ORIGINAL ARTICLE

Outpatient High-Dose-Rate Brachytherapy for Cervical Cancer in the Radiation Department

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ABSTRACT

Introduction: This report analyzes a standardized high-dose-rate (HDR) brachytherapy protocol in an urban, outpatient cancer center and compares feasibility and outcome measures with earlier, non-standardized processes. **Method:** A standard protocol for HDR brachytherapy was developed for patients with locally advanced cervical cancer (FIGO stages IIB-IVA). Data regarding the development and results of the protocol were analyzed. Multiple disciplines including gynecologic oncology, radiation oncology, anesthesiology, nursing, and administration are addressed, and the planning and execution of the protocol are critiqued. **Results:** A total of 15 patients underwent treatment with the standardized protocol, compared to 10 patients treated earlier in a non-standard fashion. Average time spent in the facility by patients was shortened by 3–4 h. Further, using the standardized protocol, 17 applications necessitated an operating room (OR), and there were no inpatient admissions. 10 patients treated off-protocol required 48 applications in the OR and 7 inpatient admissions. 71/72 (98.6%) applications prescribed using the protocol were completed. 21/48 (43.8%) applications were prescribed off-protocol ($P < 0.5$). **Discussion:**The utilization of protocol-based HDR brachytherapy minimized OR utilization eliminated inpatient admissions and improved compliance. Challenges include maintaining necessary equipment/drugs, in the radiation oncology suite for intra-operative pain management. Furthermore, some brachytherapy applications could not be done successfully in the radiation suite due to poor tumor response and/or pelvic anatomy of the subject. Due to the time-sensitive nature of this treatment, the procedures must be quickly rescheduled in the OR, which can be very difficult. Finally, one-on-one nursing care is required to provide patient reassurance and improves workflow management. This protocol can greatly facilitate the care of women with locally advanced cervical cancer despite these challenges and is strongly recommended for these challenging patients.

Key words: Cervical Cancer, Radiotherapy, Outpatient

INTRODUCTION

Brachytherapy for Cervical Cancer

Intracavitary therapy, also known as brachytherapy, has been used for the treatment of cervical cancer for over a century. Numerous systems for applying brachytherapy in an intracavitary fashion (i.e., within the vaginal/uterine cavity) have been proposed over the years. Many of the lessons learned from those treatment systems were combined by Drs. Felix Rutledge and Gilbert Fletcher, whose long collaboration resulted in the development of what has become the international standard for locally-advanced cervical cancer. Drs. Rutledge and Fletcher realized that larger, grossly irregular cervical tumors could be more effectively treated by utilizing external beam radiation therapy as the first step in the treatment process, with the intent of restoring cervical/vaginal anatomy as close to its original state as possible. Restoring the uterus, cervix, and vagina to a relatively normal anatomic configuration greatly facilitates effective dosing with brachytherapy, making radiation therapy with curative

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intent feasible. This basic regimen has been used around the world for almost 5 decades and has successfully treated tens of thousands of previously incurable women.[1]

Today, the standard treatment for locally advanced cervical cancer continues to utilize external beam radiation therapy followed by intracavitary therapy with concurrent cisplatin chemotherapy. Recent advances have allowed for the transition from low-dose-rate (LDR) brachytherapy using isotopes with half-lives measured in years, to high-dose-rate (HDR) brachytherapy, using isotopes whose half-lives can be measured in days. LDR brachytherapy application typically required 36–48 h, necessitating inpatient hospitalization. In contrast, HDR brachytherapy applications are much shorter, typically requiring 15–20 min, thereby making outpatient therapy feasible.

Rationale behind brachytherapy

HDR brachytherapy for cervical cancer provides several therapeutic advantages compared to LDR. HDR can deliver an effective dose of radiation to the tumor in much less time, thus minimizing the risk of cervix and tumor movement during the application, and also reducing the dose to adjacent organs.[2] HDR also eliminates the prolonged recumbency associated with LDR, potentially lessening the risk of deep vein thrombosis, in addition to reducing the time burden on the patient.[3] Furthermore, the HDR applicators (tandem and ovoids) are typically smaller in diameter than standard LDR devices, potentially allowing for placement without using general anesthesia (as typically required for LDR). By eliminating the need for both inpatient admission and general anesthesia, the use of outpatient HDR brachytherapy performed becomes feasible (and potentially more cost-effective) for most clinical radiation therapy departments.

Safe, effective, and convenient delivery of HDR brachytherapy requires accurate placement and immobilization of the applicators, dosimetry planning, and adequate patient monitoring both while awaiting and during the administration of the radioactive material.[4] This report analyzes the development of a standardized HDR brachytherapy protocol for use in the radiation department of a busy, urban, outpatient clinical cancer center, and compares feasibility and outcome measures with earlier, non-standardized processes.

