The Result of Radiation Therapy of Superior Vena Cava Syndrome

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To access the result of radiation therapy for 8 years experiences, 21 patients who were treated with superior vena cava syndrome had been analysed according to dose fractionation and total dose.

The results are as follows;

1. In high fractionate dose group, six of eleven patients (54.5%) exhibited relief of symptoms in 1-2 days, and additional three patients of nine (81.7%) within 3-4 days, while standard fractionated dose treatment is not effective to achieve initial relief of symptoms.
2. Graded response by total dose was correlated with total dose rather than dose fractionation.
3. Overall one year survival rate with superior vena cava syndrome was 9.1% and mean survival was 4.2 months.

Key words: SVC, Radiotherapy, Fractionation.

INTRODUCTION

Superior vena cava syndrome was first reported by Willam Hunter in 1757 and characterized by obstruction of venous drainage of the upper part thorax and neck in the superior mediastinum. It is almost always caused by a malignant neoplasm, most commonly bronchogenic carcinoma.[1, 2, 3]

Traditionally, superior vena cava syndrome has been considered an oncologic emergency requiring radiotherapy for palliation,[5, 6] and considerable discussion has been existed about the proper dose time schedule of this kind of treatment. Based on clinical and experimental evidence, high daily dose irradiation was introduced for superior vena cava obstruction.[5), 6)]

We reviewed 21 patients who were treated with superior vena cava syndrome over the past 8 years, and compaired the effectiveness of high fractionated dose technique to standard fractionated dose technique.

METHOD AND MATERIAL

A retrospective review was performed of 21 patients with superior vena cava syndrome who were treated at the department of therapeutic radiology of Kyung Hee University Hospital between 1978 and 1985.

There were 16 men and 5 wemen who ranged in age from 29 to 70 years and had a mean age of 58 years.

The diagnosis of obstruction of the superior vena cava was largely determined by symptoms and clinical signs but diagnostic work-up also included chest roentenogram, bronchoscopy, thoracotomy, scalene node biopsy and a variety of other procedures.

Specific etiology was determined in all 21 patients as a bronchogenic carcinoma. Histologic diagnosis was established either before or after treatment began; it revealed eight patients had squamous cell carcinoma, seven patients presented with small cell carcinoma, three patients had adenocarcinoma and three patients were un-

classified carcinoma respectively(Table 1)

Superior vena cava syndrome was presented as first symptom in 17 of 21 patients and in four patients during chemotherapy as a disease progression.

The patients were divided into two major categories; those who received standard fractionated dose(10 of 21 patients), and those who received high fractionated dose with initially 300-400 cGy daily(11 of 21 patients). The number of patients treated by different modality together with their distribution according to the histology is shown in Table 1.

Radiation therapy was used with cobalt machine. All patients were treated through anterior and posterior portals that encompassed the radiographic mass and the adajacent mediastinum including one or both supraclavicular regions. Total radiation dose varied over a wide range with nine of 21 patients receiving less than 3,000 cGy total radiation dose, nine of the patients received between 3,000 and 5,000 cGy, whereas only three patients received a full course of 5,000 cGy or more to the mediastinum.

Evaluation of response to treatment was estimated subjectively based on symptoms and signs recorded in case record on a scale I to V on the last day of treatment[7] and evaluated the initiation of symptom relief, too. We considered scale I to III patients as a responder, and scale IV and V patients as a non-responder.

Table 1. Incidence by Histology and Treatment Schedule

Histology	High dose	Standard dose	Total
Squamous cell carcinoma	4	4	8
Small cell carcinoma	5	2	7
Adenocarcinoma	1	2	3
Undifferentiated carcinoma	1	2	3
Total	11	10	21

RESULT

1. Evaluation of symptoms and signs(Table 2)

The presenting symptoms and signs are shown in table 4. The shortness of breath(21/21), facial swelling(18/21), and cough(17/21) were noted in the majority of patients with superior vena cava syndrome. The common signs were facial edema (18/21), neck vein engorgement(15/21), and upper extremity edema (13/21).

