A Study on the treatment of Esophageal Cancer through Irradiation of Conformation Fields with High Energy X-rays

(The Studies of Linac Therapy Part VI)

by

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高エネルギーX線変形照射野による食道癌治療に関する研究

(Linac 治療に関する研究　第6報)

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狭窄範囲が主として10cm以上の食道悪性腫瘍20例に対し10MV X-rays に変形照射野（照射範囲はX線像上異常部より上下1cm，側方食道基底線より最小5mm）を用いて，前2門後1門のY方向照射を行ない嚥下困難の改善，その他の自覚症を軽減し，生命の延長を計ろうと試み，次の結論を得た．

1．本法で使用した分割多片絞りによる変形照射野の線量最高部分の容積は，同一条件の矩形照射野の場合の50～70%であつた．

2．病巣線量は計算値と食道挿入硝子細桿線量計による測定値とを比較したところ，その差は±3%に過ぎなかつた．

3．死亡した18例の1年生存率は28%，平均生存月数 8.4ヶ月，半数生存月数7ヶ月，中央値7ヶ月，最長生存月数15ヶ月，最短生存月数4ヶ月で，現在生存中の者の最長は20ヶ月であり，十分治療効果があつたものと認める．

4．副障害としては，肺放射線症2例，照射による瘢痕狭窄4例を認めた．後者のうち3例は病巣線量10,000rads，1例は 8,000rads であつた．その他の副障害は軽微であつた．

5．本法は自覚症の改善には有効であり，特に嚥下困難は75%に著しい改善をみた．

6．食道ファイバースコープによる生検で，6,000 rads では50%，8,000 rads では80%，10,000rads では全例に癌細胞を証明できなかつたが，7～13ヶ月後に剖検した3例（10,000rads

照射）には多少とも癌細胞を認めた.

7. 剖検例のうち，原発巣より上下に進展を認めたもの1例，下方のみへの進展は2例で胃体上部に及んでいた.

以上により食道癌進行症例に対して高エネルギーX線変形照射野法による治療は十分有効であることが明かとなつたが，尚病巣線量は6,000～8,000radsに止め，照射野は更に癌病巣の上下に延長し，胃上部への照射を行なう方がより良い結果が得られるものと思う.

Introduction

Cancer of the Esophagus is a difficult disease to treat. Even with excellent surgical treatment, the 5 year survival rate only reaches 10–20% according to Nakayama,[6] Sweet[11] and Mustard.[5] With radiation therapy, a pessimistic survival rate of less than 5% is usually obtained, with the exception of 21% by Watson[14] and 20% by Pearson.[9] Even if excellent results are reported with surgical treatment, strict criteria of operability rule out many patients. The rates are also calculated by exclusion of operative death or so-called hospital death. Consequently, the cure rate for all patients with esophageal cancer is extremely poor.

In many of the cases of esophageal cancer encountered in our daily experience, the lesion is already widespread at the time of detection, and only a few cases are subjected to radical operation or radical radiation therapy. In advanced cases, palliative radiation therapy or anticancer drugs are used to improve symptoms of stenosis and other subjective symptoms.

In our department, since the beginning of 1968, radiation therapy was carried out mainly on inoperable esophageal cancer with range of stenosis measuring more than 10 cm by using conformable field technique. This conformable field is obtained automatically by the device of comformation collimator on 13 MV linear accelerator ("Toshiba Linac for medical use model LMR-13", subsequently abbreviated as Linac). Method of treatment and results of treatment up to August 1971 are reported.

Method of Study

A. Subjects of study

1. Patients:

In our department, all of 44 patients with esophageal cancer were subjected to high energy X-rays therapy for January 1968 to December 1970 and administered as follows. Preoperative irradiation is given in 14 cases, postoperative irradiation in 7 and irradiation before and after operation in 3 cases. In 20 cases, only radiation therapy was administered. An outline of these 20 cases is shown in Table 1. Gastrostomy was performed in 3 cases with marked distrubance in swallowing, since aggravation of the nutritional state of patient was expected. Gastrostomy was closed in 1 case after improvement.

2. Examination of the irradiation method:

Isodose curves were prepared by the radiographic film method reported by Noda et al.[7], to examine various methods of irradiation. The difference between the calculated dose to apply the intraesophageal lesion and actual dose measured with a fine fluoro glass rod dosimeter (Toshiba Type FGD-3B) are examined. While Linac X-rays are used to the treatment of esophageal cancer in our department, a similar study is conducted on cobalt-60 therapy unit (Shimazu Type RTGS-2) because of the attachment of a simplified conformation collimator.

3. Observation of the course based on X-rays, endoscopy and biopsy:

Table 1. In 20 cases, only radiation therapy was administered from January 1968 to December 1970.

Case No.	Sex	Age	Location	Length (cm)	Type	Tumor Dose (rad)	Survival Time (months)
*1 H. U.	♀	62	Iu	11	Saw Type	4400	14 Dead
2 S. H.	♂	69	Ce	10	Spiral Type	10000	9 Dead
3 S. M.	♂	76	Ei	8	Saw Type	10000	15 Dead
4 S. T.	♂	69	Im	10	Saw Type	10000	4 Dead
5 Y. U.	♂	48	Im	12	Spiral Type	10000	7 Dead
6 M. K.	♀	67	Iu	13	Spiral Type	10000	12 Dead
7 M. K.	♂	60	Ce	8	Funnel Type	10000	7 Dead
8 Y. A.	♂	65	Im	10	Funnel Type	10000	7 Dead
9 T. S.	♂	46	Im	11	Spiral Type	10000	8 Dead
*10 K. K.	♂	59	Iu	11	Spiral Type	10000	5 Dead
°11 K. T.	♂	54	Im	10	Polyp Type	10000	13 Dead
*12 H. T.	♂	55	Im	9	Spiral Type	6000	7 Dead
13 M. H.	♀	58	Im	10	Spiral Type	8000	20 Alive
14 T. M.	♂	58	Im	9	Spiral Type	10000	4 Dead
15 K. F.	♂	75	Ei	7	Spiral Type	10000	7 Dead
16 M. M.	♀	66	Ei	10	Funnel Type	8000	6 Dead
17 K. N.	♂	68	Ei	8	Spiral Type	8000	6 Dead
18 S. T.	♂	62	Im	11	Spiral Type	10000	9 Dead
19 M. W.	♂	51	Ei	9	Funnel Type	8000	14 Alive
20 S. H.	♂	63	Im	11	Spiral Type	8000	12 Dead

Cases of Esophageal cancer
* Gastrostomy ° Leiomyosarcoma

In all cases, X-ray examination was carried out before irradiation, after 3,000 rads, 6,000 rads, 8,000 rads and 10,000 rads at the time of irradiation. The degree of shrinkage of the filling defect in the esophagography are measured by planimeter. As a rule examination was repeated every month following discharge. In 10 of these cases, direct visualization of the lesion was observed by fiverscope (Olympus Type EF) and biopsy for histological examination under HE stain, before and after irradiation of 5,000–6,000 rads and 10,000 rads.

