

# Analysis of Postoperative Vaginal Vault Radiotherapy of Stage I Endometrial Cancer with Different Radionuclides

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Acta Oncologica Vol. 37, No. 1, pp. 61–63, 1998

A total of 213 patients in stage I grade I endometrial cancer were treated postoperatively with either radium or caesium vaginal applicators. The rate of complication and the incidence of second malignancies were studied in both groups. The frequency of grades 2 and 3 vaginal complications was higher among patients treated with caesium applicators but not statistically significant. The observed number of second malignancies was significantly higher than expected in the radium-treated group, in which the observed number of second malignancies with distant location was also significantly higher than expected, which could not be found in the caesium group.

Received 30 May 1997

Accepted 6 November 1997

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The treatment policy in stage I grade I endometrial cancer at Radiumhemmet has in previous years been primary surgery with total abdominal hysterectomy and bilateral salpingo-oophorectomy followed by postoperative intracavitary vaginal irradiation. Over the years, radium was the only source in brachytherapy, but since 1980 Cs-137 sources have also been available. Between 1980 and 1986 about half the number of patients were treated with radium and the other half with caesium. The aim of this study is to determine whether radium and caesium, administered at the same calculated radiation dose, give the same outcome regarding complication rate, recurrence rate, and second tumor incidence.

## MATERIAL AND METHODS

Between 1980 and 1986, 213 patients in stage I grade I carcinoma of the endometrium were admitted to Radiumhemmet for postoperative vaginal treatment. The two applicators compared in this study were identical in size, shape, and weight but one was loaded with caesium and the other with radium. At this time the Gynecological Department at Radiumhemmet had two wards, each using one applicator. The patients were randomly referred to either of the wards.

Ninety-nine patients were treated with the radium applicator and 114 with the caesium applicator. With the exception of one papillary type, all cases were histologically confirmed as highly differentiated endometrial adenocarcinomas. The patient ages varied between 39 and 80 years, mean age 60. The 'bladder' and 'rectal' dose rates were measured with a special probe in each patient. For the radium and the caesium groups, the median values of the dose to the bladder were 12 Gy (range 4–20) and 14 Gy (range 6–19) respectively. For the dose to the rectum the median values were 17 Gy (range 9–23) and 16 Gy (range 9–24) respectively. The patients were followed for at least 5 years or until death.

At the Radiumhemmet the treatment complications of bladder and rectum were recorded according to Gray & Kottmeier (1) (see Table 1), which renders other glossaries inapplicable for the evaluation of the Stockholm patient file. The vaginal complications grading was modified by the authors according to Gray & Kottmeier.

## STATISTICAL METHODS

The observed numbers of second malignant tumors in the radium and caesium groups were compared with the expected number of malignant tumors as calculated by age groups and observed calendar period on the basis of

**Table 1**  
Definitions and grading of complications following radiation therapy

	Bladder	Rectum	Vagina
Grade 1	Mild symptoms, cystoscopy findings: mild atrophy, telangiectasia	Mild proctitis	Dryness, discharge, small bleedings, adhesions in upper half of vagina
Grade 2	Urgent discharge, cystitis, bleedings, cystoscopy findings: necrosis with ulcer or fibrine	Severe subjective symptoms, ulcers and necrosis, moderate stenosis	Severe bleedings, pains, adhesions in lower half of vagina
Grade 3	Fistulas	Severe stenosis	Ulcers, necrosis
Grade 4		Fistulas	Fistulas

incidence data from the Swedish Cancer Registry. The differences between the observed and expected numbers were tested using the  $\chi^2$  statistic.

### PHYSICAL PROPERTIES

Two cylindrical applicators of the same construction and dimensions were used. One contained radium with a source strength of 1 080  $\mu\text{Gy h}^{-1} \text{m}^2$  (150 mg Ra; 5 490 MBq) and the other Cs-137 with a source strength of 1 096  $\mu\text{Gy h}^{-1} \text{m}^2$  (150 mg Ra eq; 13 838 MBq) year 1979. The relative dose rate around the applicators was measured with a diode in a water phantom (Radiation Field Analyzer, RFA-7, Scanditronix, Sweden). The diode was a p-type silicon detector with no wall shielding (2). The absorbed dose at 1 and 2 cm distance from the surface in the mid-plane of the applicators was measured with thermoluminescent dosimeters (LiF-7, Harshaw) in the form of extruded rods. At that time intracavitary irradiation was still based on the concept mgh Ra (milligram hour of radium) or its corresponding amount of Cs. According to the measurements, the absorbed dose at 1 and 2 cm tissue depth amounted to  $21 \pm 2$  Gy and  $12 \pm 1$  Gy, respectively, during one treatment session.

### RESULTS

#### Complication rate

Among 99 patients treated with the radium applicator there were six bladder complications, ten rectal complications and 40 vaginal complications at the grade 1 stage, two rectal complications and four vaginal complications at the grade 2 stage and eight vaginal complications in patients at grade 3 stage (Table 2).

