

THE COMBINATION OF EXTERNAL IRRADIATION AND CURIETHERAPY USED PREOPERATIVELY IN ADENOCARCINOMA OF THE ENDOMETRIUM*

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CARCINOMA of the endometrium is a form of cancer of increasing importance in highly developed communities; as we increase the measures to diminish the morbidity from invasive carcinoma of the cervix, endometrial cancer will gradually become the predominant form of gynecologic cancer. In Puerto Rico carcinoma of the uterine cervix has been and continues to be the number one form of cancer in women; however, carcinoma of the endometrium is increasing in incidence, as observed in the data from the Puerto Rico Cancer Registry¹⁰ and in the experience at the I. González Martínez Oncologic Hospital. In 1956 only 4 cases of carcinoma of the endometrium were registered at the I. González Martínez Oncologic Hospital, whereas in 1966 a total of 28 cases were seen. The reported incidence of cancer of the endometrium (excluding choriocarcinoma) at the Puerto Rico Cancer Registry for the year 1965 was 2.9 cases/100,000 women. Table I shows the ratio of cervical cancer to endometrial carcinoma cases as observed at the Puerto Rico Cancer Registry and at the I. González Martínez Oncologic Hospital during the years 1958-1966. We believe that the hospital data regarding accuracy of diagnosis are more reliable in differentiating cervical carcinoma from endometrial carcinoma. This ratio at the Hospital ranged from 18 to 1 in 1958, to 5 to 1 in 1966; we believe that this is a reflection of the changing age and socio-economic patterns of the Puerto Rican population. It is to be expected that as the average age of our female population rises and our socio-economic level improves, to-

TABLE I
RATIO OF CARCINOMA OF CERVIX UTERI TO CARCINOMA OF CORPUS UTERI CASES

	Puerto Rico Cancer Registry	I. González Martínez Hosp
1958	10:1	18:1
1959	13:1	17:1
1960	16:1	17:1
1961	13:1	10:1
1962	16:1	28:1
1963	16:1	14:1
1964	13:1	9:1
1965	14:1	10:1
1966	10:1	5:1

gether with a reduction in parity we will observe a reduction in incidence of invasive carcinoma of the cervix and a relative increase in endometrial carcinoma to approach a ratio of 1 to 1 between these two conditions. One of us (V.A.M.) has previously reported on the socio-economic aspects of the incidence of cancer in Puerto Rico and has pointed out that carcinoma of the endometrium is more frequently seen in the higher socio-economic groups of women.⁹

The role of radiation therapy in the management of carcinoma of the endometrium has been considerably debated in the medical literature; the opinions vary from a complete rejection of this modality in the early operable cases⁴ to its acceptance as the primary treatment of adenocarcinoma of the endometrium.⁷ The majority of reports in the literature consider radiation therapy of great value as an adjunct to surgery in the management of this for

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of cancer. Kottmeier,⁷ in his compilation of the international results of treatment of cancer of the uterus for the years 1951-60, reported that out of 42 reporting centers in 20 institutions preoperative radiotherapy was applied as a rule, while 21 centers used surgery without preoperative irradiation for tumors limited to the uterus in good surgical risk cases.

The purpose of this report is to present the experience with radiation therapy for this condition at the I. González Martínez Oncologic Hospital, with emphasis on the combination of external and intracavitary irradiation in the preoperative treatment.

MATERIAL

During the period January 1, 1956 to December 31, 1966 a total of 105 not previously treated cases of carcinoma of the endometrium were treated at the Radiotherapy Department of the I. González Martínez Oncologic Hospital. During the same period 28 patients received postoperative irradiation after surgery outside our Hospital, 2 cases were not treated because of critical health, and 1 case was submitted to surgery only, because carcinoma of the cervix had been treated by irradiation several years before. Three cases with sarcoma of the uterus and 5 patients with carcinoma *in situ* or questionable diagnoses were also excluded.

Our institution receives charity patients from a geographic area corresponding to two-thirds of the island of Puerto Rico, with a great concentration on radiotherapeutic cases. Although the number of pri-

vate cases in the institution has usually been less than 10 per cent of the total work load during the study period, the percentage of private cases in this series was 46 per cent (Table II).

