

# Changes of the Vagina After Concurrent Radiochemotherapy and Brachytherapy in Cervical Cancer Anatomical and Physiological Changes

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**Abstract:-** The objective of the study: The aim of our study was to highlight the anatomical and physiological changes of the vagina after external radiotherapy and brachytherapy in cervical cancer. **Materials and Methods:** This was a prospective descriptive study conducted over a period of 6 months, from March to August 2022. A total of 123 women with cervical cancer, treated with concurrent radiochemotherapy and uterovaginal brachytherapy, who reported having had sexual intercourse in the six months prior, were included in the study. Patients were interviewed and examined during post-therapeutic follow-up consultations. **Results and Statistical Analysis:** The age of the patients (n=123) ranged from 33 to 67 years, with a mean of  $49.35 \pm 9.84$  years. The post-therapeutic follow-up duration ranged from 6 months to 7 years. The most common histological type was squamous cell carcinoma, and the most common FIGO stage was stage II. Treatment consisted of concurrent radiochemotherapy and uterovaginal brachytherapy. Interviews revealed several changes related to the vagina after treatment. More than 65% of patients (n=81) reported the onset or worsening of vaginal dryness, over 50% (n=63) reported the onset or worsening of dyspareunia. Nearly 70% (n=83) reported a decrease in sexual desire frequency or dissatisfaction, and over 60% (n=78) became indifferent to sexual life. Gynecological examination revealed a vaginal length ranging from 2 to 10 cm with a mean of  $5.66 \pm 2.09$  cm, the presence of synechiae and/or stenosis in nearly 43% (n=53), and bleeding in nearly 40% (n=47). In univariate analysis, vaginal dryness and dyspareunia significantly increased with age. Resumption of sexual activity was slower in younger and older women. Among patients followed for two years or less, there was a significant increase in synechiae or stenosis, as well as bleeding. Conversely, the prevalence of vaginal dryness and dyspareunia increased with follow-up duration, especially in those exceeding two years. In groups with vaginal dryness or dyspareunia, a large proportion of patients reported a decrease in sexual desire and indifference to their sexual life. **Conclusion:** This study revealed that patients with cervical cancer experienced significant anatomical and physiological changes in the vagina after treatment with concurrent radiochemotherapy and uterovaginal brachytherapy, leading to chronic sequelae

and sexual disorders. It is therefore essential to implement measures to prevent or limit certain side effects associated with these treatments.

**Keywords:-** Vagina, Concurrent Radiochemotherapy, Brachytherapy, Cervical Cancer.

## I. INTRODUCTION

When discussing the physiology and anatomy of the vagina, it becomes essential to understand the complex mechanisms underlying its functioning and natural balance. This musculo-membranous canal, vital for reproduction and sexual health, measures between 7 and 12 cm in length. Located in the female pelvis, it connects the vulva to the cervix and can undergo significant anatomical and physiological variations after irradiation of the pelvic region in the context of cervical cancer.

Cervical cancer, often treated at the localized stage with concurrent radiochemotherapy and uterovaginal brachytherapy, can lead to significant changes in the vagina. These changes can affect the mucosa, vascularization, sensitivity, and various functionalities of the vagina, resulting in dryness, reduced elasticity and blood flow, as well as discomfort or dyspareunia during intercourse. This poses significant challenges in terms of sexual health and quality of life for treated patients.

This article therefore examines the alterations in the anatomy and physiology of the vagina in women treated with concurrent radiochemotherapy and uterovaginal brachytherapy for cervical cancer. It is based on knowledge of vaginal structure, its hormonal and immune responses, as well as on clinical changes and functional signs reported by patients' post-therapy.

## II. OBJECTIVE OF THE STUDY

The objective of our study was to highlight the anatomical and physiological changes of the vagina after concurrent radiochemotherapy and uterovaginal brachytherapy in cervical cancer.

### III. MATERIALS AND METHODS

This was a prospective cross-sectional, descriptive, and analytical study conducted over a period of six months, from March to August 2022, at the National Institute of Oncology in Rabat. This institute is the largest national oncology center in Morocco and is a collaborator of the International Atomic Energy Agency (IAEA). It recruits the largest number of patients.

