Remote Afterloading High Dose Rate Brachytherapy AMC EXPERIANCES

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Remote afterloading high dose rate brachytherapy (HDRB) is a new technology and needs new biological principle for time and dose schedule. Here, authors attempt to evaluate the technique and clinical outcome in 116 patients, 590 procedures performed at Asan Medical Center for 3 years. From Sep. 1989 to Aug 1992, 471 procedures of intracavitary radiation in 58 patients of cervical cancer and 26 of nasopharyngeal cancer, 79 intraluminal radiation in 12 of esophageal cancer, 11 of endobronchial cancer and 1 Klatskin tumor and 40 interstitial brachytherapy in 4 of breast cancer, 1 sarcoma and 1 urethral cancer were performed. Median follow-up was 7 months with range 1~31 months. All procedures except interstitial were performed under the local anesthesia and they were all well tolerated and completed the planned therapy except 6 patients. 53/58 patients with cervical cancer and 22/26 patients with nasopharynx cancer achieved CR.

Among 15 patients with palliative therapy, 80% achieved palliation. We will describe the details of the technique and results in the text. To evaluate biologic effects of HDRB and optimal time/dose/fractionation schedule, we need longer follow-up. But authors feel that HDRB with proper fractionation schedule may yield superior results compared to the low dose rate brachytherapy considering the advantages of HDRB in safety factor for operator, better control of radiation dose and volume and patients comfort over the low dose brachytherapy.

Key Words: HDR, Brachytherapy, TDF

INTRODUCTION

Remote Afterloading High Dose Rate Brachytherapy (HDRB) has several advantages as compared with conventional Low Dose Rate Brachytherapy which include the patient comfort, safety factor for the operator and exellent control of radiation dose and treatment volume. HDRB delivers the radiation over a shorter periods of time, generally about a few minutes, but often in fractionated schedule.

The radiobiologic potential for disastrous late complications is present with a few big HDR fractions and it must be avoided by careful packing to displace the normal structure from the radioactive sources and careful fractionation schedule. In recent years, there has been a rapid increase in use of HDRB. HDRB is a new technology and we need a new biologic principle for time/dose/fractionation for HDRB. Here, authors review our 3 year HDRB experiances with an attempt to analyse for the effectiveness of therapy and complications of HDRB. Also, authors present our HDRB techniques for intracavitary radiation, intraluminal and interstitial irradiation.

MATERIALS AND METHODS

1. Patients

From September 1989 to August 1992, 116 patients were treated with 590 HDRB procedures at Asan Medical Center. Threre were 471 procedures of intracavitary radiation in 58 patients of cervical cancer and 26 patients of nasopharyngeal cancer, 79 procedures of intraluminal radiation in 12 patients of esophageal cancer, 11 patients of endobronchial cancer (8 lung and 3 trachea) and 1 patients of Klatskin tumor, and 40 interstitial brachytherapy in 4 patents of breast cancer, 1 patient of soft tissue sarcoma of thigh and 1 patient of urethral cancer. Performance status of HDRB patients ranged from 30 to 90 in Karnofsky scale with mode scale of 90. Median follow-up periods was 7 months with range 1~31 months. Of toal 116 patients, only 15 patients were treated with palliative aim (10 of lung cancer and 5 of esophageal cancer). 13 patients were treated for recurrent disease (10 patients with curative intent and 3 lung patients with palliative intent). 99 patients underwent HDRB in combination with external beam

irradiation with curative intent and among them, one sarcoma patient and 7 patients of cervical cancer were treated after curative surgery.

The characteristics of these patients including stage, pathology, patients' age, performance scale and intent of HDRB are shown in Table 1.

