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Carcionoma of the endometrium : a report on the incidence of visible tumor following preoperative radiotherapy

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CARCINOMA OF THE ENDOMETRIUM: A REPORT ON THE INCIDENCE OF VIABLE TUMOR FOLLOWING PREOPERATIVE RADIOTHERAPY

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INTRODUCTION

Carcinoma of the endometrium is a slowly growing neoplasm which spreads by direct invasion of surrounding structures, surface extension, and invasion of lymphatic or vascular channels (1, 2, 3). Invasive growth is very slow. Months or years may pass before the tumor reaches the serosal surface of the uterus (2). Although it was once felt that this neoplasm was much less common than carcinoma of the uterine cervix, present evidence (1, 3, 4) indicates that the incidence of these tumors is very nearly equal.

Since the advent of radium, the treatment of corporeal carcinoma has been generally accepted as combined radiotherapy and surgery (1, 3). The surgical procedure of choice in this combined regime is a total hysterectomy with bilateral salpingo-oophorectomy (1, 5, 6). The role of surgery in this disease is well defined. There seems to be little question that, in operable patients, parahysterectomy plays a primary role in definitive treatment (1, 3, 4, 5, 7). Due to the relatively high incidence of obesity, hypertension and diabetes in association with endometrial carcinoma, many patients may be considered poor surgical risks (1, 4). Improvement in surgical technique, however, has greatly increased the number of clinically operable cases (5).

Radiotherapeutic methods have not been as distinctly

defined. It is the purpose of this thesis to review these methods and evaluate their efficacy on the basis of histopathologic findings in uteri so treated.

RADIOTHERAPY OF ENDOMETRIAL CARCINOMA

Hunt (4) has summarized the various plans of treatment in endometrial carcinoma as follows:

1) Immediate hysterectomy without radiotherapy.
2) Panhysterectomy with postoperative irradiation of the vaginal vault.
3) Initial radiotherapy with immediate panhysterectomy.
4) Radiotherapy, followed by panhysterectomy six to twelve weeks later.
5) Radiotherapy, with subsequent surgery limited to those operable cases showing tumor on follow-up examination.

Primary radiotherapy with total exclusion of surgery is not currently advocated.

Various methods of intracavitary radium application have been described. Single radium or radon tubes, and short or long intrauterine tandems have been shown to give generally unsatisfactory results (7, 8). Schmitz (9), in 1935, described the use of a "Y-applicator" designed to provide a more uniform dose to the uterine cavity. In 1940, Friedman (10) described a "Hysterostat" which is constructed of multiple sections de-

signed to produce a triangular distribution of radium sources within the uterus.

The multiple packing method advocated by Heyman (11) has been adopted by many others in various forms (4, 6, 8, 12). In this technique, multiple tubes containing radium are packed individually into the uterine cavity until all space is filled. The dose from each source is small, therefore the risk of local necrosis is lessened and the total irradiation is evenly distributed (11). In 1944, Corsacaden (6) reported 70% five-year survival when all techniques of radium application were considered. He indicated that the multiple packing methods promised five-year survivals of 80% or better. Arneson (12) reported 50% five-year survivals, with combined therapy, when intrauterine tandems were used and 75% five-year survivals when multiple capsules were employed. He reported similar comparative results when intracavitary radium was used alone because of clinical contraindications to surgery.

The finding of persistent tumor in the operative specimen, the significance of which will be discussed later, also bears out these results. Arneson (12) reported residual tumor in 77% of cases where tandems were used. He found a 26% incidence of residual in those cases treated with multiple capsule methods. Freed and Pendergrass (8) have reported an evaluation of application techniques based on a physical analysis of dose distribution. They conclude that a minimum cancerocidal dose,

which will not exceed normal tissue tolerance, can only be delivered by use of the packing methods.

