

Perioperative HDR brachytherapy in the treatment of recurrent carcinoma of the cervix and endometrium – a report of three cases

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Purpose. To present early results of perioperative brachytherapy HDR in the treatment of recurrent cervical and endometrial cancer.

Material and methods. We present two cases of two patients with recurrent carcinoma of the cervix and one case of patient with endometrial cancer. Their treatment consisted of surgical removal of the tumour with intraoperative implantation of flexible catheters for interstitial brachytherapy. Ir-192 source with nominal activity of 10Ci was used. A total dose of 30 Gy was delivered in 5-6 fractions in the case of the two patients who did not require external beam irradiation, and 20 Gy for the patient who needed additional teletherapy.

Results. Early observation of the patients confirmed a good postoperative course with satisfactory bowel function allowing the start of brachytherapy usually in the 3rd postoperative day. Fraction dose of 5-6 Gy and total dose of up to 30 Gy was well tolerated. The position of the catheter was stable over the treatment time.

In the follow-up of 9 months no early complications of brachytherapy and progression of the tumour have been observed.

Conclusion. According to these early experiences perioperative interstitial brachytherapy HDR offers a very promising potential for a more successful treatment of recurrent cervical and endometrial cancer. It is well tolerated and effective in achieving local control of the disease. This early results justify a further exploration of clinical value of this novel approach to the treatment of recurrent gynecological cancer.

Okolooperacyjna brachyterapia śródtkankowa – nowe perspektywy leczenia nawrotów raka szyjki i błony śluzowej macicy

Cel pracy. Przedstawienie wstępnych doświadczeń z zastosowaniem okolooperacyjnej brachyterapii śródtkankowej HDR w leczeniu nawrotów raka szyjki i błony śluzowej macicy.

Materiał i metoda. Przedmiotem analizy były trzy chore, leczone z powodu nawrotu miejscowego raka szyjki macicy (2 przypadki) i raka błony śluzowej macicy (1 przypadek). Leczenie polegało w I-szym etapie na operacyjnym usunięciu wznowy z jednoczesnym wszczepieniem aplikatorów do brachyterapii śródtkankowej.

W brachyterapii okolooperacyjnej zastosowano źródło Ir192 o nominalnej aktywności 10Ci (HDR). Leczenie prowadzono, stosując frakcje 5-6 Gy do łącznej dawki 30 Gy lub 20 Gy – w przypadku zastosowania uzupełniającej teleradioterapii.

Wyniki. Przeprowadzone obserwacje potwierdziły dobry przebieg pooperacyjny u chorych, manifestujący się prawidłowym powrotem funkcji perystaltycznej jelit i bezobjawowym przebiegiem. Przeprowadzenie brachyterapii HDR w dawce frakcyjnej 5Gy i dawce całkowitej 30 Gy charakteryzowało się dobrą tolerancją wczesną. Zastosowana technika implantacji zapewniła dobrą stabilizację położenia aplikatorów. W okresie trzy miesięcznej obserwacji nie stwierdzono znacznych odczynów popromiennych ani cech progresji nowotworu.

Wnioski. Wczesne doświadczenia z zastosowaniem okolooperacyjnej brachyterapii śródtkankowej potwierdza duży potencjał terapeutyczny tej metody i uzasadnia kontynuację dalszych badań klinicznych w tej dziedzinie.

Key words: perioperative brachytherapy, recurrence, cervix, carcinoma endometrium

Słowa kluczowe: brachyterapia okolooperacyjna, wznowa, rak szyjki macicy, endometrium

Introduction

Carcinoma of the cervix is the most frequent malignancy of the female genital tract in Poland. Despite a steady decrease of its incidence and improvement in early detection and treatment every year about 2500 women die from the disease [1].

Local recurrences are the leading cause of treatment failure in carcinoma of the cervix. The rate of central failures is closely related to the clinical stage of the disease: 10-15% in clinical stage I, 30-40% in stage II and about 60% in stage III. The prognosis in those women is usually poor, with a 5-year survival of 0-25% [2, 3].