2. HDRB Technique

All patients were treated on microSelectron-HDR-Iridium 192 after placing an appropriate afterloading device under local anesthesia except interstitial implant. For an boost therapy to external beam irradiation, the HDRB was performed within a week after the completion of external beam irradiation. Prior to the HDRB, patients were mildly sedated with demerol 50 mg I.M. and valium 10 mg I.M. and buscopan 20 mg I.M. was given for esophageal and endobronchial HDRB. Under endoscopic or fluoroscopic visualization, the applicators were placed. After proper packing and proper stabilization of applicator in situ, dummy sources were inserted into the HDRB applicators and orthogonal simulation films were taken. The treatment volume was defined and then Nucletron brachytherapy planning computer optimized the dwell position and time of the sources to fit the isodose curve in the target volume. And then, these applicators were connected to microSelectron-HDR-Ir-192 and the treatment was given under the observation by audio/visual monitor.

1) The HDR Intracavitary Brachytherapy for Cervical Cancer:

The applicators with a tandem and 2 ovoids were used for intact uterus and applicator with 2 ovoids (5 cases) or vaginal cylinder (2 cases) was used for the patients s/p hysterectomy (Fig. 2). Fig. 1 shows various applicators for brachytherapy of cervix and various sites. The fraction size of 500 cGy was given at the reference point A and 45~80% of point A dose was given at the urinary bladder, 55~85% of point A dose at the rectum and 25~30% of point A dose at the point B. The total doses combined external beam irradiation and HDRB were ranged 65~80 Gy at the point A and 60~70 Gy at the point B. Table 2 shows the details of time/dose/fractionation.

2) The HDR Intracavitary Radiation for Nasopharyngeal Cancer:

Foley catheters were utilized as an outer applicator with 6 French endobronchial catheters as an inner applicators. Fig. 2 shows the applicators for HDRB. Local anesthesia with 2% xylocaine packing was applied in the nasal cavity. Two Foley catheters with 2 endobronchial tubes were introduced through the nares into the nasopharynx with the head hyperextended. The tips of catheters were pushed up to the level of soft palate. A 5 cc balloon with contrast, which is attached to the distal

Table 1. Charateristics of Patients for HDRB

	Intracavitary		Intraluminary				Interstitial		
	CERVIX	Nasopharynx	Esophagus	Lung	Trachea	Klstskin	Breast	Sarcoma	Urethra
Patient#	58	26	12	8	3	1	4	1	1
Procedure#	367	104	32	21	18	8	23	5	12
Age(mean)	23-82(54)	23-81(50)	47-81(61)	51-77(63)	29-54(38)	68	33-50(45)	70	76
Karnofsky scale(mode)	70-90 (90)	80-90 (90)	80-90 (90)	30-90 (50)	30-90 (50)	80	90	80	80
Pathology	squamous:54 adeno:3 adenosqua:1	squamous:13 undiff:9 P/D diff:4	squamous:10 P/D diff:1 adeno:1	squamous:8	squamous:2 adenocysitic:1	adeno:1	invasive ductal:4	MFH	adeno
Stage *R;relapse *P;primary	I A:- I B:5 II A:3 II B;28 III A:- III B:15 IV A:2 IV B:- R:5	I:- II:3 III:3 IV:17 R:3	I:- II A:2 II B:1 III:7 IV:- R:2	I:- II A:1 II B:- III A:2 III B:3 R:2	P:2 R:1	II	I:1 II A:2 III A:1		III
curative T×#	58	26	7	3	1	1	4	1	1

