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# THE ROLE OF RADIATION THERAPY IN THE TREATMENT OF ADENOCARCINOMA OF THE CORPUS UTERI STAGE I

## A ten year experience (1970–1979)

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**Abstract**

A series of 93 cases of endometrial adenocarcinoma stage I, of which 87 were treated by surgery in combination with pre- or postoperative irradiation, is analysed with respect to recurrence rate, survival and effect of preoperative irradiation on myometrial invasion. According to the authors, the treatment of choice remains a combination of surgery and radiation therapy in order to control the primary tumor and prevent vaginal recurrence. The authors recommend uterovaginal intracavitary irradiation followed by total abdominal hysterectomy and bilateral salpingo-oophorectomy with or without lymphadenectomy, and with adjunctive postoperative external irradiation reserved for the rare cases at high risk for locoregional failure (persistence of deep myometrial invasion, lymph node involvement).

An increase in the incidence of endometrial adenocarcinoma has been noted by several authors (2), with lesions limited to the body of the uterus (stage I) largely predominating. The principle of the combination of surgery and radiation therapy is not disputed (3, 7, 13) and in terms of survival excellent results have been obtained. However, in practice, radiation therapy differs from one team to another concerning method to be adopted (intracavitary or external irradiation), order with regard to surgery and irradiation (pre- or postoperative), and treated volume. In the light of ten years' experience, we have analysed the factors underlying different therapeutic protocols in order to arrive at what could be considered the optimal policy.

### Material and Methods

Between 1970 and 1979, 93 patients with clinical stage I adenocarcinoma of the endometrium (4) were treated at this hospital.

By measurement of the uterine cavity, 73 patients were classified as stage I A (uterine cavity <8 cm) and 20 as stage I B (uterine cavity >8 cm). The ages ranged from 36 to 86 years with a mean of 60 years, 68 per cent of the patients being between 50 and 70 years. Eighty-four per cent of the patients were post-menopausal and in 92 per cent the disease was revealed by post-menopausal bleeding.

*Treatment modalities and outline of treatment policy.* The type of radiation therapy employed, i.e. pre- or postoperative irradiation, depended, as far as this department was concerned, only on whether the patient was seen before or after surgery.

*Patients seen before surgery (50 patients).* The treatment most often used was uterovaginal intracavitary therapy to a dose of 60 Gy (39 patients) delivered to a target volume encompassing the entire uterus, the immediately adjacent parametria and the upper third of the vagina and paravagina; only

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rarely was vaginal irradiation alone used (7 patients). Radiation therapy was followed 4 to 6 weeks later by surgery in the form of total abdominal hysterectomy with bilateral salpingo-oophorectomy often combined with a bilateral lymph node dissection. In cases with lymph node involvement or deep muscle invasion, additional pelvic irradiation was given by 25 MV roentgen rays or $^{60}Co$ gamma rays to a total dose of 45 Gy with protection of the volume treated by intracavitary irradiation (2 patients).

Four patients presented with severe hemorrhage and received external radiation therapy preoperatively. One of them was treated to a total dose of 45 Gy and the other 3 with external radiation therapy to a dose of 30 Gy followed by additional intracavitary therapy to a dose of 30 Gy (2 preoperatively, 1 postoperatively).

*Patients seen after primary surgery (37 patients).* When the surgical specimen showed no lymph node metastases and only superficial muscle invasion (i.e. less than half the myometrium invaded), only vaginal intracavitary therapy to a dose of 60 Gy was given to the remaining upper third of the vagina at a depth of 4 to 5 mm (20 patients).

Patients with lymph node involvement and/or deep muscle invasion (i.e. more than half the myometrium invaded) received pelvic external irradiation to a dose of 45 Gy (14 patients) followed, in 3 patients, by an additional 20 Gy from vaginal intracavitary therapy.

*Inoperable cases (6 patients).* These patients were judged as being inoperable for medical reasons and were treated with radical radiation therapy.