METHODS

Interdisciplinary coordination: gynecologic oncology, radiation oncology, anesthesiology, nursing, and administration

Multi-disciplinary planning must precede the utilization of outpatient HDR brachytherapy. A working group was created at this center, which included representatives of gynecologic oncology, radiation oncology (including medical physicists), anesthesiology, nursing, and administration (including social work). This group required several meetings and much discussion to develop a protocol that was acceptable to all.

A standardized step-by-step protocol was developed, which includes an initial treatment planning discussion for each individual patient, as significant variation will exist in both clinical presentation and personal needs. In this and many facilities, patients with locally advanced cervical cancer (FIGO stages IIB-IVA) generally enter the system initially as a referral to the gynecologic oncologist, who will typically prescribe combined radiation/chemotherapy. This treatment, described in detail elsewhere,[5] includes external beam radiation to a pelvic field with weekly intravenous cisplatin, followed by intracavitary brachytherapy. Chemotherapy may or may not be administered during the brachytherapy. The next step is a referral to the radiation oncologist, followed by a treatment planning discussion between these specialties. This can be in the context of a multi-disciplinary meeting, or a simple personal conversation, depending on the circumstances. In this facility, it is preferred that new cases be discussed at a scheduled Tumor Board, so that representatives of other disciplines may understand/contribute to the treatment plan.

A treatment schedule is then created, with the patient's input. Facility administration is notified early so that insurance approvals can be obtained in a timely fashion. As cervical cancer disproportionately affects low socioeconomic status women, often of ethnic minorities, trained social workers are asked to address a variety of issues, including transportation, child care and paying for prescriptions. Non-local patients may require assistance with housing during treatment. A workflow that is minimally disruptive, but that addresses the major contingencies are planned, with appropriate documentation in the patient's electronic medical record. Treatment is typically four to five individual treatments over 10–14 days per patient.

Administration of brachytherapy

The protocol in this institution is to perform the first application in the OR, usually with general anesthesia. This facilitates both the performance of a pelvic examination and dilation of the cervix as needed. A Schmitt-type cervical sleeve can be placed at this time if needed. The type of brachytherapy applicator used can be based on the preference of the physicians. This facility primarily utilizes a tandem and ring design, although traditional tandem and ovoids are acceptable as well.

Once the patient is under anesthesia, she is placed in lithotomy position. Pelvic examination is done to precisely determine the extent of the residual disease and estimate the size and position of the uterus, and to select the specific size of the applicator. The tandem/ovoids (ring) are then placed and moistened cotton gauze is packed in the vagina around the

device(s) for stabilization. A Foley catheter is placed in the bladder, and the bulb is filled with a 50:50 mix of radiopaque dye and sterile water. While the gynecologic oncologist may be more comfortable with the actual placement of the applicator, the radiation oncologist should be present to confirm optimum location and immobilization. Then, the patient is awakened from anesthesia. In this facility, all patients undergoing general anesthesia must go to the Post Anesthesia Care Unit for recovery, lasting approximately 1 h.

After recovery, the patient is moved to the radiation department while dosimetry planning is begun. It must be stressed that one-on-one nursing care during this entire period is both necessary and beneficial to the patient to assess vital signs, address any patient complaints, and provide reassurance that the procedure is going well. When the dosimetry plan is completed, the patient is moved to the adjacent treatment vault, and the remote afterloading device is connected as per manufacturers' direction, allowing the radioactive elements to be applied as planned. After the treatment is completed and the radioactive elements are removed, the patient is moved to a treatment room where the gauze packing and the applicators are removed.

For the remaining three to four treatments, the applicator is typically placed in the radiation department, as general anesthesia is rarely necessary. Conscious sedation, with monitoring by a CRNA, is typically adequate for the remaining placements. This eliminates several steps and facilitates the process for the patient. On the day of the application, the patient is instructed to arrive at the facility no later than 1 h before the procedure start time. An RN who is dedicated to monitoring the patient through the entire treatment until the patient leaves the facility assesses the patient's baseline vital signs on arrival. If the patient has a primary recognized oncology nurse, it is recommended that this individual should be as closely involved in the brachytherapy process as possible, preferably including performance of the primary nursing assessments on the day of the application.

A CRNA meets and prepares the patient. The CRNA is committed in advance by anesthesiology to be present for the duration of the placement and (if needed) for the removal of the applicators. The RN or CRNA will obtain intravenous access, and the patient will then be moved to the treatment room. The treatment room contains a functioning anesthesia machine and full resuscitative capability. A gynecologic exam table with movable stirrups is helpful but not absolutely required for the procedure. In this facility, the procedure is done on the CT simulation table, to minimize the number of movements the patient must make once the applicators are placed. After adequate sedation is obtained, the tandem/ovoids can typically be placed with no additional dilation of the cervix, followed by placement of the Foley catheter. It is recommended that both the gynecologic oncologist and radiation oncologist be present for at least the initial department-based application, and available for subsequent applications. At this institution, the physical availability of both gynecology oncologist and radiation oncologist is facilitated by the proximity of radiation oncology suite to the gynecologic oncology clinic but is not absolutely necessary.