The dosage of radiation delivered to the tumor should be individualized (4). Factors such as the size and shape of the uterus (14), obesity (4) and the probability of subsequent panhysterectomy (13) are important. Several authorities have set up minimum standards on the basis of clinical results. Corsacaden (6) in 1944, recommended 3000 to 4000 milligram-hours of intracavitary radium in one dose. Gray and Friedman (5) indicate that the radium dose must exceed 5000 milligram-hours and that it should be given in two divided doses about 10 days apart. Schmitz (15) has defined "adequate therapy" as 6000 milligram-hours of intracavitary radiation in three weekly divided doses, plus deep roentgen therapy to a tumor dose of 4000 roentgens in 28 days. Freed and Pendergrass (8) indicate that 7000 gamma roentgens, delivered to the tumor within two or three weeks, is the minimum cancerocidal dose. They further indicate that 15,000 gamma roentgens is the maximum dose attainable without causing tissue necrosis. They state that this limit should not be exceeded. Their studies (8) indicate that this optimal ratio can only be attained by use of multiple packing methods of radium implantation. Hunt (4) advocates fractionated external roentgen therapy coexistent with intracavitary radium application. He delivers from 5000 to 7000 gamma roentgens to encompass a zone one to 1.5 centimeters beyond the periphery of

the uterine cavity and upper vaginal tract. Arneson (4) considers a dose of 7000 gamma roentgens at a depth of 1.5 centimeters into the myometrium as mandatory. In reference to the manner of reporting dosages, Freed and Pendergrass (8) state that the value in gamma roentgens is the only significant figure. A dose reported in milligram-hours does not give an accurate indication of the actual tumor irradiation (8) until it is correlated with the geometrical position of the radium sources in relation to the target.

RESULTS OF TREATMENT

A classification, related to the anatomic extent of the carcinoma, would appear necessary for a critical analysis of end results in treatment. Only a clinical classification is pertinent in those patients undergoing radiotherapy (4). Hunt (4) uses the Stockholm League of Nations classification (Table I). Javert and Douglas (3) have proposed a surgical-athologic classification of endometrial carcinoma based on their histologic study of 345 uteri removed without antecedent radiotherapy. Of their total cases, 83.5% had a clinically normal to small uterus. In this classification only the extent of tumor spread is considered. Their findings are summarized in Table II. Many clinical classifications stress the size of the uterus (17) as a factor. Palmer's statistical study of endometrial carcinoma (17)

indicates that the size of the uterus, as determined by the usual clinical methods, is not reliable. He states that the common coexistence of obesity, leiomyomata and adenomyosis with corpus carcinoma predisposes to frequent error.

When considering the clinical results of therapy, in terms of survival rates, it is significant that death from intercurrent disease limits the potential absolute five-year survival to 90% of less (4, 13). In 1944, Corsacaden (6) reported a 60% five-year survival rate in patients treated by panhysterectomy alone. Radium therapy alone yielded a 55% five-year survival (6). He found that combined therapy resulted in a 70% survival. Hyeman (11), in 1946 reported a five-year survival of 65% in 316 patients receiving radiotherapy. He found this result comparable to collected statistics for hysterectomy alone. Arenson (12), in 1948 reported 32 cases of combined therapy with 68% five-year survival. In 18 "favorable" cases, surgery alone yielded an 84% survival. Palmer's (17) statistics show a 41.1% absolute five-year survival in 272 cases treated with radiation alone. In 30 similar cases receiving combined therapy he found an 80% absolute five-year survival. Radiotherapy alone yielded a 64.3% absolute five-year survival in the series reported by Nugent and Gleichert (19). McGoogan and Hunt (18) advocate parallel radium and external roentgen therapy, followed in six to twelve weeks with panhysterectomy. In 18 selected patients so treated they have a 100% absolute five-year survival.

