Volume 1 Issue 1 January, 2025

Maiden Edition

NIGERIAN JOURNAL OF ONCOLOGY

NJO

ARCON
Association of Radiation and Clinical Oncologists of Nigeria

w.w.w.ngjoncology.com

Printed by Ahmadu Bello University Press Ltd.,
P.M.B. 1094 Samaru, Zaria, Nigeria. Tel: 08065949711.
E-mail: abupress@abu.edu.ng, info@abupress.com.ng
Website: www.abupress.com.ng

USE OF LOW-DOSE RATE BRACHYTHERAPY IN THE TREATMENT OF GYNAECOLOGY MALIGNANCIES IN A LOW-RESOURCE SETTING: A TEN-YEAR REVIEW

Charles Okwonna[1], Shehu Salihu Umar[2,3], Ali Abba Tijjani[4,5], Oiza Tessy Ahmadu[6], Aisha Mustapha[7,8], Aisha Jamila Ahmad[8], Tajudeen A. Olasinde[2,3]

1. St Luke's Cancer Centre, Royal Surrey County Hospital, Guildford, Surrey
2. Department of Radiology, Ahmadu Bello University Zaria, Kaduna State, Nigeria
3. Department of Radiation and Clinical Oncology, Ahmadu Bello University Teaching Hospital, Zaria, Kaduna State, Nigeria
4. Department of Radiology, University of Maiduguri, Maiduguri, Borno State, Nigeria
5. Department of Clinical Oncology, University of Maiduguri Teaching Hospital, Maiduguri, Borno State, Nigeria
6. Department of Oncology, Federal Medical Centre, Abuja, FCT, Nigeria
7. Department of Obstetrics and Gynecology, Ahmadu Bello University, Zaria, Kaduna State, Nigeria
8. Department of Obstetrics and Gynecology, Ahmadu Bello University Teaching Hospital, Zaria, Kaduna State, Nigeria

Corresponding Author:
Dr. Charles Okwonna, St Luke's Cancer Centre, Royal Surrey County Hospital, Guildford, Surrey, charles.okwonna@npmcn.edu.ng

Citation: Okwonna C, Umar SS, Tijjani AA, Ahmadu OT, Mustapha A, Ahmad AJ, et al. Use of Low-Dose Rate Brachytherapy in the Treatment of Gynaecology Malignancies in a Low-Resource Setting: A Ten-Year Review. *Niger J Oncol 2025;*1(1):90-109

ABSTRACT

Introduction: Gynaecological cancers are among the most common cancers worldwide and vary in incidence geographically. In Nigeria, cervical cancer is the most common gynaecological cancer and the second most common cause of cancer-related mortality. Cervical cancer constitutes a huge percentage of the cases treated with radiotherapy in developing nations. This study aims to assess the impact of low dose rate intracavitary brachytherapy (BT) on treatment outcome of gynaecological cancers in Zaria.

Methodology: This was a retrospective descriptive study that involved all patients with gynaecological cancers that were treated with brachytherapy at the Radiotherapy and Oncology Department, Ahmadu Bello University Teaching Hospital (ABUTH), Zaria from January 2006 to December 2015.

Result: A total of 351 patients with gynaecological cancers were treated between January 2006 and December 2015 and were entered into this study. Mean age of the patients was 52 years. Cancers treated with brachytherapy during

this period were Cervical (97.4%), Endometrial (1.7%) and Vaginal (0.9%). Most (46.7%) of the patients had stage IIIB cervical cancer. Majority (77%) of the patients had no evidence of disease at 2 years post treatment. Factors associated with disease relapse were pretreatment tumors >4cm in diameter, interval between External Beam Radiotherapy (EBRT) and brachytherapy >12 weeks, cumulative radiation dose <70Gy and the type of applicators used for BT.

Conclusion: The study demonstrated the effectiveness of brachytherapy in the management of cervical cancer especially for smaller tumor sizes. Prioritization of patients with smaller size tumors for brachytherapy should be made in our setting with limited brachytherapy facilities.

KEYWORDS: Gynaecological, Malignancy, Intracavitary, Brachytherapy

INTRODUCTION

Gynaecological cancers are amongst the most common cancers worldwide and vary in incidence geographically.[1] These include cancers of the ovary, endometrial, corpus uteri, vagina, vulva and cervical.[2,3] According to the International Agency for Research on Cancer (IARC), gynaecological cancers accounted for 20% of the 14.1 million new cases, 8.2 million cancer deaths and 13 million 5-year prevalent cancer cases among women in the world in 2018.[1] While ovarian and endometrial cancers are commoner in Caucasian population and Western nations, cervical cancers are by far more prevalent in developing countries.[1] Among these, cancer of the uterine cervix is by far the commonest, accounting for 569,843 new cases and 311,000 deaths in 2018; and 604,127 new cases and 341,831 deaths in 2020.[1,4] Over 80% of the incident cervical cancer cases occur in developing countries.[1] In Northern Nigeria, cervical cancer is the most common gynaecological cancer and the second most common cause of cancer-related mortality.[5,6] Cervical cancer constitutes a huge percentage of the cases treated with external beam radiation therapy in developing nations.[7]

The most preponderant aetiologic factor in almost all gynaecological cancers is infection with Human Papillomavirus (HPV).[8] The virus is implicated as a causative agent in over 70% of cervical cancers, 50-60% of vaginal cancers and some endometrial cancers.[8] There are over 200 HPV serotypes, out of which about 40 are known to infect man, with 13 of them capable of infecting the lower female genital tract.[9] However, serotypes 16 and 18 are most implicated, hence are often referred to as the oncogenic serotypes.[9]

Majority of cervical cancer patients are either pre- or peri-menopausal at diagnosis, with the median age being 54 years in most studies.[10,11] Endometrial and vaginal cancer patients mostly present post-menopausal.[12] Majority of women with cervical cancer in developing nations, just like malignancies in other anatomical parts, largely present with locally advanced diseases due to various reasons.[13] Late presentation of cancer patients is a common finding in most developing nations despite the fact that most gynaecological malignancies often start with abnormal vaginal bleeding.[14,15] Majority of patients present with locally advanced and/or inoperable diseases.[16] This is also a regular finding in most other low/middle-income cancer patients in such climes.[17,18]

The diagnosis of gynaecological cancer involves detailed history taking, thorough physical examination including examination of the lower genital tract under anaesthesia.[18] Biopsies of any suspicious lesions or obvious masses are taken; and in case of suspected endometrial cancer, curettage is done to obtain biopsy.[12,18] The biopsied specimens are

subjected to histopathology review. The patients are then subjected to radiological investigations in order to establish the site and extent of spread (stage) of the cancer. Some of these investigations include abdominopelvic ultrasound scan, computed tomography (CT) scan, magnetic resonance imaging (MRI) scan, intravenous urography (IVU) and chest X-ray.[19] According to Bourgioti et al, the preferred imaging method for local cervical cancer evaluation is Magnetic Resonance Imaging.[19] The commonly used staging system for all gynaecological malignancies is that of the International Federation of Gynecology and Obstetrics (FIGO) which has undergone many revisions with the latest being FIGO 2018.[20] The staging incorporates clinical, pathological and radiological findings.[20]

