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Intra-Cavitary Brachytherapy practice in COVID times: A prospective analysis of time durations of various procedural steps in the practice

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ABSTRACT

***Background and purpose:** During the COVID19 pandemic many radiotherapy centers have found it difficult to continue with their brachytherapy program. The apprehension was that the brachytherapy procedures may become unacceptably cumbersome, unsafe and time consuming under the prevailing pandemic. We undertook the present study to estimate and analyze the time durations of various steps during high dose rate (HDR) intracavitary brachytherapy (ICBT) procedure for carcinoma cervix while adhering to the safety protocols. **Material and methods:** The study was conducted at a government run hospital from Jan till Apr 2021. We prospectively estimated the time durations of each step of the HDR-ICBT procedure starting from the time a patient was taken into the operation theater till sent to the ward. Institutional safety protocols were followed. A total of 70 consecutive ICBT procedures involving 18 patients were included in the study. In all 1048 time-duration measurements were done. **Results:** The average time-durations were 24 minutes, 54 minutes, 54 minutes, 63 minutes and 26 minutes for induction of spinal epidural anesthesia, completion of brachytherapy applicator placement, CT/MRI imaging and patient transport to the brachytherapy room, completion of planning and execution of treatment, and for applicator removal, respectively. The average time-duration for the entire brachytherapy procedure till the patient reached to ward was 4 hrs. **Conclusion:** The average time of four hours for completion of an HDR-ICBT procedure with Covid-19 restrictions is reasonable and has scope for further reduction. Radiotherapy centers having adequate logistic and related support may, therefore, consider continuing with their ICBT program during the pandemic.*

Keywords: *COVID 19, HDR-ICBT, Time duration, Brachytherapy practice, Carcinoma cervix.*

1. INTRODUCTION

In the past two years, starting sometime in Nov-Dec 2019, the novel SARS-COV2 which caused COVID 19 pandemic has wreaked havoc on mankind resulting in severe economic, mental, physical, and social tragedies beyond any comprehensible words. World Health Organization (WHO) declared SARS-COV2 COVID 19 as a pandemic on 11 March 2020. The SARS-COV2 virus is transmitted via droplet or close contact with an infected patient with a secondary attack rate of more than 90%. It has been noted with concern that there is a high death rate in oncology patients who contract COVID-19 infection especially in the elderly population with preexisting comorbidities especially pulmonary diseases like chronic obstructive pulmonary disease (COPD) (1).

The guidelines and management protocols have been changing constantly impacting the healthcare including the management of oncological cases. Delaying the treatment for want of negative RT-PCR report is considered essential for protection of the healthcare workers and the patients. Brachytherapy is a component of management of malignancies of various sites. However, it has been proven beyond doubt as the mainstay of management in locally advanced carcinoma cervix to achieve a reasonable EQD_2 (equivalent dose with 2 Gy per fraction) of 85 Gy for optimal response and overall survival (OS)rates. Delays in treatment have been occurring due to the pandemic effects causing progression of disease. At times stoppage of further treatment has occurred for varied reasons. The delays in starting external beam radiotherapy (EBRT) or unscheduled gaps during EBRT have been witnessed in our day to day practice. Expecting similar delays in delivering high dose rate intracavitary brachytherapy (HDR-ICBT) during the pandemic is logical. Such delays in brachytherapy, an irreplaceable part of radiation therapy in cervical cancer, will negatively impact the overall outcome and prognosis of the patient (2,3).

Quantification of the time taken in completing the HDR-ICBT procedure while observing institutional Covid-19 safety protocols for staff and patients is relevant and useful for reasons such as planning of logistics and the impact of prolongation of time duration, if any, on the ICBT delivery. The ICBT efficacy could get affected if implementation of HDR-ICBT protocols such as bladder and rectum protocol becomes difficult due to longer time durations in the ICBT procedures. We could not find such information in the published literature, especially in Indian context. Hence, the present study was conducted to assess the feasibility of ICBT practice in terms of time factors involved during the ICBT procedures.

2. METHOD AND MATERIALS

A total of 70 consecutive ICBT procedures involving 18 patients were included in the study during Jan till Apr 2021. The ICBT procedure was divided into six main steps as shown in Table 1. In all, 1048 time-duration measurements for these six steps were carried out. All patients were cases of locally advanced carcinoma cervix who had completed planned EBRT and were due for their ICBT procedure. Written informed consent was taken from all patients to undergo the ICBT procedure and anesthesia clearance was taken a week prior to the procedure. All patients were admitted in a ward as part of COVID-19 protocol of the hospital and no visitors were allowed.