TABLE I

STAGE 0	.....	Questionable Cancer. (atypical hyperplasia)
STAGE I	.....	Definite Carcinoma, clinically confined to the Uterus.
STAGE II	.....	Carcinoma which has spread beyond the Uterus (irregular extrauterine mass, obvious invasion of surrounding tissue, or evident metastases)

ENCOMETRIAL CARCINOMA : STOCKHOLM CLASSIFICATION [1]

TABLE II

		Cases	%
STAGE 0	... (Primary lesion limited to Endometrium) ...	35	10.1
STAGE I	... (Myometrial invasion only) ...	225	65.2
STAGE II	... (Direct extension to adjacent organs) ...	51	14.8
STAGE III	... (Lymph Node metastases) ...	16	4.6
STAGE IV	... (Carcinomatosis, Hematogenous spread) ...	18	5.2
		345	99.9%

SURGICAL - PATHOLOGIC CLASSIFICATION OF ENDOMETRIAL CANCER [2]

[1] From Hunt (4).

[2] From Javert and Douglas (3).

HISTOPATHOLOGY OF IRRADIATED UTERI

Evidence of destruction of cancer within the uterus is an accurate indicator of the biologic response attained through radiotherapy (12). Arneson (12) states that the most reliable prediction of clinical result is based on persistence of viable tumor within the operative specimen. He reported 32 cases treated by combined methods. Persistent tumor was found in 47%. Of this group, only 46% survived five years. In the remainder of cases, where no residual tumor was found, 88% survived five years. Taylor and Becker (20) summarized 119 cases receiving intracavitary radiation averaging 3600 milligram-hours with tandem application. Panhysterectomy was performed after a six week interval. Residual carcinoma was found in 49.6% of cases. The five-year survival rate in these patients was 44.1%. The cases in which no residual tumor was evident had a five-year survival rate of 73.8%. These figures are presented in Table III.

Webb (13) reports an absolute five-year survival of 89% of patients in which no residual tumor was discovered in the uterus after combined therapy. This figure approaches "tumor control" (13) and agrees closely with Hunt's (4) finding regarding optimum potential survival.

Stowe (7) states that little attention has been paid to correlation of radiotherapeutic measures with histopathology in endometrial carcinoma. A review of the literature reveals an

TABLE III

		Residual Cancer	No Residual
Arneson (12): 32 Cases	....	15 cases (47%)	17 cases (53%)
Five year survival	....	46%	88%

		Residual Cancer	No Residual
Taylor and Becker (20): 119 Cases	...	59 Cases (49.6%)	60 Cases (50.4%)
Five year survival	...	44.1%	73.8%

SURVIVAL OF PATIENTS RECEIVING COMBINED RADIOTHERAPY & SURGERY
Illustrating the lower survival rate in cases with Residual Carcinoma in the Operative Specimen.

incidence of persistent viable tumor ranging from 12.5% to 100% (4, 5, 7, 8, 20, 21, 22). These results are summarized in Table IV.

The wide variation in frequency of residual tumor indicates a wide range of variables. A few of these are listed below:

1) Techniques of intracavitary radium application differ widely (7).
2. The duration of irradiation may vary, depending on such things as fractionation of dosage and use of external roentgen therapy.
3) The interval between radiotherapy and surgery differs. Hunt (4) states that from six to 12 weeks are required for resolution of irradiated tumor.
4) The size and configuration of uteri vary (4, 7, 13).
5) It is conceivable that, in some cases, all tumor tissue was removed at curettage (7).
6) The extent and diligence of the search for residual tumor can be expected to vary widely. Stowe (7) re-examined the uteri in his series of 53 cases which were reported free of tumor on the basis of routine pathologic examination. He removed the entire endometrium and superficial myometrium, making subserial sections. His discovery of viable tumor cells in this material raised his total incidence by 10%.
7) Criteria for tumor cell viability may differ among several