Surgery remains the most definite treatment modality for early cervical, vaginal or uterine body cancers.[21] Treatment for locally advanced cervical and other gynaecological cancers has gradually progressed over the years from external beam radiotherapy (EBRT) only, to EBRT along with brachytherapy boost, EBRT and brachytherapy with concurrent cytotoxic chemotherapy.[22] Treatment with EBRT is to the primary tumor, parametria, pelvic lymph nodes and other areas with potential for microscopic disease involvement like the external inguinal lymph nodes.[23] The dose ranges from 45 to 54 Gray (Gy) in 25 to 30 fractions using 2D and other non-conformal forms of therapy.[23] Thereafter, brachytherapy is used to eradicate residual tumor so as to increase the chances for local disease control and overall survival.[23,24] The required tumoricidal dose of 70 - 80Gy for cervical cancer can only be achieved without untoward side effects by the use of brachytherapy.[24] Brachytherapy for cervical, endometrial or vaginal cancers is usually done using gynaecological applicators; in which the radiation source is inserted into the cavity of the affected organ.[25,26] However, in a study carried out on 116 patients with locally advanced cervical cancer, it was reported that interstitial brachytherapy provided excellent loco-regional control (85.3%) and 5-year disease free survival (60%) in patients with locally advanced cervical cancer for which intra-cavitary brachytherapy was unsuitable.[27]

Radiation in brachytherapy is delivered majorly using either a low dose rate (LDR) machine where the radiation rate is <2Gy/hour or a high dose rate (HDR) machine that emits radiation at a rate >12Gy/hour.[28] Most institutions world over have gradually switched over from low dose rate to high dose rate brachytherapy modes, which has the advantage of treating many patients in a day. [26, 29] Various radioactive isotopes are used for intra-cavitary brachytherapy and include Caesium-137, Iridium-192, Cobalt-60, etc.[30] The choice of radio-isotope to be used depends on the physical characteristics of the particular isotope and the type of brachytherapy machine available at the center.[30] There is no study that has been able to establish superiority of one isotope over the other, however, Cesium-137 was shown to have higher dose delivery to tumour.[30]

During brachytherapy, radioactive sources are placed in close contact with the tumor, such that minimal radiation gets to the normal tissues and organs, which they tolerate.[31] Brachytherapy obeys the inverse square law of radiation, such that the dose of radiation at any particular point is inversely proportional to the square of the distance from the radiation source emitting uniformly in all directions.[31] This

implies that smaller tumor bulks tend to benefit more from brachytherapy while sparing the surrounding structures.[31]

The side effects from intra-cavitary brachytherapy are usually tolerable within the commonly prescribed doses.[32] The effects are commonly on the rectum and bladder, with the predominant symptoms being diarrhea, hematochezia and increased urinary frequency.[32] Although, side effects could occur with any of the brachytherapy techniques, rectal and bladder acute side effects are more commonly seen with LDR compared to HDR.[33]

This study, therefore set out to document our experiences with the use of Low Dose Rate (LDR) intracavitary brachytherapy in the treatment of gynaecological malignancies over a 10- year period from 2006- 2015, in a low-resource setting. The specific objectives included assessment of tumor response, treatment toxicities and outcomes.

METHODS

Study Area

This study was carried out in the Radiotherapy and Oncology Department of Ahmadu Bello University Teaching Hospital, Zaria, northwestern Nigeria. It is a tertiary health facility providing specialist oncology care for cancer patients in Northern Nigeria as well as neighboring countries like Niger, Benin and Cameroun Republics. It is one of the six centers of excellence in oncology nationwide.

Study Design

This was a cross-sectional retrospective study.

Recruitment of study population

All patients with gynaecological cancers that were treated with low dose rate brachytherapy using Cesium-137 machine in Ahmadu Bello University Teaching Hospital over the ten-year period covering January 2006 to December 2015, were recruited for the study. A total of 351 patients were recruited in the study (see Figure 1).

Inclusion Criteria

All patients with histologically confirmed cervical, vaginal and endometrial cancers that had low dose rate brachytherapy after radical EBRT +/- chemotherapy.

Exclusion Criteria

i. Patients who did not complete brachytherapy radiation dose prescribed to point A for whatsoever reason.
ii. Patients who did not attend follow-up visits for up to 2 years after treatment.
iii. Patients who had previous pelvic irradiation
iv. Patients who previously received chemotherapy before presenting to the index hospital
v. Patients with pelvic comorbidities like renal impairment, etcetera

Data Collection

A proforma was used to extract relevant data from patients' case files and treatment cards. Information obtained include bio-data, site and size of tumor, dose of radiation prescribed to point A or any other reference point, date of brachytherapy, date of completion of EBRT as well as dose of radiation received from EBRT, interval between both therapies, side effects on discharge and follow-up, disease status on follow-up period. Abdominopelvic ultrasound scan was used to assess the size of the cervical mass before and after completing brachytherapy.

Data Analysis

Data was manually entered, cleaned and analyzed using Statistical Package for Social Sciences (SPSS) version 21. Analyses that were done included univariate, bivariate & multivariate analyses.

Univariate analysis for quantitative variables included mean and standard deviation, while frequencies and proportions were computed for qualitative variables. Bivariate analysis using Chi-square or Fisher's exact test was used to test significance of association between disease status at 2 years and treatment variables like prolonged treatment intervals, pre-brachytherapy tumor size and cumulative radiation dose. Multivariate analysis using Cox regression was used to establish direct causal relationship of disease recurrence with treatment variables. $P<0.05$ was considered to indicate a statistically significant difference.

Ethical Considerations

Ethical approval that enabled the study to be conducted was duly sought and obtained from the Health Research and Ethics Committee of Ahmadu Bello University Teaching Hospital (ABUTHZ/HREC/B09/2018). The information of patients obtained using proforma was securely entered into a password-protected computer, treated with utmost confidentiality and was only privy to the researcher and supervisors.

RESULTS

A total of three hundred and fifty-one (351) patients who met the study inclusion criteria were enrolled in the study (see Figure 1). The average age of respondents was 52.8 ± 11.6 years. Over half of the patients, 191(54.4%), were between 40- 59 years of age, with 256 (72.9%) married and 275 (78.3%) having parity of 5 and above (see Table 1).

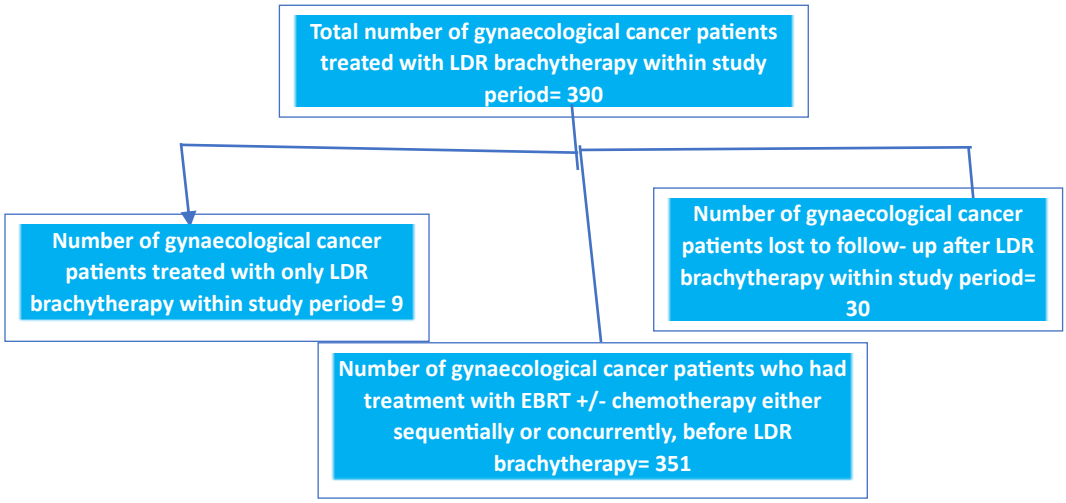

Figure 1. Flow chart showing recruitment of eligible participants of the study (LDR= Low dose rate, EBRT= external beam radiotherapy)