A total of 123 patients were included in this study aimed at screening the anatomical and physiological changes of the vagina after treatment for cervical cancer with concurrent radiochemotherapy and uterovaginal brachytherapy. This information was collected during post-therapeutic follow-up consultations, based on interviews and clinical examination. Data regarding the disease, histological type, stage, and treatment received were extracted from medical records retrospectively.

During the interview, four questions were asked:

- Have you noticed the onset or worsening of vaginal dryness after treatment?
- Have you observed the onset or worsening of dyspareunia after treatment?
- Have you experienced a decrease in sexual desire or sexual dissatisfaction after treatment?
- Do you feel indifferent towards your sexual life with your partner after treatment?

During the clinical examination, the following elements were specified: vaginal length, presence or absence of vaginal synechiae or stenosis, and presence or absence of bleeding.

All data were entered and analyzed using the Statistical Package for the Social Sciences (SPSS) version 21. The significance level for all statistical analyses was set at  $p < 0.05$ .

The inclusion criteria were as follows:

- Patients with localized cervical cancer
- Patients who received concurrent radiochemotherapy and uterovaginal brachytherapy
- Patients who reported having had sexual intercourse in the six months prior
- Patients in good local and distant control
- Obtaining informed consent from patients who were previously informed about the purpose and confidentiality of the study.

The exclusion criteria were as follows:

- Patients with cervical cancer in poor local or distant control
- Patient refusal
- Presence of cognitive disorders or major illiteracy preventing understanding and physician-patient communication.

### IV. RESULTS

One hundred twenty-three (n=123) patients were included in this study. The median age was 47 years (range: 33 to 67 years), with a mean of  $49.35 \pm 9.84$  years.

The most common histological type was squamous cell carcinoma in 117 patients (95.12%). The most common FIGO stage was stage II in 84 patients (68.29%).

All patients received conventional 3D external radiotherapy, with a total dose ranging from 46 to 66 Gy and a median of 56 Gy, delivered in 23 to 33 fractions over a 5-fraction-per-week schedule, in combination with weekly cisplatin-based chemotherapy at a dose of 40 mg/m<sup>2</sup>. Additionally, uterovaginal brachytherapy was administered using two schedules: 4x7 Gy and 3x8 Gy, with a duration ranging from 53 to 78 days and a mean of  $60.05 \pm 7.80$  days. Sixty-two women (50.40%) had a duration  $\leq 55$  days, while 61 women (49.59%) had a duration  $> 55$  days.

The resumption of sexual activity varied after the end of treatment, with 88 patients (71.54%) resuming before 3 months and 35 patients (28.45%) resuming after 3 months.

The post-therapeutic period ranged from 6 months to 7 years, with a median of 2 years and 6 months, with 45 patients (36.58%) having a duration of 2 years or less and 78 patients (63.41%) having a duration of more than 2 years. (Table I)

**Table 1 : Socio-Demographic, Medical, and Therapeutic Characteristics of the Patients**

	Population Size	%
<b>Age (years)</b>		
33-39	21	17,07
40-49	48	39,02
50-59	30	24,39
60-67	24	19,51
<b>FIGO stage</b>		
I	9	07,31
II	84	68,29
III	30	24,39
<b>Histological type</b>		
Squamous cell carcinoma	117	95,12
Others	6	04,87
<b>External radiotherapy</b>		
46 Gy	39	31,70
56 Gy	58	47,15
60 Gy	16	13,00
66 Gy	10	08,13
<b>Brachytherapy</b>		
4x7 Gy	119	96,74
3x8 Gy	4	03,25
<b>Duration</b>		
$\leq 55$ days	62	50,40
$> 55$ days	61	49,59
<b>Resumption of sexual activity</b>		
Avant 3 months	88	71,54
Après 3 months	35	28,45

<b>Post-therapeutic period</b>	45	36,58
≤ 2 years	78	63,41
> 2 years		

Interviews revealed that after treatment, there was onset or worsening of vaginal dryness in 81 patients (65.85%), onset or worsening of dyspareunia in 63 patients (51.21%), decrease in sexual desire or sexual dissatisfaction in 83 patients (67.47%), and a feeling of indifference towards sexual life in 78 patients (63.41%). (Table 2)