*Treatment technique.* Intracavitary therapy was delivered by $^{192}Ir$ with the help of a plastic mould. In the case of uterovaginal therapy one single uterine and two vaginal sources were used with size and position of the sources in the plastic mould according to the recently published Méthode de Créteil (11) which was initially developed for treatment of cervical cancer. This system defines a reference isodose of fixed value encompassing the target volume. The dose is calculated at the reference isodose of 4 Gy/day assuming a linear nominal exposure rate of 1 mR–1 m2 cm-1. This corresponds to an effective dose rate which varies between 8 and 16 Gy/day when the actual linear exposure rate of the $^{192}Ir$ wires is taken into account. When the vagina alone had to be treated, an imprint of the vagina was made and the various dimensions estimated. It was then decided whether 2 linear sources arranged in an anteroposterior direction or a single linear source placed in the frontal plane would be required in order to obtain a dose distribution such that the reference isodose would include a minimum of 4 to 5 mm of tissue from the surface of the plastic mould.

**Table 1**

*Distribution according to histologic grade, muscle invasion and lymph node involvement*

| | Stage | | Total |
|---|---|---|---|
| | IA | IB | |
| Histologic grade | | | |
| G1 | 64 | 16 | 80 |
| G2 | 7 | 3 | 10 |
| G3 | 0 | 1 | 1 |
| Unspecified | 2 | 0 | 2 |
| Muscle invasion | | | |
| None | 28 | 4 | 32 |
| <1/2 | 30 | 9 | 39 |
| >1/2 | 11 | 5 | 16 |
| Unspecified* | 4 | 2 | 6 |
| Lymph node involvement N+/number of dissections performed | 2/35 | 2/10 | 4/45 |

* Patients treated with radical radiation therapy.

The distribution according to histologic grade, myometrial invasion independently of initial treatment, and lymph node involvement is shown in Table 1.

## Results

*Tumor control and survival.* Two of the 93 patients were lost to follow-up. As far as disease control was concerned two locoregional failures were observed: one patient, in stage IA, treated with uterovaginal intracavitary therapy followed by surgery and pelvic external irradiation, presented a retrourethral recurrence (inferior third of the vagina) at thirty months, which was treated by interstitial radiation therapy. Another patient, in stage IB, treated with pelvic external irradiation alone, developed at twenty-eight months a recurrence in the uterus which was salvaged by uterovaginal intracavitary irradiation. Thus the percentage of vaginal vault recurrence in this series was only 1.1 (1/93).

Three patients developed distant metastases, two of them died and the third was salvaged by lobectomy.

The NED survival at 4 years (93 patients) and 5

**Table 2**

*Muscle invasion as a function of the initial treatment (per cent in parentheses)*

| | Muscle involvement | | |
|---|---|---|---|
| | None | <1/2 | >1/2 |
| Pre-operative utero-vaginal radiation therapy* | 23/43 (53) | 18/43 (42) (95) | 2/43 (5) |
| Initial surgery or vaginal radiation therapy | 9/44 (20) | 21/44 (48) (68) | 14/44 (32) |

* Intracavitary therapy or external radiation therapy.

years (82 patients) was 94 per cent (87/93) and 92 per cent (75/82), respectively.

*Complications.* Only one complication after the treatment was observed, in the form of a bilateral ureteral stenosis which occurred 22 months later in a patient who had received surgery followed by external radiation therapy. Surgical re-implantation of the ureters was successfully carried out and the patient is doing well. It is to be noted that no complications were observed in this series after treatment by uterovaginal or vaginal intracavitary irradiation alone.

*Myometrial invasion as a function of the locoregional treatment employed.* Table 2 compares the depth of myometrial invasion as judged from the surgical specimen, according to whether or not the patients received preoperative radiation therapy (uterovaginal intracavitary therapy or external radiation therapy). The only factor influencing the decision to give preoperative radiation therapy was whether the patient was seen by us before or after surgery. Therefore, the two treatment groups are not strictly comparable from a statistical point of view. However, it may be assumed that primary surgery was performed in prognostically more favorable cases. Thus the slight bias in patient selection could rather have disfavored the preoperative irradiation group.

Seven patients received preoperative vaginal intracavitary therapy during which the uterus was excluded from the treated volume. For this reason they were considered as not having received preoperative radiation therapy to the corpus of the uterus for this part of the analysis.