Table 1. Sociodemographic characteristics of study population

Socio-demographic factors (N=351)	Frequency (%)

Age group (years)	
<40	53 (15.1)
40 - 49	85 (24.2)
50 – 59	106 (30.2)
60 – 69	82 (23.4)
≥70	25 (7.1)
Marital status	
Single	10 (2.8)
Married	256 (72.9)
Divorced	22 (6.3)
Widowed	63 (18.0)
Ethnicity	
Hausa/Fulani	96 (27.4)
Yoruba	35 (10.0)
Igbo	63 (17.9)
Others	157 (44.7)
Level of Education	
No formal	160 (45.6)
Primary	80 (22.8)
Secondary	75 (21.4)
Tertiary	36 (10.2)
Parity	
< 5 births	76 (21.7)
≥ 5 births	275 (78.3)

Clinicopathological characteristics of Gynaecological tumors

The overwhelming majority of respondents had cervical cancer, 342 (97.4%), with endometrial and vaginal cancers accounting for the remaining 9(2.6%) (Figure 1). The commonest histological type was squamous cell carcinoma accounting for 320 (91.2%) of the cases (see Table 2). Most of the patients treated, 312 (88.9%) had locally advanced tumors (FIGO Stage IIB to IVA) (see Table 2). The commonest comorbid conditions were hypertension, 211(60.1%) and Diabetes Mellitus 70 (19.9%) (see Figure 3).

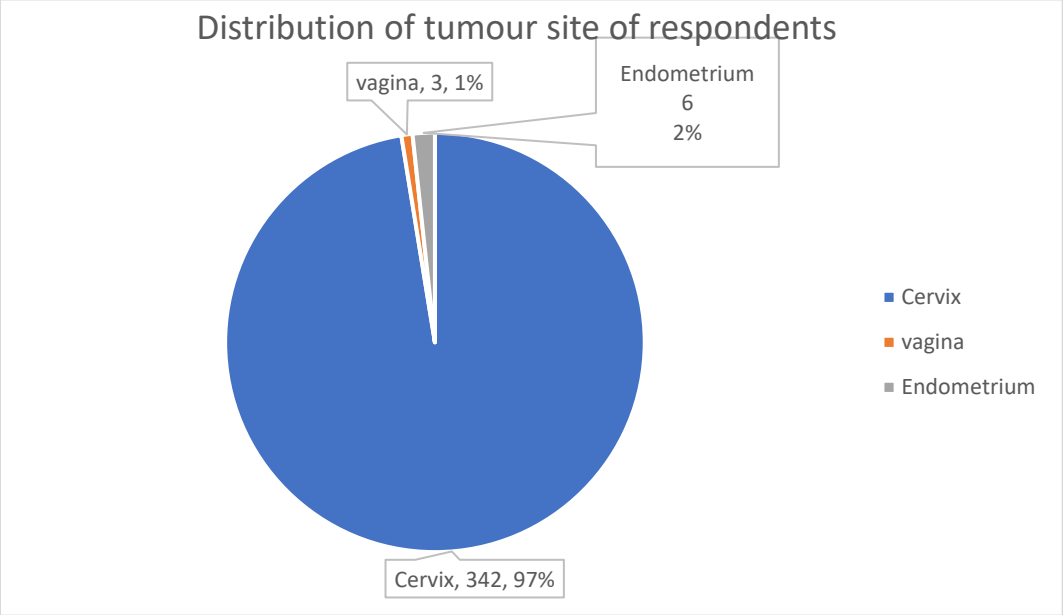

Figure 2. Distribution of tumor site of study population (n= 351)

Procedure and Dose received

The total dose of radiation received by patients ranged from 45Gy to 54Gy. However, doses of 50Gy and 54Gy received by 180 (51.3%) and 154(43.9%) respectively were the commonest doses given. Conversely, this was followed by brachytherapy to point A or to any other reference point of prescription to doses between 15Gy and 30Gy. Also 187 (53.3%) and 101 (28.8%) had total doses of 20Gy and 25Gy prescribed to Point A. Most of the patients 281 (80.1%) received a cumulative total dose (EBRT + Brachytherapy) of ≥70Gy, while only 70 (19.9%) received less than 70Gy (Table 4). The majority, 221 (63.0%), of patients had brachytherapy using the *Delouche* Applicator while 130 (37.0%) had a Vaginal Cylinder used (Table 4). Most patients, 336 (95.7%) had chemotherapy administered either as concurrent chemoradiation and/or adjuvant chemotherapy following EBRT. Only 151 (43.0%) received brachytherapy within 12 weeks following completion of EBRT while 200 (57.0%) received it more than 12 weeks following completion of EBRT (Table 4).

Table 2. Clinicopathologic characteristics of study population

Characteristics (n= 351)	Frequency (%)
Histology type	
Squamous Cell Carcinoma	320 (91.2)
Adenocarcinoma	21 (6.0)
Clear Cell/Small Cell	5 (1.4)
Others	5 (1.4)
Grade	
Well-differentiated	69 (19.6)
Moderately differentiated	105 (29.9)
Poorly differentiated	114 (32.5)
Undifferentiated	7 (2.0)
Unspecified	56 (16.0)
FIGO 2018 Staging	
Cervix	
IB	10 (2.8)
IIA	20 (5.7)
IIB	23 (6.6)
IIIA	122 (34.8)
IIIB	158 (45.0)
IVA	9 (2.6)
Vagina	
III	3 (0.8)
Endometrium	
II	2 (0.6)
III	4 (1.1)

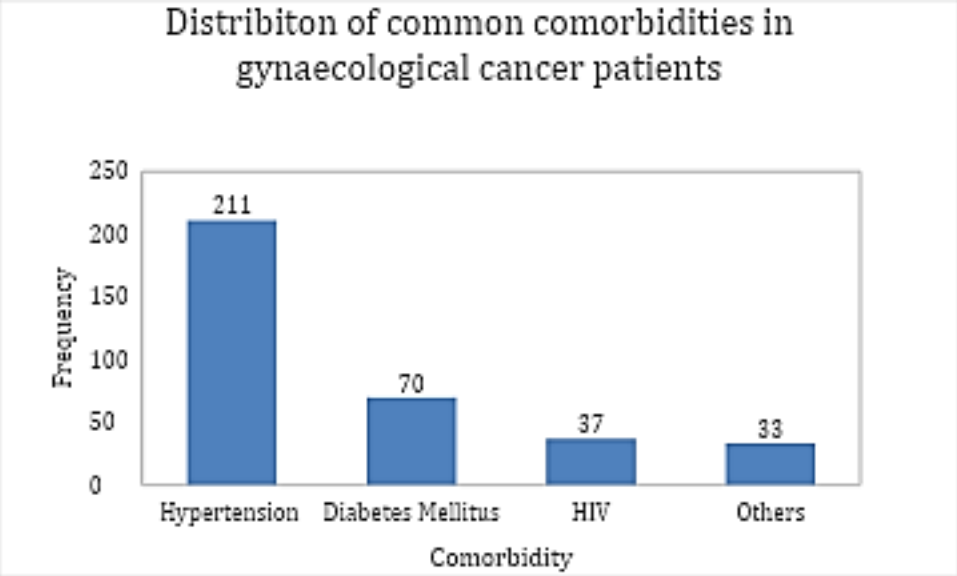

Figure 3. Common comorbid conditions in study population

Tumor response and treatment outcomes

The patients with tumor size 3 cm or less before brachytherapy had no evidence of tumor remnant upon completion of brachytherapy while with tumors 4 cm and greater, there were tumor remnants on completion of brachytherapy, the size of which was significantly correlated with pre-brachytherapy tumor size (see Table 3).