Clinical examination revealed a vaginal length ranging from 2 to 10 cm, with a mean of 5.66 ± 2.09 cm. The presence of synechiae and/or stenoses was observed in 53 patients, representing 43.08%, and abnormal discharge or bleeding was noted in 47 patients, representing 38.21%. (Table 3)

**Table 2 Interview Data**

	Population size	%
<b>Vaginal dryness</b>		
Yes	81	65,85
No	42	34,14
<b>Dyspareunia</b>		
Yes	63	51,21
No	60	48,78
<b>Decrease in sexual desire or sexual dissatisfaction</b>		
Yes	83	67,47
No	40	32,52
<b>Feeling of indifference towards sexual life</b>		
Yes	78	63,41
No	45	36,58

**Table 3 Clinical Examination Data**

	Population Size	%
<b>Vaginal length</b>		
2-4 cm	35	28,45
5-7cm	62	50,40
8-10 cm	26	21,13
<b>Vaginal synechiae and/or stenosis</b>		
Yes	53	43,08
No	70	56,91
<b>Bleeding</b>		
Yes	47	38,21
No	76	61,78

In univariate analysis, the prevalence of onset or worsening of vaginal dryness and dyspareunia increases with age. This increase is significant, with p-values of 0.000 and 0.045 respectively. These rates increase from 28.57% and 23.57% in the 33-39 age group to 83.33% and 62.50% in the 60-67 age group. (Table 4)

We also observed that the resumption of sexual activity is slower in younger and older women (p=0.028).

Among patients who did not exceed 2 years of follow-up, we noticed a significant increase in the prevalence of synechiae or stenosis, as well as bleeding, with a significant p-value of 0.000. These prevalences decrease from 80% in the group of patients followed for two years or less, to 21.79% and 14.10% respectively in the group that exceeded 2 years of follow-up. (Table 5)

However, the prevalence of onset or worsening of vaginal dryness and dyspareunia increases with the duration of follow-up, being more frequent in the group of patients who exceeded 2 years, with p-values of 0.026 and 0.008 respectively. (Table 6)

In the group with onset or worsening of vaginal dryness (n=81), 71 patients (87.65%) also reported a decrease in sexual desire (p=0.00), and 68 patients (83.96%) reported indifference towards sexual life (p=0.00).

In the group with onset or worsening of dyspareunia (n=63), all patients also reported a decrease in sexual desire and vaginal dryness (p=0.00), and almost all, 60 patients (95.23%), expressed indifference towards their sexual life. Our study also revealed a strong association between sexual desire and indifference. All patients reporting indifference towards their sexual life also reported a decrease in desire, with a p-value of 0.00.

## V. DISCUSSION

This study addressed the delicate issue of the vagina and its crucial role in post-treatment sexuality, as a key organ for reproduction and sexual health. Subject to significant alterations after cancer treatment, the vagina is composed of smooth and striated muscle tissues, as well as a folded mucosa that allows it to stretch during sexual intercourse and childbirth. Moreover, it is influenced by hormones and endowed with a local immune system that protects it against infections and pathogens. Furthermore, the vagina is an erogenous zone playing a crucial role in female sexual response, facilitating sexual intercourse, enhancing pleasure, and providing pleasant sensations during sexual arousal.

Although radiotherapy targets tumor cells, it can damage surrounding tissues, leading to acute and chronic effects such as inflammation, vaginal thinning, adhesions, atrophy, and fibrosis. These progressive alterations result in a loss of vaginal elasticity, narrowing, and shortening of the total length of the vagina. [1] [2]

The consequences go beyond physical structure, as radiotherapy can also induce sexual disorders such as decreased libido and premature ovarian failure, leading to vaginal dryness, hot flashes, and emotional imbalance, which have an extremely negative impact on sexual function. [3] [4] [5]

Other causes of sexual disorders reported in the literature include limited ability to reach sexual arousal and orgasm, decreased sensitivity of the sexual organs, a sensation of

numbness, and fear that sexual intercourse will not occur. [6] [7] [8] [9]

However, sexual dysfunction is also attributable to other socio-economic factors such as age, medical insurance, sleep disorders, and level of education. [10]