4. Survey on months of survival:

Days from the beginning of treatment to death were counted and months of survival calculated assuming 30.5 days constitute one month. As to patients who died after discharge, the course of the disease, date and causes of the death were surveyed through visiting or writing to the family or regular physician of the patients. Average months of survival were calculated on all patients in whom irradiation was started, without exception.

5. Complications and side effects of treatment:

In order to detect radiation pneumonitis, postirradiation esophageal stenosis, gastric deformity, esophagobronchial fistula, mediastinitis and bronchitis, chest X-ray and esophagogastric fluoroscopy examinations were performed every 2 weeks along with the survey on subjective symptoms before, during and after irradiation. In 3 patients, posmortem examinations was carried out to study the

changes of the lesion, state of metastasis, and changes in the lungs, aorta and other structures within the field of irradiation.

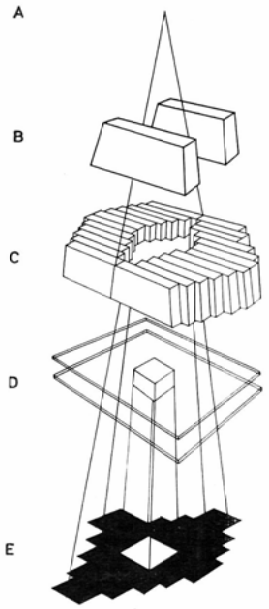
B. Practical aspects of irradiation

1. Device of the conformation collimator:

The collimator of Linac consists of one pair of tungsten alloy monoblock in an axis of the focus side, while 12 pairs of tungsten alloy collimator are placed anteriorly in another axis. The thickness of one piece of this collimator is 72.5 mm, and the dose ratio between useful beam and after passage through the collimator is less than 1/1000. The structure is shown in Fig. 1. Fig. 2-a, b, c shows the shape of field, the control panel in the treatment room and the main control panel in the operation room. After defining the shape of the field at the depth of the lesion and preparing the paper pattern of this shape in 1/2 scale and set in the potentiometer of controller as Fig. 2-b, the shape of the field for treatment as Fig. 2-a is obtained readily by the servo motor driving mechanism for 12 pairs collimator. By using of this paper pattern, identical conformation field is repeatedly obtained at each treatment. Moreover, this field may be set from the operation room with the use of main controller.

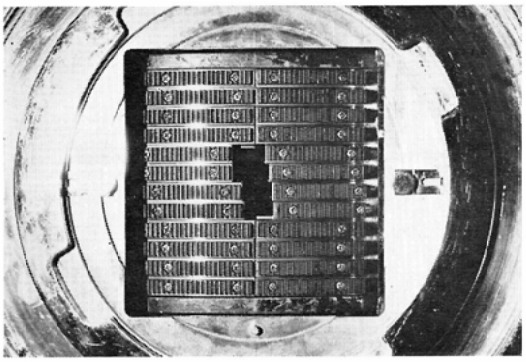
2. Positioning of field by a simulator:

The patient is placed in the supine position on the couch of the simulator. Esophagrams are obtained in the frontal and lateral projections. As shown in Fig. 3, a minimum rectangle field compltely covering the esophagus lesion are supposed. The long axis of this rectangle should coincide

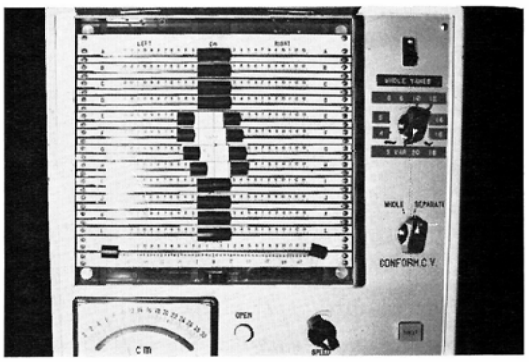


A: target.
B: on pair of tungsten alloy monoblock.
C: 12 pairs of tungsten alloy collimator.
D: lead block for hollow out irradiation.
E: radiation field.

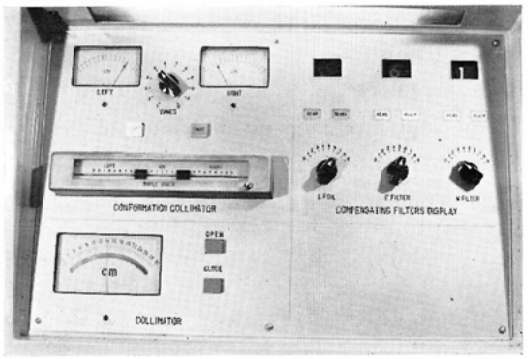
Fig. 1. The structure of collimator of LMR-13Linac.



a: 12 pairs of tungsten alloy collimator and radiation portal.



b: control panel of collimator in the treatment room.



c: main control panel in the operation room.

Fig. 2.

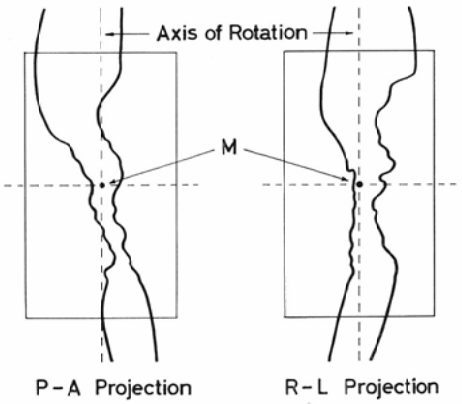


Fig. 3. A minimum rectangle completely covering the entire esophagus previously determined by examination is determined. The long axis of this rectangle should coincide with the rotation axis of the simulator.