Many of the patients had no significant early side effects following brachytherapy. However, the commonest early side effects included cystitis, proctitis and venous thromboembolism (VTE) (see Figure 4). The common late side effects included vaginal stenosis and fistula (see Figure 5).

Two years after completion of EBRT +/- chemotherapy and brachytherapy, 269 (76.7%) of patients had no evidence of tumor recurrence while 82 (23.3%) had clinical evidence of disease progression/recurrence (Figure 6). On bivariate analysis using $\chi 2$ analysis, recurrence was significantly associated with interval between EBRT and brachytherapy (p= 0.0029); cumulative radiation dose (p= 0.0001); pre-brachytherapy tumor size (p= 0.005) and type of applicator used (p= 0.004) (Table 4). There were no significant association with age, education status, parity, tumor type, histology type or stage of tumor.

On multivariate analysis, recurrence was significantly associated with the interval between EBRT and brachytherapy (OR=2.356; CI, 95% = 0.947-5.863); cumulative radiation dose (OR=2.303; CI, 95% = 1.258-4.129); pre-brachytherapy tumor size (OR=2.321; CI, 95% = 1.287-4.183); and type of applicator used (OR=2.573; CI, 95% = 1.344-4.928).

Table 3. Tumor response to brachytherapy in study population

Tumor size pre brachytherapy (cm)	Frequency (n)	Average tumor size post brachytherapy (cm)	95% CI	t- test	P value
1.0 – 3.0	229	0.00 ± 0.00		------	-------
4.0- 4.9	76	0.615 ± 0.328		------	---------
5.0- 5.9	24	1.00 ± 0.02	0.252 to 0.518	5.73	<0.0001
6.0- 6.9	22	2.16 ± 2.45	0.153 to 2.166	2.32	0.025

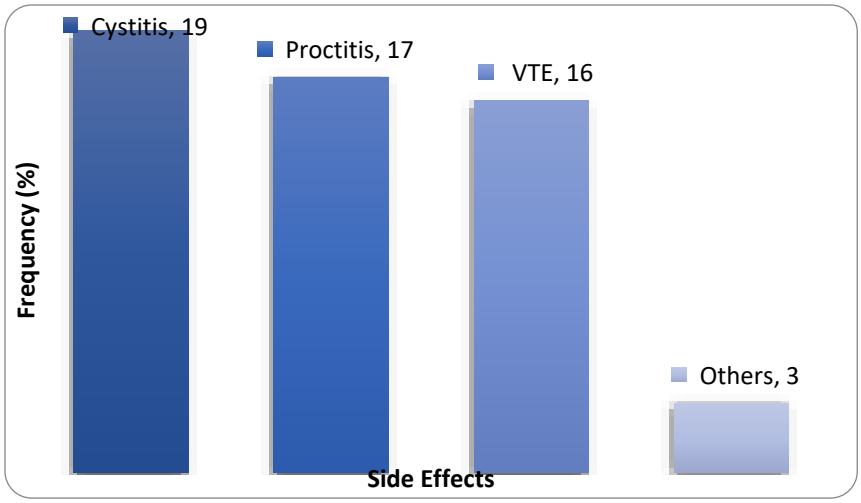

Figure 4. Common early side effects in patients following brachytherapy in study population

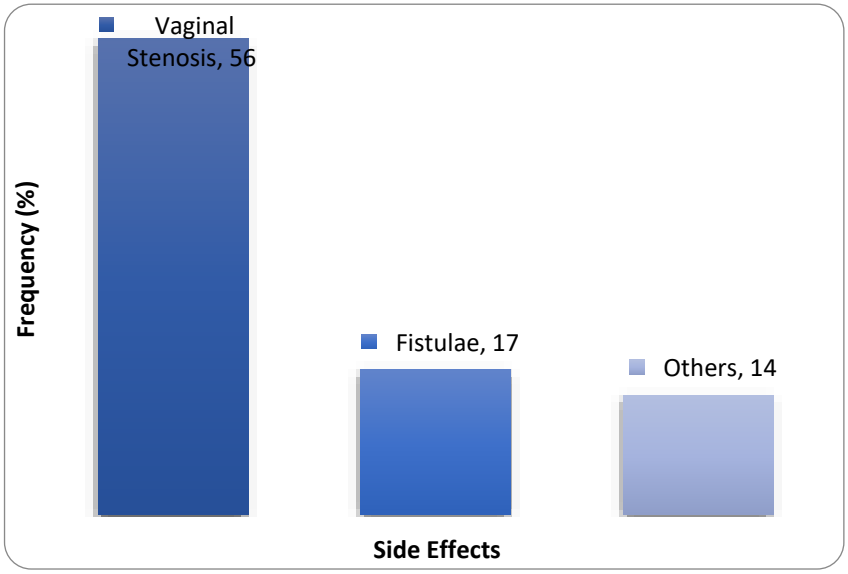

Figure 5: Distribution of type of late side effects of brachytherapy seen on follow up in study population

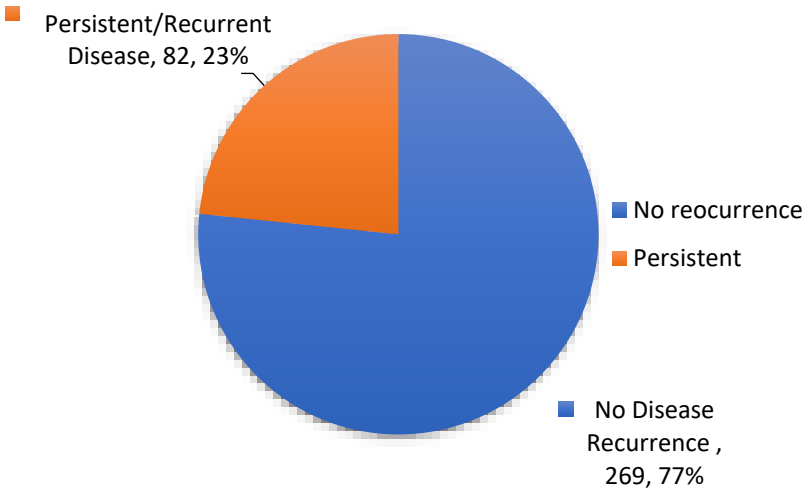

Figure 6: Disease outcome 2 years after completion of EBRT +/- chemotherapy + brachytherapy in study population.

