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Endobronchial Brachytherapy for Malignant Airway Obstruction: Low Dose Rate Versus High Dose Rate

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= Abstract =

Purpose : This is a retrospective study to compare the palliation rates, survival rates and complications of low dose rate and high dose rate endobronchial brachytherapy in the management of malignant airway obstruction.

Materials and Methods : Forty three consecutive patients with malignant airway compromise from primary or metastatic lung tumors were treated with low dose rate(LDR) endobronchial Iridium-192 insertion(21 patients) between October 1988 and June 1992, and high dose rate(HDR) endobronchial brachytherapy(22 patients) between August 1992 and April 1994 with palliative aim. Flexible fiberoptic bronchoscopy under fluoroscopic control was utilized in all 91 procedures. Twenty seven LDR procedures delivered a dose of 5-7.5 Gy to a 1.0 cm radius respectively.

Results : Subjective and objective responses to treatments were evaluated on follow-up examinations by clinical examination, chest x-rays and CT scan of the chest on some patients. Fifteen of 21 LDR patients and 19 of 22 HDR patients showed subjective improvement in terms of better breathing and less productive cough as well as complete disappearance of hemoptysis. Objective improvement on chest x-rays and CT scan of the chest had been demonstrated on 8 LDR patients and 10 HDR patients.

Conclusion : The technique of LDR and HDR endobronchial brachytherapy is simple and well tolerated procedure with minimal morbidity. It provides excellent palliation by keeping airway patent in these short life-spanned patients.

Key Words : Endobronchial Brachytherapy, Low Dose Rate, High Dose Rate, Radiation Therapy, Palliation, Malignant Airway Obstruction

INTRODUCTION

Endobronchial irradiation is not a new idea. The first report of endobronchial irradiation for malignant airway obstruction came out in the literature in 1921. Yankauer reported treating two cases with encapsulated radium placed by bronchoscope[1]. About ten years later, Kerman used radon seeds in seven patients[2]. He reported that 4 of 7 patients showed 2 years survival. In 1961, Poole reported the use of radon seeds in 42 cases. In recent years, there has

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been a widespread interest in this modality alone or in conjuction with the use of laser beam therapy utilizing Iridium-192 ribbons for LDR procedures and HDR afterloading brachytherapy machines for HDR procedures[3-10].

Lung cancer is the most common form of cancer diagnosed in the United States and also the major cause of cancer death. In 1995, there were approximately 169,900 new cases and 157,400 deaths from lung cancer[11]. The incidence of lung cancer has increased about 240% over the past 5 years with a similar increase in mortality. However, there has been a decrease in incidence recently among white males which indicates positive signs associated with a reduction in cigarette smoking since 1965.

Treatement options for lung cancer are primary surgical resection, radiation therapy, chemotherapy or any combination of the above. Surgical resection offers the best hope for cure. However, only 20-25% of lung cancer cases are suitable for attempted curative resection. 5-year survival rate of these patients is about 30%. Response rate of chemotherapy for non-small cell lung cancer is approximately 20-40%. External beam radiation therapy combined with chemotherapy for non-small cell lung cancer is now actively under investigation. Response rate of the combined modality is about 40-75%.

Overall 5-year survival rate of lung cancer remains at 10-12%. More than 90% of lung cancer cases require palliative treatment because of distressing local symtoms due to airway compromises such as productive cough, hemoptysis, dyspnea and obstructive pneumonia. External beam radiation therapy is the mainstay of palliative therapy for these predominantly central tumors. However, the dose of external radiotherapy is limited by the tolerance of surrounding normal tissues. 40% of patients die of local disease and 25% of patients develop endobronchial disease.

When patients present primary or recurrent endobronchial tumor, they may already have distressing local symptoms or may develop those symptoms during their clinical courses. After the initial external beam radiotherapy, those patients with local symptoms who are proven to have endobronchial recurrence require palliative treatment. In some patients with primary proximal airway lung cancers which are medically and/or technically inoperable, curative intent with endobronchial brachytherapy in conjunction with external beam radiotherapy should be aimed.