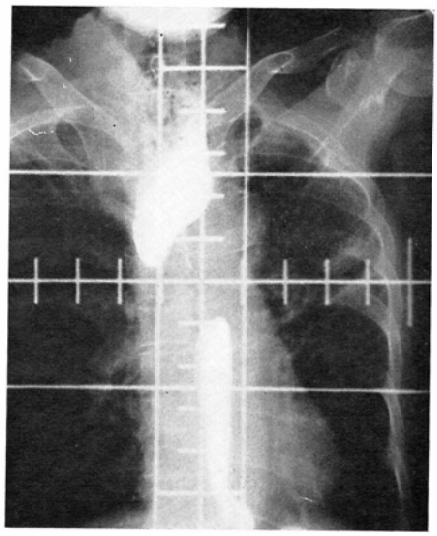


Fig. 4. Dorso-ventral esophagram taken by simulator. One scale in this picture is 2 cm at the depth of the lesion.

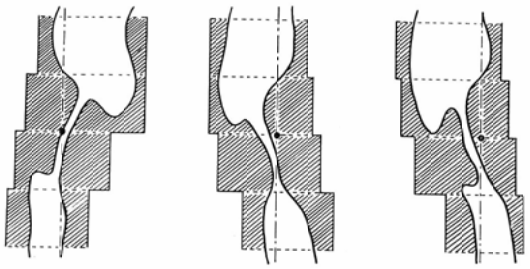


Fig. 5. The outline of the esophagrams and shape of the conformation fields.

with the rotation axis of the simulator, that is therapy unit. And then a correction is made the isocenter of the simulator should coincide with the center of this square. So that a point M (that is the center of the square field) in Fig. 3 is adjusted to the isocenter of simulator, irradiation from any direction would cause the central ray to pass through M. Radiographs are then obtained from two anterior fields (Angle between two fiels is 90°) and single posterior field (dorsoventral direction) from which subsequent irradiation is planned. Fig. 4 shows an example of such a radiograph. One scale in this picture is 2 cm at the depth of the lesion.

3. Determination of the field:

In the determination of the field of irradiation, the upper and lower ends of the field are placed 1 cm superiorly and inferiorly to the edge of abnormal tissue detected by X-ray studies, while at least 5 mm outside the basal esophageal line is taken as the lateral border. Fig. 5 shows the outline of the esophagrams and shape of the transformed irradiation fields. This shape of the field is made to 1/2 scale to use as the paper pattern for control panel as shown in Fig. 6.

4. Confirmation of the treatment field:

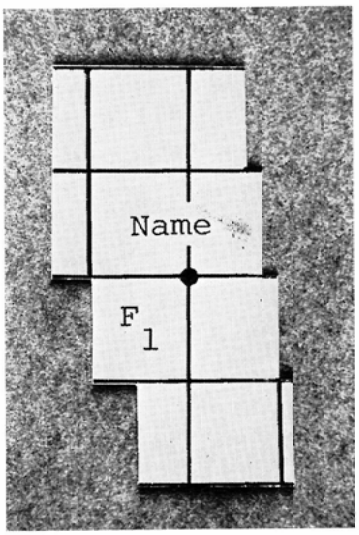


Fig. 6. The paper pattern for setting of control panel.

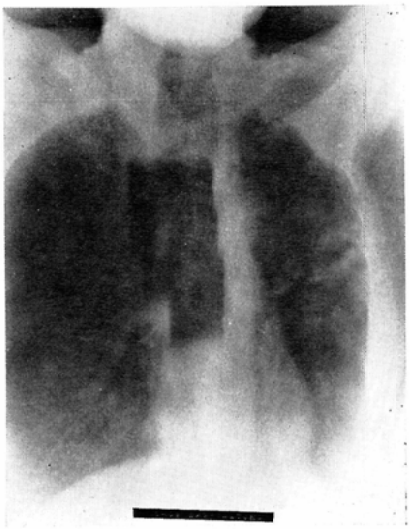


Fig. 7. Linacography is carried out to confirm accurate irradiation. This picture taken by 6 MV X-rays.

The patient is placed in the supine position on the treatment couch of Linac, and the collimator is adjusted. Next, according to the Method of Tsuji[13] of our department, Linacography is carried out to confirm accurate irradiation. One example of Linacography is shown in Fig. 7.

5. Treatment conditions:

As a rule, dose of 200 rads per day for single field of 10 MV X-rays at STD 90 cm and a total dose of 10,000 rads to the lesion are applied. Under unusual cases, 4,400–8,000 rads are used. (4,400 rads in 1 case, 6,000 rads in 2 cases, 8,000 rads in 5 cases, and 10,000 rads in 12 cases)

C. Regional classification of esophageal carcinoma:

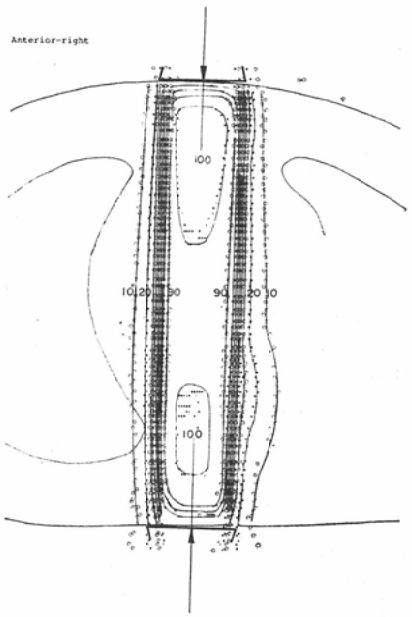
The description of the site of the esophageal cancer in this paper is based on the regulations of the Japanese Society for the study of diseases of the esophagus. They are as follows: Cervical esophagus (from the entrance of esophagus to upper sternal border, as Ce), upper thoracic esophagus (from the upper sternal border to the lower edge of the tracheal bifurcation, as Iu), middle thoracic esophagus (upper half of the portion between the lower edge of bifurcation and esophagocardiac junction, as Im), lower thoracic esophagus (intrathoracic part of the lower half of the portion between the lower edge of bifurcation and esophagocardiac junction, as Ei), and abdominal esophagus (intra abdominal part of the lower half of the portion between the lower edge of bifurcation and esophagocardiac junction, as Ea).