Painful sexual intercourse remains the most commonly reported sexual problem by cancer patients, with nearly 70% of gynecological patients at risk of dyspareunia associated with vaginal elasticity alterations, which hinder orgasm and reduce sexual pleasure. [11] [12] [13]

Other issues such as loss of interest in sexual life and a negative change in body image perception, which can lead to a decrease in quality of life, satisfaction in the relationship, depression, and anxiety, especially among women of

childbearing age who become sterile due to treatment, can be perceived as incomplete, insufficient, or worthless. [14] [15] [9]

This decline in performance often threatens the quality of life, creating a need for emotional support to improve sexual function, reinforcing the importance of counseling by healthcare professionals for women and their partners on illness and sexuality. [16]

Most patients believe that partners should receive information and education on how to support their spouse in case of sexual problems and also be able to respond to any need for support from them. This psychosexual support should therefore not only encompass the physical aspect but also consider the relationship and the partner's perspective. [17]

**Table 4 Sociodemographic, Medical and Therapeutic Data, and Variables Related To the Interview**

	Vaginal Dryness	p	Dyspareunia	p	Decrease in Sexual Desire or Sexual Dissatisfaction	p	Feeling of Indifference Towards Sexual Life	p
<b>Age (years)</b>		<b>0,000</b>		<b>0,045</b>		<b>0,816</b>		<b>0,491</b>
33-39	6 (28,57%)		5 (23,57%)		13 (61,90%)		12 (57,14%)	
40-49	30 (62,50%)		26 (54,17%)		32 (66,67%)		28 (58,33%)	
50-59	25 (83,33%)		17 (56,67%)		20 (66,67%)		20 (66,67%)	
60-67	20 (83,33%)		15 (62,50%)		18 (75,00%)		18 (75,00%)	
<b>FIGO stage</b>		<b>0,127</b>		<b>0,402</b>		<b>0,589</b>		<b>0,896</b>
I	4 (44,44%)		3 (33,33%)		6 (66,67%)		6 (66,67%)	
II	60 (71,42%)		46 (54,76%)		59 (70,24%)		54 (64,29%)	
III	17 (56,66%)		14 (46,67%)		18 (60,00%)		18 (60,00%)	
<b>Histological type</b>		<b>0,085</b>		<b>0,369</b>		<b>0,067</b>		<b>0,117</b>
Squamous cell carcinoma	79 (67,52%)		61 (52,14%)		81 (69,23%)		76 (64,96%)	
Others	2 (33,33%)		2 (33,33%)		2 (33,33%)		2 (33,33%)	
<b>External radiotherapy</b>		<b>0,015</b>		<b>0,199</b>		<b>0,010</b>		<b>0,024</b>
46 Gy	26 (66,67%)		20 (51,28%)		27 (69,23%)		25 (64,1%)	
56 Gy	42 (72,41%)		33 (56,9%)		42 (72,41%)		39 (67,24%)	
60 Gy	11 (68,75%)		8 (50,00%)		12 (75,00%)		12 (75,00%)	
66 Gy	2 (20,00%)		2 (20,00%)		2 (20,00%)		2 (20,00%)	
<b>Brachytherapy</b>		<b>0,497</b>		<b>0,960</b>		<b>0,448</b>		<b>0,571</b>
4x7 Gy	79 (66,39%)		61 (51,26%)		81 (68,07%)		76 (63,87%)	
3x8 Gy	2 (50,00%)		2 (50,00%)		2 (50,00%)		2 (50,00%)	
<b>Duration</b>		<b>0,487</b>		<b>0,930</b>		<b>0,654</b>		<b>0,315</b>
≤ 55 days	39 (62,90%)		32 (51,61%)		43 (69,35%)		42 (67,74%)	
> 55 days	42 (68,85%)		31 (50,82%)		40 (65,57%)		36 (59,02%)	
<b>Resumption of sexual activity</b>		<b>0,214</b>		<b>0,668</b>		<b>0,871</b>		<b>0,454</b>
Before 3 months	55 (62,50%)		44 (50,00%)		59 (67,05%)		54 (61,36%)	
After 3 months	26 (74,29%)		19 (54,29%)		24 (68,57%)		24 (68,57%)	
<b>Post-therapeutic period</b>		<b>0,026</b>		<b>0,008</b>		<b>0,344</b>		<b>0,324</b>
≤ 2 years	24 (53,33%)		16 (35,55%)		28 (62,22%)		26 (57,78%)	
> 2 years	57 (73,07%)		47 (60,25%)		55 (70,51%)		52 (66,67%)	