Treatment strategies for the treatment of recurrent cervical cancer include exenterative radical surgery, irradiation and chemotherapy. Over the years pelvic exenteration emerged as the most effective method of treatment of central recurrences after both primary radiotherapy and surgery [4-6]. Five year survival of about 30-40% can be expected with microscopically confirmed radical excision of the relapsing tumor [6, 7]. The prognosis is usually fatal in patients who cannot be salvaged by surgery. There is no standard approach to the treatment of patients with a microscopic and macroscopic residual tumor after radical surgical intervention. The use of external beam irradiation as an adjuvant has many limitations, such as past history of previous radiotherapy including intracavitary brachytherapy. Its effectiveness is further diminished by poor tolerance of the previously irradiated area and a high risk of severe complications [8-11]. The introduction of intraoperative radiation therapy (IORT) has improved the effectiveness of irradiation by delivering a high dose of radiation to the tumor site while sparing of the surrounding organs [12, 13]. Intraoperative radiation therapy can be performed by either of two techniques: electron beam and high dose rate (HDR) brachytherapy [13, 14]. With the electron beam technique a planned radiation dose is delivered by a linear accelerator optimally installed in the operating room. The HDR technique has gained in popularity in recent years due to technical and practical advantages over the electron beam IORT. In the HDR technique a set of flexible catheters is placed in the tumor bed conforming to the area of treatment. The treatment usually begins in the perioperative time and is completed within a few days depending on the fractionation schedule.

In this report we present our early experience with the IORT - HDR as an adjuvant to surgical excision of recurrent carcinoma of the cervix and endometrium.

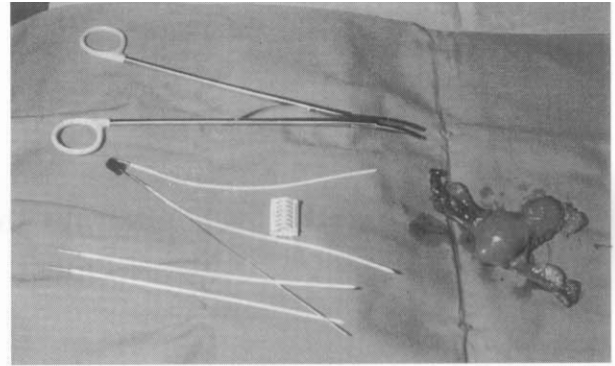


Figure 1. Catheters and titanium clips used for interstitial applications

Material and methods

Between January 2000 and December 2000 a pilot group of 3 patients with microscopically confirmed locally recurrent carcinoma of the cervix and endometrium were admitted to the Department of Gynecologic Oncology of the Maria Skłodowska-Curie Memorial Cancer Centre-Institute of Oncology.

After a comprehensive clinical evaluation with the use of modern imaging techniques the presence of central recurrence with no evidence of distant metastases was confirmed. The recurrence was located in the cervix in two patients (of cervical and endometrial cancer treated primarily with radiotherapy alone). One patient was treated initially with radical Wertheim's hysterectomy and adjuvant vaginal brachytherapy and subsequently developed a central recurrence in the vaginal apex. More detailed clinical information is presented in Table I.

The treatment of the recurrence was radical hysterectomy with wide parametrial excision in two patients, and radical upper colectomy in one case. The decision to place brachytherapy catheters for IORT-HDR treatment was made on the suspicion of persistent infiltration of the distal parametria in the proximity of the ureter and the iliac vessels. Once the tumor excision was completed the boundaries of the tumor bed were defined and marked with titanium clips. Flexible applicators (GammaMed interstitial applicator 200 mm) were used for IORT-HDR.

To obtain the desired dose distribution 4-6 applicators were placed in the tumor bed.

The position of the catheters was secured by placing absorbable sutures at their tips. The distant parts of the catheters were led out of the abdominal cavity through a 28 gauge vaginal catheter.

The HDR treatment was initiated on the second postoperative day, after the return of normal bowel function. The position of the catheters was confirmed by two orthogonal films. Abacus planning system was used for 3D reconstruction and treatment planning.

The Ir -192 source with a nominal activity of 10Ci was used for irradiation. A total dose of 30Gy was given to non irradiated patients, and of 20Gy to the patient with the prior external beam radiotherapy. Daily fractions of 5Gy were given. The

Table I. Patients characteristics

	1	2	3
Age	58	56	66
Diagnosis	ca colli ut. IIB	ca colli ut. IB	ca corp. ut. III
Microscopic type	ca plano G-2	ca plano G-2	adenoca G-3
Primary treatment	radiotherapy	surgery+BTH	radiotherapy
Site of recurrence	cervix	vaginal apex	cervix
Time to diagnosis of recurrence	22 months	19 months	8 months



Figure 2. Application of interstitial catheters into the parametrium

dose was prescribed at 1cm from the source. The catheters were removed immediately after completion of the treatment. One patient received a course of external beam irradiation- 9MeV photons, total dose of 44Gy.