Results

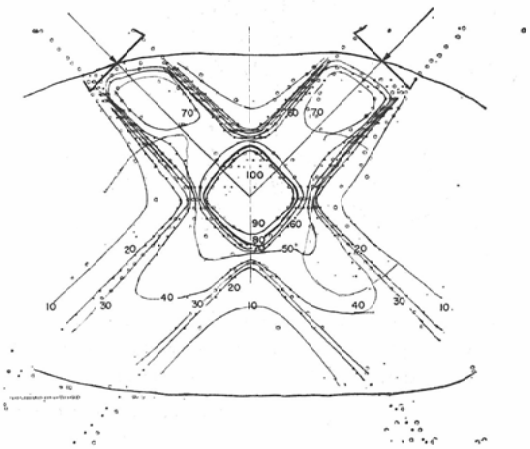
1. Examination on the method of irradiation:

a. Isodose curve for each method of irradiation; Various irradiation methods are possible in the treatment of the esophagus. The methods of irradiation are studied those of two anterior and posterior opposing fields, two fields placed anteriorly in a V configuration, two anterior and two

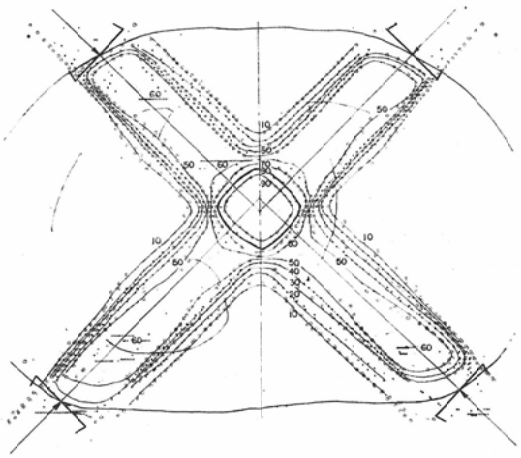
posterior fields placed in X configuration, and two anterior fields adding one posterior fields placed in Y configuration. In the Y shape distributions, three methods are examined. Fig. 8-a, b, c, d, e and f show the isodose curves in the mix DP chest phantom for each of these methods. As the result of examination of all these, the Y shape of Fig. 8-e proved to be the best and this method was mainly employed in actual treatment.



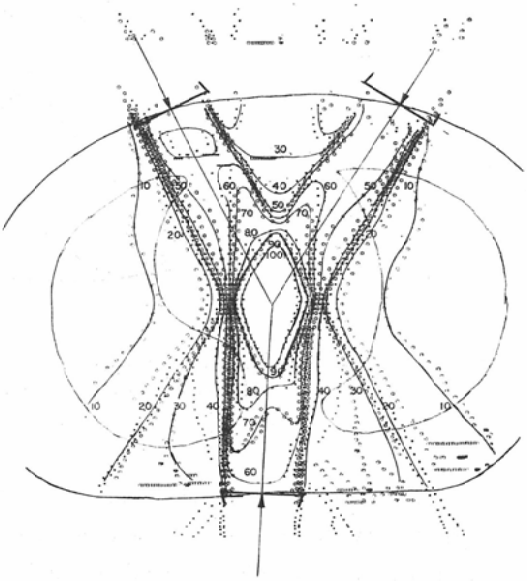
a: 2 Fields: Opposed, 10 MV X-rays, chest phantom, STD 90 cm, Field size 4×12 cm, Dose ratio 1:1



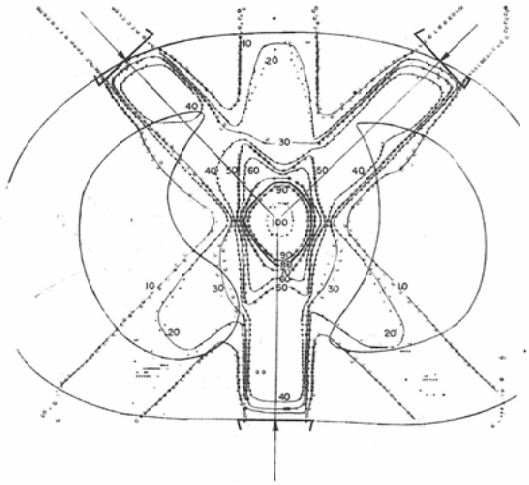
b: 2 Fields: V Configuration' 10 MV X-rays, Chest phantom, STD 90 cm, Field size 4×12 cm, Angleθ = 90°, Dose ratio 1:1



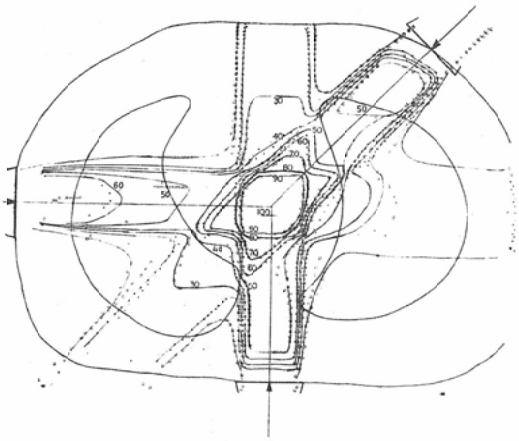
c: 4 Fields: X Configuration, 10 MV X-rays, Chest phantom, STD 90 cm, Field size 4×12 cm, Angleθ = 90°, Dose ratio 1:1:1:1



d: 3 Fields: Y Configuration, 10 MV X-rays, Chest phantom, STD 90 cm, Field size 4×12 cm, Angleθ = 60°, Dose ratio 1:1:1



e: 3 Fields: Y Configuration, 10 MV X-rays, Chest phantom, STD 90 cm, Field size 4×12 cm, Angleθ = 90°, Dose ratio 1: 1: 1



f: 3 Fields: deformed Y Configuration, 10 MV X-rays, Chest phantom, STD 90 cm, Field size 4×12 cm, Angleθ = 90°, 135°, 135°, Dose ratio 1: 1: 1

Fig. 8. Isodose curves for each method of irradiation.