TABLE IV

Author	Cases	Radium Technique	Radium Dose mg. hr.	Roentgen Therapy (r)	Operation Interval	Residual %
Donovan and Warren (8)	13	Tandem	1700-3000	none	6-10 weeks	85
Healey and Brown (14)	24	Tandem	1200-2700	none	6-10 "	88
	25		3000-3300	none	6-10 "	48
	20		3400-4000	none	6-10 "	40
Smith (8)	24	Tandem	2400-3600	?	6-10 "	83
Marquis (7)	29	?	7260-7920	?	6 "	72
Arneson et al (12)	13	Tandem	3000-5000	1200-1600	1-6 "	77
Palmer et al (8)	86	Tandem	4500-9000	none	6 "	69.7
Brindley (8)	34	Tandem	800-4500	none	6 "	55.8
Scheffey et al (22)	30	Tandem	2000-5000	none	8-10 "	50
Taylor and Becker (20)	119	Tandem	Av. 3600	?	6 "	49.6
Corsacaden (6)	70	Tandem	1200-5000	none	1-20 "	75.7
Stowe (7)	7	Tandem	2000-4900	(2190	4-6 "	43
			(4500	(2190	4-6 "	67
			) 4500	) 2190	4-6 "	50
Schmitz and associates (15)	5	Y applicator	(6000	) 4000	?	100
	6		6000-	4000-	12-34 "	16.5
Friedman (10)	8	Hysterostat	4000-8000	none	?	12.5
Gray, Friedman and Randall (5)	7	Hysterostat	6000-12000	?	7-24 "	85
Arneson, Stanbro and Nolan (12)	19	Packing method	3500-7000	1200-1600	1-6 "	26.3

REPORTED INCIDENCE OF RESIDUAL TUMOR IN OPERATIVE SPECIMENS *
A Comparison of Results Found with Various Techniques

* Adapted from Freed and Pendergrass (8).

examiners.

An analysis of Table IV leads to the following conclusions:

1. High incidence of residual tumor is found in cases where tandem applicators are used.
2. Significant decrease in residual tumor is found as the intracavitary radium dose exceeds 6000 milligram-hours.
3. External roentgen therapy seems to have little effect on the intrauterine tumor.
4. Even with massive dosages of intracavitary radiation, residual tumor can be demonstrated.

The report of Gray, Friedman and Randall (5) is remarkable in that, (a) 85% incidence of residual tumor was reported with radium dosages ranging from 6030 to 12,480 milligram-hours, and, (b) the residual carcinoma was manifested as nests of apparently viable cells within the superficial myometrium. It is noted, however, that they employed the hysterostat application method which has been deemed inferior to packing procedures (8). The results of Healey and Brown (14) demonstrate that persistence of viable tumor is inversely related to the magnitude of radium dose. Schmitz and his associates (15) described a meticulous method of pathologic examination of their specimens. The entire endometrium was blocked and multiple sections were examined from each block.

REPORT OF CASES

MATERIAL:

Eighteen patients were studied in this series whose age ranged from 45 to 74 years. The average age was 62. All diagnoses were made by histologic examination of uterine curettings. The course of treatment consisted of preliminary radiotherapy, followed, at an average interval of 10 weeks, by panhysterectomy. The only selectivity in these cases was based on the following four criteria:

1) All cases had a planned course of combined therapy.
2) All cases were clinically classified as Stockholm Stage I.
3) All patients were treated under the direction of one radiotherapist.
4) All uteri were examined under the supervision of one pathologist.

METHODS:

Radiotherapeutic measures in these cases, although individualized, had basic uniformity. The patients, with one exception, received fractionated external roentgen therapy over a period averaging two to three weeks. Anterior and posterior ports, with mid-line shielding, were used in all cases. Additional lateral and gluteal ports were used as indicated. The tumor dose was calculated in tissue roentgens by applying suit-

able coefficients relative to (a) tumor depth, (b) field area, (c) half-value layer, (d) TSD and (e) shielding procedures, to the air dose (23). Backscatter was also considered.

Intracavitary radium was applied, in all cases, by packing the cavity with multiple capsules as advocated by Heyman (4). Tandems were used, in addition to the capsules, in order to increase the dose to the endocervical area. The radium therapy was fractionated into two courses spaced at one to two weeks. The placement of the capsules was recorded radiographically in two planes. The external roentgen therapy was administered concurrently with the radium. This extended the zone of cancerocidal dosage and improved the homogeneity of the radiation (4).