Table 4: Association between disease status at 2 years and prognostic variables in study population

Variable (N= 351)	Disease Recurrence N (%)	No Disease Recurrence N (%)	Total N (%)	X^2	P-Value
EBRT – BT Interval					
0 – 12 weeks	10(2.8)	141(40.2)	151(43.0)	**2.618**	**0.0029**
>12 weeks	72(20.5)	128(36.5)	200(57.0)		
Cumulative Radiation Dose					
<70Gy	50(14.2)	20(5.7)	70(19.9)	**2.864**	**0.0001**
≥70Gy	32(9.2)	249(70.9)	281(80.1)		
Pre-Brachytherapy Tumor Size					
<4cm	16(4.6)	154(43.8)	170(48.4)	**2.310**	**0.005**
≥4cm	66(18.8)	115(32.8)	181(51.6)		
Applicator Used					
Delouche	21(6.0)	200(57.0)	221(63.0)	**3.331**	**0.004**
Vaginal Cylinder	61(17.4)	69(19.6)	130(37.0)		

Table 5. Causal Relationship of variables with disease recurrence on Multivariate Analysis in study population

Variable	Odds Ratio	CI 95%	*P-Value*
Pre-Brachytherapy Tumour Size >4cm	**2.321**	1.287-4.183	***0.005***
EBRT – BT Interval >12 weeks	**2.356**	0.947-5.863	***0.0029***
Use of Vaginal cylinder	**2.573**	1.344-4.928	***0.004***
Total Radiation dose <75Gy	**2.303**	1.258-4.129	***0.0001***
Stage >IIB	0.75	0.480-1.172	*0.309*
No Chemotherapy	0.912	0.524-1.589	*0.396*

DISCUSSION

The commonest age group was 50-59 years, which constituted 30.2% of the total patients and the mean age was 52 years. This is in keeping with most epidemiological studies on gynaecological cancers in Nigeria[34, 35] and data

from cancer registries.[36] Majority of the patients were grand multiparous. This is in keeping with the established epidemiological fact that multiparity is associated with cervical cancer.[37, 38] However, there were few nulliparous patients diagnosed of cervical cancer from this study. Though uncommon, a few studies have however established the occurrence of cervical cancer in nulliparous women.[39, 40]

Most of the patients presented with locally advanced (FIGO Stage IIB – IVA) disease at diagnosis with stage IIIB being the commonest category. This finding reflects one of the major challenges of management of gynaecological tumors in developing countries as highlighted in many studies.[41] Advanced stages at diagnosis of cancers in low-resource settings has been attributed to several factors like hesitancy in seeking health care, paucity of funds, dearth of hospitals with adequate diagnostic facilities and inadequacy of personnel with the requisite experience in the management of cancer.[42,43]

A significant proportion of the patients (45.5%) had one form of comorbid condition or the other comorbidities prior to undergoing brachytherapy. This finding is in tandem with those from Lagos[44] and Zaria,[45] where hypertension was seen as the most common comorbidity among cancer patients undergoing radiation therapy.

The treatment of locally advanced cervical, vaginal and endometrial cancers usually involves EBRT and chemotherapy as initial treatments either concurrently or sequentially, followed by intracavitary brachytherapy.[46] Dose of radiation from EBRT ranged from 45Gy to 70Gy depending on the type of machine and degree of conformity. However, most Radiation Oncologists prefer to stop at 50Gy when doing non-conformal therapy.[47, 48] Majority of the patients in this study had EBRT to the whole pelvis to a dose of 50Gy. This is also in tandem with the American Brachytherapy Society guidelines on Gynaecological brachytherapy following EBRT,[49] and the gynaecological arm of European Society for Therapeutic Radiation Oncologists (ESTRO).[50]

The total brachytherapy dose prescribed in this study is in keeping with standard dose prescribed by most Radiation Oncologists which range between 22 and 30Gy to point A using LDR brachytherapy.[51] Majority of patients in the study received brachytherapy using *Delouche* gynecologic applicator with the central uterine tandem and 2 lateral ovoids, while those with inadequate vaginal room to accommodate the applicator or those that already had surgery (Hysterectomy) had theirs using vaginal cylinders. This was consistent with a multi-institutional study on brachytherapy for cervical cancer in USA which demonstrated that most facilities using LDR brachytherapy technique made use of the *Delouche* and/or *Paris* applicators more.[52] The *Delouche* applicator has consistently been proven to demonstrate superior dosimetry qualities compared to other gynecologic applicators used for brachytherapy.[53, 54]

This study revealed that majority of patients had delays beyond 12 weeks after EBRT before commencing brachytherapy. This finding was very much in contrast with several studies done world over that showed a maximum interval of 4 weeks between completion of EBRT and start of brachytherapy. [55-57] The delays had significant

association with recurrence of disease after 2 years of follow-up. This finding is validated by a study in the United States where an increased local relapse rate was associated with treatment intervals above 6 - 8 weeks.[58] Several other studies have also reported similar outcomes with prolonged treatment intervals.[59,60] The delays in assessing brachytherapy in Sub-Saharan Africa and Nigeria in particular have been attributed to financial constraints on the patients' side, lack of qualified health personnel and most importantly the dearth of brachytherapy and other radiation facilities.[61] In addition, though the center of study within the duration of study had both functional EBRT and brachytherapy; what is practically obtainable are centers with disjointed access to this treatment. A patient requiring both EBRT and brachytherapy for treatment may have to go to a center for EBRT and then get referred to another center (usually far apart geographically) for brachytherapy. This is a major cause of significant delay or even abandonment of treatment by gynaecological cancer patients.

Although brachytherapy produced significant tumor reduction across all sizes of tumor in this study, the greatest benefits were seen in tumors 3 cm or less where there was consistent tumor sterilization, six weeks post treatment and less probability of disease recurrence two years following treatment. These findings were supported by other studies. [62-64] In a randomized clinical trial carried out on 256 patients in New York, USA proved that cervical tumors with pretreatment size >4cm was one of the highest prognostic factors determining local relapse.[63] Likewise, a prospective study demonstrated similar findings which showed a 5-year cumulative pelvic failure rate of 16% against 9% for cervical tumors >3cm and <3cm respectively, after treatment.[64] These finding emphasize the importance of tumor size as a determinant of response to brachytherapy treatment and tumor control in the long run. The study demonstrated high tumor control in patients who had EBRT, +/- chemotherapy and brachytherapy.

Though majority of patients experienced no significant acute side effects, a total of 15.6% of the patients experienced early side effects of the brachytherapy within the first three months after their treatment, which was much higher than the maximum degree of acute side effects reported from brachytherapy in any institution as noted in the systematic review in which reported 6.6%.[65] The high rate of acute effects recorded in this study may be attributed to the higher proportion of patients who had their brachytherapy using vaginal cylinder. High degree of localized side effects from brachytherapy has been attributed to increased use of cylinders, rings and other applicators instead of tandem-ovoid applicators.[66] A study which retrospectively reviewed patients who had brachytherapy, reported cystitis and proctitis as the most frequently encountered acute side effects which was in keeping with findings from this study.[67] The pattern of long-term side effects from brachytherapy in this study; which include vaginal stenosis, fistulous tracts, sexual dysfunction; were replicated from similar studies. [68, 69]

The proportion of patients who had no evidence of disease at 2 years of follow-up (76.7%) was similar to another study with a value of 81%,[69] but much higher than a study done in Ibadan where complete response rates of 68%, 57% and 41.2% were achieved in 2 years in patients with stages IIB, III and IVA cervical cancers respectively.[70] These findings underscore the importance of complete

treatment with EBRT and brachytherapy in the treatment of locally advanced cervical cancers, and other gynaecological tumors.