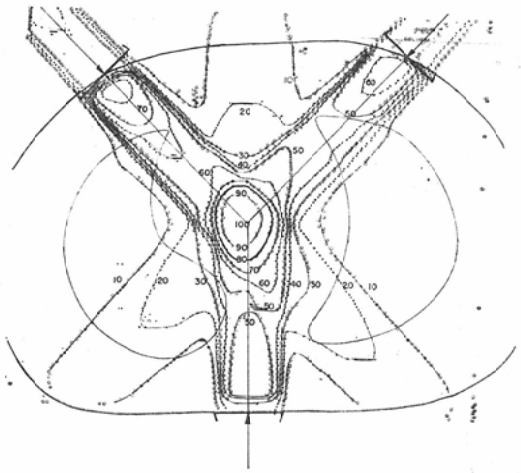


Fig. 9. Isodose curve of cobalt-60 unit in the Y field configuration. STD 65 cm, Field size 4×12 cm, Chest phantom, Angleθ = 90°, Dose ratio 1: 1: 1

For cobalt-60 unit, isodose curves are also obtained in this Y shape irradiation, and compared with 10 MV X-rays. Fig. 9 shows an isodose curves for cobalt-60 in this Y field. As a frame of treatment couch of Linac is made of alminum alloy, the decrease in dose due to this structure appeared to be about 30% as shown in Fig. 10.

b. Penumbra of the irradiation field; Fig. 11 and 12 indicate the positional relationship among

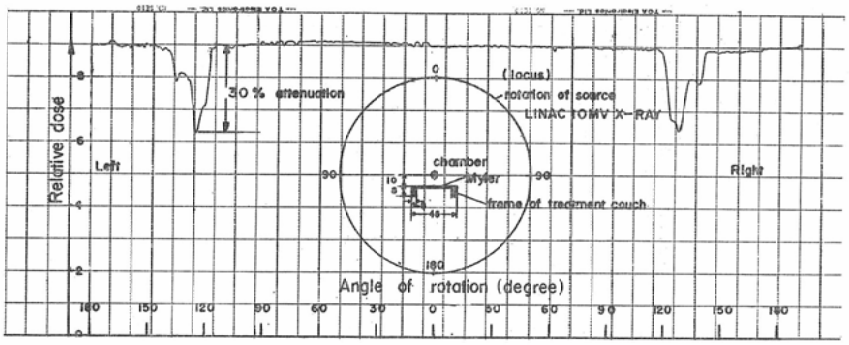


Fig. 10. Dose attenuation due to the frame of treatment couch.

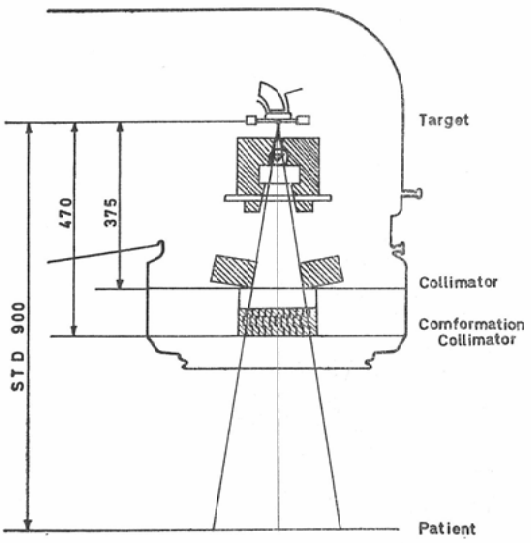


Fig. 11. The positional relationship among] radiation source, collimator and rotation center (Toshiba, LMR-13 Linac).

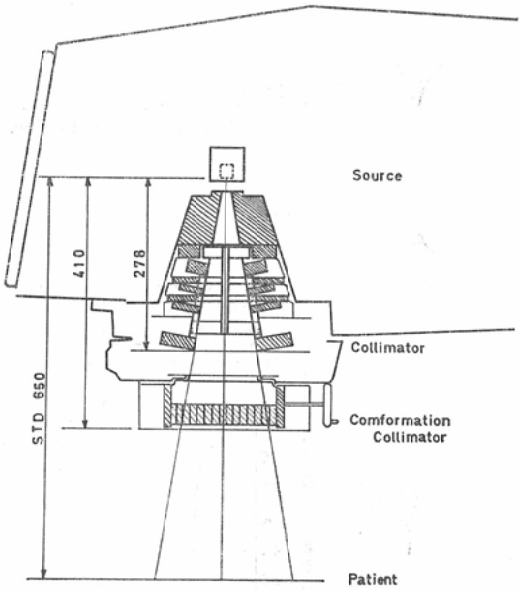


Fig. 12. The positional relationship among radiation source, collimator and rotation center (Shimazu, RTGS-2 cobalt-60 therapy unit).

radiation source, collimator, and rotation center in Linac and cobalt-60 unit. The dose distribution of Linac and cobalt-60 unit delivered by the apparatus described above in the same conformation fields size is shown in Fig. 13. The profile of dose distribution across beams is shown in Fig. 14.

c. Irradiated volume in body; As the volume irradiated is increased, more side effects are produced and the result of treatment is naturally affected. On the irradiation with Y configuration three fields, the volume of tissue enclosed to the lesion by the each geometrical fields are estimated and compared with rectangular field and conformation field. For example, in a case with range of stenosis of 10 cm on X-ray, the volume defined with the rectangular fields extended to 1 cm above and below the limit of the lesion is 370 ml. While the conformation field is used to same case, the

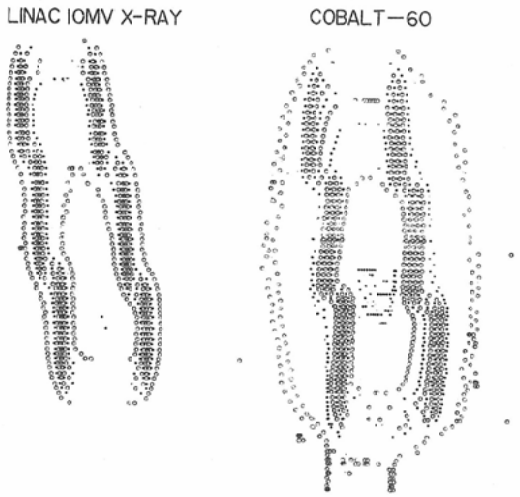


Fig. 13. The dose distribution of Linac and cobalt-60 unit in the same conformation field size.