Additional radium applications were made to the upper vagina by the use of colpostats.

The radium dose or its radiocobalt equivalent was calculated in gamma roentgens as advocated by Freed and Pendergrass (8). Several volume calculations were made by use of the geometric data supplied by lateral radiographs of the application. The length of the packed cavity was measured directly from the lateral film with a 30% correction for magnification. It was found that the dose, in gamma roentgens, as calculated from all point sources could be related to the Patterson-Parker Curves for Linear Sources (23). Using the dose to the cavity in milligram-hours, along with the measured length of the application, and

applying a 10% correction for the 0.5 m.m. platinum filter, the dose in gamma roentgens was calculated. The value, as reported, represents the tumor dose to a depth of five millimeters or more beyond the uterine lining, (derived from the intracavitary application only). The radium in the colpostats delivered a dose in gamma roentgens approximately equivalent to one-third of the milligram-hour value as measured at the center of the uterus (23).

The uteri, when examined after hysterectomy, had a total length ranging from eight to 10 centimeters. Sections of endometrium and underlying myometrium were taken with special emphasis on areas showing irregularities of texture or color. When no suspicious areas were evident, two or three random areas were blocked and sectioned. In the four most recent cases, the endometrium and underlying superficial myometrium were "filleted". In this process the entire endometrium is removed. As many as 66 micro sections were made in these cases. The criteria of tumor cellular viability included (1) Integrity of cellular outline, (2) Preservation of a sharp nuclear membrane, and (3) Normal staining reaction of the cytoplasm and nucleus.

RESULTS:

The results of this study are tabulated in Table V, and summarized in Table VI.

TABLE V

Case No.	Intra-cavitary Radium mg. hr.	Colpostat Radium mg. hr.	Deep X-ray Tissue r.	Intra-cavitary gamma r.	Total Dose	Tumor r.	RESI-DUAL
1	8970	-	2200	7400	est.	9500	No
2	5660	1040	1560	5930	"	6500	Yes
3	5600	1400	2550	5250	"	6200	Yes
4	5325	2225	2000	5050	"	6200	Yes
5	4550	2100	1100	4600	"	5800	Yes
6	5500	2000	1500	5300	"	6200	Yes
7	6840	2200	2620	5800	"	7500	No
8	7200	-	1000	7280	"	7500	Yes
9	6132	2190	2300	5750	"	6900	Yes
10	4690	2142	1900	5100	"	6100	No
11	3780	2130	2000	5650	"	6500	No
12	4800	2825	1400	5400	"	6900	No
13	6000	3240	1260	6480	"	7700	No
14	5040	3200	2260	5200	"	6400	No
15	4320	-	1700	5000	"	5800	Yes
16	5670	1820	1700	5800	"	6800	Yes
17	5770	3790	-	6000	"	7200	No
18	7480	2000	2250	7120	"	8100	No

TABULATION OF 18 CASES COMPARING RADIATION DOSAGE TO RESIDUAL CANCER WHEN OTHER VARIABLES ARE FAIRLY WELL CONTROLLED (See Text)

TABLE VI

No. Cases	Stockholm Stage	Radium Technique	Radium Dose mg. hr.	Tissue Roentgens	Intracavitary Dose gamma r.
18	I	Packing method plus tandem.	4000-9000	1000-2500	4600-7400

Operation Interval	Residual Carcinoma %
av. 10 wk.	50

REPORT OF INCIDENCE OF RESIDUAL TUMOR IN OPERATIVE SPECIMENS
A summary of Results Found in the Current Study.