**Table 5 Sociodemographic, Medical and Therapeutic Data, and Variables Related To Clinical Examination**

	Vaginal length			p	Vaginal synechia and/or stenosis	p	Bleeding	p
	2-4 cm	5-7 cm	8-10 cm					
<b>Age (years)</b>				<b>0,745</b>		<b>0,346</b>		<b>0,149</b>
33-39	7 (33,33%)	8 (38,10%)	6 (28,57%)		12 (57,14%)		10 (47,62%)	
40-49	15 (31,25%)	22 (45,83%)	11 (22,92%)		22 (45,83%)		22 (45,83%)	
50-59	7 (23,33%)	18 (60,00%)	5 (16,66%)		10 (33,33%)		10 (33,33%)	
60-67	6 (25,00%)	14 (58,33%)	4 (16,67%)		9 (37,50%)		5 (20,83%)	
<b>FIGO stage</b>				<b>0,885</b>		<b>0,066</b>		<b>0,039</b>
I	2 (22,22%)	4 (44,44%)	3 (33,33%)		7 (77,78%)		7 (77,78%)	
II	25 (29,76%)	43 (51,19%)	16 (19,05%)		32 (38,10%)		29 (34,52%)	
III	8 (26,67%)	15 (50,00%)	7 (23,33%)		14 (46,67%)		11 (36,67%)	
<b>Histological type</b>				<b>0,094</b>		<b>0,232</b>		<b>0,542</b>
Squamous cell carcinoma	31 (26,50%)	61 (52,14%)	25 (21,37%)		49 (41,88%)		44 (37,61%)	
Others	4 (66,67%)	1 (16,67%)	1 (16,67%)		4 (66,67%)		3 (50,00%)	
<b>External radiotherapy</b>				<b>0,839</b>		<b>0,615</b>		<b>0,821</b>
46 Gy	9 (23,08%)	20 (51,28%)	10 (25,64%)		18 (46,15%)		17 (43,59%)	
56 Gy	18 (31,03%)	28 (48,28%)	12 (20,69%)		23 (39,66%)		21 (36,21%)	
60 Gy	4 (25,00%)	10 (62,50%)	2 (12,50%)		6 (37,50%)		5 (31,25%)	
66 Gy	4 (40,00%)	4 (40,00%)	2 (20,00%)		6 (60,00%)		4 (40,00%)	
<b>Brachytherapy</b>				<b>0,103</b>		<b>0,777</b>		<b>0,580</b>
4x7 Gy	32 (26,89%)	61 (51,26%)	26 (21,85%)		51 (42,86%)		46 (38,66%)	
3x8 Gy	3 (75,00%)	1 (25,00%)	0 (0,00%)		2 (50,00%)		1 (25,00%)	
<b>Duration</b>				<b>0,276</b>		<b>0,405</b>		<b>0,627</b>
≤ 55 days	21 (33,87%)	27 (43,55%)	14 (22,58%)		29 (46,77%)		25 (40,32%)	
> 55 days	14 (22,95%)	35 (57,38%)	12 (19,67%)		24 (39,34%)		22 (36,07%)	
<b>Resumption of sexual activity</b>				<b>0,419</b>		<b>0,100</b>		<b>0,072</b>
Before 3 months	28 (31,82%)	42 (47,73%)	18 (20,45%)		42 (47,73%)		38 (43,18%)	
After 3 months	7 (20,00%)	20 (57,14%)	8 (22,86%)		11 (31,43%)		9 (25,71%)	
<b>Post-therapeutic period</b>				<b>0,326</b>		<b>0,000</b>		<b>0,000</b>
≤ 2 years	16 (35,56%)	19 (42,22%)	10 (22,22%)		36 (80,00%)		36 (80,00%)	
> 2 years	19 (24,36%)	43 (55,13%)	16 (20,51%)		17 (21,79%)		11 (14,10%)	

**VI. CONCLUSION**

The topic of vaginal changes after treatment for pelvic cancers is largely underestimated. It is crucial for gynecologists, sexologists, and oncologists-radiation therapists to work together to design programs aimed at preventing these alterations in the vagina. This small organ can be responsible for sexual dysfunctions and impair the quality of life of women. It is imperative to continue research and randomized controlled trials to better understand the extent of the problem and explore possible avenues for improvement.

