CERVICAL CANCER - BRACHYTHERAPY

Archive of Oncology 2001;9(Suppl 2):47-8.

S. ČIKARIĆ

INSTITUTE FOR ONCOLOGY AND RADIOLOGY OF SERBIA, BELGRADE, YUGOSLAVIA

Low-dose-rate *vs.* high-dose-rate brachytherapy and the external beam therapy of the cervical carcinoma: our 25-year experience

KEYWORDS: Cervical cancer; Brachytherapy; Radiotherapy

INTRODUCTION

Cervical carcinoma has traditionally been treated with low-dose-rate brachytherapy. High-dose-rate brachytherapy was developed to overcome potential disadvantages of LDR brachytherapy (radiation exposure to medical staff, prolonged treatment time, mandatory hospitalization and applicator movement). Both, LDR and HDR brachytherapy have been combined with the external beam therapy (EBT).

At the Institute for Oncology and Radiology of Serbia in Belgrade, the treatment of the cervical carcinoma with the radiological methods has been existing for more than 70 years. Intracavitary brachytherapy of this malignancy with gamma emitters began in 1932 using Ra-226 (LDR). Co-60 sources were introduced in the clinical practice in 1964 and Cs-137 (LDR) in 1977. The Parisian technique was applied in 1964, when a modification of the Manchester technique was introduced. External pelvic irradiation has continuously been applied for the treatment of the cervical carcinoma: ortovoltage EBT since 1923, Co-60 teletherapy since 1960, 42 MeV Betatron since 1970, and 10 MeV Linear accelerator since 1976. In Belgrade, afterloading technique was started in 1970 with manual Co-60 LDR afterloading by Henschke and in 1977 with manual Cs-137 LDR afterloading by V. Vujnić. In 1974 we started with remote HDR afterloading using Cathetron (Co-60 HDR), in 1989 Selectron (Co-60 HDR), in 1993 - Microselectron (Ir-192 HDR).

MATERIALS AND METHODS

Patients

From February 25, 1974 to May 20, 1997, a total number of 18,141 patients with gynecological malignancy were irradiated at the Institute for Oncology and Radiology of Serbia in Belgrade using HDR afterloading technique:

- Cathetron (Feb. 25, 1974 - May 20, 1997) - 14,250 patients (first appl. by Z. Merkaš, S. Čikarić, V. Vujnić),
- Selectron HDR (May 30, 1989 - May 20, 1997) - 2,434 patients (first appl. by S. Čikarić, V. Vujnić)
- Microselectron (Feb. 23, 1993 - May 20, 1997) - 1,457 patients (first appl. by S. Čikarić, Lj. Gržetić).

From this clinical material we made a retrospective analysis of 1,330 patients with the cervical carcinoma treated with HDR brachytherapy (Table 1). From July 1, 1997 to August 31, 1978, a group of 187 patients with the cervical carcinoma have been irradiated radically using manual Cs-137 LDR afterloading technique (Table 1).

Table 1. Cervical carcinoma: treatment time and stage distribution (FIGO) treatment

Treatment	Stage	1974/75	1977/78 HDR	1977/78 (LDR)	1984	1989/90	Total HDR	Total (LDR)
Surgery + Radiation	I+IIa	188	111	(-)	119	39	457	(-)
Radiation only	I	11	3	(1)	8	-	22	(1)
	IIb	169	85	(66)	125	46	425	(66)
	III (a+b)	171	52	(120)	136	58	417	(120)
	IVa	-	-	(-)	3	6	9	(-)
Total		539	251	(187)	391	149	1,330	(187)

Squamous cell carcinoma was dominant in both groups (HDR-94.8%, LDR - 96.8%). There were no patients younger than 20 years and the peak incidence occurred in the age group of 50-55 years in both, HDR and LDR series (peak incidence in surgery + radiation HDR series was in the age group of 40-44 years (X = 51.8) (LDR series).

RADIATION TREATMENT

Intracavitary brachytherapy

We used uterine tube and two vaginal ovoids with both techniques (HDR and LDR),. Total activity of sources (uterine tube + 2 vag. ovoids) was 333 GBq and 8.88 GBq at the and of August 1978. Dose rate at point A was 180 and 1.4 cGy/min; number of fractions 4-5 and 2 doses per fraction at point A 950-1000 and 3000-3200 cGy; time of 1 fraction 5-6 min and 33-39 h; interval between 2 fractions 1 week and 2 weeks, total treatment time 21 and 15 days, total dose at point A was 3.800-4.000 and 6.000-6.400 cGy (Table 2).

External beam therapy

In all cases we combined intracavitary brachytherapy and the external megavoltage beam therapy (Table 2).