This study also demonstrated the inferior dosimetric value of cylinders when compared to tandem-ovoid applicators, as evidenced by higher recurrence in the former than the latter. This was supported by a similar study which compared the dose distribution from various intracavitary applicators for gynaecological tumours.[71]

Patients who received optimal cumulative radiation dose (≥ 70Gy) in this study had better chance of loco-regional disease control. This finding was very much in keeping with a study which found the mean loco-regional disease-free survival of 55.2 months (+/-4.4 months) was achieved for patients with locally advanced cervical cancer with a total radiation dose of 70.2Gy.[72] Similarly, three- and five-year disease-free survival of 63.7% and 60.2% respectively were recorded in a prospective cohort study carried out on patients with locally advanced cervical cancer in whom a cumulative radiation dose of about 75Gy was given.[73] These findings emphasize the need for Radiation Oncologists to ensure that cervical cancer patients receive optimal cumulative radiation doses to ensure tumor control in the long term.

CONCLUSION

Most of the patients seen in the study were of the age group 50-59 years, with cervical cancer being by far the commonest gynaecological cancer treated with intracavitary LDR brachytherapy. Majority of the cases were diagnosed at stage IIIB. The most commonly prescribed radiation dose from EBRT and brachytherapy were 50Gy and 20Gy respectively.

The study showed that the chances of having poor tumor control/persistent disease in patients with locally advanced gynaecological cancer was higher in patients with tumors ≥4cm prior to brachytherapy, those who had a delay interval of more than 12 weeks between completing EBRT and commencing brachytherapy, as well as those who received cumulative radiation dose <70Gy.

Limitation of the Study

i. Being a retrospective study, some information could not be obtained from patients' case files and records. Also, some of the patients excluded due to inability to continue follow-up for two years may represent those who responded poorly to treatment and might have been lost due to death. Their exclusion represents loss of vital information from an important block of potential respondents.
ii. The specific data on indication for use of vaginal applicator was not gotten. This would have enabled us rule them out as potential confounders in multivariate analysis to determine if the type of applicator used was truly significantly associated with disease recurrence.

REFERENCES

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394–424.
2. Barman D, Sharma JD, Barmon D, Kataki AC, Sharma A, Kalita M. Epidemiology of gynecological cancers in Kamrup Urban

District cancer registry. Indian J Cancer. 2017 Mar;54(1):388–91
3. Gebretsadik A, Bogale N, Dulla D. Descriptive epidemiology of gynaecological cancers in southern Ethopia: restrospective cross-sectional review. BMJ Open 2022;12:e062633. Doi: 10.1136/bmjopen-2022-062633.
4. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021;0:1-41.
5. Oguntayo O, Zayyan M, Kolawole A, Adewuyi S, Ismail H, Koledade K. Cancer of the cervix in Zaria, Northern Nigeria. Ecancer medical science [Internet]. 2011 Aug 19 [cited 2019 Aug 2];5
6. Zubairu IH, Theyra HE, Nuhu T. Demographic Pattern of Cervical Cancer Patients Seen in a Radiotherapy Treatment Facility in Northern Nigeria. Indian J Gynecol Oncol. 2017; 15(3): 52.
7. Aliyu UM, Jimoh AO, Yunusa A, Umar M. Pattern of Cancers Treated with Radiotherapy in UDUTH Sokoto: A New Center Experience. J Clin Diagn Res JCDR. 2015 Aug;9(8):XC01–4
8. Manga MM, Fowotade A, Abdullahi YM, El-Nafaty AU, Adamu DB, Pindiga HU, et al. Epidemiological patterns of cervical human Papillomavirus infection among women presenting for cervical cancer screening in North-Eastern Nigeria. Infect Agent Cancer. 2015;10:39.
9. De Vincenzo R, Conte C, Ricci C, Scambia G, Capelli G. Long-term efficacy and safety of human Papillomavirus vaccination. Int J Womens Health. 2014; 6:999–1010.
10. Jain A, Ganesh B, Bobdey SC, Sathwara JA, Saoba S. Sociodemographic and Clinical Profile of Cervical Cancer Patients Visiting in a Tertiary Care Hospital in India. Indian J Med Paediatr Oncol Off J Indian Soc Med Paediatr Oncol. 2017;38(3):291–5.
11. Alsbeih G. Exploring the Causes of the Low Incidence of Cervical Cancer in Western Asia. Asian Pac J Cancer Prev APJCP. 2018;19(6):1425–9.
12. Evans T, Sany O, Pearmain P, Ganesan R, Blann A, Sundar S. Differential trends in the rising incidence of endometrial cancer by type: data from a UK population-based registry from 1994 to 2006. Br J Cancer. 2011 Apr 26;104(9):1505–10.
13. Forbes LJL, Warburton F, Richards MA, Ramirez AJ. Risk factors for delay in symptomatic presentation: a survey of cancer patients. Br J Cancer. 2014 Jul 29;111(3):581–8
14. Anorlu RI, Orakwue CO, Oyeneyin L, Abudu OO. Late presentation of patients with cervical cancer to a tertiary hospital in Lagos: What is responsible? Eur J Gynaecol Oncol. 2004;25(6):729-732.
15. Ouasmani F, Hanchi Z, Haddou Rahou B, Bekkali R, Ahid S, Mesfioui A. Determinants of Patient Delay in Seeking Diagnosis and Treatment among Moroccan Women with Cervical Cancer. Obstet Gynecol Int. 2016;2016:4840762.doi:10.1155/2016/4840762.
16. Mathew A, George PS, Ramadas K, Mathew BS, Kumar A, Roshni S, et al. Sociodemographic Factors and Stage of Cancer at Diagnosis: A Population-Based Study in South India. J Glob Oncol [Internet]. 2019 Jul 19 [cited 2019 Oct 6]; Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6690651/
17. Perri T, Issakov G, Ben-Baruch G, Felder S, Beiner ME, Helpman L, et al. Effect of treatment delay on survival in patients with cervical cancer a historical cohort study. International Journal of Gynecological Cancer. 2014;24(7):1326-1332.