The age distribution of this group of cases is shown in Table III; the largest group was constituted by patients 50 to 59 years of age with a median age of 58.7 and an average age of 59.7. The youngest patient was 30 years of age and the oldest 87.

Parity of these cases is shown in Table IV. It is observed that 32 per cent of the women reported had no children and 27 per cent had 1 or 2 children only. This is considered low for the Puerto Rican community, where fertility in women is high.

The menopausal status of women in the study is shown in Table V; only 20 per cent

TABLE III
CARCINOMA OF ENDOMETRIUM
AGE DISTRIBUTION

Age Group	No. of Cases	Per Cent
30-39	4	4
40-49	16	15
50-59	38	36
60-69	26	25
70-79	16	15
80-89	5	5
Total	105	100
Median age—58.7	Youngest—30 yr. of age	
Average age—59.7	Oldest—87 yr. of age	

TABLE II
CARCINOMA OF ENDOMETRIUM
SOCIO-ECONOMIC STATUS

	No. of Cases	Per Cent
Indigent	57	54
Nonindigent	48	46
Total	105	100

TABLE IV
CARCINOMA OF ENDOMETRIUM
PARITY

Para	No. of Cases	Per Cent
0	34	32
1-2	28	27
3-4	13	12
5-6	8	8
7-8	8	8
9-	14	13
Total	105	100

TABLE V
CARCINOMA OF ENDOMETRIUM
MENOPAUSAL STATUS

	No. of Cases	Per Cent
Premenopausal	84	80
Postmenopausal	21	20
Total	105	100

of the cases were considered postmenopausal.

The associated medical conditions encountered are shown in Table VI. A complicating medical condition was not mentioned in the chart in only 38 per cent of the cases. The following associated medical conditions were reported in order of diminishing frequency: obesity, hypertension, and diabetes.

For the purpose of classification of extent of the disease, we have used the staging system adopted by the International Federation of Obstetrics and Gynecology in January, 1961. This is as follows: Stage I—the carcinoma is confined to the corpus uteri; Stage II—the carcinoma has involved the corpus and the cervix; Stage III—the carcinoma has extended outside the uterus but not outside the true pelvis; Stage IV—

TABLE VI
CARCINOMA OF ENDOMETRIUM
ASSOCIATED MEDICAL CONDITIONS

	No. of Cases	Per Cent
Obesity	15	14
Obesity and hypertension	15	14
Obesity and diabetes	7	7
Obesity, diabetes, and hypertension	12	11
Hypertension	8	8
Hypertension and diabetes	2	2
Diabetes	6	6
Subtotal	65	62
None stated	40	38
Total	105	100

the carcinoma has extended outside the true pelvis or has obviously involved the mucosa of the bladder or rectum. Table VII shows the stage distribution of the cases in the study; the largest number is constituted by the Stage I category, with 72 per cent of the patients. A fractional curettage was not done in the majority of patients that we have classified as Stage I, for the initial diagnostic dilation and curettage was frequently done outside of our Hospital. Consequently, an unknown number of cases with endocervical extent of the disease must have been included in the Stage I group of patients. All cases classified as Stage II had histologic evidence of involvement of the endocervix by carcinoma. The size of the uterus could not be properly evaluated in a significant number of our cases because of associated obesity.

All patients had histologic proof of the disease. In 80 per cent of the cases the diagnosis was reported as adenocarcinoma without reference to grading, and in 10 per cent of the cases this was reported as Grade 2, 3 or anaplastic carcinoma. The diagnosis of adenoacanthoma was made in 4 cases and carcinosarcoma in 1 case.

TREATMENT POLICY

Our treatment policy throughout the years has been to administer preoperative irradiation to all stages of carcinoma of the endometrium and then to follow this by total hysterectomy, approximately 6 weeks after irradiation. Cases who have had primary surgery elsewhere have been accepted for postoperative irradiation but were not

TABLE VII
CARCINOMA OF ENDOMETRIUM
STAGE DISTRIBUTION

Stage	No. of Cases	Per Cent
I	76	72
II	16	15
III	10	10
IV	3	3
Total	105	100

included in this study. When a patient has been considered inoperable she has been submitted to irradiation only by intracavitary curietherapy, by external irradiation or by a combination of both modalities. In the early years covered by this study the preferred form of preoperative irradiation was intracavitary curietherapy, usually by means of the Heyman capsules and a vaginal applicator, for a total of 6,000 to 8,000 mg. hr. Gradually throughout the years we adopted the policy of employing a combination of preoperative irradiation followed by intracavitary curietherapy and preserved curietherapy alone for the very obese patients; in the last 3 years of the study only 3 patients received preoperative curietherapy, while 38 were submitted to preoperative external irradiation followed by curietherapy.