Due to the pandemic the number of elective procedures in a hospital had to be decreased substantially as per the guidelines given by the national authorities. Hence, a written permission was taken for each patient. A dedicated operation theatre (OT) was provided for the ICBT procedures. Only essential OT staff including radiation therapy staff was allowed in the OT who took necessary precautions in the form of wearing of personal protective equipment (PPE) kits. Anesthesia given was spinal epidural anesthesia. Patients were placed in lithotomy position and bladder protocol was followed by inserting a Foley's catheter and administering 300 ml normal saline. All patients were given laxatives one night prior to the procedure for bowel preparation. After adequate cleaning and draping, ultrasound (USG) pelvis was done to ascertain the bladder filling, uterine contour and endometrial canal. Appropriate uterine sound was inserted to ascertain the length of the uterine canal and appropriate size central tandem was placed in the uterine canal. Adequate size ovoid's were placed. Rectal marker was placed for CT planning. After completion of procedure a repeat USG pelvis was conducted to ascertain the application in both sagittal and axial sections (Fig 1). Subsequent to the satisfactory placement of the applicator, patients were shifted for MRI/CT planning scans.

The OT is located on the 2nd floor and the CT scan center on the ground floor of the hospital in the same block. Lift was used to transport the patient on a stretcher from the OT to the CT scan room. The MRI center is located on ground floor in a separate building of the hospital. It takes about three minutes to take patient on wheeled stretcher from the OT to the MRI center. The patient is brought to the brachytherapy room located in the basement of the hospital from the imaging center. It takes about 2-3 minutes from the CT center and 4-5 minutes from the MRI center to reach the brachytherapy room. The treatment planning system is located within the brachytherapy suite.

For ICBT planning and delivery Micro-Selectron-HDR brachytherapy unit (model V3), Oncentra Treatment Planning System (TPS) Ver 4.5.1, Fletcher Williamson Asia Pacific stainless-steel ICBT applicators and CT/MR ICBT plastic applicators, all from Nucletron BV (The Netherlands) were used. CT imaging was performed on a helical CT model Lightspeed VXR 16 (GE Medical Systems, USA) with 3 mm contiguous slice thickness protocol. For MRI, T2 weighted 3mm contiguous slice thickness was performed in paraxial, parasagittal and para-coronal planes with respect to the uterus plane and inclination on model Magnetom-Avanto-1.5 Tesla (Siemens, Germany) machine. The images were transferred through a DICOM network to the TPS and planning was performed that included contouring of organs at risk (OAR) namely bladder, rectum and sigmoid and high risk-clinical target volume (HR-CTV). Prescription was done at point A as per the ICRU definition. In some cases, manual dwell time adjustment on the standard dosimetry plan was needed to optimize the dose to point A and OARs. Fig 2 shows staff working with PPE kit and other safety precautions.

3. RESULTS

A total of 18 consecutive patients were included in the study with 70 ICBT procedures among them. Sixty-six ICBT procedures were planned with CT imaging and 04 with MR imaging. In all 1048 measurements of time-durations for various steps/stages involved in each ICBT procedure were done. Each step was defined as shown in Table 1. Table 2 depicts the demographic profile of our patients, Table 3 depicts the concurrent treatment with EBRT profile and table 4 depicts the ICBT details. Usual time to start the ICBT post EBRT was within a week however, in two patients ICBT was started after 10 days due to non-availability of OT and awaiting negative RT-PCR report since 1st sample was inconclusive, in four patients there was adverse event of low counts and the ICBT had to be delayed for 11 to 14 days. In two patients ICBT was interdigitated in the last week of EBRT to reduce OTT (Table 4).