DISCUSSION:

The tables of results, in general, speak for themselves. The residual tumor in cases 2, 3 and 4 (Table V) was located in the endometrium, none appearing to invade myometrium. In cases 5 and 6, the residual acini were deep within the myometrium. Case 8 was a "filleted" specimen in which several well defined residual areas were seen, showing preservation of nuclear membranes and nucleoli. Case 9 was another "filleted" uterus in which 66 microscopic sections were examined. Eight of these sections showed definite infiltrative adenocarcinoma both deep within the myometrium and in superficial areas. Cases 15 and 16 both showed definite viable acini, staining well, within the superficial 0.3 to 0.4 cm of myometrium.

The rather ominous reports of five-year survival in cases where residual tumor was found, have been shown in Table III. The findings of Javert and Douglas are also significant. As noted in Table II, they found tumor invading the myometrium in 65.2% of 345 cases primarily operated. With a finding of invasive carcinoma in over half of a series primarily operated, it does not seem surprising when incidence of residual tumor is reported as high as 70 and 80% with inadequate radiotherapeutic measures.

The 18 cases, reported in this paper received an average of 6000 gamma roentgens, to a depth greater than 0.5 of a centimeter, from the intracavitary radium alone. When the

radiation from the colpostat applications and the deep roentgen therapy is added to this, it would seem apparent that these cases received adequate therapy as defined in this paper. The cases were all clinically stage I. The interval between radiation and surgery averaged 10 weeks. Definite residual carcinoma was found in 50% of these cases.

SUMMARY

The current concepts of treatment in endometrial carcinoma include surgical and radiotherapeutic regimes. The primary role of panhysterectomy is generally accepted. Radiotherapeutic methods and results show wide variation. The best results have been attained by use of intracavitary packing methods of radium application, in conjunction with external roentgen therapy. Most authors recommend that the dose of intracavitary radiation should be no less than 6000 gamma roentgens, delivered to a depth of one to 1.5 centimeters.

Examination of uteri for viable tumor six to twelve weeks after completion of irradiation is a valuable method of evaluating results. Five-year survival rates, in cases where residual is evident in the uterus, are much lower than in cases where no viable tumor is demonstrable.

The reports found in the literature, concerning the incidence of residual tumor in previously irradiated uteri, show

wide variation. Such reports can be expected to vary because of differences in radiotherapeutic methods and pathologic examination procedures.

Eighteen cases of endometrial carcinoma, treated by preoperative irradiation, have been reported. These cases were treated by adequate radiotherapeutic methods as defined in this paper. The method of pathologic examination employed has been reviewed. The entire endometrium and superficial myometrium should be examined microscopically if an accurate report of residual tumor is to be made. A method of approximating this goal has been discussed.

Viable carcinoma was found in 50% of the 18 cases discussed in this paper.

CONCLUSIONS

1) A search for viable carcinoma in uteri irradiated six to twelve weeks prior to surgery is an effective method of evaluating results.

2) Five-year survival is significantly less in cases where residual carcinoma is demonstrated.

3) The best radiotherapeutic methods, as currently defined, will not eradicate carcinoma within the uterus in all cases.

4) Routine pathologic examination of previously irra-

diated uteri should include complete removal of the endometrium and superficial myometrium. This tissue should be carefully examined microscopically if an accurate report of residual carcinoma is to be made.

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BIBLIOGRAPHY

1. Novak, Emil and Novak, E. R., Textbook of Gynecology, Baltimore, Williams and Wilkins Company, 1956. p. 384.

2. Anderson, W. A. D. ed., Pathology, St. Louis, C. V. Mosby Company, 1953. p. 1084.

3. Javert, C. T. and Douglas, R. G., Treatment of Endometrial Carcinoma: A Study of 381 Cases at the New York Hospital, Am. J. Roentgenol. 75:508-514, (March) 1956.

4. Hunt, H. B., Comparative Radiotherapeutic Results in Carcinoma of the Endometrium as Modified by Prior Surgery and Post Irradiation Hysterosalpingo-Oophorectomy, Radiology 66:653-666, (May) 1956.

5. Gray, L. A., Friedman, Milton and Randall, W. S., Observations on the Treatment of Adenocarcinoma of the Uterus, Surg. Gynec. & Obst., 82:386-404, (April) 1946.