After initial radiation therapy, deep muscle invasion (more than half the thickness of the myometrium) was observed in 5 per cent and no muscle invasion in 53 per cent of the cases. The corresponding figures for those treated initially with surgery were 32 per cent and 20 per cent, a difference which was highly significant ($p<0.002$). On the other hand, the incidence of superficial muscle invasion (less than half the thickness of the myometrium) was similar in the two groups (42% and 48%). Since myometrial invasion was not influenced by initial surgery the observations in this group of patients could serve as a reference. From these observations it was obvious that radiation therapy often reduced the degree of infiltration or caused a complete disappearance of muscle invasion. It should be noted that after initial uterovaginal intracavitary therapy, complete histologic absence of tumor was observed in 44 per cent of the cases (17/39).

## Discussion

The exact role of radiation therapy in the treatment of stage I endometrial adenocarcinoma remains controversial (3). Even if the irradiation should have no effect on survival it certainly reduces significantly the incidence of vaginal and/or pelvic recurrences (1–3, 5). Thus, after surgery alone the incidence of vaginal recurrences is between 8 and 12 per cent whereas with surgery and radiation therapy combined it is only about 3 per cent (5, 10, 13) whatever the histologic grade. The latter seems to be more a risk factor for distant metastases than for locoregional recurrences (6). When myometrial invasion exceeds half of the thickness, postoperative external irradiation significantly reduces the incidence of pelvic recurrences (1).

The results in this series are similar to those described in the literature with regard to NED survival, incidence of lymph node involvement (estimated by MORROW et coll. (9) to be 10.6% in stage I), and efficiency of radiation therapy in the prevention of vaginal and/or pelvic recurrences. In fact, we observed only one vaginal recurrence (1%), and the other locoregional failure (uterine recurrence) could be explained by insufficient treatment (external irradiation alone). Furthermore, none of the 16 patients who received postoperative external irradiation because of a deep muscle invasion developed pelvic recurrence.

Analysis of the myometrial invasion in relation to initial treatment method (radiation therapy or sur-

gery) showed a lower incidence of deep muscle invasion when radiation therapy was performed first; moreover, in 44 per cent of the patients treated by preoperative uterovaginal intracavitary irradiation, no residual tumor was found in the surgical specimen. Although the modality of initial treatment was not randomized, but depended solely on whether the patient was seen before or after surgery, these data confirmed the efficiency of initial radiation therapy. They cannot be interpreted as a bias in the patient selection, since in 20 per cent of the cases no myometrial invasion was found after initial surgery. Many authors have regarded the change in myometrial invasion after irradiation as a prognostic factor. MCCABE & SAGERMAN (8) observed failures in 14 per cent of the cases when residual tumor was present in the surgical specimen and in only 3 per cent when the tumor had totally disappeared. In addition the percentages of pelvic recurrence were 75 and 33 per cent, respectively. Furthermore, PIVER et coll. (13) reported that the incidence of failures increased with the depth of myometrial invasion. Similarly, CHUNG et coll. (3) did not note any pelvic recurrence when the residual tumor, after irradiation, was confined to the inner third of the myometrium, compared with an incidence of 12 per cent in cases with deeper invasion. Thus the persistence of deep myometrial invasion after irradiation seems to be an important risk factor for locoregional failure.

The combination of surgery and radiation therapy in the treatment of endometrial adenocarcinoma stage I is consequently, in our opinion, justified in order to prevent locoregional failures (in the vagina regardless of the pathologic findings and/or in the true pelvis when the myometrium is deeply involved). The methods used for radiation therapy vary from one author to the other, and the possible morbidity induced by the treatment must be taken into consideration, especially when surgery and irradiation are combined. We therefore recommend preoperative uterovaginal intracavitary irradiation, which ensures an efficient vaginal prophylaxis and reveals the rare cases with persistent deep myometrial invasion for which adjunctive external irradiation is indicated (5% in the present series). On the other hand, the use of postoperative external irradiation should, theoretically, be relevant only in patients with a high risk of pelvic recurrence (3), according to the pathologic findings (32% in this series). However, a not negligible number of these patients would be exposed to a higher risk of complications by undergoing a laparotomy followed by adjunctive external irradiation, whereas preoperative uterovaginal intracavitary therapy would in almost all cases (95% in our series) reduce myometrial invasion without sequelae and make external irradiation unnecessary.

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