Table 2. Cervical carcinoma: treatment regimens (HDR Brachytherapy +EBT)

		1974/75-1977/78	1984	1989/90
Technique		Dose/Fr./Fi.(Pb±)	Dose/Fr./Fi.(Pb±)	Dose/Fr./Fi.(Pb±)
Cath./Sel.		R:36-40Gy/.A/4/(-)	same	35-40Gy/.A/4-5/(-)
	S+	R:30-40Gy/0.5cm/4/(-)	same	same
Co-60 TT		R:37.8Gy/.B/24/2/(+)	-	-
	S+	R:30-35Gy/18/2/(-)	-	-
Betatron		R:36-46Gy/.B/16-22/2/(+)	-	-
	S+	R:30-35Gy/8/2/(-)	-	-
Linac		R:35-46/.B/16-22/2/(+)	46Gy/.B/22/2/(+)	same (±)
10 MeV	S+	R:35-40/18-20/2/(-)	same	same
TDFf/.A		≤140	≤165	≤175

Fr. - Fraction, Fi. - Fields, Pb - central lead shield, R - radiation, S - surgery, TDFf - timedose-fractionation-factor, A,B - dosimetric points in pelvis, Co-60 TT - Co-60 teletherapy

In LDR series (1977/78) EBT regimen was as follows: total midplane pelvic dose 45-50 Gy, 22-30 fractions, 4-5 fractions/week, 2 parallel opposite fields and the central lead shield.

As shown in Table 2, TDFf at point A was enlarged in 1984 and from 1989 to 1990.

Address correspondence to:
Prof. Dr. Slobodan Čikarić, Institute for Oncology and Radiology of Serbia, Pasterova 14, 11000 Belgrade, Yugoslavia

The manuscript was received: 12. 10. 2001.

Accepted for publication: 19. 10. 2001.

RESULTS

Survival

The 5-year crude survival rates for all radically irradiated cases classified into high and low-dose-rate groups (HDR Co-60 vs. LDR Cs-137) treated in period July 1977 - August 1978, were as follows: HDR vs. LDR - st. I - 3/3 (100%) vs. 0/1 (0%), st. II - 46/85 (54%) vs. 44/66 (69.7%), st. III - 19/52 (36.5%) vs. 52/120 (43.3%) and all stages - 68/140 (48.6%) vs. 98/187 (52.4%). The results are better in the LDR series (stage II-III), but difference in the survival rates is not statistically significant ($p<0,01$).

The 5-year crude survival rates for cases treated from 1974 to 1990 (HDR brachytherapy + EBT) are shown in Table 3.

Table 3. Cervical carcinoma: (HDR + EBT): 5-year survival (raw data)

Treatment	Stage	1974/75	1977/78	1984	1989/90	Total
Surgery+ Radiation	I+IIa	162/188 (86.2%)	92/111 (82.9%)	98/119 (82.4%)	31/39 (80.0%)	383/457 (83.8%)
	I (a+b)	9/11 (81.8%)	3/3 (10.0%)	5/8 (62.5%)	-	17/22 (77.3%)
	IIb	91/169 (53.8%)	46/85 (54.0%)	90/125 (72.0%)	32/46 (69.6%)	259/425 (60.9%)
Radiation only	III (a+b)	57/171 (33.3%)	19/52 (36.5%)	55/136 (40.0%)	29/58 (50.0)	160/417 (38.4%)
	IVa	-	-	0/3 (0%)	3/6 (50.0%)	3/9 (33.3%)
Total		319/539 (59.2%)	160/251 (63.7%)	248/391 (63.4%)	95/149 (63.7%)	822/1330 (61.8%)
Lost to follow-up		4%	6%	8.9%	4%	

We compared our results with the average world results (FIGO 1988). As we can see in Table 4, Belgrade results are better (statistically significant for total survival).

Table 4. Cervical carcinoma: % of 5-year survival (Belgrade vs. FIGO 1988)

Stage	% of 5-year survival	
	Belgrade N = 133 pts.	FIGO 1988 N = 31543 pts
I	83.8	75.7
II	60.9	54.7
III	38.4	30.6
IVa	33.3	7.3
Total	61.8	53.5

As we can see in Table 3, a 5-year survival of stages IIb and IIIa+b was statistically more significant in 1984 and between 1989-1990 versus 1974-1975 and 1977-1978 (TDF_f: ≤165 ≤175 vs. ≤140).

Late postirradiation sequelae

Only the complications that developed at least 2 months after irradiation were considered late complications (Table 5).

Table 5. Cervical carcinoma: Late postirradiation sequelae (G+)

Gradus (G)	1974/75 n = 539	1977/78 n = 251	1984 n = 391	1989/90 n = 149	Total n = 1330
G1	42 (7.8%)	16 (6.4%)	68 (17.4%)	37 (24.8%)	163 (12.3%)
G2	-	2 (0.8%)	-	15 (10.1%)	17 (1.3%)
G3	30 (5.6%)	9 (3.5%)	6 (1.5%)	13 (8.7%)	58 (4.4%)
G4	-	-	-	7 (4.7%)	7 (0.5%)
Total	72 (13.4%)	27 (10.8%)	74 (18.9%)	72 (48.3%)	245 (18.4%)
TDFf	≤140	≤140	≤165	≤175	

Severe late postirradiation sequelae (G3+4) in Belgrade group of patients between 1989-1990 were high (13.4%) but they are compared with same sequelae in other world centers: Horiot - 14.8% (LDR), Rodrigus - 14.3% (LDR), Clark - 5.0% (HDR) and 28.0% (HDR + CT).