All patients were followed regularly at bimonthly intervals for the median time of 9 months. After six months a CT of the abdomen was obtained in all patients. A special emphasis was put on the detection of post irradiation reactions.

Results

A preliminary assessment of the early results of HDR-IORT has focused on the following issues: postoperative course, stability of the implanted catheters, early tolerance of irradiation and local control of the relapsing tumor.

The postoperative course in all 3 patients was uneventful allowing a start of IORT on the second or third postoperative day.

The system of applicator fixation has proved to be very effective in assuring adequate stability during the entire treatment. The fractionation of 5Gy and a total dose range of 20-30Gy was well tolerated. All patients completed the planned treatment. A full course of external beam irradiation given to one patient was well tolerated with only transient reaction from the bladder.

None of the treated patients presented with recurrent or progressive disease after a 9 month long follow up period.

Discussion

Local recurrences are the leading causes of treatment failure in invasive carcinoma of the cervix [2, 15]. More than 60% of cancer – related deaths are caused by central recurrences in the vagina or parametria of patients treated with radical surgery and radiotherapy [2, 9]. Survival of patients with recurrent cervical and endometrial cancer is poor. The techniques of radical exenterative surgery developed in the fifties [4] proved to be effective in curing isolated central recurrences. The progress in surgical techniques and postoperative care has resulted in lowering the rate of fatal complications to about 5%, with 5 year survivals of 40-50% [5]. Similar results can be achieved with less radical surgery, such as hysterectomy or vaginal resection [6, 16, 17]. In any circumstances the success of surgical intervention can be assured only if the resection margins are free of cancer. Positive surgical margins on microscopic examination are encountered in 15-25% of what appeared to be a radically resected tumor and lead to treatment failure in about 80% of patients [7, 16-18]. Adjuvant external beam irradiation was commonly used in this setting. However its effectiveness was limited due to high incidence of bowel and urinary tract complications, especially in patients with a past history of radiotherapy or urinary diversion [10, 12]. Brachytherapy has proved to be a more effective method of treatment of local recurrences of cervical and endometrial cancer. The principal advantage over external beam irradiation is the possibility of delivering a high dose of irradiation to a well defined volume of tissue with a relatively low risk of damage of vital organs [18-20]. As early as in the seventies Evans and al.[10] reported a high rate of local control, exceeding 60%, after brachytherapy for recurrent carcinoma of the cervix. The introduction of interstitial brachytherapy with computerized optimization of dose distribution has improved the tumor control rate to the same level as radical surgery [21-24]. Intraoperative radiotherapy in the form of HDR brachytherapy is the most promising method of adjuvant treatment of local recurrences after surgical excision [21]. The use of IORT-HDR in this setting improves local control especially if the surgical margins were positive on microscopic examination [16, 21]. The overall local control rate of about 60-70% was reported by several authors [16, 17, 21]. Some advocate the application of interstitial catheters to the tumor bed in every case of surgical excision of recurrence of endometrial or cervical cancer. The decision to conduct IORT-HDR is made after microscopic examination. In the presence of positive surgical margins interstitial irradiation is commenced [16, 21]. Complications still remain a serious issue in IORT. Treatment related toxicities, such as delayed return of bowel function, wound infections, ureteral stenosis and fistulas were reported [21,23,24]. They may be the result of radical surgery, irradiation or a combination of these. In the opinion of many investigators peripheral nerve toxicity is the dose limiting toxicity for IORT. The dose of 15-20Gy should not be exceeded to avoid peripheral nerve damage [21]. Many techniques have be-



Figure 3. Distal parts of brachytherapy catheters protruding from the vagina

en developed to prevent the occurrence of severe complications. The use of ureteral stents, omental and rectus muscle flaps to shield bowel has contributed to a significant reduction of grade 3 complications [17, 21]. In our experience the treatment with daily fractionation of 5Gy and total dose of 20-30 Gy was well tolerated, however a much longer follow up period is needed to evaluate the late morbidity of interstitial therapy.

To conclude: perioperative interstitial brachytherapy HDR as an adjuvant to surgical resection offers a good chance of local control and cure to women with local recurrences of cervical and endometrial cancer. Our early results justify further exploration of clinical value of this novel approach to the treatment of recurrent gynecological cancer.

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