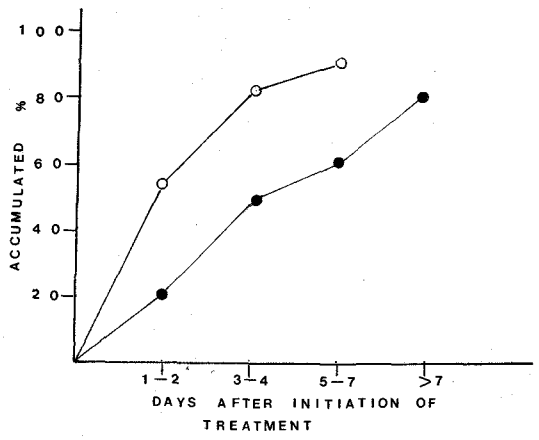

Fig. 1. Accumulated percent of patients exhibiting improvement in shortness of breath at various time after treatment of high fractionated dose (○ -○) and standard fractionated dose (● -●).

Table 2. Presenting Symptoms and Signs of Superior Vena Cava Syndrome in 21 Patients

Symptoms	No.	%	Signs	No.	%
Shortness of breath	21	100.0	Facial edema	18	85.7
Face swelling	18	85.7	Neck vein distension	15	71.4
Cough	17	80.9	Upper extremity swelling	13	61.9
Headache	7	33.3	Arm vein distension	10	47.6
Orthopnea	4	19.0	Upper body plethora	5	23.8
Dysphagia	2	9.5	Mental change	2	9.5
Hoarseness	1	4.7	Glossal edema	1	4.7
Syncope	1	4.7			
Epistaxis	1	4.7			

Table 3. Initiation of Symptom Relief

Days	High dose	Standard dose	Total
1-2	6	2	8
3-4	3	3	6
5-7	1	1	2
7	-	2	2
No relief	1	2	3
Mean days	3.1 days	4.1 days	3.8 days

2. Evaluation of immediate relief of subjective symptoms(Table 3)

Response to standard fractionated dose: Ten patients in the standard dose group presented with shortness of breath. Two patients(20%) exhibited improvement within 1-2 days and an additional three patinets or total of five(50%) had relief within 3-4 days. Of remaining five patients, two patients failed to achieve response.

Response to high fractionated dose: Of eleven patients who presented with shortness of breath, six patients(54.5%) exhibited relief in 1-2 days