CONCLUSIONS

1. Our clinical material of 1,330 patients with the cervical carcinoma treated between 1974 and 1990 was very similar to the clinical material of FIGO'94 (distribution by stage, by age, by histology, etc.).

2. The difference between disease control rates of intracavitary brachytherapy of the cervical carcinoma using either LDR or HDR was not statistically significant.

3. The 5-year survival rates were better and late postirradiation complications were more frequent and severe in those patients who were treated (radiation only, HDR) in 1984 and between 1989-1990 (TDF_f at point A was: ≤165 and ≤175).

4. All patients (6 patients with stage IIIb) treated with doses higher than 175 TDFf at point A have died within five years after treatment.

5. The 5-year survival rate for 1,330 Belgrade patients of all stages was 61.8% and for 31,543 FIGO'88 patients was 53.5% (crude data). This difference is statistically significant ($p < 0.01$).

6. Severe late postirradiation complications (G3+4) in Belgrade group of patients between 1989-1990 were high (13.4%) but they are compared with the same sequelae in other centers of the World: Horiot - 14.8% (LDR), Rodrigus - 14.3% (LDR), Clark - 5.0% (HDR) and 28.0% (HDR+CT).

SUGGESTED LITERATURE

Čikarić S. Radiation Therapy of Cervical Carcinoma using either HDR or LDR Afterloading: Comparison of 5-Year Results and Complications, Supplements to Strahlentherapie und Onkolgie. Vol. 82. Munchen - Wien - Baltimore: Urban & Schwarzenberg; 1988. p. 119-2.

Čikarić. S. The treatment of carcinoma or the uterine cervix by cathetron at the Institute of Oncology and Radiology in Belgrade - our 6 years experience. Proceedings - sixth meeting of international working party on the use of radionuclides and afterloading techniques in the treatment of cancer of the uterus in developing areas and International conference on gynecological cancer. Istanbul, 1980;179-88.

Atahan IL. High dose rate (HDR) vs. low dose rate (LDR) brachytherapy in the management of cervical cancer. Radiother Oncol 2001;58(Suppl. 1):S3,9.

Deehan C, O'Donoghue JA. Biological Equivalence of LDR and HDR Brachytherapy. In: Mould RF, Battermann JJ, Martinez AA, Speiser BL, eds. Brachytherapy from Radium to Optimization. Wageningen: Veenman Drukkers; 1994. p. 19-33.

Ellis F. Nominal standard dose and ret. Br J Radiol 1974;44:101-8.

Horiot JC, Fric D, Barillot I, et al. Carcinoma of the Cervix Treated with Radiotherapy Alone: Results & Prevention of Complications. In: Mould RF, Battermann JJ, Martinez AA, Speiser BL, eds. Brachytherapy from Radium to Optimization. Wageningen: Veenman Drukkers; 1994. p. 79-90.

Joslin CAF, Liversage WE, Ramsey NW. High doserate treatment moulds by afterloading techniques. Br J Radiol 1969;42:108-12.

Nag S, Erickson B, Thomadsen B, et al. The American brachytherapy society recommendations for high-dose-rate brachytherapy for carcinoma of the cervix. Int J Radiat Oncol Biol Phys 2000;48:201-11.

Pettersson F. Annual Report on the results of treatment in gynecological cancer. Stockholm: Radiumhemmet 1988; p. 45-60.

Pettersson F. Annual Report on the results of treatment in gynecological cancer. Stockholm: Radiumhemmet 1994; p. 51-64.

Extended abstract
UDC: 616.146-006:616-085:615.849.1

V. PLEŠINAC
S. ČIKARIĆ

INSTITUTE FOR ONCOLOGY AND RADIOLOGY OF SERBIA, BELGRADE, YUGOSLAVIA

Stepping source (Ir-192 HDR) vs. linear distributed and fixed sources (Co-60 HDR) in brachytherapy of cervical cancer: a single-center experience

KEYWORDS: Cervical cancer; Brachytherapy; Radiotherapy

INTRODUCTION

Based on experience and basic investigations (radiobiology), generally accepted attitude is that combined radiotherapy of malignant cervical cancer with brachytherapy and transcutaneous therapy (X-rays of high energy obtained on supervoltage machines) is the optimal method for achieving success in either post-operative or radical treatment (1).

The advanced production of artificial isotopes in last decades and the introduction of manual and remote afterloading techniques allowed the use of radionuclides of high- dose- rate radioactivity (HDR). In addition to the maximal protection of health care personnel, possibilities for out-hospital treatment, shorter term of application, better fixation of applicator, individual planning and optimization, we had even better survival results with reduced complication frequency (2).

Modern practice offers various technical solutions in source positioning during the same radiation regimes (HDR), along the applied catheters (3).

Selectron is a machine for mechanic afterloading in intracavitary brachytherapy in HDR therapeutic regimen, with Co-60 foci. A source train consists of combination of active and inactive pellets which are linearly distributed and fixed, making possible the adequate distribution of desired radiation dose and which are pneumatically transferred into applicator (4).