6. Corsacaden, J. A., An Evaluation of Radiation in the Treatment of Carcinoma of the Corpus Uteri, J. A. M. A. 126: 1134-1138, (Dec. 30) 1944.

7. Stowe, L. D., A Histologic Study of the Effect of Irradiation on Adenocarcinoma of the Endometrium, Am. J. Obst. & Gynec. 51:57-66, (Jan.) 1946.

8. Freed, J. H. and Pendergrass, E. P., An Evaluation of the Efficiency of Various Techniques in the Treatment of Cancer of the Corpus Uteri, Am. J. Roentgenol., 71:253-265, (Feb.) 1954.

9. Schmitz, Henry and Schmitz, H. E., An Improved Technique for Radium Treatment of Carcinoma of the Uterine Body, Am. J. Roentgenol., 34:759-765, (Dec.) 1935.

10. Friedman, Milton, Treatment of Carcinoma of Corpus Uteri: Description of New Hysterostat, Radiology 35:28-35, (Jan.) 1940.

11. Heyman, J. and Benner, Sven, Futher Experience with Radiotherapy in Cancer of Corpus of Uterus, Acta. radiol. 27:328-331, 1946.

12. Arneson, A. N., Stanbro, W. W. and Nolan, J. F., The Use of Multiple Sources of Radium within the Uterus in the Treatment of Endometrial Cancer, Am. J. Obst. & Gynec. 55:64-78, (Jan.) 1948.

13. Webb, G. A., Margolis, A. J. and Traut, H. F., Adenocarcinoma of the Endometrium: An Evaluation of Factors Influencing Prognosis and an Outline of a Plan of Therapy Based on these Factors, Tr. Pacific Coast Obst. & Gynec. Soc. 22:69-81, 1954.

14. Healey, W. P. and Brown, R. L., Experience with Surgical and Radiation Therapy in Carcinoma of the Corpus Uteri, Am. J. Obst. & Gynec. 38:1-13, (Jan.) 1939.

15. Schmitz, H. E., Sheehan, J. F. and Towne, J. E., Effect of Preoperative Irradiation on Adenocarcinoma of the Uterus, Am. J. Obst. & Gynec. 45:377-390, (March) 1943.

16. Arneson, A. N., Clinical Results and Histologic Changes Following Radiation Therapy of Cancer of Corpus Uteri, Am. J. Roentgenol. 36:461-476, (Oct.) 1936.

17. Palmer, J. P., Reinhard, M. A., Sadugor, M. G. and Goltz, H. L., A statistical Study of Cancer of the Corpus Uteri, Am. J. Obst. & Gynec. 58:457-467, (Sept.) 1949.

18. McGoogan, L. S. and Hunt, H. B., Treatment of Carcinoma of the Fundus Uteri, Arch. Surg. 56:172-177, (Feb.) 1948.

19. Nugent, F. B. and Gleichert, J. E., Carcinoma of the Endometrium: Survey of Treatment and Results in a Community Hospital, Obst. & Gynec. 7:406-411, (April) 1956.

20. Taylor, H. C., Jr. and Becker, W. F., Carcinoma of Corpus Uteri: End Results of Treatment in 531 Cases from 1926 to 1940, Surg. Gynec. & Obst. 84:129-139, (Feb.) 1947.

21. Smith, G. V., Carcinoma of Endometrium: Review with Results of Treatment through 1935, New England J. Med. 225:608-615, (Oct. 16) 1941.

22. Scheffey, L. C., Thudium, W. J. and Farell, D. M., Further Experience in Management and Treatment of Carcinoma of Fundus of Uterus, Am. J. Obst. & Gynec. 46:786-802, (Nov.) 1943.

23. Glasser, Oliver, Quimby, E. H., Taylor, L. S. and Weatherwax, J. L., Physical Foundations of Radiology, New York; Paul Hoeber, Inc., 1952. p. 351, 524-528.