Table VIII shows the distribution of cases by irradiation modality and stage. Preoperative external irradiation followed by intracavitary curietherapy was used in 58 cases and preoperative curietherapy was employed in 22 cases. Fourteen cases had a combination of external and intracavitary irradiation without subsequent surgery. Five cases had intracavitary curietherapy as the only form of therapy. In 3 cases postoperative irradiation was administered in view of the findings in the operative specimen, after previous preoperative curiether-

apy. Three cases were submitted to external irradiation only.

IRRADIATION TECHNIQUES

In the early years covered by the study the external irradiation was administered by orthovoltage x rays of 250 kvp., a half-value layer of 3 mm. of Cu, a treatment distance of 70 cm., and by a combination of anterior, posterior, and sacrosclatic fields, with exposures of 4,000 r calculated in the mid-pelvis. Since 1958 most cases have been treated with an "El Dorado" cobalt 60 teletherapy unit with a treatment distance of 80 to 100 cm., anterior and posterior fields 16×12 or 16×14 cm. Some cases have been treated with a rotational technique utilizing a Jr. Theratron cobalt 60 teletherapy unit with a 15×15 cm. field. The preferred exposure with cobalt 60 teletherapy has been 5,000 r calculated in the mid-pelvis region administered over a period of approximately 45 days. The fractionation employed has been 5 exposures per week of 150 r each, or 3 exposures of 250 r each per week. The external irradiation has been followed by intracavitary curietherapy by means of a long linear source constituted by four to six 10 mg. sources of radium or a substitute radioisotope such as Co⁶⁰ or Cs¹³⁷ in a tandem arrangement within a plastic or a metal tube to cover the uterine cavity and the upper half of the

TABLE VIII
CARCINOMA OF ENDOMETRIUM
RADIATION THERAPY MODALITY AND STAGE

	Stage				Total
	I	II	III	IV	
Preoperative external and intracavitary irradiation	41	11	6	—	58
Preoperative intracavitary irradiation	18	3	1	—	22
External and intracavitary irradiation only	10	1	2	1	14
Intracavitary irradiation only	5	—	—	—	5
Preoperative intracavitary and postoperative irradiation	2	1	—	—	3
External irradiation only	—	—	1	2	3
Total	76	16	10	3	105

TABLE IX
 CARCINOMA OF ENDOMETRIUM
 3 YEAR SURVIVAL BY STAGE AND TREATMENT

	Stage								
	I		II		III		IV	Total	
	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	No.	Per Cent
Preoperative external and intracavitary irradiation	18/21	86	5/7	71	4/5		—	27/33	82
Preoperative intracavitary irradiation	12/17	70	3/3		1/1		—	16/21	76
External and intracavitary irradiation only	1/4		0/1		0/1		0/1	1/7	14
Intracavitary irradiation only	3/4		—		—		—	3/4	
Preoperative intracavitary and postoperative irradiation	2/2		1/1		—		—	3/3	
External irradiation only	—		—		0/1		0/2	0/3	
Total	36/48	75	9/12	75	5/8	62	0/3	50/71	70

vagina. Curietherapy doses have been calculated at a point 2 cm. from the center of the linear source, with a preferred exposure of 3,000 r.

TREATMENT RESULTS

For the purpose of evaluating the results of treatment in this study, we have limited the analysis to cases with a minimal follow-up period of 3 years. Survival results have been determined at 3 and 5 years. Follow-up information is available on all cases.

Table IX shows the 3 year survival by stage and treatment modality in 71 cases that qualify for this analysis. The largest group (33 cases) was submitted to preoperative external and intracavitary irradiation. The 3 year survival for the group was 82 per cent, with a Stage I survival of 86 per cent in 21 cases. Preoperative intracavitary curietherapy was administered to 21 cases with a resulting 3 year survival of 76 per cent; in 17 Stage I cases the 3 year survival was 70 per cent. Other subgroups submitted to irradiation are shown in Table IX. The over-all 3 year survival for all Stage I cases (48) was 75 per cent and the same for 12 Stage II patients. Stage III patients had 3 year survival in 5 out of 8 cases. The

over-all 3 year survival for the entire group of 71 patients was 70 per cent. No Stage IV patient survived 3 years.