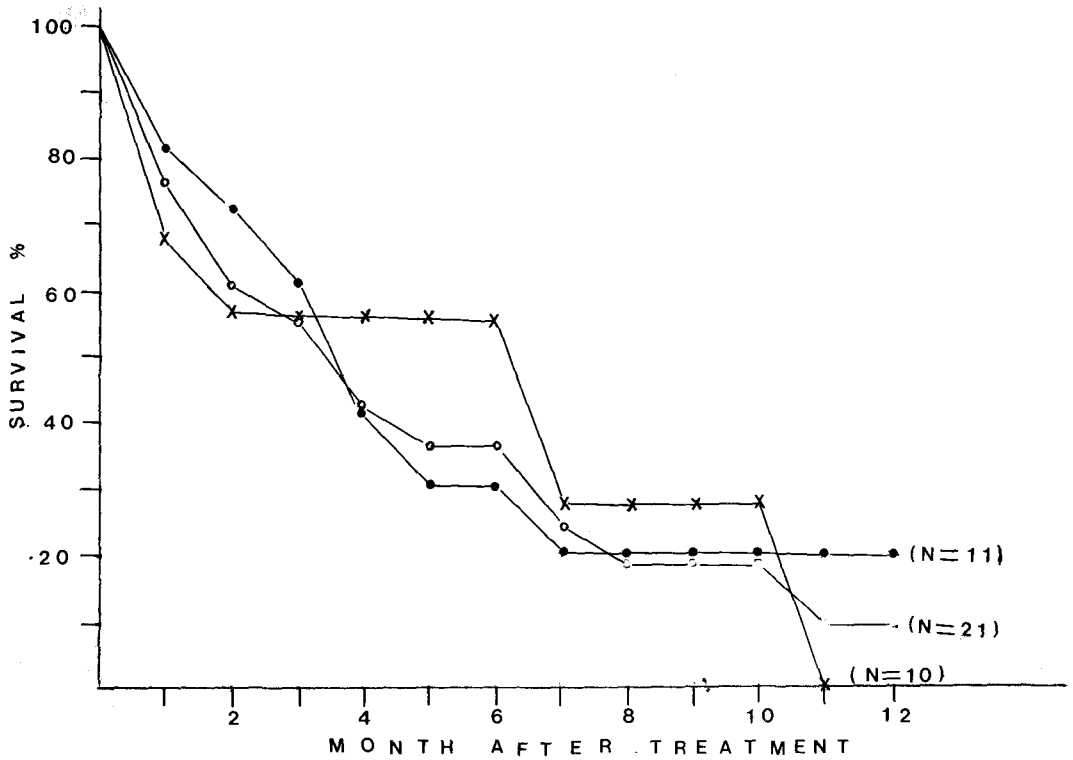

Fig. 2. Actuarial survival surce of high fractionated dose (●—●), standard fracrionated dose (×—×), and overall (o—o).

Table 4. Graded Response to Treatment

Grade	> 3,000 cGy	3,000-5,000 cGy	5,000 cGy	Total
I. Asymptomatic without signs	-	1	1	2
II. Moderate decrease in symptoms and signs	2	4	2	8
III. Some decrease in symptoms and signs	2	3	1	6
IV. Minimal change	1	-	-	1
V. No change or worse	4	-	-	4

and additional three patients of nine(81.7%) within 3-4 days. Of the remaining two patients in this group, one patient showed improvement within 7 days and one patient failed to achieve a relief symptoms.

3. Evaluation of graded response to treatment (Table 4)

It was correlated with total dose rather than dose fractionation. The majority of the patients who were given irradiation more than 3,000 cGy were responded within 7 days, whereas non-responders (5/21) all were treated less than 3,000 cGy. And two of five patients were expired during treatment.

4. Evaluation of metastatic foci

Fifteen of 21 patients(71.4%) had one or more metastatic lesions; more than half patients(12/21) had metastatic focus in supraclavicular lymph node, bone metastasis was in 4 patients, liver metastasis was in 2 patients and brain, adrenal gland, skin, and axillary lymph node were revealed metastatic sites in every one patient.

5. Evaluation of survival

Overall one year survival rate with superior vena cava syndrome were 9.1% and mean survival were 4.2 months.

Association between survival and dose fractionation(Fig. 2)

The mean survival rate of high fractionated dose group was 4.5 months and standard fractionated dose group was 3.8 months. The actuarial survival curves are represented in figure 2. But there was no statistcal significance between two groups.

Accociation between survival and total dose (Fig. 3)

The mean survival who were irradiated above 3,000 cGy was 5.7 months and who were irradiated less than 3,000 cGy was 1.4 months. We considered that the great part of the patients irradiated less than 3,000 cGy had far advanced disease, so the result of this group is poor.

The actuarial survival curve is shown in Figure 3.