Images are immediately obtained for dosimetry planning. It is recommended that imaging be repeated with subsequent applications, as maintaining the initial dosimetry plan may result in a dose excess to the organs at risk because of the variable positioning of the applicator and organ mobility between applications. The remainder of the procedure continues as described above. The CRNA is available to administer sedation to facilitate device removal as the patient may express significant discomfort. In this facility, de-briefings are held after each session to discuss problems encountered and to jointly formulate solutions to apply to the next session.

Study design

This study compared 15 patients treated for locally advanced cervical cancer with the new protocol to 10 patients treated for locally advanced cervical cancer before its' implementation. Patients were followed throughout the entire day of treatment to track the timing of the protocol. Patient compliance was measured comparing prescribed applications to completed applications. Patient satisfaction was subjectively measured through conversations with patients.

RESULTS

Patient compliance was measured as stated above, and the results are summarized in Table 1. 10 patients treated before the implementation of the new protocol ranged between ages 32 and 71, with seven African-American (Black) patients, one Asian patient, and two Caucasian patients. Seven patients had Stage IIB cervical cancer, and three had Stage IIIB. Eight patients were prescribed five brachytherapy applications, with five patients completing two brachytherapy applications and three patients completing three applications. Two patients were prescribed four applications, and both completed two applications. Time per application was measured to the nearest quarter hour and is summarized in Table 1. Before implementation of the protocol, the mean time/application was 5.35 h, compared to 3.5 h using the standardized protocol.

Fifteen patients were treated according to the new protocol. They ranged between ages 29 and 61 and included 12 African-American (black), 2 Caucasian (white), and one Hispanic patient. Eight had FIGO Stage IIB cervical cancer, one had Stage IIIA, 4 had Stage IIIB, and 2 had Stage IVA cervical cancer. 10 patients were prescribed five applications, and 9 completed five applications, while 1 completed only 4. Five patients were prescribed four applications, and all completed four applications.

Table 1: Patients Treated for Locally Advanced Cervical Cancer, 9/13-9/16

Patient	Age	Ethnicity B-black W-white A-Asian H-Hispanic	Stage (FIGO)	Standard protocol	Brachytherapy applications prescribed	Brachytherapy applications completed	Time/Application (h)
1	58	W	IIIB	No	5	3	7.0
2	32	W	IIB	No	5	2	6.0
3	28	B	IIB	No	5	2	6.5
4	34	A	IIB	No	5	3	5.5
5	51	B	IIIB	No	5	3	5.0
6	53	B	IIB	No	5	2	5.25
7	48	B	IIB	No	5	2	5.75
8	39	B	IIIB	No	4	1	6.0
9	60	B	IIB	No	5	2	6.75
10	71	B	IIB	No	4	1	5.5
11	51	B	IIB	Yes	4	4	4.5
12	38	B	IIB	Yes	5	5	4.0
13	53	B	IVA	Yes	4	4	3.0
14	40	B	IIB	Yes	5	5	3.25
15	39	B	IIB	Yes	5	5	3.5
16	57	B	IIB	Yes	5	5	3.0
17	44	B	IIIB	Yes	5	5	4.0
18	60	W	IIIA	Yes	5	4	3.75
19	41	B	IIIB	Yes	4	4	5.0
20	46	H	IIB	Yes	5	5	3.5
21	53	B	IIB	Yes	4	4	3.0
22	29	B	IVA	Yes	4	4	3.25
23	47	B	IIIB	Yes	5	5	4.5
24	59	W	IIIB	Yes	5	5	3.0
25	43	B	IIB	Yes	5	5	3.25

Table 2: Brachytherapy applications prescribed versus completed, before and after implementation of a standard protocol

Timing of Applications	Applications prescribed	Applications completed
Before standard protocol	48	21
After standard protocol	70	69*

*$P < 0.05$

Table 2 compares the total number of brachytherapy applications prescribed versus applications completed between patients treated before and after the implementation of the standard protocol. In the pre-protocol group, 48 applications were prescribed, and 21 were completed. In the group of patients treated according to the new protocol, 70 applications were applied, and 69 were completed. This was shown to be statistically significant with $P < 0.05$.

DISCUSSION

The standardized protocol allowed for patients with locally advanced cervical cancer to receive exclusively outpatient therapy, with no more than one episode of general anesthesia. The commitment of each involved department before the planning of the project was critical to it's success. The planning process required multiple meetings, with various members of the team, demonstrating the need for universal "buy in" to the concept in advance. The result was an effective and efficient protocol, with multiple advantages and minimal challenges.

