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INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI:10.21474/IJAR01/19016
DOI URL: http://dx.doi.org/10.21474/IJAR01/19016

RESEARCH ARTICLE

HIGH DOSE RATE BRACHYTHERAPY IN THE TREATMENT OF OPERATED ENDOMETRIAL CANCERS: ABOUT 60 CASES

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Manuscript Info

Manuscript History
Received: 05 May 2024
Final Accepted: 09 June 2024
Published: July 2024

Key words:-
Brachytherapy, Dosimetry, Endometrial Cancer, Toxicity

Abstract

Introduction: Endometrial cancer is the third gyneco-mammary cancer in the radiotherapy-brachytherapy department of the RABAT national oncology institute.Brachytherapy has an important place in the therapeutic strategy.

The objective of the study:Is to analyze the coverage of target volumes as well as the dose to organs at risk with three-dimensional dosimetric planning and toxicity assessment.

Material and methods: This is a retrospective study of 60 cases of operated endometrial cancers treated by high dose rate brachytherapy without external radiotherapy or chemotherapy collected in the radiotherapy department of the National Institute of Oncology RABAT between January 2018 and December 2020. A dosimetric scan without injection was performed at the first session and was used to delineate the clinical anatomic target volume (CTV). We evaluated the D100 of the clinical target volume and the D2 cm3 of the bladder, rectum and small intestine. We also analyzed acute genitourinary and gastrointestinal toxicity.

Results: The average age of the patients was 49 years. Endometrioid carcinoma accounted for 98.5%, with one case of mucinous carcinoma. All patients underwent surgery.The brachytherapy protocol used was 3 × 7 Gy (75%) or 4 × 5.5 Gy (17%) in weekly sessions; A single patient received a reduced total dose of 19.8 Gy in 3 fractions of 5.5 Gy due to a high rectal dose.The average target volume coverage (D100) was 96.50%.The average D2 cm3 per session received by the bladder, rectum and small intestine were 4.06 Gy, 4.9 Gy and 2.8 Gy, respectively.Regarding genitourinary toxicity, we noted two grade 1 cystitis, one grade 2, two grade 1 mucositis and one grade 2.For gastrointestinal toxicity, no cases of grade greater than 1 were noted.No grade 3 or 4 toxicities were recorded.

Conclusion: High dose rate brachytherapy has an important place in the therapeutic strategy for endometrial cancer.The very low toxicity recalls the good tolerance of this treatment whichapplies to the entire population.

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Introduction:-

Endometrial cancers are the third most common tumor site in women.

The positive diagnosis is based on the histological study of an endometrial biopsy or the staged curettage product.

CT or MRI evaluates penetration into the myometrium, towards the isthmus and the cervix and looks for ectopic lesions and iliac or lumbo-aortic lymphadenopathy.

The main treatment remains total hysterectomy with bilateral adnexectomy and bilateral iliac subvenous lymph node sampling. However, after surgery alone, the locoregional recurrence rate is 4 to 20%, reduced from 0 to 5% after postoperative brachytherapy of the vaginal fundus. Postoperative brachytherapy is most often carried out on an outpatient basis using three or four fractions, at a high dose rate.

Our study aims to analyze the coverage of target volumes as well as the dose to organs at risk with three-dimensional dosimetric planning and toxicity assessment.

Materials and Methods:-

The patients:

Patients were identified using medical records

Computerized, between January 2018 and December 2020 within the radiotherapy department of the National Institute of Oncology Rabat.