18. Rudd P, Gorman D, Meja S, Mtonga P, Jere Y, Chidothe I, et al. Cervical cancer in southern Malawi: A prospective analysis of presentation, management and outcomes. Malawi Med J. 2017;29(2):124-129
19. Bourgioti C, Chatoupis K, Moulopoulos LA. Current imaging strategies for the evaluation of uterine cervical cancer. World J Radiol. 2016 Apr 28;8(4):342–54
20. Salib MY, Russell JHB, Stewart VR, Sudderuddin SA, Barwick TD, Rockall AG et al. 2018 FIGO Staging Classification for Cervical Cancer: Added Benefit of Imaging. Radiographics 2020;40(6):1807-1822
21. Chhabra S. Editorial: Management of Gynaecological Cancers - An Update. Rev Recent Clin Trials. 2015;10(4):252–4
22. Todo Y, Watari H. Concurrent chemoradiotherapy for cervical cancer: background including evidence-based data, pitfalls of the data, limitation of treatment in certain groups. Chin J Cancer Res. 2016 Apr;28(2):221–7.
23. Logsdon MD, Eifel PJ. Figo IIIB squamous cell carcinoma of the cervix: an analysis of prognostic factors emphasizing the balance between external beam and intracavitary radiation therapy. Int J Radiat Oncol Biol Phys. 1999 Mar 1;43(4):763–75
24. Romano KD, Hill C, Trifiletti DM, Peach MS, Horton BJ, Shah N, et al. High dose-rate tandem and ovoid brachytherapy in cervical cancer: dosimetric predictors of adverse events. Radiat Oncol. 2018 Jul 16;13(1):129.
25. Koushik K, Bilimagga R, Rao N, Janaki MG, Ponni A, Rajeev AG. Positional variation of applicators during low dose rate intracavitary brachytherapy for cervical cancer: a prospective study. J Contemp Brachytherapy. 2010 Sep;2(3):93–7.
26. Ntekim A, Adenipekun A, Akinlade B, Campbell O. High Dose Rate Brachytherapy in the Treatment of cervical cancer: preliminary experience with cobalt 60 Radionuclide source-A Prospective Study. Clin Med Insights Oncol. 2010 Aug 19;4:89–94.
27. Pinn-Bingham M, Puthawala AA, Syed AMN, Sharma A, Disaia P, Berman M, et al. Outcomes of high-dose-rate interstitial brachytherapy in the treatment of locally advanced cervical cancer: long-term results. Int J Radiat Oncol Biol Phys. 2013 Mar 1;85(3):714–20
28. Ferrigno R, Nishimoto IN, Novaes PER dos S, Pellizzon ACA, Maia MAC, Fogarolli RC, et al. Comparison of low and high dose rate brachytherapy in the treatment of uterine cervix cancer. Retrospective analysis of two sequential series. Int J Radiat Oncol Biol Phys. 2005 Jul 15;62(4):1108–16.
29. Wang X, Liu R, Ma B, Yang K, Tian J, Jiang L, et al. High dose rate versus low dose rate intracavity brachytherapy for locally advanced uterine cervix cancer. Cochrane Database Syst Rev. 2010 Jul 7;(7):CD007563
30. Bakhshabadi M, Ghorbani M, Khosroabadi M, Knaup C, Meigooni AS. A comparison study on various low energy sources in interstitial prostate brachytherapy. J Contemp Brachytherapy. 2016 Feb;8(1):74–81
31. Ehlers A, Makanjee CR. Exploration of gynaecological cancer high dose-rate brachytherapy treatment: a pilot study. Pan Afr Med J [Internet]. 2018 May 15 [cited 2019 Oct 7];30.
32. Warnock C. Patients' experiences of intracavity brachytherapy treatment for gynaecological cancer. Eur J Oncol Nurs Off J Eur Oncol Nurs Soc. 2005 Mar;9(1):44–55
33. Perez S, Néron S, Benc R, Rosberger Z, Vuong T. The Meaning and Experience of Patients Undergoing Rectal High-Dose-Rate Brachytherapy. Cancer Nurs. 2016 Feb;39(1):42–50.

34. Yakasai IA, Ugwa EA, Otubu J. Gynecological malignancies in Aminu Kano Teaching Hospital Kano: a 3-year review. Niger J Clin Pract. 2013 Mar;16(1):63–6.
35. Sowunmi AC, Alabi AO, Fatiregun OA, Olukiran GE, Alabi B a. M, Ibitoye AZ. Trend of gynecological cancers in a tertiary centre in Lagos, Nigeria. Niger Q J Hosp Med. 2016 Jan 1;26(2):439-442–442.
36. Mohammed AZ, Edino ST, Ochicha O, Gwarzo AK, Samaila AA. Cancer in Nigeria: a 10-year analysis of the Kano cancer registry. Niger J Med J Natl Assoc Resid Dr Niger. 2008 Aug;17(3):280–4.
37. Muñoz N, Franceschi S, Bosetti C, Moreno V, Herrero R, Smith JS, et al. Role of parity and human Papillomavirus in cervical cancer: the IARC multicentric case-control study. Lancet Lond Engl. 2002 Mar 30;359(9312):1093–101
38. Tekalegn Y, Sahiledengle B, Woldeyohannes D, Atlaw D, Degno S, Desta F et al. high parity is associated with increased risk of cervical cancer: Systemic review and meta-analysis of case-control studies. Women Health (Lond) 2022;18:17455065221075904.
39. Nnadi DC, Nwobodo EI, Ekele BA, Sahabi SM. Screening for Cervical Cancer: A Review of Outcome among Infertile Women in a Tertiary Hospital in North-West Nigeria. Ann Med Sci Res 2014;4(3):383-387.
40. Tompkins P. Cancer of the Cervix Uteri in Nulliparous Women: A Report of 53 Cases. Am J Cancer. 1935 Jun 1;24(2):397–401.
41. Adefuye PO, Adefuye BO, Oluwole AA. Female Genital Tract Cancers in Sagamu, Southwesr Nigeria. East Afr Med J. 2014 Nov;91(11):398–406.
42. Ibrahim NA, Oludara MA. Socio-demographic factors and reasons associated with delay in breast cancer presentation: a study in Nigerian women. Breast Edinb Scotl. 2012 Jun;21(3):416–8
43. Ouasmani F, Hanchi Z, Haddou Rahou B, Bekkali R, Ahid S, Mesfioui A. Determinants of Patient Delay in Seeking Diagnosis and Treatment among Moroccan Women with Cervical Cancer. Obstet Gynecol Int. 2016;2016:4840762.doi:10.1155/2016/4840762.
44. Salako O, Okediji PT, Habeebu MY, Fatiregun OA, Awofeso OM, Okunade KS, et al. The pattern of comorbidities in cancer patients in Lagos, South-Western Nigeria. Ecancer medical science [Internet]. 2018 Jun 13 [cited 2019 Aug 23]; 12.
45. Adewuyi SA, Mbibu NH, Samaila MOA, Ketiku KK, Durosinmi-Etti FA. Clinico-pathologic characterisation of metastatic prostate cancer in the Radiotherapy and Oncology Department, Ahmadu Bello University Teaching Hospital, Zaria-Nigeria: 2006-2009. Niger Postgrad Med J. 2013 Mar;20(1):45–51.
46. Rijkmans EC, Nout RA, Rutten IHHM, Ketelaars M, Neelis KJ, Laman MS, et al. Improved survival of patients with cervical cancer treated with image-guided brachytherapy compared with conventional brachytherapy. Gynecol Oncol. 2014 Nov;135(2):231–8.
47. Strauss H-G, Kuhnt T, Laban C, Puschmann D, Pigorsch S, Dunst J, et al. Chemoradiation in cervical cancer with cisplatin and high-dose rate brachytherapy combined with external beam radiotherapy. Results of a phase-II study. Strahlenther Onkol Organ Dtsch Rontgengesellschaft Al. 2002 Jul;178(7):378–85.
48. Mahmoud O, Kilic S, Khan AJ, Beriwal S, Small W. External beam techniques to boost cervical cancer when brachytherapy is not an option—theories and applications. Ann Transl Med [Internet]. 2017 May [cited 2019 Aug 24];5(10).
49. Nag S, Erickson B, Thomadsen B, Orton C, Demanes JD, Petereit D. The American

Brachytherapy Society recommendations for high-dose-rate brachytherapy for carcinoma of the cervix. Int J Radiat Oncol Biol Phys. 2000 Aug 1;48(1):201–11.