Among 114 patients treated with the caesium applicator there were five bladder complications, four rectal complications and 46 vaginal complications at the grade 1 stage, one bladder complication, two rectal complications, and ten vaginal complications at the grade 2 stage and ten vaginal complications in patients at grade 3 stage (Table 2). The number of grade 2 and grade 3 vaginal complica-

tions was higher among patients treated with caesium applicators but this result was not statistically significant.

#### Recurrence rate and survival

Out of a total of 213 patients only one, treated with caesium, died of distant recurrence 4 years after primary treatment, while 29 patients died of intercurrent disease. The crude survival rate was 86%, disease-free survival rate 99.6%.

#### Second malignancies

Through the regional cancer registry 25 patients with second malignancies were identified, 15 of them in the radium group and ten in the caesium group. The observed numbers of second malignancies were compared with the expected number as calculated by age group and observed period on the basis of incidence data from the Swedish Cancer Registry. Among the radium-treated patients, 6.08 malignancies were expected, compared with the 15 tumors observed,  $p < 0.001$ ,  $\chi^2$  13.1. In the caesium-treated group the observed ten cases of second malignancies did not reflect a significant increase over the expected number of 7.15, ( $p = 0.287$ ,  $\chi^2$  1.14) (Table 3).

Two patients in the radium-treated group and two patients in the caesium-treated group developed a second malignancy in the organ located within a short distance from the applicators. Among the radium-treated patients, 13 patients developed a second malignancy in a distant organ vs. eight in the caesium-treated group. The expected

**Table 2**  
Complications after radium (99) respectively caesium (114) vaginal treatment

	Grade 1		Grade 2		Grade 3	
	Ra	Cs	Ra	Cs	Ra	Cs
Bladder	6	5	0	1	0	0
Rectum	10	4	2	2	0	0
Vagina	40	46	4	10	8	10

**Table 3**  
Second primary malignancies

Organs	Ra (no. 99)		Cs (no. 114)	
	Expected	Observed	Expected	Observed
Breast	1.84	4	2.25	3
Lymphoma	0.19	1	0.23	1
Gall bladder	0.23	1	0.26	0
Lip	0.01	0	0.01	1
Colon	0.57	1	0.64	0
Rectum	0.30	0	0.34	2
Pancreas	0.23	1	0.26	0
Leukemia	0.16	0	0.18	1
Salivary gland	0.02	1	0.02	0
Bladder	0.18	1	0.21	0
Brain	0.23	1	0.28	0
Myeloma	0.09	1	0.11	1
Vagina	0.06	1	0.07	0
Thyroidea	0.07	1	0.08	0
Melanoma	0.19	0	0.24	1
Skin	0.18	1	0.18	0
All sites	6.08	15	7.15	10

All sites  $p < 0.001$  Ra  $\chi^2$  13.1  
 $p = 0.287$  Cs  $\chi^2$  1.14.

numbers were 5.54 and 6.53, respectively. In the radium-treated group the observed number of second malignancies with distant location was significantly higher than expected— $p < 0.002$ ,  $\chi^2$  10.1. No significant difference could be observed in the caesium-treated group— $p = 0.556$ ,  $\chi^2$  0.33.

## DISCUSSION

The potential hazards associated with the use of radium together with the problems of radiation protection arising from the high energy of gamma rays emitted were such that during recent decades radium has been replaced successively by radionuclides such as caesium 137, cobalt 60, iodine 125 and iridium 192.

Still, it is of interest to investigate whether these two different isotopes, radium and caesium, when applied at the same absorbed dose, differ in adverse effects. In order to facilitate the use of other radionuclides, it has been practical to specify other sources in milligram radium equivalent. The mass of radium contained in a point source filtered by 0.5 mm thick 90% Pt will yield the same exposure rate in air as the actual radioactive sources at the same distance (3). Using these measures and considering the half life of Cs, the treatment times for caesium applicators, to be equivalent in activity to radium applicators,

were established. However, the clinical impression was that, despite the equal activity, the complication rate was different for patients treated with radium and caesium applicators, respectively.

There was a numeric difference in grades 2 and 3 complication rates between the two groups. Caesium 137 is a very popular radium substitute because of its 30-year half life. Its single gamma ray is less penetrating than the gamma rays from radium, which could explain the trend seen in complication rate.

Still, even if the complications tend to be more frequent in the caesium-applicator-treated patients, all the severe complications occurred in the vagina and neither fistulas to bladder or rectum nor stenosis of the rectum was observed. This observation justifies the conclusion that even though the complication rate was higher among the patients treated with caesium, the severity of the side effects was not of the kind to create long-term problems for the patients.

An increased risk of second primary malignancies has previously been described among patients irradiated for cervical cancer or benign gynecological disorders (4, 5).

Such an increased risk was found to be significant only in the radium-treated group of patients with endometrial carcinoma presented here. The risk between the two groups did not differ with respect to second malignancies in organs within a short distance, but there was an unexpected statistically significant difference in risk of second malignancies with distant location. The difference could possibly be explained by the fact that radium has a complex gamma energy spectrum and a higher mean energy than caesium. Organs with distant location can receive a 2–3 times higher absorbed dose from radium compared to caesium. Could a different pattern of adverse effects also be seen in comparison with other isotopes?

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