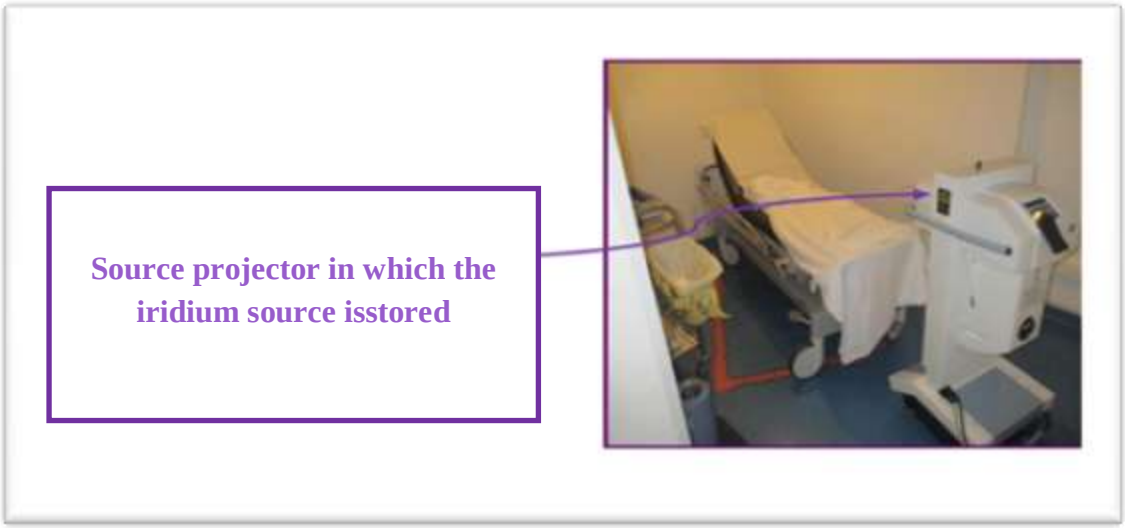
All patients underwent primary surgery (hysterectomytotal colpohysterectomy with or without lymph node dissection) and without external radiotherapy or chemotherapy and were treated with high dose rate brachytherapy.

Planning technique:

Before the first HDR-VB procedure, dosimetric and localization planning was undertaken. Patients underwent a pelvic examination to assess the integrity of the vaginal cuff and to look for signs of residual or recurrent disease.

The brachytherapy device was a standard applicator placed at each session after gynecological examination (figure 1). A dosimetric scan without injection was performed at the first session and was used to delineate the anatomoclinical target volume (CTV) equal to the vaginal mucosa over a height ranging from the upper third to the upper two thirds of the vagina and the organs at risk (rectum, bladder, small intestine). We evaluated the D100 (dose receiving 100% of the prescribed dose) of the clinical target volume and the D2 cm3 (dose in 2 cm3 of the volume) of the bladder, rectum and small intestine.

Figure 1:-Brachytherapy room.



Results :-

Patient and tumor characteristics are described in Table (1). The average age of the patients was 49 years; the majority of patients included in this study were pathological stage I (85%), 15% of patients were stage II.

Among patients with stage I disease, 88% were atstage IA and 12% at stage IB. 45% of patients had grade 1 disease, 35% of patients had grade 2 disease, and 20% of patients had grade 3 tumors