MATERIALS AND METHODS

From October 1988 to June 1922, 27 procedures in 21 patients were performed with LDR techniques and from July 1992 to April 1994, 64 procedures in 22 patients were performed with HDR technuques using a Microselectron Afterloading system at JFK Medical Center in Edison, New Jersey. The age range was 43 to 94 in LDR patients and 39 to 79 in HDR patients. The average ages were 65.7 in LDR patients and 63.2 in HDR patients. All patients had biopsy-proven primary lung cancers or metastatic endobronchial tumors. The distribution of cell type (Table 1) was almost identical between LDR and HDR patients. The most common cell type was the squamous cell carcinoma. The pattern of

Table 1. Primary Tumor(Cell Type)

		LDR	HDR	Total
Lung Primary	Squamous Cell Ca.	13	10	23
	Adenocarcinoma	3	6	9
	Large Cell Undiff.	2	2	4
	Small Cell Undiff.	1	0	1
Metastatic	Brease, Kidney(2). Ovary	2	4	6
	Rectum and Bladder			
	Total	21	22	43

previous treatments(Table 2) was also almost same in both modalities. Four patients in LDR cases underwent 6 procedures of laser therapy prior to endobronchial irradiation. Seven patients in HDR group had concurrent or sequential external beam radiation therapy.

All patients had clinical symptoms listed on Table 3. The majority of the patients had been suffering from one or more symptoms. Half of the patients had episodes of hemoptysis which cleared after the endobronchial brachytherapy.

All LDR patients were treated on an inpatient but most HDR patients were treated on an outpatients basis except for those who were inpatients due to medical problems. The procedure was performed in fluoroscopy suite with a pulmonologist who does the exact same preparation as for a bronchoscopy. Fiberoptic bronchoscope is introduced nasally and advanced to the area of obstruction. Flexible, blind end nylon catheter is advanced through the working channel of bronchoscope to the point approximately 2-3 cm beyond the distal extent of disease.

The catheter is held in position as bronchoscope is withdrawn over it and then grasped at its exit from the nasal cavity. The catheter is taped onto the nose and forehead after painting the skin with Benzoin tincture. Fluoroscopy is performed with dummy line sources in the catheter. After obtaining AP and lateral orthogonal simulation films, the patient is sent to the floor for LDR patients or taken to the HDR brachytherapy suite for HDR patients. In the meantime, computer generated planning and isodose curves will be ready prior to the actual treatment.

The dose for LDR was calculated at 0.75 cm from the line of sourses. One patient had incomplete treatment and 4 patients had retreatments a few months after the initial procedures. Twenty one procedures had 20 to 30 Gy prescribed dose as the initial treatments. The average treatment time for LDR procedures was 21.5 hours which required overnight hospital stay. One treatment was aborted because the patient pulled the catheter out accidentally before the actual treatment.

The dose for HDR was given at 1 cm from the catheter. One patient had incomplete treatment and 7 patients received 15 Gy in 3 weekly fractions combined with concurrent or sequential external beam radiation therapy while 14 patients had 22.5 Gy in 3 weekly fractions as the initial treatments for recurrent endobronchial disease after external beam therapy.

Table 2. Previous Treatments

	LDR	HDR	Total
External Beam Radiation	21	18	39
Surgery	3	4	7
Chemotherapy	4	2	6
Laser Treatments	4(6)*	0	4(6)
Concurrent or Sequential External Beam Radiation	0	7	7

* Four patients had six procedures

Table 3. Major Symptoms

	LDR	HDR	Total
Dyspnea	13	14	27
Hemoptysis	10	12	22
Cough	16	15	31
Pain	0	5	5
Weight Loss	2	3	5
Hoarseness	0	4	4
Wheezing	0	1	1
Total	41	54	95