Table 1

Sr No	Brachytherapy Stage/Step	Average time duration (range)
a.	Patient wheeled in the OT till spinal epidural anesthesia is induced	24 min (6 min- 58 min)
b.	Brachytherapy implant procedure in the OT after anesthesia	54 min (19 min- 105 min)
c.	Patient wheeled out from the OT till completion of the CT/MRI imaging followed by shifting to the brachytherapy room (MR imaging takes on an average 20 min longer than CT imaging).	54 min (14 min- 70 min)
d.	Completion of the brachytherapy treatment including contouring of bladder, rectum and sigmoid, dosimetry planning and execution of the treatment after being shifted to brachytherapy room	63 min (23 min – 190 min)
e.	Removal of implant/ applicator after completion of treatment	21min (10 min – 40 min)
f.	Total time taken for the completion of the entire ICBT procedure including shifting of patient back to the respective ward.	4 hrs 01 min (2.30 hrs – 06 hrs)

4. DISCUSSION

Cervical cancer is the second most common cancer in the female population worldwide after carcinoma breast (4), and ICBT is an integral part of the management. As per all the available guidelines including ABS the overall treatment time (OTT) i.e. EBRT plus ICBT should be less than 8 weeks and beyond this time the survival and local control decreases to 1% per day delay (5). Hence, the ABS guidelines and other major studies recommend that ICBT should not be delayed in patients without Covid-19 symptoms and negative reports (6,7,8,9). ICBT can be interdigitated along with EBRT to reduce the OTT with equivalent response and toxicities to sequential ICBT along with a distinct advantage of decreased OTT (10). During the COVID 19 pandemic it is important to recognize that prolonging the treatment duration has been shown to negatively impact tumor control outcomes through tumor repopulation (11).

We at our center have seen the ICBT process evolving from 2 D orthogonal planning to the present CT/ MRI based 3D planning process. Also, at our center we practice ultrasound guidance for proper placement of brachytherapy applicators, visualization of the uterine contours and bladder filling. CT/MRI has a distinct edge over 2D planning in better delineation of soft tissue contours and dosimetry planning involving HR-CTV and OAR's(12).

ABS (American Brachytherapy Society) guidelines provide various fractionation schedules for HDR ICBT (13). The standard fractionation used is 7 Gy in three to four fractions. Patel et al also used 9 Gy in 2 fractions with good local control and decreased toxicity (14). However, the IAEA in its guidelines favors 4 fractions of 6 GY each schedule (15). We at our center followed 7 Gy in 4 fractions post 46 Gy EBRT with EQD_2 of 85.7 and 6 Gy in four fractions post 50 Gy EBRT schedule with EQD_2 of 82 Gy.

Anesthesia for brachytherapy is the most important aspect of any good brachytherapy procedure in terms of adequate analgesia and pelvic floor relaxation. At our center spinal epidural anesthesia is the first preference for our patients. During the pandemic, getting an OT slot with anesthesia support became difficult due to factors such as limited OT staff and lack of ventilators. The hospital resources were being allocated elsewhere for Covid management.

As seen in Table 1there are wide variations in time-duration within each stage/step of the ICBT procedure. A variety of factors were responsible for such variations. For step 'a' related to wheeling-in of a patient into the OT till the time spinal epidural anesthesia was induced, the average time duration was 24 minutes with the minimum time as short as 6 minutes and the maximum time of 58 minutes. Factors such as timely availability of the anesthesiologist once a patient reaches the OT, occasional need of repeating the spinal anesthesia process because of its ineffectiveness in the first attempt or converting spinal anesthesia into general anesthesia, and even ensuring availability of a female attendant in the OT. At times, arranging a lady attendant, however trivial it may appear, could lead to prolongation of time duration of this step. Presence of a lady attendant when a male staff examines and treat a female patient is a mandatory requirement at our institution. The factors mentioned here either alone or in combination contributed towards prolongation of time duration of this step. When most of these factors were favorable, the completion of this step took shorter time. Similarly, factors involved in time duration variation (19 min to 105 min) for applicator placement (shown as step 'b' in the table) were normal anatomy versus effaced cervix/ distorted anatomy, and at times requirement of support of a gynecologic oncologist in the OT.