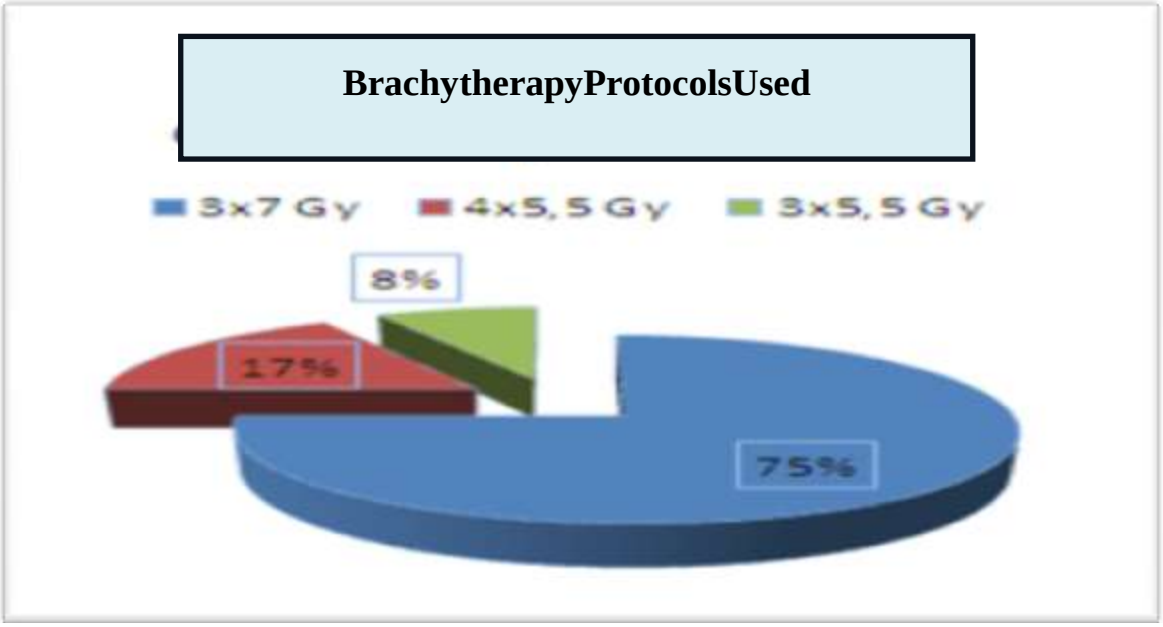
Endometrioid carcinoma accounted for 98.5%, with one case of mucinous carcinoma. All patients underwent surgery

Table 1:-Patient characteristics (N=60).

Clinical data	%
Middle age	49
STADIUM **I** **II**	 85 15
Grade **1** **2** **3**	 45 35 20
Histological type **Endometrioid carcinoma** **mucinous carcinoma**	 98.5 1.5

The brachytherapy protocol used (figure 2) was 3 × 7 Gy (75%) or 4 × 5.5 Gy (17%) in weekly sessions; A single patient received a reduced total dose of 19.8 Gy in 3 fractions of 5.5 Gy due to a high rectal dose.

Figure 2:- Brachytherapyprotocolsused.



The average target volume coverage (D100) was 96.50%.

The average D2 cm3 per session received (Table 2) by the bladder, rectum and small intestine were 4.06 Gy, 4.9 Gy and 2.8 Gy, respectively.

Table 2:- The average D2 cm3 per session received by the organs at risk.

Organs at risk	D2 cm3 /session
Bladder	4.06 Gy
Rectum	2.9Gy
Small intestine	2.8Gy

No cases of significant bladder toxicity have been reported for thegroup of patients analyzed. The rate of acute urinaryreactions (<90 daysfrom start of RT) grades 1 and 2 was 14%and 2%, respectively. The rate of lateurinaryreactions(>90 daysafter RT) grades 1 and 2 were 7% and 3%,respectively .Urinaryreactionsmostcommonlyincludeddysuria, as well as urinary frequency and tract infectionsurinary, whichmay be due to insertion of the bladder catheter.

No grade 3 or greater urinary toxicity was observed.

There have been no reports of significant rectal toxicity in ourstudy population (Table 3).

Table 3:-Assessment of brachytherapy toxicity.

Toxicities	%
Urinary	
Acute grade 1	14
Grade 2	2
Late grade 1	7
Grade 2	3
Gastrointestinal	_

The 3-year overall survival rates were 95%. Of the 60 patients included in this study, there were a total of 4 failures (5%). Tworecurrenceslocoregionallocalizationsdevelopedmainly at the lymph node level and 2 patientspresentedsecondarylocalizations at the pulmonarylevel.There was no recurrence at the vaginal cuff.

Discussion:-

Endometrial cancer is the most common gynecological cancer in developed countries. In 2019, 63,000 new cases were diagnosed worldwide (1).

The overall prognosis is favorable because more than 80% of these cancers are diagnosed at an early stage.

It is a cancer preferentially affecting women after menopause because in nine out of ten cases, it occurs in a patient over 50 years old (2). Philippe and Charpin place the average age between 59-60 years (3). Other studies reveal an average age of 57.5 years, (4).