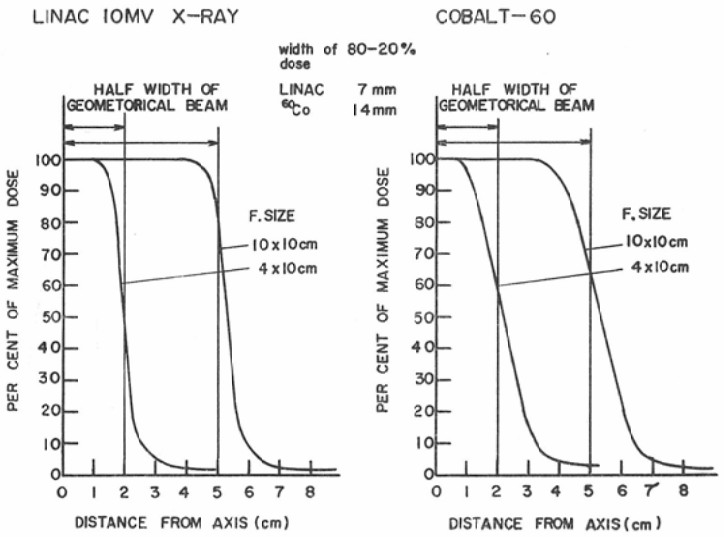


Fig. 14. The profile of dose distribution.

volume in body is 213.4 ml, and decreased to 57.7% of rectangular field.

d. Actual measurement of the dose of irradiation on the lesion; The dose of 300 rads to the lesion is decided by the calculation from the out put measurement of Linac. In actual treatment, as the measured dose in patient with fluoro-glass dosimeter is 292 rads, then the deviation from the estimation is about 3% shown in Table 1. The doses shown in this paper are all obtained by calculation.

3. Therapeutic results:

Table 2. Actual dose measurement.

	calculated applied dose	measured dose	deviation
phantom	300 rad	301 rad	+ 0.3%
patient	300 rad	292 rad	− 3 %
fluoro-glass		Toshiba FD-1	
radiation source		Linac 10 MV X-rays	
number of fields		3 : bilateral, $F_1F_2F_3$	
depth of $F_1F_2F_3$		12.5cm, 12.0cm, 10.0cm	
STD		90cm	
field size		4 × 12cm	
angle between F_1F_2		90°	
applied dose ratio		1 : 1 : 1	

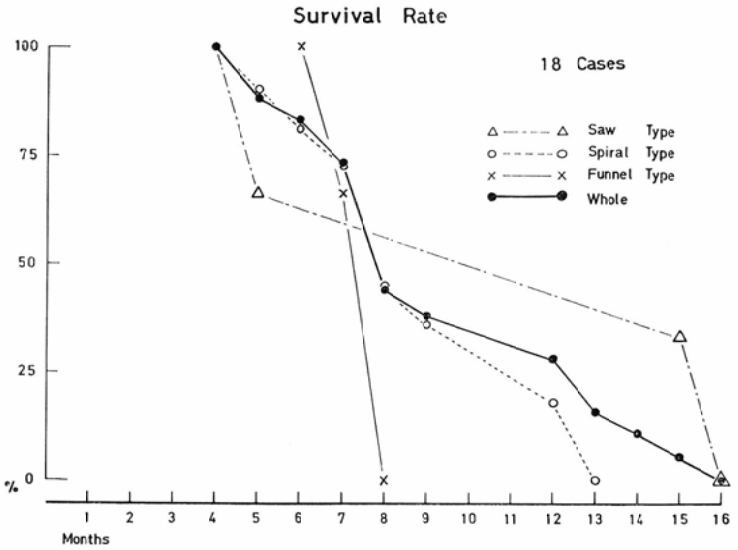


Fig. 15. The survival curves of 18 deceased cases.

Among 20 cases, the survival curves of 18 deceased cases are summarized in Fig. 15. Course of each of the 20 cases is shown in Fig. 16. Average months of survival was 8.4 months, one year survival rate was 28%, survival of one-half of the cases was 7 months, median value 7 months, longest survival 15 months, shortest survival 4 months, and the longest survival among those who are surviving is 20 months.

Fig. 17, 18, 19 shows the course of X-ray, endoscopic, and histologic findings in the case surviving 20 months after an excellent result. Cases with less dramatic results are shown in figures 20 and 21.

The area of filling defect relative to the original esophageal contour is measured by planimetry, correcting for the magnification in X-ray picture, and decrease in size of the filling defect after

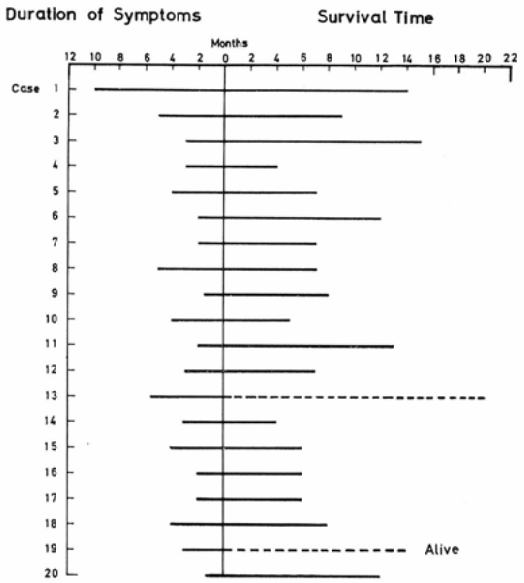


Fig. 16. Course of each of the 20 cases.