DISCUSSION

Superior vena cava syndromes is nealy always

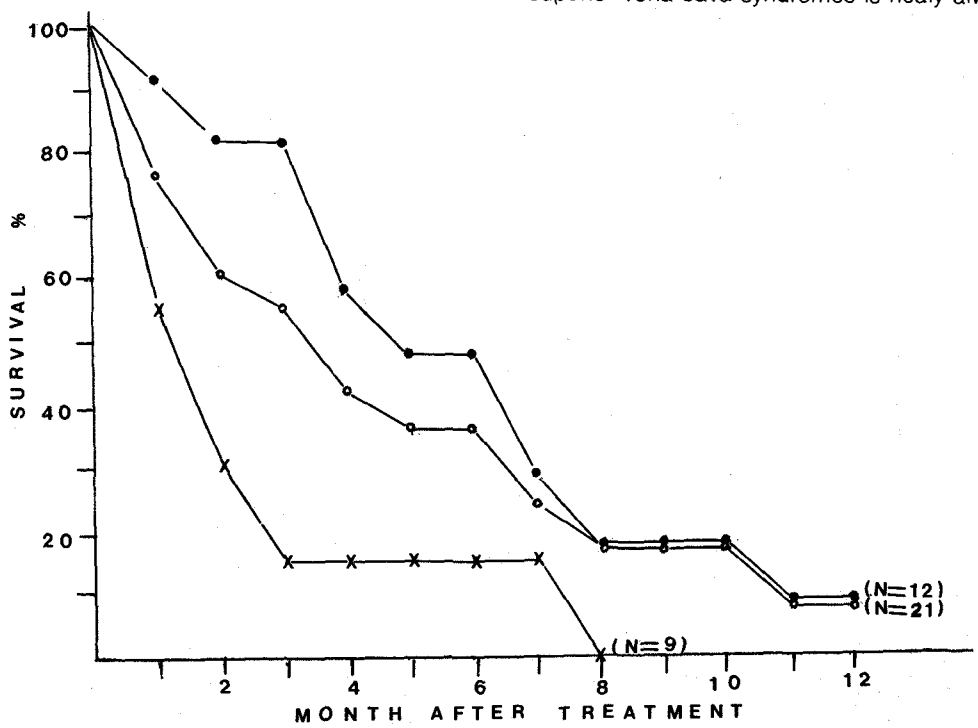

Fig. 3. Actuarial survival curve of treating more than 3,000 cGy (●—●) less than 3,000 cGy (×—×) and overall (○—○).

cause by malignant disease.[1, 2, 7, 8] By combining different series, Lokich and Goodman[2] reported 97% of such cases due to malignant disease; 75% due to bronchogenic cancer; 15% to lymphoma; and 7% to metastatic cancer. The remaining 3% were due to benign condition such as thyroid goiter, fibrosing mediastinitis, tuberculosis and aortic aneurysm. Before the advent of penicillin, 40% of the superior vena cava syndromes were related to syphilis. In last 5 years iatrogenic superior vena cava syndromes has become increasingly common to utilized long-term central venous catheter for hyperalimentation therapy, or for chemotherapy in patients requiring long-term venous access.[9]

The superior vena cava is locked tightly into the compartment of the right anterior superior mediastinum and is in intimate proximity to the right main stem bronchus. It is completely encircled by chains of lymph node, which drain all structures of the right thoracic cavity and the lower part of the left. Signs of the superior vena cava syndromes are edema and plethora of the neck and face, dilatation of collateral veins of the chest wall and necks, and usually respiratory distress. There may also be edema of conjuntiva, with proptosis and central nervous system effects such as headache, visual disturbance and disturbed states of consciousness.[10] In our series all cases were revealed bronchogenic cancer, and the majority of the patients had symptoms and signs such as shortness of breath, facial swelling, and cough.

Based on the symptomatic and clinical findings alone, the diagnosis of superior vena cava syndromes can be made easily when the syndrome is well established. In order to determine the primary cause and location of the obstruction and development of venous collateral, further investigation is necessary.[7, 11, 12] But life-threatening respiratory obstruction, aspiration, and hemorrhage have resulted from attempts to establish specific histo-pathological diagnosis.[2,7] Lokich[2] protest that "pitfalls in mangement of superior vena cava syndromes are related to the overzealous efforts to establish the site of obstruction and determine a specific histopathological diagnosis. Immediate treatment is indicated even when the diagnosis of malignancy has not been established histologically"

The basic therapeutic modalities to consider in the management of superior vena cava syndromes first, since nearly all obstructions are due to surgically unresectable malignancy, radiation therapy is the primary therapeutic modality with the other treatment consideration general employed as adjuvantive measures; second, medical measures consisting of diuretics for symptomatic relief of thrombosis, steroid for relief of cerebral edema or respiratory distress, and chemotherapy to reduce tumor bulk; third, surgical methods represent the least used, but perhaps the most useful intervention for patients with severe obstructive syndromes.

Radiation therapy has been used for palliative therapy in superior vena cava syndromes due to malignant tumors for many years. This is one of the few instances when radiation therapy is indicated as an emergency procedure. On this basis, the approach has been to initiate a rapid high daily dose schedule of irradiation to obtain immediate relief of symptoms through relief of obstruction.[11, 13, 14] Palliation of symptom is usually rapid and demonstratable increase in survival is obtained.[13, 14]

Previously the initial use of low daily dose irradiation was considered appropriate since it was considered it would avoid the production of cellular edema which further aggravates an already patient.[15]

Geller[16] suggested that chemotherapy and/or low initial daily dose irradiation are required in the treatment of superior vena cava obstruction. However Green et al.[5] showed that low dose irradiation(less than 200 cGy daily) had no effect in relieving superior vena cava obstruction in rat. Subsequently Rubin et al.[6] showed that a rapid high irradiation was more effective than the low dose irradiation in the immediate relief of syndromes in superior vena cava obstruction; they found that five of seven patients who were treated with the high fractionated dose noted excellent improvement of symptom within five days whereas only two of who were treated with standard fractionation responded within the same time period.