The last generation of brachytherapy machines is Microselectron that has one Ir-192 source with small dimenzions, moving "step by step" along the applicator, with previously defined steps (stepping source). The desired isodose distribution is obtained by programming dwell positions and times for the single source within each applicator (4).

Having in mind various technical solutions in source positioning we wished to compare treatment results in patients with cervical cancer treated in the frame of combined radiation treatments: brachytherapy with Selectron (linear distributed and fixed sources Co-60 HDR) or with Microselectron (stepping source Ir-192 HDR). We analyzed clinical parameters, therapeutic efficacy, complication level and the speed of radiation dose in certain points of interest.

Address correspondence to:
Dr Vesna Plešinac, Institute for Oncology and Radiology of Serbia, Pasterova 14, 11000 Belgrade, Yugoslavia

The manuscript was received: 12. 10. 2001.

Accepted for publication: 19. 10. 2001.

MATERIALS AND METHODS

At the Institute of oncology and radiology, Selectron (linear distributed and fixed sources Co-60 HDR γ–rays of 1,25 MeV) has been used for brachytherapy in cervical cancer from 1989. Microselectron (stepping source Ir -192 HDR g. rays of 0,35 MeV) has been used from 1992.

The retrospective study involved 216 patients with cervical cancer of all stages (FIGO), treated with brachytherapy on Microselectron or Selectron (Ir-192 group versus Co-60 group) within postoperative or radical combined radiation treatment. During 1995, a group of 108 patients were treated on Microselectron, and the same number of patients - 108 was in the group treated on Selectron during 1993. Stage distribution of patients in both groups (Ir-192 group versus Co 60 group) was similar: St. I - 32 versus 17, St. II - 36 versus 49, St. III - 34 versus 37, St. IV - 6 versus 5 (Table 1).

Table 1. Cervical cancer: Method of treatment, number of patients and stages (FIGO) (period of treatment: Ir-192 HDR group -1995, Co-60 HDR group 1993)

Treatment	Stage (FIGO)	Number of patients		Total
		Ir - 192 HDR	Co – 60 HDR	
Surgery + radiation	I b	31	17	48
	II (a+b)	4	3	7
	III b	1	2	3
	IV (a+b)	0	0	0
Radiation only	I b	1	0	1
	II (a+b)	32	43	75
	III b	33	37	70
	IV (a+b)	6	6	12
Total		108	108	216

The dominant histopathological type in both groups was planocellular cancer (cca 95% of all patients). Other patients had adenocarcinoma of the cervix which belong to less frequent histopathological type (1). The youngest patient in this study had 20 years, and the oldest 80 years, while the majority of patients belonged to the age group 40-55 in both groups.

All patients experienced combined treatment with transcutaneous radiotherapy and brachytherapy. Transcutaneous radiotherapy (X ray of 6-10 MeV) was conducted with TD of 36 to 46 Gy in 16-22 fractions with or without central lead shield.

In cases of radical radiation treatment, brachytherapy was delivered with uterine probe and two ovoids in 4 to 5 applications and TD of 7 to 8Gy in the point A. In postoperative radiation treatment brachytherapy was delivered with two vaginal ovoids and TD of 7 to 8 Gy in 4 applications and the dose calculated at 0.5 cm from the applicator (Table 2).

Table 2. Delivered radiotherapy regimens

Treatment	Brachytherapy (Ir – 192 HDR or Co – 60 HDR)	Teleradiotherapy (Linear accelerator)
Radiation only	4-5 x 7-8 Gy/A (uterine tube + 2 vaginal ovoids)	40 – 50 Gy/22-25f (with or without central Pb shield)
Surgery+ Radiation	4 x 7-8 Gy/0,5 cm (2 vaginal ovoids)	36-40 Gy/18/20f (without central Pb shield)

Two investigated groups of patients were uniform regarding age, histologic type, and disease stage and treatment regimen.

RESULTS AND DISCUSSION

Four years survival of patients, according to stages, presented in percentage, treated with Microselectron and Selectron (Ir-192 versus Co-60 group) was equalized: St. I - 24/27 (89%) vs. 14/16 (88%), St. II - 24/31 (77%) vs.

28/36 (78%), St. III - 8/27 (30%) vs. 10/22 (45%), St. IV - 0/3 (-) vs. 0/4 (-), and all stages 56/88 (64%) vs. 52/78 (67%), except in the group of patients with stage III with better survival in the group of patients treated with Selectron (45% versus 30%) than patients treated with Microselectron (Figure1).