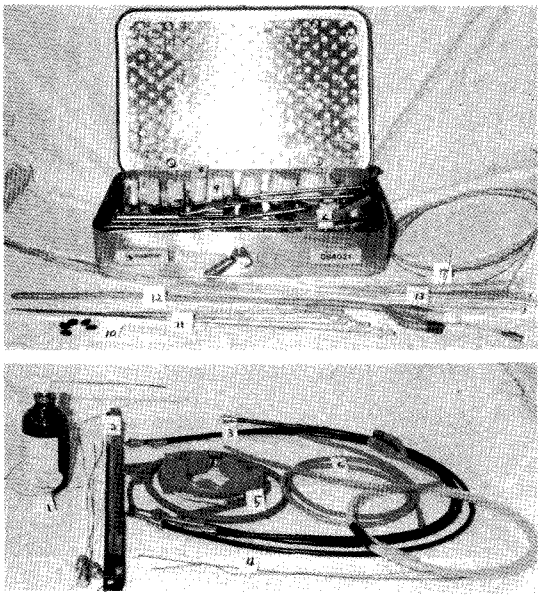


Fig. 1. 1. mouth piece & 2% xylocaine splay
2. dummy & source position stimulation ruler
3. treatment tube
4. guidewire 5. S-B tube 6. L tube
7. bronchial applicators & tandems
8. shieded caps of ovoids
9. ovoids 10. buttons 11. stylets
12. rectal or urethral marker
13. flexible interstitial catheters with one end button

end of the Foley catheter, was inflated for the purposes of anchoring and displacing the catheter to the roof of the nasopharynx to improve the dose to the nasopharynx. The dose was 500 cGy at a radius 0.5 cm or 1 cm from the center of the source (Fig. 3). Table 2 shows the details of time/dose/fractionation.

3) The HDR Endobronchial/Intraluminal Brachytherapy:

The endobronchial catheters (5 or 6 French) were used for endobronchial tumor and Klatskin tumor. Esophageal applicators or Levin or Sengstaken-Blakemore tube with endobronchial catheter inside were utilized for esophageal cancer.

In the HDRB for endobronchial tumor, patient was premedicated with demerol 50 mg I.M. and buscopan 20 mg I.M. and kept the vein open with D5W. 1% lidocaine and 0.25% bosmine 1~2 ml could be used in the tracheobronchial tree for topical anesthesia during the bronchoscopic procedure. Under bronchoscopic visualization, the tip of the bronchscope was placed at the distal portion of tumor. The guidewire was inserted in the lumen of the catheter which was introduced through the biopsy channel of the bronchoscope and then, the bronchscope was slowly withdrawn. The catheter was taped to the perioral area to prevent movement at the proximal end. To assure the catheter position, the bronchoscope was reintroduced in

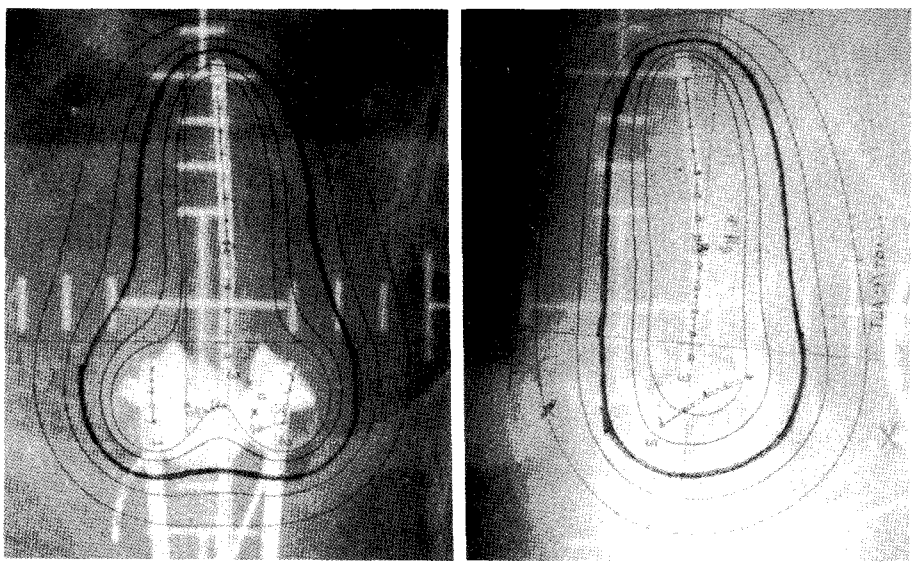


Fig. 2. HDR intracavitary radiation for cervix cancer using 1 tandem & 2 ovoids.
1. anterior view 2. lateral view