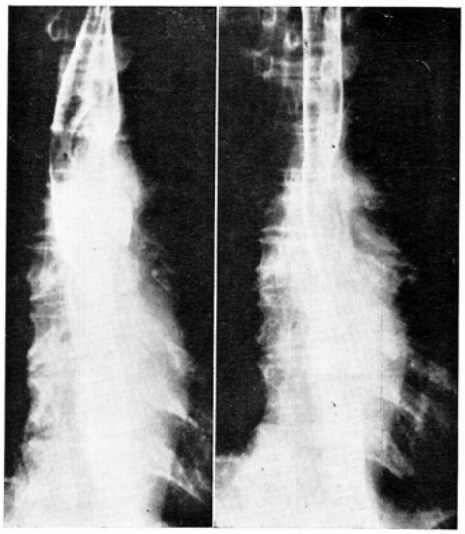
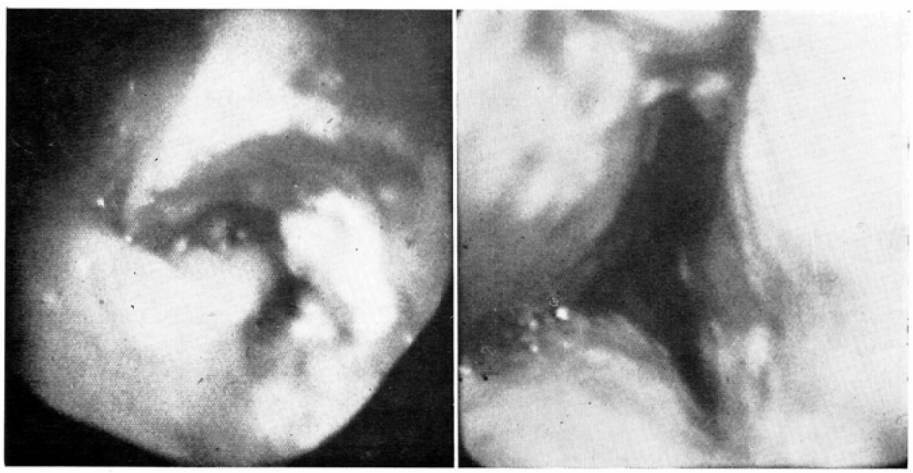


Fig. 17. Case 13. Esophagography before (left) and after (right, 10,000 rads) irradiation reveal an average reduction in size of 13%.



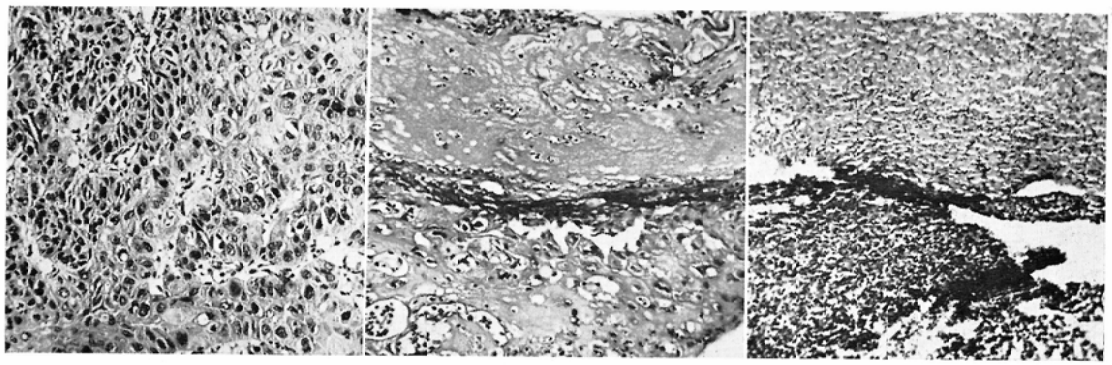
a　　b

Fig. 18. Case 13. Endoscopic pictures before (left) and after irradiation (right) show decrease in tumor size.

irradiation is calculated. As the result, average decrease in size is 54%, maximum 100%, minimum 12.5%, and median 60.8%. The rate of reduction in size from morphologic view-point is greater in polypoid leiomyosarcoma but not much different among others as shown in Table 3.

4. Side effects and complications of irradiation:

a. Radiation pneumonitis and fibrosis; In the initial stage of treatment with high energy X-rays therapy, 10,000 rads is irradiated with 12×8 cm field using a V configuration in a 69 year



a b c

a: Biopsy before irradiation reveal squamous cell carcinoma.
b: Biopsy with 6,000 rads reveal abundant necrotic, with partially degenerated cancer cells and inflammatory findings.
c: Biopsy with 10,000 rads no cancer cells are detected, only leaving necrosis, inflammatory cells.

Fig. 19. Case 13. Histologic findings.

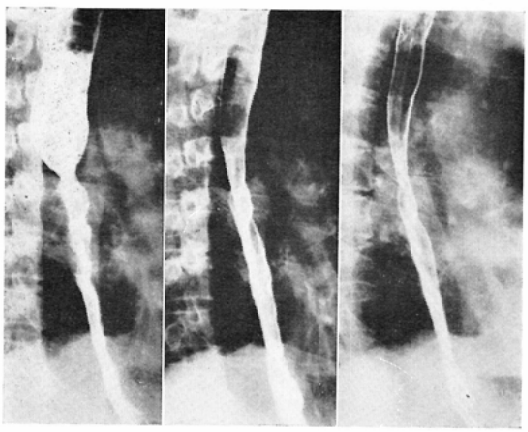


Fig. 20. Case 19. The case with moderate result. Esophagography before (left), during (middle, 6,000 rads), after (right, 10,000 rads) reveal reduction in size of 63%.

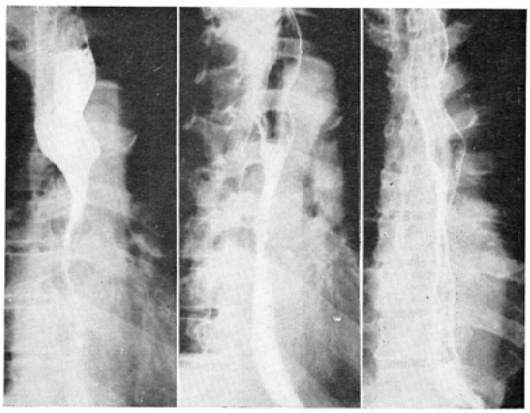


Fig. 21. Case 8. The case of funnel type with moderate result. Esophagography before (left), during (middle, 6,000 rads), after(right, 10,000 rads) irradiation reveal reduction in size of 72 %.

old male. One and half months after the end of irradiation, radiation pneumonitis and fibrosis is noted in both upper and middle lung fields. In case 13, 8,000 rads is delivered to the middle thoracic esophagus (Im), followed by an additional 6,000 rads after 1 month. Similar lesions are found in both hilar areas. Radiographs before and after irradiation are shown in Fig. 22. In other cases, no radiation pneumonitis or fibrosis are noted.

b. Mediastinal pleurisy; In the PA radiograph of the chest, the cardiophrenic angle is obscured in 4 cases. A case (case 8) is shown in Fig. 23.