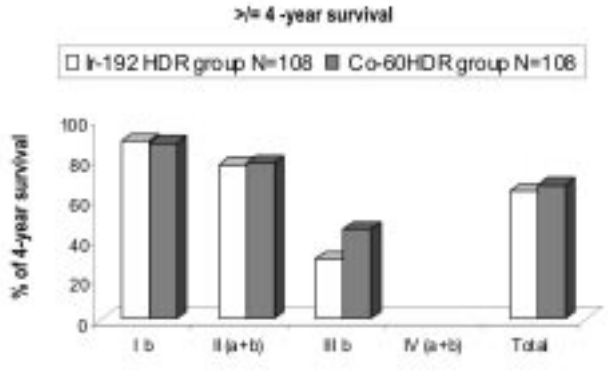

Figure 1. 4-year survival corrected for the cases lost to follow-up in groups Ir-192 and Co-60

The analysis of the late post-irradiation sequelae (French-Italian glossary) was also performed: G1-20% vs. 14%, G2 - 8% vs. 10%, G3 - 10% vs. 7%, G4 - 4% vs. 1% and total - 42% vs. 32%. The complications were with slightly higher percentage in the group of patients treated with Microselectron.

Based on the results obtained, the Department for radiotherapy physics and dosimetry of the Institute analyzed the medium and maximal dose speed at the point A on Selectron and Microselectron with the same total activity of the machines and in the same clinical conditions. The analysis revealed that:

- Medium dose speed in the point A on Selectron was 2 to 3 times higher than on Microselectron in any point in referent volume but in the relevant part out of it also (Figure 2).

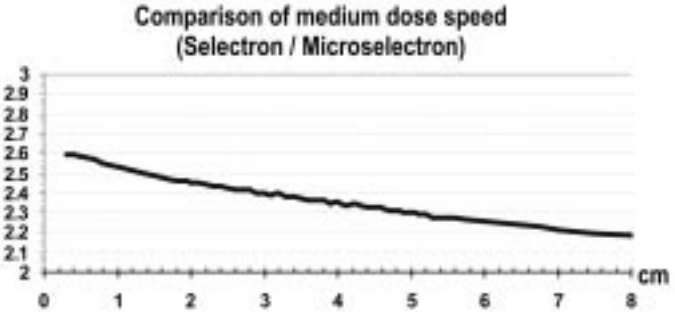

Figure 2. Comparison of medium dose speed

- Maximal dose speed in the point A on Microselectron was lower from 15 to 20 percent than on Selectron, during the same activity. In the point B, the speed was lower approximately for 50%. At the surface of the intrauterine probe the condition was inversely proportional. Maximal dose speed was 4 to 5 times higher on Microselectron than on Selectron (Figure 3).

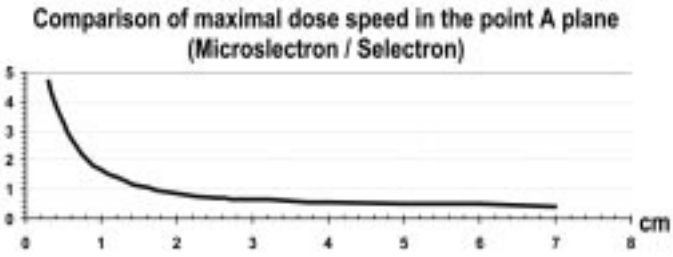

Figure 3. Comparison of maximal dose speeds in the point A plane

In accordance with the obtained results of clinical investigation and physical analyses, the question arises: would the evidence of higher medium dose speed on Selectron (Co-60) in the point A and apart of it in the referent volume, and in the relative part out of it, be the explanation for slightly worse therapeutic response in treatment on Microselectron (Ir -192) in case of patients with advanced cervical carcinoma (St.IIIb FIGO), especially in conditions when the activity of the source declines? Or, another question: can high speed of contact dose on Microselectron be significant both from aspect of tumor degradation and from aspect of applicator and healthy tissue and postirradiation sequelae, concerning that our clinical study revealed that late post-irradiation sequelae were represented in the group of patients treated on Microselectron? Unfortunately, data in literature dealing with these problems are very poor (5,6).

CONCLUSION

To conclude, we can say that, from the standpoint of our results, and according to the of various technical solutions in source positioning, further clinical investigation in strictly controlled studies with dosimetric investigations are necessary in order to define the most optimal therapeutic approach in treatment of cervical carcinoma.

REFERENCE

1. Perez CA, Brady LW. Principles and Practice of Radiation Oncology. Philadelphia: J.B. Lippincott Company; I987.

2. Nag S, Erickson B, Thomadsen B, et al. Int J Radiat Oncol Biol Phys 2000;48(1):201-11.

3. ICRU Report 38: Dose and volume specification for reporting intracavitary therapy in gynecology. Bethesda, MD: ICRU; 1985.

4. Stanković J. Osnovi radiološke fizike u radioterapiji. Beograd: Fakultet za fizičku hemiju Univerziteta u Beogradu; 1997.

5. Kagei K, Shirato H, Nishioka T, Kitahara T, Suzuki K, Tomita M, et al. High -dose - rate intracavitary irradiation using liner source arrangement for stage II and III squamos cell carcinoma of the uterine cervix. Radiother Oncol 1998;47(2):207-13.

6. Čikarić S, Stupar S, Marjanov I, Rudan Lj, Plešinac V. Stepping source (Ir - 192 HDR) versus linear distributed and fixed source Co - 60 HDR) in brachitherapy of cervical cancer: Our clinical experience. Eur J Cancer 1999;35(4):235-26.