Table 2. Treatment Information of HDRB

	EXT.RT dose cGy (mean)	#of FX (mode)	Dose of FX (cGy)	FX Interval
Cervix	3960~11000 (5067)	2-10 (6)	A point; 500 cGy B point: 25-30% of A point bladder; 45-80% rectum; 5-84%	#2/wk
Naso-Pharynx	5940-7020 (6189)	2-10 (4)	500 cGy/0.5 cm: 8 pts 200 cGy/0.5 cm: 1 pt **(BID) 500 cGy/a cm; 17 pts	#2/wk
Esophagus	5040-6120 (5885)	1-3 (3)	300 cGy/0.5 cm; 4 pts 300 cGy/1 cm; 8 pts	#2/wk
Lung	6480-3720 (5523)	1-4 (3)	500 cGy/0.5 cm; 2 pts 500 cGy/1.0 cm; 3 pts 500 cGy/2.0 cm; 1 pt 800 cGy/0.5 cm; 2 pts	#2/wk
Trachea	4500-5960 (5300)	3-8 (6)	500 cGy/0.5 cm; 2 pts 500 cGy/1.0 cm; 1 pt	#2/wk
Klastskin	5040	8	250 cGy/0.7 or 1 cm	#2/day
Breast	4900-5080 5015)	4-9 (6)	300 cGy/0.5 cm; 1 pt 300 cGy/1.0 cm; 2 pts 150 cGy/1.0 cm;1 pt **(BID)	#1/day #2/day
Thigh	4500	5	300 cGy/0.5 cm; 1 pt	#1/day
Urethra	5940	12	250 cGy/0.5 cm; 1 pt	#2/day

the bronchoscopy suite and the position of the catheter was fluoroscoped in the simulator. Dummy sources were inserted into the catheter and orthogonal simulation films were taken and define the treatment volume (Fig. 4). Nucletron planning computer could optimize the dwell position and dwell time of the sources to fit the isodose curve in the target volume. The treatment dose and fractionation are shown in Table 2.

In the HDRB for Klatskin tumor, a transhepatic cholangiogram was performed through the T-tube under fluoroscopic control. After the site of obstruction was identified, flexible catheters were inserted into the T-tube in biliary tree to appropriate length. 500 cGy was given at 0.7 or 1 cm from the source (Fig. 6). The patient would develop pain and fever after the insertion of the catheter. These symptoms were usually controlled with antibiotics. The detailed dose and fractionation are shown in Table 2.

In the HDRB for esophageal cancer, 2% lidocaine viscus was used in topical anesthesia and demerol 50 mg I.M. and buscopan 20 mg I.M. were used in premedication. Esopahgeal applicator or Levin or Sengstaken-Blakemore tube with endobronchial catheter was inserted to tumor bed. The position of catheter tip was determined under fluorscopic control. Treatment volume en-