The 5 year survival by stage and treatment is shown in Table X. The highest survival was observed in the group submitted to preoperative external irradiation and intracavitary curietherapy, with 75 per cent of 16 cases surviving at the end of 5 years. The over-all survival in 49 cases qualifying for 5 year evaluation is 59 per cent. Noteworthy is the fact that 7 of the 49 patients died of intercurrent disease before the end of 5 years; correcting for this we have a net 5 year survival of 69 per cent. The causes of failure at the end of 5 years are shown in Table XI. Only 1 case was alive with disease at 5 years.

The effectiveness of the various modalities of irradiation in eliminating the tumor from the surgical specimen can be observed in Table XII. More than 50 per cent of the removed specimens did not have recognizable tumor on histologic examination. We must emphasize the fact that several pathologists were involved in the examination of these specimens (some from outside our institution) and that no effort was made to review the corresponding histopathology

TABLE X
CARCINOMA OF ENDOMETRIUM
5 YEAR SURVIVAL BY STAGE AND TREATMENT

	Stage								
	I		II		III		IV		Total
	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	No.	Per Cent
Preoperative external and intracavitary irradiation	6/8	75	2/3		4/5		—	12/16	75
Preoperative intracavitary irradiation	9/15	60	3/3		1/1		—	13/19	68
External and intracavitary irradiation only	1/3		0/1		0/1		0/1	1/6	17
Intracavitary irradiation only	1/3		—		—		—	1/3	
Preoperative intracavitary and postoperative irradiation	1/2		1/1		—		—	2/3	
External irradiation only	—		—		0/1		0/1	0/2	
Total	18/31	58	6/8	75	5/8	62	0/2	29/49	59

slides by a single pathologist. An analysis of the time interval between irradiation and surgery did not show the relationship between the length of time and the presence or absence of tumor in the specimen. The majority of cases had the uterus removed 4 weeks or more after irradiation. Likewise,

no relationship was found between the presence or absence of tumor in the specimen and survival.

The employed irradiation techniques have resulted in no significant morbidity or complications. Postsurgical healing took place uneventfully in all cases.

TABLE XI
CARCINOMA OF ENDOMETRIUM
ANALYSIS OF 5 YEAR FAILURES

Irradiation	Alive 5 Years with Disease	Died with Disease				Died, Cause Unknown	Died, Inter-current Disease
	Stage I	Stage I II III IV				Stage I	Stage I
	I	I	II	III	IV	I	I
Preoperative external and intracavitary irradiation	—	2	1	1	—	—	—
Preoperative intracavitary irradiation	1	3	—	—	—	1	2
External and intracavitary irradiation only	—	—	1	1	1	—	2
Intracavitary irradiation only	—	—	—	—	—	—	2
Preoperative intracavitary and postoperative external irradiation	—	—	—	—	—	—	1
External irradiation only	—	—	—	1	1	—	—
Total	1	5	2	3	2	1	7

TABLE XII
 CARCINOMA OF ENDOMETRIUM
 EFFECTIVENESS OF RADIATION THERAPY TECHNIQUE, BY STAGE

	Stage				Total
	I	II	III	IV	
Preoperative External and Intracavitary Irradiation					
Tumor present	12	2	1	—	15
Tumor absent	9	5	4	—	18
Preoperative Intracavitary Irradiation*					
Tumor present	7	2	1	—	10
Tumor absent	11	2	0	—	13
Total					
Tumor present	19	4	2	—	25
Tumor absent	20	7	4	—	31

* Excluding 1 case, Stage I with no pathologic report of surgical specimen.

DISCUSSION

The modest number of cases in this series makes it impossible to arrive at statistically valid conclusions regarding the factors of importance in determining the prognosis of carcinoma of the endometrium. Nevertheless, there are some striking findings that deserve discussion. One of these concerns the similarity in survival results obtained in the Stage I and II cases, and in the Stage III cases. This may be attributable to the whole-pelvis technique of external irradiation employed. Extension of the tumor into the endocervix resulted in a 3 and 5 year survival of 75 per cent in 12 and 8 cases, respectively. Gusberg and Yannopoulos⁶ have reported a 27.3 per cent 5 year survival in 14 cases with this type of tumor extension. Davis⁴ has also reported a low 5 year survival of 24 per cent in endometrial carcinoma involving the cervix and endocervix.