Archive of Oncology 2001;9(Suppl 2):51-2.

K. DABIĆ-STANKOVIĆ[1]
J. BABIĆ[2]

[1]INSTITUTE FOR ONCOLOGY AND RADIOLOGY OF SERBIA, BELGRADE, YUGOSLAVIA
[2]INSTITUTE OF ONCOLOGY SREMSKA KAMENICA, RADIOTHERAPY DEPARTMENT, SREMSKA KAMENICA, YUGOSLAVIA

Late complications following combined radiotherapy for advanced cervical cancer (external beam therapy and MDR intracavitary brachytherapy)

KEYWORDS: Cervical cancer; Brachytherapy; Radiotherapy

INTRODUCTION

Since the beginning of the combined radiotherapy approach in patients suffering advanced cervical cancer, the goal of radiation oncologists has been oriented towards determination of the total therapy dose, relation between the doses given by external beam (EBRT) and brachythearpy (BHRT), etc., which would give the best therapy result that assumes the highest degree of tumour control while minimizing acute and late complications predominantly on the urinary bladder, rectum and small bowel. When EBRT as a part of combined treatment is concerned, some kind of consensus was established assuming that the pelvic side wall dose should be kept in a range 50 Gy for early stages, to 65 Gy for advanced ones (1). However, one has to keep in mind that the pelvis sidewall dose is generated not only by EBRT but also with BHRT (with less extent). On the other hand, brachytherapy depends on various circumstances that include irradiation regimen (LDR, MDR or HDR), the initial tumour volume, ability to displace the urinary bladder and rectum. But there is agreement among therapists that the total therapy dose to the point A (in a term of LDR equivalent dose) should be kept to at least 80 Gy for early stages, or 90 Gy for advanced disease stages (1). Porurquier and collaborators (2) report that the total dose of 75-80 Gy generates G2-G3 complications in 5% of treated patients, while the total doses greater than 80 Gy enrolls more than 10% of treated patients. Although pathophysiologic mechanisms of sequel generation are well known (3-5), strict limits of a tissue tolerant total dose are not known. The problem seems open when different therapy approaches and brachytherapy regimens (from LDR to HDR) are assumed. Only few authors reported results on MDR brachytherapy regimen, as a part of combined radiotherapy treatment in patients with cancer of the cervix (6). On the other hand numerous authors report that patients suffering from late postirradiation sequels have statistically significant benefit in the overall survival than patients without complications (2,7), which points out significance of magnitude of the total dose for cancer control.

It seems that sophisticated brachytherapy units, computer treatment planning, dose optimization and individualization, can be powerful tools that can insure good therapy results (maximum tumour control and overall survival with minimum late complications), in this patient group.

In this paper we would like to report therapy results in group of patients, suffering advanced cancer of the uterine cervix, treated at the Institute of Oncology in Sremska Kamenica, from 1987 to 1993. End point of this study is to correlate the total dose and volume dose to the urinary bladder and rectum with late complication (8).

MATERIALS AND METHODS

Group of 100 patients with advanced cervical cancer (FIGO stages IIb and IIIa) underwent combined radiotherapy (EBRT + BHRT) to the total pelvic EBRT dose of 50 Gy (20 Gy/10 fractions; open field + 30 Gy/20 fractions; central shielding) + BHRT dose 51 Gy/2 fractions (1 fraction weekly; mean dose rate 250 cGy/h - MDR). In all patients rectum and the urinary bladder maximum BHRT dose was planed to be 62% of the total BHRT dose, i.e. 31.62 cGy), that was in accordance with ICRU 38 recommendations (9). However, some of patients received less than maximum BHRT dose. All patients survived more than 5 years post irradiation. Group was divided into two subgroups: I - patients without late complications and II - patients with late complications. Other patient characteristics can be found elsewhere (8). Appropriate statistical tests were applied to find difference between groups and facilitate final conclusion (8).

RESULTS AND DISCUSSION

Doses to the critical organ (rectum and/urinary bladder) were higher in patients suffering from late complications than in patients with no complications.

For G3 rectal complications we found difference in patients that received BHRT dose from 33.16 Gy (65%) to 43.35 Gy (80%) which in combination with EBRT totaled 53-63 Gy. However, it is shown that influence of BHRT dose for G3 rectal complications is dominant (10), but only in the involved rectum part that receives total dose higher than 75 Gy. On the other hand G2 complications are not in strong correlation with BHRT dose, and depend mainly on EBRT dose in a range above 70 Gy. Also, therapy dose volume plays significant role in generation of late sequels on rectum. Sismondi et al. (1990) (11) reported it, too.

Acute complications on the urinary bladder were greater when organ-point (ICRU 38) total dose exceeded 62% dose limit, but for late complications no correlation was observed. This is contrary to the result reported by Crook et al. (1987) (10); however the authors (10) discuss degree of that correlation, pointed out the urinary bladder referent point definition (9) and associated marking and reconstruction problems. Barillot et al. (1993) (12) introduced ultrasonography technique as promising technique for visualization of the urinary bladder reference points.