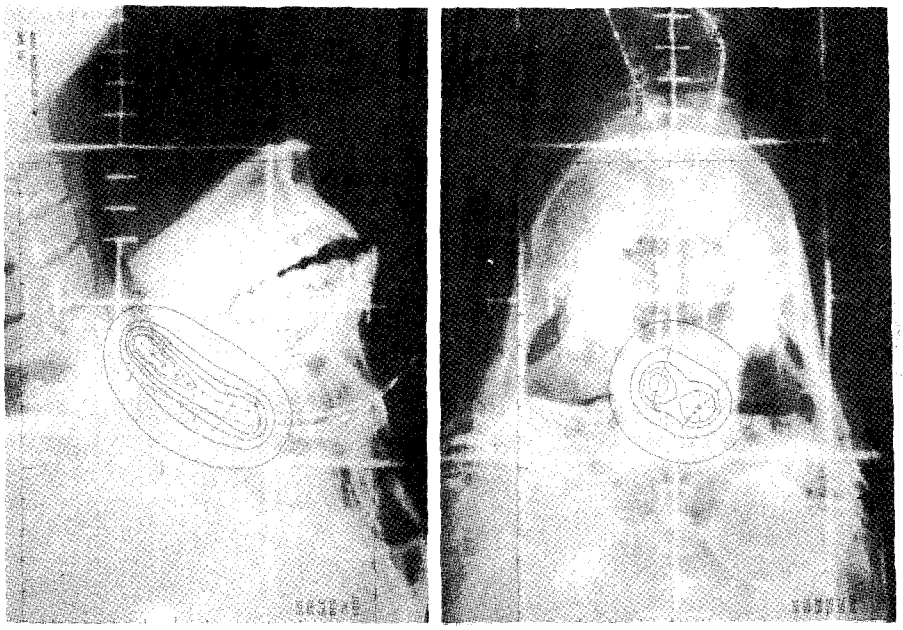


Fig. 3. HDR intracavitary radiation for nasopharynx cancer using 2 Foley catheters with 2 bronchial applicators.
1. anterior view 2. lateral view

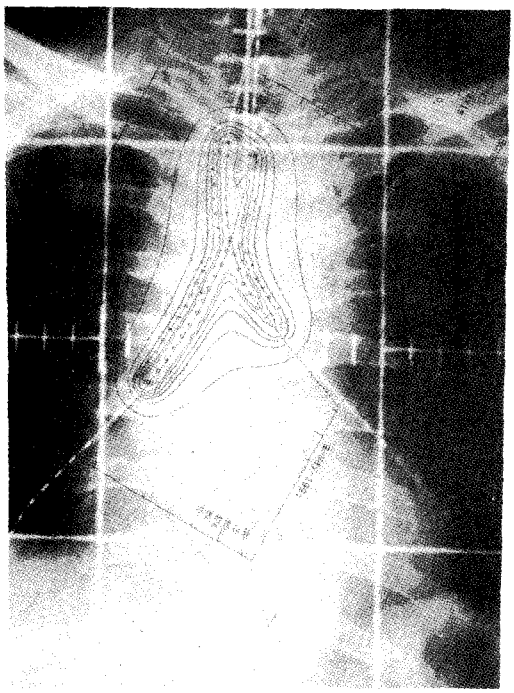


Fig. 4. HDR endobronchial radiotherapy of trachea using 2 endobronchial applicators.

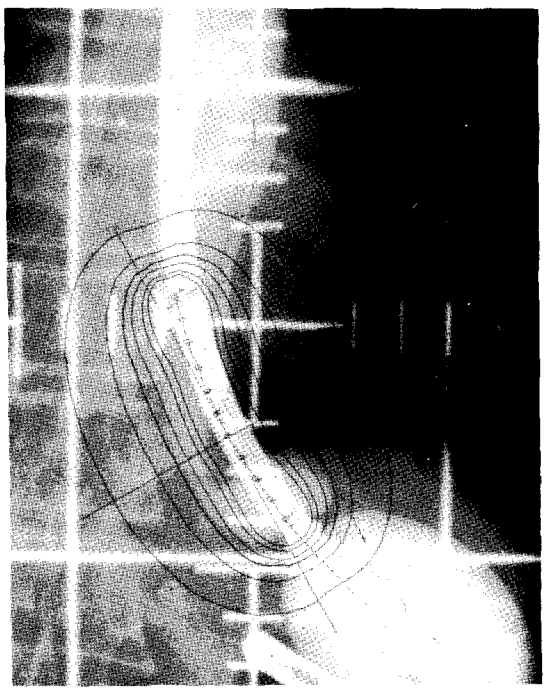


Fig. 5. HDR intraluminal radiation for esophageal cancer using S-B tube.

compasses the primary tumor site with a margin of 2~3 cm both proximally and distally. 250~500 cGy at 0.5~1 cm from the source was prescribed (Fig. 5). Fractionation and dose are shown in Table 2.