Challenges

Most Radiation Oncology suites will not typically possess the equipment necessary for brachytherapy applicator placement.

Ideally, a table with movable stirrups to facilitate lithotomy positioning should be used for placement of the applicator. Adequate access can be obtained using a table without stirrups, by elevating the patients' buttocks with an upside down emesis basin while in "frog-leg" (hips/knees flexed) position. This practice is followed in this facility, while the patient is situated on the CT simulation table. As stated previously, this reduces the number of position transfers that must be done with the applicator in place. Further, a strong, directional light source needs to be available during the placement. Appropriate lighting fixtures should be secured in advance, as they are not usually available in most radiation therapy departments.

Pain control needs vary greatly by the patient. Most radiation treatment facilities will not have an adequate variety or supply of intravenous medications for pain control on hand for immediate use. Hydromorphone (1.0 mg IV) and lorazepam (1.0 mg IV) can be used as standard agents for pain and anxiety control while the device is in place and should be immediately available. The individual responsible for administering these agents (either RN or CRNA) should be experienced and comfortable with the management of perioperative pain medications.

As stated above, the experience at this facility supports the initial placement of the applicators in the OR, with or without placement of a Schmitt sleeve. This allows the physician to perform a more thorough examination and any necessary cervical dilation with minimal discomfort for the patient. It is recognized, however, that depending on a patient's specific anatomy and pattern of disease, that tandem placement in the OR may be necessary for each treatment session for some patients.

Advantages

Utilization of this protocol eliminated the need for an OR setting, general anesthesia, and recovery in a PACU after the first application. As a result, the length of the treatment day for subsequent applications is decreased by about 2 h. In addition, the patient could remain in a familiar setting, with trusted personnel. The proximity of the radiation oncology suite to the gynecologic oncology clinic within this facility facilitated the process for the physicians and allows for more immediate consultation if/when problems arise. Furthermore, improvement of the workflow (quality improvement) is facilitated by the proximity of the involved teams and shared space.

Compliance is critical to the successful treatment of locally advanced cervical cancer. However, the episodic nature of the standard Radio/chemotherapy regimen can be quite demanding, particularly for patients with limited social and/or financial resources. If all recommended applications are not completed, under-dosing and suboptimal tumor control may occur. 15 prescribed applications were not completed in the pre-protocol group, compared to the only one after implementation of the protocol. The reason for the non-completions was patient-driven in all cases. Typically, patients who did not complete the prescribed applications said that they were "worn out" by the treatments already received, and/or that the application itself was painful or otherwise uncomfortable.

Role of one-on-one nursing

Compassionate, one-on-one nursing is also critical to the success of this protocol. Close communication between the nurse, patient, and family at this point will greatly improve the overall perception of the procedure, and in the experience of this facility, is critical to ensuring compliance with subsequent planned applications. The relationship between the primary oncology nurse and the patient is typically unique and provides opportunities for education and reassurance that cannot be easily duplicated. This continuity of care is not only reassuring to the patient but also provides insight into the team's workflow. The nursing staff can direct the ancillary staff regarding the transport of the patient from station to station and coordinate all actions of the multidisciplinary team. Continuous monitoring will help achieve adequate pain control and provides reassurance to the patient throughout the procedure.

CONCLUSION

The treatment of locally advanced cervical cancer is complex, time-consuming, and physically and mentally demanding. Patients often struggle to complete the prescribed therapy. Patients who are uninsured and/or of low socioeconomic status frequently have limited family and social support and therefore are disproportionately affected by the demands of complex cancer therapy. These circumstances are exacerbated by the fact that cervical cancer disproportionately affects women of low socioeconomic status.

The utilization of HDR brachytherapy can minimize or eliminate the need for prolonged immobilization and inpatient hospital admissions. HDR does, however, increase the level of complexity of the treatment plan. The development of a standard protocol for the utilization of HDR brachytherapy will facilitate the treatment process for patients, physicians, and staff. In this facility, the use of the standard protocol reduced the time required for individual applications after the initial placement by approximately 2 h. In addition, implementation of this protocol improved compliance by reducing the number of applications missed by patients. Patient perception of the brachytherapy experience was much improved after implementation of the protocol, and the physicians and staff expressed increased satisfaction with the associated workflow. This protocol may be easily translated to other facilities. As the incidence of cervical cancer is

declining in many parts of the U.S and may continue to fall based on the success of ongoing Human Papilloma Virus vaccination programs, it is likely that the treatment of women with locally advanced cervical cancer will be concentrated in a relatively small number of specialized centers. This protocol is strongly recommended for such centers, as it is likely to greatly facilitate the care of these challenging patients.

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