Perez et al.[8] studied on a large series of patients; they reported slightly higher rate(70%) responded more to higher dose than to standard dose(50%), although the difference was not statistically significant.

Davenport et al.[13] reported subjective improvement in respiratory symptoms in 17 of 19 patients within 72 hours who were treated with initial high dose. Finally, Scarantino et al.[14] reported that rapid relief of the symptoms occurs in 60% of patients in 1-2 days, and in 86% within 3-4 days.

The result of the present study reveals an

advantage in high fractionated dose compaired to more standard fractionated dose irradiation; six of eleven patients(54.5%) showed improvement of within 1-2 days and nine of eleven(81.7%) noted improvement within 3-4 days. Whereas in standard fractionated group; two of ten patients(29%) had a relief of symptoms within 1-2 days and five of ten patients(50%) had improvement of symptom within 3-4 days.

Although no randomized study exists, comparing initial high fractionated irradiation to standard fractionation, several reports[6, 8, 13, 14] indicate more rapid relief of symptoms when initial high fractionation was used.

Rosenbloom[17] who reported on a series of seven untreated patients with superior vena cava obstruction secondary to bronchgenic carcinoma. The mean survival was 6 weeks. In this report, we got the similar result that the mean survival who received less than 3,000 cGy(9 patients) was 1.4 months.

Initial studies in which various dose of irradiation were utilized to improve survival up to 6 months. Recently however, Perez et al.[8] reported an overall survival of 25% at one year, and 10% at 30 months. Scarantino et al.[14] reported overall survival was 27% and mean survival was 11.6 months.

In this series, mean survival was 4.2 months and overall one year survival was 9.1%. This result is worse than that of recent reports.[8, 14] We think it was because that great proportion of patients were received less than tumoricidal dose.

Various subgroups have been identified with improved survival.[8, 14, 15, 18] These include a group of patients who exhibited a more immediate response of symptoms, a group with undifferentiated lung carcinoma, and a group treated with tumoricidal dose.

Recently improvement in chemotherapy of small cell carcinoma of the lung results in objective tumor response in the majority of patients treated with chemotherapy.[12, 16, 18] A recent study[12] observed alleviations of symptoms and signs of superior vena obstruction due to small cell carcinoma within 7 days in patients treated with chemotherapy alone.

Although radiation therapy may provide initial relief of symptoms from superior vena cava syndrome, the majority of patients with non small cell lesion have no tumor shinkage on chest roentgenogram. Of 30 patients described by Scarantino et al.[14] Who had chest roentgenogram after radiation therapy for superior vena cava obstruction, 18 patients(54%) had improvement in their primary chest lesion. All but one of these patients had either small cell cancer cancer or lymphoma. Of the 12 patients who showed either worsing or no change roentgenographically, 11 had non-small cell lung cancer.

We reviewd chest roentgenogram in 15 patients. Seven were small cell lung cancer and nine were non-small cell lung cancer. Seven of 15 patients (46.7%) showed improvement of primary lesion. Five of seven patients showed improvement were small cell lung cancer.

The total dose of radiation is determined by two factors both the type and the extent of the malignant disease. Lymphoproliferative disease, such as lymphosarcoma or Hodgkin's disease, are more radioresponsive than adenocarcinoma or squamous cell carcinoma and may be effectively irradiated to doses of 3,000-4,000 cGy, while the epithelial tumor require 5,000 to 6,000 cGy, to achieve adequate local control.[3]

In summary, although the population in this series was too small to elicit more meaningful conclusion, we believe that in the superior vena cava syndrome complicating bronchogenic carcinoma, therapy with a tumoricidal dose of about 5,500 cGy with initial high fractionated dose or more total dose should be begun promptly.