4) The HDRB Interstitial Brachytherapy:

The procedure was performed under the general anesthesia. After the volume to be implanted was determined, lines were drawn on the surface of the HDRB site to determine the position of the single or the double plane implant. Then, 18 gauge needles with stylet were inserted into the determined sites. The interstitial catheters with one end button were inserted through the needle. The proximal end of the catheter was secured by suturing buttons at skin surface. These catheters were placed for 5~7 days for HDRB. The length of active source was determined on orthogonal simulation films taken with dummy sources and caution

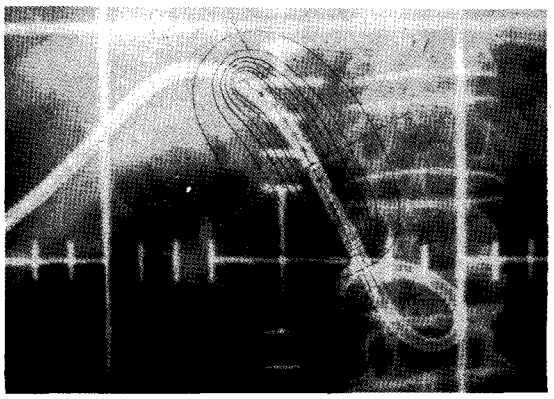


Fig. 6. HDR intraluminal radiation for Klatskin tumor using PTBD tube with endobronchial catheter.

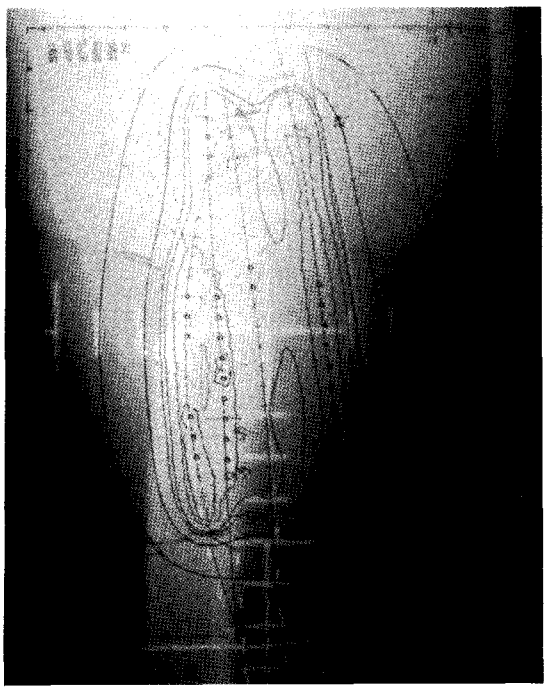
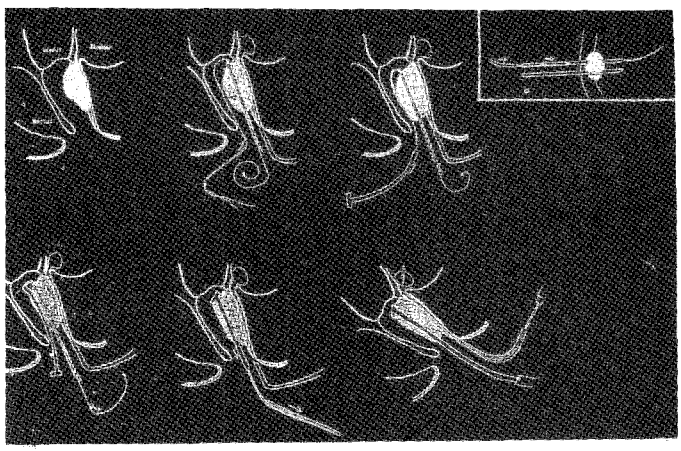


Fig. 7. HDR interstitial implant radiation for thigh sarcoma.