Taking into consideration that regional lymph node metastases have been reported as high as 20 per cent¹¹ and that a significant number of cases with endometrial carcinoma tend to metastasize to the ovary, it makes sense to employ a preoperative technique that would irradiate all points in the pelvis to a significant dosage. For this purpose we have utilized external irradiation

followed by curietherapy by means of long linear source. Adequate irradiation of the uterus and the entire pelvis, with precise dosimetry, is afforded by this technique. This technique has achieved sterilization of the tumor from the specimen in over 50 per cent of the cases. Lampe⁸ has reported that roentgen irradiation followed by radium gave a 53 per cent sterilization of the tumor in the removed specimen *versus* 28 per cent by roentgen irradiation alone and 32 per cent for preoperative radium.

No vaginal metastases were noted during the first 5 years post-treatment in this series; however, 2 cases developed massive pelvic recurrent carcinoma, one, 10 years post-treatment. The reported incidence of vaginal metastases in nonirradiated cases has been 5 to 17.7 per cent.¹³

No correlation between histologic type of the tumor, size of the tumor and age of patients, and prognosis, could be found in our cases. This could be due to the limited size of our clinical sample. We are left with a number of unanswered questions.

IS RADIATION THERAPY INDICATED AS THE PRIMARY TREATMENT OF CARCINOMA OF THE ENDOMETRIUM?

Table XIII shows the international results of treatment of carcinoma of the corpus reported by Kottmeier for the years 1951 to

1960.⁷ The over-all 5 year recovery rate for 14,796 patients (excluding 1,001 cases with endocervical extent) was 62.6 per cent in 42 institutions. The 5 year disease-free survival in the Stage I, Group 1 cases, which are the cases with disease confined to the uterus and constituting a good surgical risk, was 77.1 per cent. On page 401 of the report, the editor states that it is of interest that at 20 institutions reporting 3,985 cases of Stage I, Group 1 in which, as a rule, preoperative irradiation was applied, the 5 year recovery rate was 73.8 per cent, while for 21 institutions reporting 4,668 cases of Stage I, Group 1 in which, as a rule, surgery was performed without preoperative irradiation, the corresponding figure was 76.2 per cent. In an effort to determine the value of irradiation in carcinoma of the corpus, we have prepared Table XIV, based on the reported international results for the years 1951-1960. This table takes into consideration all patients that were registered with a view for treatment at each of the reporting institutions and the survival results were determined using the entire examined population as a basis and not just the cases that were submitted to therapy, as is shown in Table XIII. We expect that if a given treatment influences the outcome of cancer cases seen at an institution, this should reflect on the survival results of the entire group; consequently, the survival analysis should not be limited to a selected group disregarding the fate of the rest of the cases.

TABLE XIII
CARCINOMA OF THE CORPUS
INTERNATIONAL RESULTS OF TREATMENT
1951-60

Stage	No. of Cases	Per Cent 5 Year Recovery Rate
I Group 1	8,963	77.1
I Group 2	3,850	47.1
II	1,983	26.3
	14,796*	62.6

* 1,001 cases with endocervical extent are not included.

TABLE XIV
CARCINOMA OF THE CORPUS
INTERNATIONAL RESULTS RELATED TO TREATMENT
1951-60

	Patients Registered†	Well 5 Years	
		No.	Per Cent
Irradiation	1,373	614	45
Irradiation and surgery	4,491	2,962	66
Surgery—over 50 per cent of cases	6,436	3,894	60
Surgery—less than 50 per cent of cases	3,238	1,791	55
	15,538*	9,261	60

* Includes untreated cases; excludes cases with endocervical extent.

† With a view to treatment.