**REFERENCES**

[1]. clinicaltrials.gov, MMterKuile. SPARC Study: A Nurse-led Sexual Rehabilitation Programme for Women With Gynaecological Cancers Receiving Radiotherapy: A Randomized Multicentre Trial [Internet]. and February 2020 [cited February 18, 2021]. Report No.: NCT0.

[2]. N, Singh N, Sachdeva M, Ghatage P (2021) Sexual dysfunction in cervical cancer survivors: a scoping review, Women's Health Report 2:1, 594–607, DOI: 10.1089/whr.2021.0035.

[3]. Herzog TJ, Wright JD. The impact of cervical cancer on quality of life—The components and means for management. Gynecol Oncol 2007 and Scholar, 107:572–577.

- [4]. Bukovic D, et al. Sexual life after cervical carcinoma. *Coll Antropol.* 2003 and Scholar], 27:173–180.
- [5]. Hughes MK. Alternations of sexual function in women with cancer. *Semin Oncol Nurs* 2008, [Scholar], 24:91–101.
- [6]. Aerts L, Enzlin P, Verhaeghe J, et al. Sexual and psychological functioning in women after pelvic surgery for gynecological cancer. *Eur J Gynaec Oncol.* 2009 and Scholar], 30:652–656.
- [7]. Wenzel LB, Donnelly JP, Fowler JM, et al. Resilience, reflection, and residual stress in ovarian cancer survivorship: a gynecologic oncology group study. *Psychooncology.* 2002 and Scholar], 11:142–153.
- [8]. Andersen BL, Hacker NF. Psychosexual adjustment after vulvar surgery. *Obstet Gynecol.* 1983 and Scholar], 62:457–462.
- [9]. Reis N, Beji NK, Coskun A. Quality of life and sexual functioning in gynecological cancer patients: results from quantitative and qualitative data. *Eur J Oncol Nurs.* 2010 and Scholar], 14:137–146.
- [10]. Zhou W, Yang X, Dai Y, Wu Q, He G, Yin G. Survey of cervical cancer survivors regarding quality of life and sexual function. *J Cancer Res Ther* 2016 and Scholar], 12:938–944.
- [11]. Jensen PT, Groenvold M, Klee MC, Thranov I, Petersen MA, Machin D. Early-stage cervical carcinoma, radical hysterectomy, and sexual function. A longitudinal study. *Cancer* 2004 and Scholar], 100:97–106.
- [12]. Stinesen Kollberg K, Waldenström AC, Bergmark K, et al. Reduced vaginal elasticity, reduced lubrication, and deep and superficial dyspareunia in irradiated gynecological cancer survivors. *Acta Oncol.* 2015 and Scholar], 54:772–779.
- [13]. Stead ML, Fallowfield L, Selby P, Brown JM. Psychosexual function and impact of gynecological cancer. *Best Pract Res Clin Obstet Gynaecol.* 2007 and Scholar], 21:309–320.
- [14]. Bourgeois-Law G, Lotocki R. Sexuality and gynecological cancer: A needs assessment. *Can J Hum Sex Winter.* 1999 and Scholar], 8:231–240.
- [15]. Aerts L, Enzlin P, Vergote I, et al. Sexual, psychological, and relational functioning in women after surgical treatment for vulvar malignancy: a literature review. *J Sex Med.* 2012 and Scholar], 9:361–371. [PubMed] [Google].
- [16]. Cervical Cancer: Issues of Sexuality and Fertility | Cancer Network [Internet]. [Cited May 14, 2020]. Available at: <https://www.cancernetwork.com/gynecologic-cancers/cervical-cancer-issues-sexuality-and-fertility> Accessed July 12, 2021.
- [17]. Vermeer WM, Bakker RM, Kenter GG, Stiggelbout AM, Ter Kuile MM. Cervical cancer survivors' and partners' experiences with sexual dysfunction and psychosexual support. *Support Care Cancer* 2016 and Scholar], 24:1679–1687.