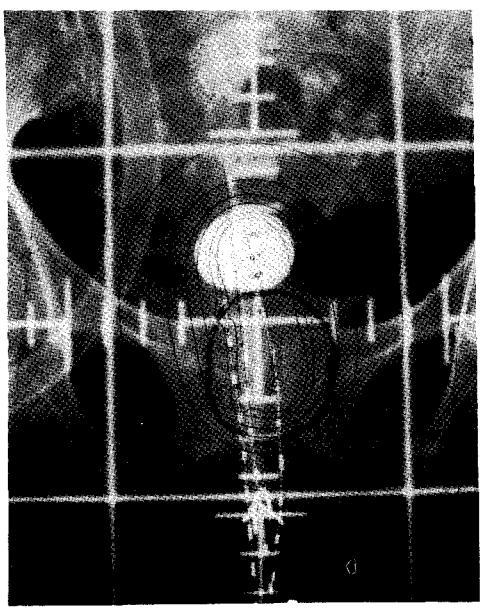


Fig. 8. HDR interstitial implant radiation for urethral cancer.
1. the procedures of implant.
2. the simulation film and isodose curve (red line: cancer mass, white round area: ballooning site of Foley cathter).

should be given to leave free space 0.5~1 cm from the skin at both ends to prevent excessive skin reaction. The proximal end was left open for travelling of the radioactive source. The dose and fractionation schedules are shown in Table 2. The simulation films of the breast, thigh and urethral cancer are shown in Fig 7, 8 and 9 respectively.

RESULTS

Tumor reponses of HDRB are summerized in Table 3. Follow-up periods were too short to estimate the median survival time. All produceres except interstitial brachytherapy were performed under local anesthesia and they were well tolerated. All patients were completed the scheduled therapy excluding 6 patients; 1 patient of lung cancer had massive hemoptysis unrelated to HDRB after the 2 fractionation, 1 patient of lung cancer refused further therapy, 1 patient of esophageal cancer developed tracheoesophageal fistula after 2 HDRB procedure and 3 patients of lung cancer

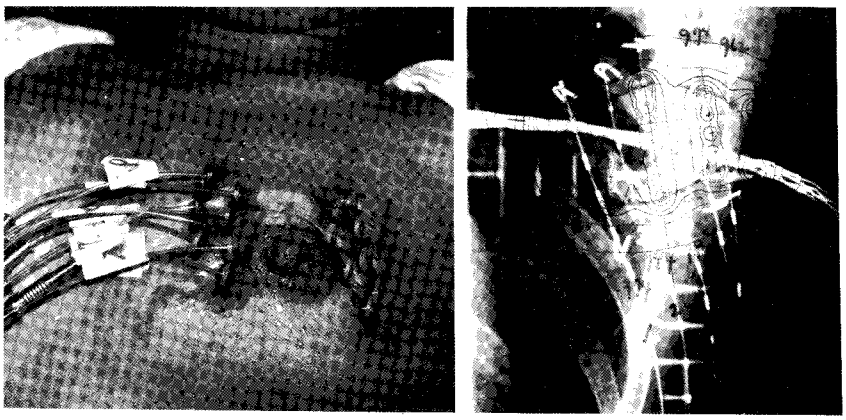


Fig. 9. HDR interstitial implant radiation for breast cancer.

Table 3. The Responses & Failure of the HDRB

	Curative TX						Palliative TX			TX falure of*	
	^T	*CR	*PR	*ST	Prog	NED (MFU)	^T	+	−	Local	Meta
CERVIX	58	52 90%	4 7%	1	1	48/52 92%) (7 mo)	·	· ·	5	4	
Naso-Pharynx	26	20 77%	3 12%	·	3 12%	19/20 (59%) (13 mo)					
Esophagus	7 29%	2 43%	3	· 29%	!!2 (13 mo)	2/2 (100%)	5 100%	5 ·	1	·	
Trachea	1	1	·	·	·	0/1 (25 mo)	2	2 100%	·	1	·
Lung	·	·	·	·	·	·	8	5 63%	3 33%	·	1
Klatskin	1	·	·	1	·	·	·	·	·	1	·
Breast	4	·	·	4	·	4/4 (100%)	·	·	·	·	·
Thigh	1	·	·	1	·	·	·	·	·	·	·
Urethra	1 ·	1	·	·	·	·	·	·	1	·	