The first treatment modality presented in Table XIV is radiation therapy. A total of 1,373 patients were registered in 4 institutions utilizing this modality as the primary treatment for carcinoma of the corpus. The lowest 5 year recovery rate was 40 per cent, the highest was 63 per cent with 45 per cent of patients well at the end of 5 years, out of the 1,772 registered cases. Irradiation given preoperatively followed by surgery was utilized on 4,498 patients at 12 institutions with a 66 per cent 5 year recovery rate, which is the highest of all types of treatment; the lowest reported recovery rate with this technique was 42 per cent and the highest 74 per cent. Primary surgery with or without postoperative irradiation for over 50 per cent of the cases was reported at 17 centers, with a 60 per cent 5 year recovery rate in 6,436 cases; the lowest 5 year recovery rate for this category was 44 per cent and the highest 71 per cent. When surgery was employed for less than 50 per cent of the cases (9 centers) the 5 year recovery rate was 55 per cent in 3,238 cases; the lowest 5 year recovery rate in this category was 38 per cent and the highest 72 per cent. Based on these data one can conclude that primary surgery (without preoperative irradiation) for a selected number of cases does not improve the curability in the en-

tire patient population seen at an institution; preoperative irradiation for all cases affords a better chance of curability for the entire group. Radiation therapy alone as the primary treatment of this disease does not achieve as good results as the other modalities of therapy mentioned in Table XIV.

A. OPTIMAL PREOPERATIVE IRRADIATION

The majority of centers utilize intracavitary curietherapy as the preferred technique for preoperative irradiation of carcinoma of the endometrium; this form of therapy affords a satisfactory rate of tumor disappearance and is more expeditious than external irradiation. The Heyman's packing technique seems to be preferred to a single linear source; however, Fletcher⁵ considers that when the uterine cavity shows no gross irregularities and the uterus is of normal size, a tandem is better than the Heyman's packing technique. We have found the tandem technique quite satisfactory, particularly after external irradiation, for it permits accurate dosimetry in the irradiated volume. Carmichael and Bean³ have found that Heyman's packing technique *versus* tandem offers no advantage, but in their hands they observe 10 per cent less specimens with residual tumor with the former. However, no difference is noted in the 5 year survival. Lampe⁸ and Sala and del Regato¹⁴ have advocated external irradiation as the preferred form of preoperative irradiation for carcinoma of the endometrium. As previously stated, we have preferred a combination of external irradiation and intracavitary curietherapy as the optimal technique for preoperative irradiation of this condition.

Significance of tumor disappearance. Arneson¹ has stated that an irradiation technique that will increase the incidence of "control" will advance the recovery of patients. Lampe⁸ does not believe that total eradication of the neoplasm is necessary before hysterectomy to achieve survival; in a group of 87 patients with residual carcinoma he obtained 92 per cent 5 year survi-

val. Roentgen irradiation alone gave him a 28 per cent sterilization rate with a resulting 5 year survival of 90.1 per cent. We found no difference in the 5 year results in the group of patients with persistent tumor *versus* the group where the tumor disappeared completely after preoperative irradiation.

B. INTERVAL BETWEEN IRRADIATION AND SURGERY

Surgery performed a few days after the termination of radiation therapy would result in a high percentage of persistent tumor in the specimen, but if practiced 6 to 8 weeks after radiation therapy most of the expected tumor disappearance would have occurred. Intervals longer than 2 to 3 months between preoperative irradiation and surgery would be expected to permit tumor regrowth in cases where complete neoplastic sterilization did not occur. We have considered an interval of 6 to 8 weeks as the optimal time for surgery after irradiation with the stated technique; by this time normal tissue radiation induced reactions have subsided and uterine tumor enlargement has been reduced.

SUMMARY

1. The experience with carcinoma of the endometrium at the Radiotherapy Department of the I. González Martínez Oncologic Hospital is presented. A total of 103 patients were seen from January 1, 1956 to December 31, 1966.

2. All patients were submitted to irradiation followed by surgery for operable cases.

3. The preferred form of preoperative irradiation was a combination of external irradiation and intracavitary curietherapy. This achieved tumor disappearance from the operative specimen in over 50 per cent of the cases.

4. The 3 and 5 year survival results have been analyzed and correlated with the stage of the disease and the treatment modalities employed.

5. A net 5 year survival of 69 per cent

was obtained in 49 patients of all stages, who qualified for 5 year evaluation.

6. An analysis of the published international results of treatment of carcinoma of the endometrium gives basis to the conclusion that preoperative irradiation affords the best chance of 5 year disease free survival for all patients with this disease.

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