-end cervical sleeves were sutured to the cervix by a gynecologic oncologist. Commercially available brachytherapy sleeves were used (Nucletron/Elekta, the Netherlands, and Varian, USA). The inner tube diameter was 4 or 6 mm. Length of sleeves was 40 or 60 mm, individually selected taking into account residual tumor size, length of the cervix by imaging, and the sounded depth of the uterine fundus. Sleeves were anchored using from 2 to 4 synthetic absorbable (2 cases) or polypropylene (2 patients) sutures. Blood loss during sleeve insertion was minimal (<50 mL) in all 4 cases.

Starting a median of 5 days after the sleeve insertion procedures, a total 14 of outpatient brachytherapy implants were uneventfully performed. Brachytherapy was given twice per week, at least 72 hours apart. Patients receiving combined antiplatelet therapy were prescribed 3 implants each, and those receiving oral anticoagulation had 4 brachytherapy insertions per case. For 2 out of 4 patients, the implants were immobilized using external fixation to the surgical table. For 2 women the brachytherapy apparatuses were kept in place by an intra-vaginal tamponade due to physician's preference. The dose was prescribed to the high-risk clinical target volume, which included the entire uterine cervix and all residual extracervical tumor at the time of brachytherapy. Median total radiation dose to the high-risk clinical target volume was 80.3 Gy, calculated in 2 Gy per fraction equivalents. Radiotherapy plans were optimized to limit cumulative dose to 2 cm^3 of the rectum and the bladder to < 70 Gy and < 80 Gy, respectively. A tandem and ovoids apparatus was used in 4 insertions and tandem and ring were utilized for 10 treatments. There was no procedural bleeding during brachytherapy. As a precaution, prepared topical thrombin solution was made available during brachytherapy for 2 women receiving antiplatelet therapy [6], but it was not used. Cervical sleeves and visible remaining sutures were removed by a brachytherapist in the outpatient brachytherapy suite on the day of the last implant under direct visualization. All 4 patients remained free of bleeding events > 180 days after brachytherapy.

In conclusion, we report 14 consecutive outpatient brachytherapy procedures for 4 women with the intact cervix during combined antiplatelet therapy or oral anticoagulation. None

of 14 treatments was complicated by procedural bleeding. Without a doubt, an intracavitary cervical implant is an intervention that is associated with risk of hemorrhage [5]. Thus, whenever possible, anti-clotting medications should be temporarily discontinued using established protocols and schedules. However, based on our preliminary experience described here, we believe that for women at high-risk of thromboembolic events, intracavitary cervical high-dose-rate brachytherapy can be considered on a case-by-case basis without change to anti-clotting agents. This observation only applies to brachytherapy employing cervical sleeve technique.

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