In step 'c', combined data of time duration for CT and MRI and shifting of patient to the brachytherapy room is presented (14 min to 70 min, average 54 min). This was the primary reason for the wide variation in time duration in completing this step. As

expected MR imaging procedure generally resulted in longer time duration as compared to CT imaging. Apart from longer scanning time, transporting the patient to the MRI center, and ensuring MRI safety before wheeling in the patient into the MR suite contributed to prolongation of the time in imaging. Another situation for prolongation of time duration in this was when slight mismatch in given time slot meant that ICBT patient had to wait till the other patient sent in for MRI is completed. This wait could be substantially longer in the case of MRI as compared to CT and hence necessitated proper coordination with the MRI center on time slot. The imaging time duration can be reduced by using CT based planning for all ICBT procedures and avoiding the MR based planning. To further reduce this time of this step, one may consider CT/MRI and USG for the first ICBT fraction and then delivering the remaining ICBT fractions for a patient using sagittal USG image (in the plane of the tandem applicator) based 2D planning. The 2D and 3D planning was correlated during the first fraction. This procedure of USG based ICBT has been in practice and will be of extreme benefit in centers where CT/MRI imaging is not available or in the context of developing countries where economics is of factor. The procedure has been well described by Sylvia et al and other related studies. (16-21)

The main factors for wide variation in time-duration(23 min to 190 min) for treatment planning and execution (step 'd' in table 1) were a) the time it took a radiation oncologist and a medical physicist to be available for the procedure and b) the availability of the HDR brachytherapy machine for treatment delivery post treatment planning. At times, arranging a lady attendant, however trivial it may appear, could lead to prolongation of time duration of this step. A weaker radiation source also could lead to extension of treatment delivery time. But this was not the case with us.

The administrative and logistics factors such as transportation of the patient from home to hospital, admission of the patient in the hospital, RT-PCR testing (at least two negative samples were required before taking the patient in the OT), coordination among the various departments, coordination among the staff, organizing a willing social worker, decision on the disinfection procedures of the equipment, applicators and department were contributors toward delays in start of ICBT. It is pertinent to mention that some patients could not get the ICBT due mainly to logistics factors and some others due to a combination of factors mentioned above. What further compounded the issue was the fact that in the initial days of pandemic, the guidelines were not clear and was constantly evolving.

5. CONCLUSION

Safe 3D image guided HDR-ICBT is possible during these pandemic times as the four-hour average time for the ICBT procedure in Covid-19 times cannot be considered unacceptable. The EBRT and ICBT procedures for cancer cervix patients should, therefore, not be deferred in the interest of treatment outcomes provided an institution is able to adhere to all recommended safety protocols. There is scope for reducing the time duration at the imaging stage by resorting to CT planning and avoiding MR based planning. This can be further reduced by adopting USG based ICBT procedure. Better coordination among the staff involved in the OT, imaging, and treatment planning and execution stages can also result in time saving in the ICBT procedure. The limitation of our study is that we did not have a similar study before the onset of the pandemic for comparison. We plan to do the same once the Covid-19 restrictions are lifted completely.

Conflict of interest: Nil

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Table 2 : Demographic Profile and Diagnosis of Patients

Characteristic		Number
Age (Year)	30-40	02
	41-50	04
	51-60	06
	61-70	06
Stage (FIGO[1]-2018)	II B	02
	IIIC1	16
HistopathologyDetails	LCKSCC[2]	02
	Adenocarcinoma	06
	PDSCC[3]	04
	KSCC[4]	06

1The International Federation of Gynaecology and Obstetrics.
2 Large cell keratinizing squamous cell carcinoma
3 Poorly differentiated squamous cell carcinoma
4 Keratinizing squamous cell carcinoma

Table 3: Details of Concurrent chemotherapy

Chemotherapy	No. of patients
Cisplatin	16
Carboplatin	02

Table 4: Time taken to start the Intracavitary brachytherapy after completion of external beam radiotherapy

05 days	02
07 days	04
08 days	02
10 days	02
11 days	02
14 days	04
Last week of EBRT	02

FIG 1:USG image during procedure

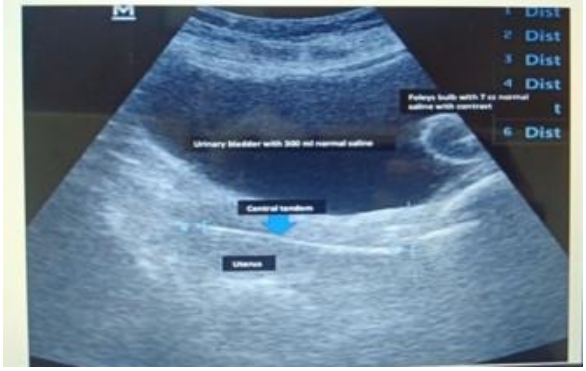

FIG 2: Performing the procedure using PPE kits (A planning) and (B treatment execution).