CONCLUSION

In contrary to LDR and HDR brachytherapy, MDR brachytherapy regimen, as a part of combined radiotherapy of advanced stages of the uterine cervix cancer, is applied in limited number of radiotherapy centers and limited number of patients. It seems that these are reasons for limited data on therapy toxicity, as well as, therapy results. When combined radiotherapy toxicity in this patient group is concerned, only correlation between the organ dose and late morbidity (G2 and G3 complications) was obtained, pointed out that brachytherapy dose significantly influences occurrence of G3 late complications on infected rectum part, while external beam therapy dose influences occurrence of G2 late complications. For the urinary bladder no strong corre-

Address correspondence to:
Dr Kata Dabić, Institute for Oncology and Radiology of Serbia, Pasterova 14, 11000 Belgrade, Yugoslavia

The manuscript was received: 12. 10. 2001.

Accepted for publication: 19. 10. 2001.

lation was observed for same parameters.

Porurquier and collaborators (2) point out that BHRT dose given to critical organ (rectum and urinary the bladder) plays significant role in therapy late morbidity and that BHRT individualization, associated with reduction of EBRT dose to 45 Gy can improve radiotherapy outcome, mainly for late G2-G3 complications, in patients suffering advanced the uterine cervix cancer. Approach of the American Brachytherapy Society (1) seems similar when HDR brachytherapy regimen is concerned.

REFERENCES

1. Nag S, Erikson B, Thomasden B, et al. The American Brachytherapy Society recommendations for high-dose-rate brachytherapy for carcinoma of the cervix. Int J Radiat Oncol Biol Phys 2000;48:201-11.

2. Porurquier H, Delard R, Achille E, et al. A quantified approach to the analysis and prevention of the urinary complications in radiotherapeutic treatment of cancer of the cervix. Int J Radiat Oncol Biol Phys 1987;13:1025-33.

3. Kottmeier H. Carcinoma of the female genitalia. Baltimore: The Wiliams Wilkins Co; 1953.

4. Oprić M. Osnovi opšte patološke anatomije. Tuzla: Univerzitet u Tuzli; 1991. p. 258-76.

5. Robbins M, Hopewell J. Renal and genitourinary system morbidity of radiotherapy. In: Plowman et al, eds. Complications of cancer management. Butterworth-Heinelman Ltd; 1991. p.193-212.

6. Rhomberg W. Intracavitary treatment with caesium-137:Consideration on Reducing Morbidity. In: Mould R, ed. Brachytherapy. The Netherlands: Nucletron; 1984. p. 22-8.

7. Perez C, Breaux S, Bedwinek J, et al. Radiation therapy alone in treatment of uterine cervix: Analysis of complications. Cancer 1984;54:235-46.

8. Dabić K. Komplikacije sprovedene nakon radiološke terapije karcinoma uterusa na rektumu i bešici i korelacija sa aplikovanom dozom. Magistarska teza. Novi Sad: Medicinski fakultet u Novom Sadu; 1996.

9. International Committee on Radiation Units and Measurements, Dose and Volume Specifications for Reporting Intracavitary Therapy in Gynaecology, ICRU Report 38, Bethesda, USA, 1985.

10. Crook J, Eshe B, Chaplin G, et al. Dose-volume analysis and the prevention od radiation sequelae in cervical cancer. Int J Radiat Oncol Biol Phys 1987;8:321-32.

11. Sismondi S, Sinistero G, Zola P, et al. Radiotherapeutic treatment of uterine cervix cancer: Analysis of complications. Cervix, 1990; 8:257-258.

12. Barillot I, Horiot JC, Maigon P, et al. Maximum and mean bladder dose defined by ultrasonography: Comparison with the ICRU reference in gynecological brachytherapy. Radiother Oncol 1994;30:231-8.

I. MARJANOV
S. ČIKARIĆ

INSTITUTE FOR ONCOLOGY AND RADIOLOGY OF SERBIA, BELGRADE, YUGOSLAVIA

HDR brachytherapy and external beam therapy of cervical cancer: late postirradiation sequelae

KEYWORDS: Cervical cancer; Brachytherapy; Radiotherapy

This is a retrospective analysis of late complications occurring after radiotherapy treatment of cervical cancer of all stages in 149 patients in the period of 1989/90.

We use well known French-Italian classification of complications of rectum and urinary bladder, by type and stage/from G1 a-f to G4.

Most patients in our clinical material were in stage III of the disease (38,9%). At the admission to the hospital patients were aged between 50-59 years, mostly. Histopathological type by far most often diagnosed was squamous cell carcinoma (96.6%).

Treatment modalities:

I. For radiation only on CTR or SEL-HDR (1) with uterine tube and 2 ovoids-5x7 Gy/.A or 4x8-10 Gy.A, combined with external beam therapy with dose of 46 Gy/22 fractions, with or without central lead shields,

2. For radiation after surgery, with 2 ovoids 4x7, 5-8 Gy/0,5 cm combined with EBT -36-45 Gy/18-22 fractions.

TDFf was within interval of 135-175 (in our materials).