RESULTS

Clinical responses(Table 4) were divided into

Table 4. Clinical Responses

	LDR	HDR	Total
Subjective Improvement	15/21(71%)	19/22(86%)	34/43(79%)
Objective Improvement	8/21(30%)	10/22(45%)	18/43(42%)
Not Evaluable	2/21(10%)	1/22(5%)	3/43(7%)

Table 5. Literature Review of Endobronchial Brachytherapy

Author	Year	Patient Number	Brachytherapy	Dose/Depth (Gy/cm × Fr.)	Palliation Rate
Schray	85	13	LDR	30/0.5-1	54%
Speiser	90	55	LDR	2-10/1	84%
Schray	88	65	LDR	30/0.5-1	83%
Roach	90	17	LDR	30/0.5	60%
Macha	87	56	HDR	7.5/1×3	79%
Speiser	91	45	HDR	9-11/1×3	65%
Nori	87	15	HDR	4-5/1×3	75%
Bedwinek	92	38	HDR	6/1×3	76%
Chang	94	76	HDR	7/1×3	95%
Cho	95	21	LDR	20-30/0.75	71%
		22	HDR	5-7.5/1×3	86%

subjective and objective improvements in our study. The evaluation of subjective improvement was performed by the survey from the patients on severity of coughing, amount of sputum production, relief of breathing difficulty, disappearance of hemoptysis and overall well-being of patients. The evaluation of objective improvement was carried out on follow-up chest x-rays and CAT scan of the chest as well as follow-up chest x-rays and CAT scan of the chest as well as follow-up bronchoscopic examinations. Fifteen of 21(71%) patients in LDR cases and 19 of 22(86%) patients in HDR cases totalling 34 of 43(79%) patients showed subjective improvement. Eight of 21(30%) patients LDR cases and 10 of 22(45%) patients in HDR cases totalling 18 of 43(42%) patients showed objective improvement. Two patients in LDR cases and one patient in HDR cases totalling 3 patients were not evaluable because of short follow-up intervals between procedures and their deaths. The evaluation of both subjective and objective improvement was measured by the criteria for response assessment(Symptom Index and Obstruction Score) used in the protocol of High Dose Rate Brachytherapy Working Group[8]. HDR cases showed slightly better results compared to LDR cases.

Average survival length from the last endobronchial brachytherapy in LDR and HDR cases was 8 months and 5 months or more respectively. Some of HDR patients were still alive at the time of this evaluation.

Side effects from the procedures include mild sore throat, transient cough and minor degree of hemoptysis. We had one catheter dislodgement in LDR era and that particular patient refused another procedure. We have never experienced a pneumothorax. We have not had any complications but literatures report rare incidences of cartilage ulceration or necrosis, acute pulmonary hemorrhage and fistulae formation.

DISCUSSION

Endobronchial brachytherapy with either LDR or HDR modalities appear to be effective methods of palliating distressful symptoms of endobronchial disease. Partial or complete subjective improvement of symptoms was achieved in 34 of 43(79%) patients. Our rate of improvement is comparable to other studies in the literature(Table 5). Objective improvement on follow-up chest x-rays, CAT scan of the chests and follow-up bronchoscopic examinations was achieved in 18 of 43(42%) patients. This rate of objective improvement is also comparable to other studies.

The disappearance rate of hemoptysis was the highest and earliest(100%) in 22 patients of both LDR and HdR cases. The improvement rate on dyspnea was the lowest and slowest(55%) in 27 patients of both modalities.

The definition of low dose rate(LDR) is the single protracted irradiation with a dose rate of 0.5 cGy/minute or less. The definition of high dose rate(HDR) is the fractionated irradiation with a dose rate of 200 to 300 cGy/minute. there are some major differences between LDR and HDR proce-

dures other than dose rates. Even though LDR procedure is afterloading, LDR procedure gives significant amount of radiation exposure to staff members including physicians, physicists, nurses and other supporting staff on the floor while HDR procedure gives almost no radiation exposure since it is done with remote computer controlled afterloading technique. HDR procedure can be performed as an outpatient basis while LDR procedure has to be done as an inpatient basis with selected private room. LDR requires higher dose, single fraction treatment though some centers do fractionate 2 to 3 times on weekly basis. HDR is given with 3 weekly fractions. In HDR cases, we are able to look and evaluate the responses on subsequent 2nd and 3rd procedures.