REFERENCES

1. **Roswit B, Kaplan G, Jacobson HG:** The superior vena cava obstruction in bronchogenic carcinoam. Radiology 61:722-736, 1953
2. **Lokich JJ, Goodman R:** Superior vena cava syndrome. JAMA 231:58-61, 1975
3. **Salsalt M, Cliffton EE:** SVOC with lung cancer. Ann Thorc Sug 6:437-422, 1968
4. **Sohraufnagel DE, Hill R, Leech JA, Pare JAP:** Superior vena cava obstruction: Is it a medial emergency? Am J Med 70:1169-1174, 1981
5. **Green J, Rubin P, Holzwasser G:** The experimental production of superior vena cava obstruction: Trial of differnet therapy schedule. Radiology 81:406-414, 1963
6. **Rubin P, Green J, Holzwasser G, Gerle R:** Superior vena cava syndrome: slow dose versus rapid high dose schedules. Radiology 81:388-401, 1963
7. **Lochridge SK, Knibble WP, Doty DB, etal:** Obstruction of the syuperior vena cava. Surgery 85:14-21, 1979
8. **Perez CA, et al:** Management of superior vena cava syndrome. Semin Oncol 5:123-134, 1978
9. **Bertrand M, Presant CA, Klein L, Scatt E:** Iatrogenic superior vena cava syndrome. Cancer

54:376-378, 1984
10. **Urschel HC, Paulson DL, et al:** Superior vena cava obstruction Dis Chest 49:155-146, 1966
11. **Lokich JJ, Goodman R:** Superior vena cava syndrome. JAMA 233:420-421, 1975
12. **Kane RC:** Superior vena cava obstruction due to small cell anaplastic lung cancer. JAMA 235:1717, 1976
13. **Davenport D, Ferree C, Blake D, Raben M:** Response of superior vena cava syndrome to radiation therapy. Cancer 38:1577-1580, 1976
14. **Charles Scarantino, et al:** The optimum radiation schedule in treatment of superior vena cava obstruction: Importance of 99m Tc scintiangiograms. Int J Radiat Oncol Biol Phys 5:1987-1995, 1979
15. **Karnofsky DA, et al:** The use of the nitrogen mustards in palliative treatment of carcinoma with particular reference to bronchogenic carcinoma. Cancer 1:634-656, 1948
16. **Geller W, et al:** The mandate for chemotherapeutic decompression in superior vena cava obstruction. Radiology 81:385-387, 1973
17. **Rosenbloom SE, et al:** Superior vena cava obstruction in primary cancer of the lung. Ann Int Med 31:470-478, 1949
18. **Kanji AM, Chao JH, Liebner EJ, et al:** Extrinsic compression of superior vena cava: an analysis of 41 patients. Int J Radiat Oncol Biol Phys 6:213-215, 1980
19. **Marc L, Citron, et al:** Superior vena cava syndrome due to non small cell lung cancer; resolution with chemotherapy alone. JAMA 250:71-72, 1983
20. **Spitzer S, Blanco G, Adam A, et al:** A superior vena cava obstruction and dissecting aneurysm. JAMA 233:165-165, 1975
21. **Pate JW, Hammon J:** Superior vena cava syndrome due to histoplasmosis in children. Ann Surg 161: 778-787, 1965
22. **Holmes KS, et al:** The treatment of superior vena cava syndrome by the high-dose grid technique. Radiology 81:402-404, 1963
23. **Stewart JR, Cohn KE, Fajardo LF, et al:** Radiation induced heart disease; A study of 25 patients. Radiology 89:302-310, 1967

=국문초록=

상행정맥 증후군의 방사선 치료 성적

경희대학교 의과대학 치료방사선과

조종희 · 김현순 · 홍성언 · 안치열

1978년 1월부터 1985년 12월까지 경희의대 부속병원 치료방사선과에서 상행정맥 증후군으로 방사선치료를 받은 환자 21명을 대상으로, 분할조사방법과 치료 총선량에 따른 초기증상의 완화와 치료에 대한 반응 및 생존율을 관찰하여 다음과 같은 결과를 얻었다.

1) 고 선량 치료군에서는 54.5%(6/11)에서 치료 1~2일후에 증상의 완화를 보였으며 81.7%(9/11)에서 치료 3~4일내에 증상의 완화를 나타내었다.

2) 일반분할조사가 각각 29%, 50%를 나타낸 것보다는 월등히 많은 환자에서 조기에 증상완화를 보였으나 두 군간의 생존율에는 유의한 차이가 없었다.

3) 치료후의 반응 판정에서는 총 선량 3,000 cGy 이상 치료한 군에서는 대부분이 반응을 나타냈으나, 3,000 cGy 이하를 치료한 군의 5예에서는 모두 반응을 나타내지 않았다.