Five-year survival rate for all patients was 63.8%. Our research showed that there was no statistically significance depending on whether lead (Pb) shield was or was not used. (2).

Occurrence of late complications in both systems, GIT and urinary, staged from G1-G4, expressed in absolute numbers and percentage in 71 patients irradiated by SELECTRON and 78 by CATHETRON, showed that regardless of the choice of machine, i.e. using either SEL. or CTR., the GI complications prevailed: 22.5% for SEL., of 149 patients complication were seen in 48.3%. There is no difference in percentage of late sequelae using either machine (3). As already said the highest percentage of complications for both machines occurred in G1.

There is statistically significant difference in percentage of G1 complications for us (25 patients of 16.8%) in relation to G1 for gastrointestinal system (12 patients or 8.1%), as well as the highest statistical difference for G4 complications (0.7% vs. 4% for GIT). Thirty patients were transcutaneosly irradiated using central lead shield, and 119 without it. Complications of all stages - G1 - G4 in patients in whom the lead shield was applied amount-per-

Address correspondence to:
Dr Ivanka Marjanov, Institute for Oncology and Radiology of Serbia, Pasterova 14, 11000 Belgrade, Yugoslavia

The manuscript was received: 12. 10. 2001.

Accepted for publication: 19. 10. 2001.

cent. There was no statistically significant difference between these groups. However, if only G3 and G4 complications are taken into consideration, statistically significant complications are seen in patients in whom the filter was used.

CONCLUSIONS

1. Late postirradiation sequelae in patients with cervical cancer were most frequently located in the gastrointestinal and urinary system.

2. Statistically significant difference in occurrence of late complications in relation to selection of machine (Cathetron of Selectron HDR) was not provided in this paper.

3. Percentage of complications of grade G1 is the highest.

4. Percentage of late complications of grade I (G1) located on urinary system is higher in relation to percentage of the ones in gastrointestinal system.

5. There is no statistically significant difference in occurrence of late complications in relation to usage of central lead shield.

6. Higher TDFf value - higher complication percentage of higher grade.

7. The higher TDFf - the higher percentage of late complications - lower rate of recurrences.

8. The French-Italian glossary is useful and applicable especially in making comparisons in clinical practice (4).

9. Our results correspond to the world results.

REFERENCES

1. Subaru N, Erickson B, Thomadsen B, Orton C, Demanes J, Petereit D. The American Brachytherapy Society recommendations for High-dose rate brachytherapy for carcinoma of the cervix. Int J Radioat Oncol Biol Phys 2000;48(1):201-11.

2. Čikarić S. Radiation therapy of cervical carcinoma using either HDR of LDR afterloading: comparison of 5-year results and complications. Strahlenther Oncol 1988;82(Suppl):119-22.

3. Čikarić S, Petrović-Stupar S, Marjanov I, Rudan Lj. Therapeutic outcome in the adjuvant radiotherapy of 526 cases of endometrial carcinoma stage I, II and III. Radiotherapy Oncology. J Eur Soc Ther Radiol Oncol 2001;12:40.

4. Chassagne D, Sismondi P, Horiot JC, Sinistero G, Bey P, Zola P, et al. A glossary for reporting complications of treatment in gynecological cancers. Radiother Oncol 1993;26:195-202.

D. PERIŠIĆ
LJ. ŠUMARAC
M. ČEKEREVAC

ONCOLOGY OUTPATIENT DEPARTMENT, MEDICAL CENTER GORNJI MILANOVAC, YUGOSLAVIA

Complications and unfavorable effects of radiotherapy in cervical cancer

KEYWORDS: Cervical cancer; Brachytherapy; Radiotherapy

Radiotherapy is used for all stages of cervical cancer. When the surgery is contraindicated, it is applied as the brachytherapy in microinvasive cervical cancer. Postoperatively, in FIGO stages Ib and IIa, it is applied as the external-beam irradiation and intracavitary brachytherapy. The radical combined radiation therapy is used in advanced carcinoma, from IIb to IVa stages. Radiotherapy is applied together with chemotherapy as the sandwich therapy for the solitary metastases in IVb stadium. The basic aim of this report is the description and analysis of the complications in cervical cancer radiation therapy. From 1995 through 2001, 77 patients with cervical cancer were treated and received follow-up care at the oncology department of the Medical Center in Gornji Milanovac. Twelve patients were treated only with surgery, 24 with surgery and further radiation, and 41 with radical radiation therapy. Most patients were in FIGO I stage. The most dominant carcinoma was squamocellular (>90%). The average age of the patients was 51.2 years. Median follow-up was 25 months (range 2-71). Median survival for the whole group was 29 months (range 6-72). Seven patients had recurrence after radiation (10.8%), and in 6 patients (9.3%) metastases occurred. The most distinctive late postirradiation complications were the rectal dysfunction and vaginal strictures - 6.1%, cystitis, ureteral strictures and consequential hydronephrosis, as well as the appearance of ileus - 4.6%. According to the number, weight and kind, postirradiation complications were in the expected limits. The expertise of the radiotherapist is vital for the destruction of the tumor tissue and preservation of the vital organs from the damage.