Four patients in LDR cases underwent six laser therapies prior to endobronchial brachytherapy. Laser therapy yields prompt palliation, making catheter placement safer and more tolerable. It may provide the only palliation for patients not responding to irradiation. Investigators who have used endobronchial irradiation following laser therapy have veen impressed with the utility of the combination. Although laser therapy is useful in quick clearance of the exophytic endobronchial lesion, early regrowth and reobstruction is common. It may be that laser and endobronchial irradiation together can give both rapid and durable palliation and are additive, not competitive, in efect. However, laser therapy is potentially hazardous with agressive approach.

The position of the catheter inside of the trachea and main stem bronchus may not be ideally located in the center of the lumen to deliver the adequate tumor dose to the endotracheal or endobronchial lesions. It is sometimes possible to do minor adjustment under the fluoroscopy. Since there is no device available to keep the catheter in the center of the lumen the optimization of the prescribed dose conforming the tumor volume should be the only another way of achieving goals in HDR cases.

In case the position of the catheter is located close to the normal mucosa rather than near to the lesion in the first week of HDR procedures, adjustments of the position of the catheter should be tried in following second and third weeks.

CONCLUSION

Therapeutic options are limited on patients who have symptomatic airway compromise by endotracheal and/or endobronchial malignant disease following definitive surgery and/or external beam irradiation. Endobronchial brachytherapy with either LDR or HDR modalities is the excellent choice to provide airway patency. the depth-dose characteristics of brachytherapy allows delivery of high doses to small volume with mild to moderate normal tissue limitations. The technique of LDR and HDR endobronchial brachytherapy is simple and well tolerated with minimum side effects and complications. Good palliation was achieved in these short life-spanned patients by providing airway patency and give them better quality of life for the remainder of their lives.

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= 국문초록 =

악성 종양에 의한 기도폐쇄시 내기관지 근접치료 : 저선량 치료 대 고선량 치료의 비교

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목 적 : 악성 종양으로 인해 기도 폐쇄가 온 환자들을 저선량 및 고선량으로 내기관지 근접치료하였을 경우의 대증치료 효과, 생존율 및 병발증을 비교 검토한다.

대상 및 방법 : 1988년 10월부터 1992년 6월까지 저선량 방법으로 21명, 1992년 8월부터 1994년 4월까지 고선량 방법으로 22명, 총 43명의 환자들에게 내기관지 근접치료를 시행하였다.

총 91회의 치료시, 모두 Fluorocopy하에서 굴절성 Fiberoptic 내시경을 이용하였으며, 저선량 방법의 21회는 15-30 Gy를 0.75 cm 원경에, 고선량 방법의 64회는 5-7.5 Gy를 Ir-192 선원으로부터 1 cm 원경에 각각 투사하였다.

결 과 : 주관적 및 객관적 치료효과의 분석은 임상재진시 나타난 환자의 증상, 흉부 방사선 사진 및 흉부 단층촬영의 결과로 이루어졌다.

저산량으로 치료한 21명 중 15명의 환자와 고선량으로 치료한 22명 중 19명의 환자들이 주관적 치료효과가 있었음을 보였고, 8명의 저선량 환자와 10명의 고선량 환자가 흉부 방사선 사진과 단층 촬영상에서 객관적 효과가 있었음을 나타냈다.

결 론 : 저선량 및 고선량 방사선에 의해 근접치료의 기술은 비교적 간단하며 환자가 별다른 후유증 없이 치료를 잘 받아 드리는 편이다. 이 치료 방법은 여생이 얼마 남지 않은 말기 폐암환자에게 내기관지 협착 내지는 폐쇄가 왔을때 기관지의 공기소통을 원활히 증진시켜주는 대증치료 방법이다.