50. Pötter R, Haie-Meder C, Van Limbergen E, Barillot I, De Brabandere M, Dimopoulos J, et al. Recommendations from gynaecological (GYN) GEC ESTRO working group (II): concepts and terms in 3D image-based treatment planning in cervix cancer brachytherapy-3D dose volume parameters and aspects of 3D image-based anatomy, radiation physics, radiobiology. Radiother Oncol J Eur Soc Ther Radiol Oncol. 2006 Jan;78(1):67–77.
51. Al Feghali KA, Elshaikh MA. Why brachytherapy boost is the treatment of choice for most women with locally advanced cervical carcinoma? Brachytherapy. 2016 Apr;15(2):191–9.
52. Erickson B, Eifel P, Moughan J, Rownd J, Iarocci T, Owen J. Patterns of brachytherapy practice for patients with carcinoma of the cervix (1996-1999): a patterns of care study. Int J Radiat Oncol Biol Phys. 2005 Nov 15;63(4):1083–92
53. Rangarajan R. Dosimetric evaluation of image-based brachytherapy using tandem ovoid and tandem ring applicators. Rep Pract Oncol Radiother. 2018;23(1):57–60.
54. Chakrabarti B, Basu-Roy S, Kar SK, Das S, Lahiri A. Comparison of dose volume parameters evaluated using three forward planning – optimization techniques in cervical cancer brachytherapy involving two applicators. J Contemp Brachytherapy. 2017 Oct;9(5):431–45.
55. Bandyopadhyay A, Mukherjee U, Ghosh S, Ghosh S, Sarkar SK. Pattern of Failure with Locally Advanced Cervical Cancer– A Retrospective Audit and Analysis of Contributory Factors. Asian Pac J Cancer Prev APJCP. 2018 Jan 27;19(1):73–9.
56. Skowronek J. Current status of brachytherapy in cancer treatment – short overview. J Contemp Brachytherapy. 2017 Dec;9(6):581–9.
57. Mazeron R, Castelnau-Marchand P, Dumas I, del Campo ER, Kom LK, Martinetti F, et al. Impact of treatment time and dose escalation on local control in locally advanced cervical cancer treated by chemoradiation and image-guided pulsed-dose rate adaptive
58. Han I, Orton C, Shamsa F, Hart K, Strowbridge A, Deppe G, et al. Combined low-dose-rate brachytherapy and external beam radiation for cervical cancer: experience over ten years. Radiat Oncol Investig. 1999;7(5):289–96,
59. Chen SW, Liang JA, Yang SN, Ko HL, Lin FJ. The adverse effect of treatment prolongation in cervical cancer by high-dose-rate intracavitary brachytherapy. Radiother Oncol J Eur Soc Ther Radiol Oncol. 2003 Apr;67(1):69–76.
60. Perez CA, Grigsby PW, Castro-Vita H, Lockett MA. Carcinoma of the uterine cervix. I. Impact of prolongation of overall treatment time and timing of brachytherapy on outcome of radiation therapy. Int J Radiat Oncol Biol Phys. 1995 Jul 30;32(5):1275–88.
61. Finocchario-Kessler S, Wexler C, Maloba M, Mabachi N, Ndikum-Moffor F, Bukusi E. Cervical cancer prevention and treatment research in Africa: a systematic review from

a public health perspective. BMC Womens Health. 2016 Jun 4;16(1):29

62. Yalman D, Aras AB, Ozkök S, Duransoy A, Celik OK, Ozsaran Z, et al. Prognostic factors in definitive radiotherapy of uterine cervical cancer. Eur J Gynaecol Oncol. 2003;24(3–4):309–14
63. Keys HM, Bundy BN, Stehman FB, Okagaki T, Gallup DG, Burnett AF, et al. Radiation therapy with and without extrafascial hysterectomy for bulky stage IB cervical carcinoma: a randomized trial of the Gynecologic Oncology Group. Gynecol Oncol. 2003 Jun;89(3):343–53
64. Grigsby PW, Perez CA, Chao KS, Elbendary A, Herzog TJ, Rader JS, et al. Lack of effect of tumor size on the prognosis of carcinoma of the uterine cervix Stage IB and IIA treated with preoperative irradiation and surgery. Int J Radiat Oncol Biol Phys. 1999 Oct 1;45(3):645–51
65. Castelnau-Marchand P, Chargari C, Maroun P, Dumas I, Del Campo ER, Cao K, et al. Clinical outcomes of definitive chemoradiation followed by intracavitary pulsed-dose rate image-guided adaptive brachytherapy in locally advanced cervical cancer. Gynecol Oncol. 2015 Nov;139(2):288–94.
66. Ma JK, Mourad WF, Allbright R, Packianathan S, Harrell LM, Chinchar E, et al. Short-term clinical outcome and dosimetric comparison of tandem and ring versus tandem and ovoids intracavitary applicators. J Contemp Brachytherapy. 2015 Jun;7(3):218–23.
67. Kirisits C, Rivard MJ, Baltas D, Ballester F, De Brabandere M, van der Laarse R, et al. Review of clinical brachytherapy uncertainties: Analysis guidelines of GEC-ESTRO and the AAPM. Radiother Oncol. 2014 Jan;110(1):199–212.
68. Lind H, Waldenström A-C, Dunberger G, al-Abany M, Alevronta E, Johansson K-A, et al. Late symptoms in long-term gynaecological cancer survivors after radiation therapy: a population-based cohort study. Br J Cancer. 2011 Sep 6;105(6):737–45.
69. Vulpe H, Asamoah FA, Maganti M, Vanderpuye V, Fyles A, Yarney J. External Beam Radiation Therapy and Brachytherapy for Cervical Cancer: The Experience of the National Centre for Radiotherapy in Accra, Ghana. Int J Radiat Oncol Biol Phys. 2018 01;100(5):1246–53.
70. O. B. Campbell IAB AO Arowojolu, BI Akinlade, A Adenipekun. Advanced cervical carcinoma in Ibadan, Nigeria: an appraisal of radiation therapy. J Obstet Gynaecol. 2000 Jan 1;20(6):624–7.
71. Basu B, Basu S, Chakraborti B, Ghorai S, Gupta P, Ghosh S, et al. A comparison of dose distribution from Manchester-style and Fletcher-style intracavitary brachytherapy applicator systems in cervical cancer. J Contemp Brachytherapy. 2012 Dec;4(4):213–8.
72. Cihoric N, Tsikkinis A, Tapia C, Aebersold DM, Zlobec I, Lössl K. Dose escalated intensity modulated radiotherapy in the treatment of cervical cancer. Radiat Oncol Lond Engl [Internet]. 2015 Nov 24 [cited 2019 Dec 20a10. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4657246/
73. Lee JE, Huh SJ, Park W, Lim DH, Ahn YC, Park CS, et al. Radical Radiotherapy for Locally Advanced Cancer of Uterine Cervix. Cancer Res Treat Off J Korean Cancer Assoc. 2004 Aug;36(4):222–7