^T; total numbers of patients, ST; Stable, PROG; Progression
!!2; Tx was stopped due to tracheoesophageal fistula/patient's refusal.
NED(MFU); no evidence of the disease (median follow-up)
(ex) [3/5 (60%); NED 3 patients /CR 5 patients, 60% NED
[(7 mo); 7 months of median follow-up
+; symptom palliation
−; no palliation

did not complete due to deterioration. 52/58 (90%) patients with cervix cancer achieved CR and 48/52 (92%) patients have remained NED state with median follow-up 7 months. 20/26 (77%) patients with nasopharyngeal cancer achieved CR and 95% (19/20 patients) remained NED state in range 2~25 months. Of total 15 patients with palliative therapy, 80% (12/15 patients) achieved symptom palliation. We did not encounter any late complication yet. The 2 serious complications seen in this study were fatal pulmonary hemorrage and tracheoesophageal fistula, but we think that these events may not be related to HDRB per se and prior therapy of extensive electrocautery may be responsible for the patient who expired with massive hemorrhage after 2 endobronchial brachytherapy. 3 patients with cervical cancer stage IVa developed chronic cystitis or proctitis and these problems were correlated with high rectal or bladder dose. All procedure for HDRB can be performed as an outpatient basis except interstitial implant. We observed excellent cosmesis in postlumpectomy breast cancer patients treated HDRB compared with electron booster.

DISCUSSION

In our evaluations, most of patients were well tolerated. some patients had only mild acute complication, but, late complications were not yet observed. It may be due to our short follow-up periods. With HDRB, the complication rate may increase with higher dose per fracton and decrease by increasing the number of fraction with similar total dose. Therefore, to evaluate biologic effects of HDRB, we need new clinical trials to test the treatment schedule. Even though we need longer follow-up, authors feel that HDRB with proper fractionation schedule may yield superior results compared with LDRB considering the adventages of HDRB in safety factor for operator and patient, better control of radiation dose and volume and patients comfort over LDRB. To establish biologic principle, we need to standaridize the dosimetry and to evaluate system for treatment response and complication. Therefore, authors hope the cooperative study to optimize technique, fraction schedule and evaluation methods for the response and complication of HDRB.

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국문초록 =

원격조정 고선량 근접 치료

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박수경 • 장혜숙 • 최은경 • 김재성 • 이병용

원격조정 고선량 근접치료는 새로운 각광받는 테크놀로지이다. 이에, 저자들은 3년간의 서울중앙병원의 590 횟수, 116 환자를 대상으로 고선량 근접치료의 그 시술과 임상적 결과를 평가해 보고자 한다. 자궁경부암 58 환자와 비인두강암 26 환자의 관내 방사선치료 471 횟수, 식도암 12 환자, 내 기관지암 11 환자, 클라스킨 종양 1 환자의 관내 방사선치료 79 횟수와 유방암 4 환자, 육종 1 환자, 요도암 1 환자의 조직내 방사선치료 40 횟수가 1989년 9 월에서 1992년 8월 사이에 시행되어졌다. 추적 관찰 기간은 1 개월에서 35 개월이었고, 그 중간 기간은 7 개월이었다. 조직내 방사선치료를 제외한 모든 시술은 국소 마취로 시행하였고, 모든 환자에서 급성 합병증은 생기지 않았다. 또한, 6 환자를 제외하고는 모두 계획 선량대로 치료를 마칠 수가 있었다. 자궁경부암 58 환자에서, 비인두강암 26 환자 중 20 환자에서 완전 관해가 일어났으며, 증상 완화 목적으로 치료한 15 환자에서 80%의 환자에서 소기의 목적을 이룰 수 있었다.

이 논문에서 원격조정 고선량 근접치료의 자세한 시술과 그에 따른 결과를 설명할 것이다. 이 치료의 생물학적인 효과와 적당한 선량/선량 횟수/분할치료를 평가하기 위해, 우리는 더욱 긴 추적 관찰을 시행하여야 하며, 이 새로운 근접치료 시술이 저선량 근접치료 시술보다 효과적이고 외래 환자로 통근 치료가 가능하며, 안전한 치료 방법이라고 생각하고 있다.