It is a hormone-dependent cancer and the main “environmental” risk factors correspond to situations of endogenous and exogenous hyperestrogenism (estrogen-progestin contraception, hormonal treatment for menopause) (5).

Other demonstrated risk factors for endometrial cancer include being overweight, diabetes, and tamoxifen treatment (5).

Genetic factors can also play a role in the genesis of endometrial cancers. They are dominated by Lynch syndrome (5).

Metrorrhagia is present in 75 to 90% at initial clinical presentation. When they occur in postmenopausal patients, they are associated with endometrial cancer in 3 to 20% of cases (6).

The diagnosis of endometrial cancer remains based on the pathological analysis of material obtained during an endometrial biopsy. According to the new European recommendations, histological types are now grouped into endometrioid or non-endometroid (serous, clear cell, carcinosarcoma), rather than type 1 and type 2.

We also note the change in the grade which is now qualified as low grade (former grade 1-2) or high grade (former grade 3) (7).

The general pre-therapeutic assessment must include family history, assessment of comorbidities with geriatric assessment if indicated, and physical examination including a pelvic examination.

The imaging assessment should include an endovaginal or endorectal pelvic ultrasound or a pelvic MRI to determine the depth of myometrial invasion and whether or not the cervical stroma is affected.

Depending on the clinical findings and the pathological analysis, other imaging examinations (thoraco-abdomino-pelvic CT, MRI, PET scanner, ultrasound) may be requested to assess ovarian, lymph node involvement, or another metastatic location. .

In addition to its crucial role in staging, surgery represents the cornerstone of curative treatment of endometrial cancer. Hysterectomy with bilateral adnexectomy is the standard surgical procedure for endometrial cancer.

The new definition of groups at risk of recurrence currently includes molecular classification if analyzes are available (7). p53abn identifies a high-risk group regardless of stage (except stage IA), histology and grade [IV,B]. POLE mut is associated with an excellent prognosis and adjuvant treatmentcouldbeavoided in stages I-II of the disease (8). In the absence of a molecularclassification, the group exposed to lowriskisdefined as havingendometrioidadenocarcinoma of pathological stage IA, limited to the endometrium or invadinglessthan 50% of the myometrium, grades 1 and 2 withembolisms. vascularsystems absent or focal.

There is no change in adjuvant treatmentcompared to the 2016 recommendations. Therapeutic abstention remainsrecommended (7). The group exposed to intermediateriskincludes patients with Stage IB low-grade endometrioidadenocarcinoma, absent or focal emboli; Stage IA high-grade endometrioid, absent or focal emboli; Non-endometroid stage IA withoutmyometrial infiltration. As in 2016, vaginal brachytherapyremainsrecommended. Therapeutic abstention can bediscussed for patients under the age of 60 (7).The brachytherapy protocol used in ourstudywas 3×7 Gy (75%);then in otherstudies the protocol usedis 5×6 Gy with good local control and minimal acute and chronic toxicity (9).In ourstudy, 60 womentreatedwith HDR-VB whopresented a goodlocal control withlow rates of acute or lateurinary toxicity.

Theseresults are similar to other reports in the literature (Table 4)

Table 4:- Results of postoperative vaginal brachytherapy.

Authors	year	NOT	Protocol	Dose rate	Median follow-up (months)	Loco-Regional control	Vaginal relapses	Grade 3 and 4 late complications (%)
Anderson et al [10].	2000	102	3×5Gy	HDD	49	97%	1%	0
Atahan et al [11]	2008	128	5×5.5Gy	HDD	48	98%	0.8%	0
Nount et al [12]	2010	213	3×7Gy	HDH	45	96%	1.8%	2 of grade 3
Sorbe et al [13]	2012	263	Variable	HDD	62	95%	2.8%	1.6%(grade3)

N: effective; HDD: high dose rate

Conclusion:-

High dose rate brachytherapy has an important place in the therapeutic strategy of endometrial cancer. It allows an improvement in the vaginal local control rate.

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