Table 3. The rate of reduction in size of the filling defect after irradiation.

Rate of Reduction %	Saw Type	Spiral Type	Funnel Type	Polyp Type	Total
81 — 100				1	1
61 — 80	1	5	2		8
41 — 60	1	2	1		4
21 — 40		1			1
0 — 20	1	1	1		3
Rate of Average Reduction	49%	52%	52%	100%	54%

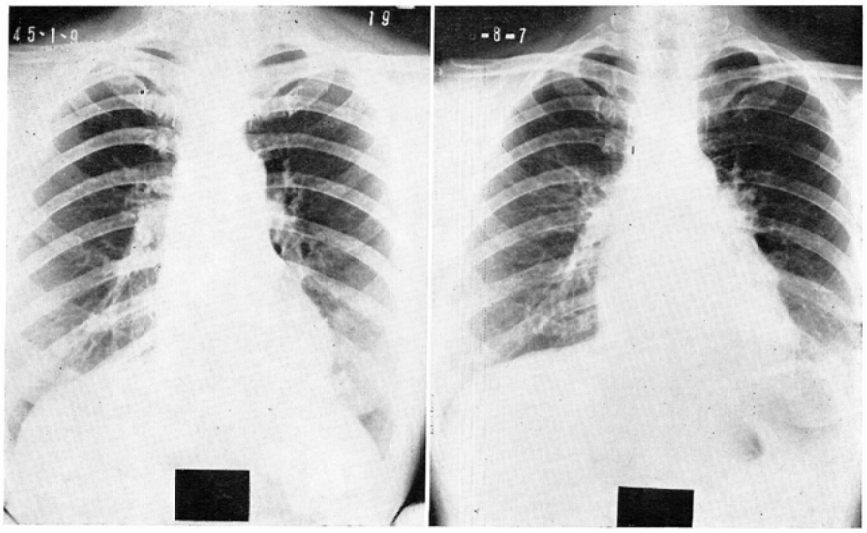


Fig. 22. In case 13, radiation pneumonitis and fibrosis are found in both hilar areas.

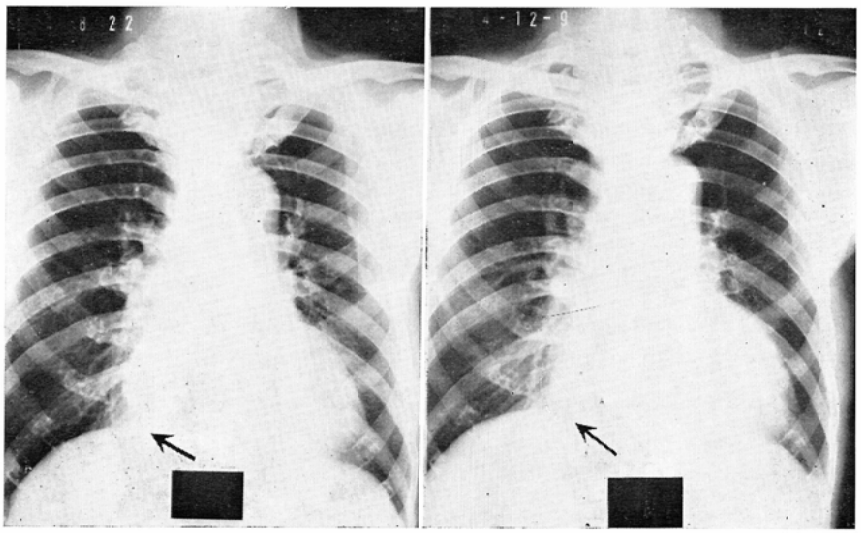


Fig. 23. In case 8, the cardiophrenic angle is obscured.

Table 4. Cicatrical stenosis of the esophagus after irradiation.

Type of Lesions	6000 rads	8000 rads	10000 rads	Total
Saw Type	0/1		0/2	0/3
Polyp Type			0/1	0/1
Funnel Type		1/2	0/2	1/4
Spiral Type	0/2	0/3	3/7	3/12
Total	0/3	1/5	3/12	4/20

c. Cicatrical stenosis of the esophagus; In 4 out of 20 cases, cicatrical stenosis of the esophagus is noted as shown in Table 3. In 3 cases, a spiral type is noted, while a funnel type is noted in another. In 3 of these cases, radiation of more than 10,000 rads is given.

d. Infiltration and metastasis; In X-ray examination of the stomach, a filling defect is noted in inferior cardia in 3 cases (including 2 cases with deformity of the greater curvature described in the next section). Pulmonary metastasis are demonstrated by X-ray in 3 cases and at autopsy in 1. In 1 case, esophagobronchial fistula developed. Fig. 24 and 25 shows the metastasis to the stomach and lung in different cases.

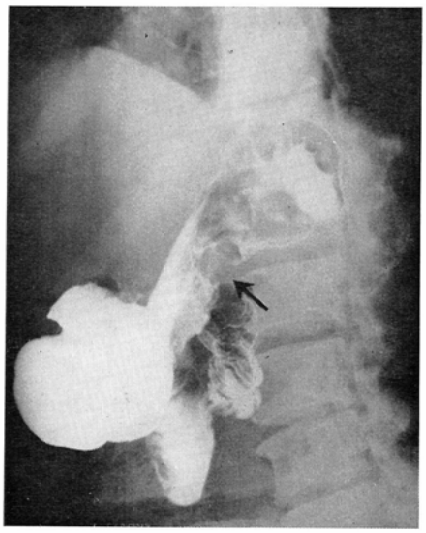


Fig. 24. The metastasis to the stomach.

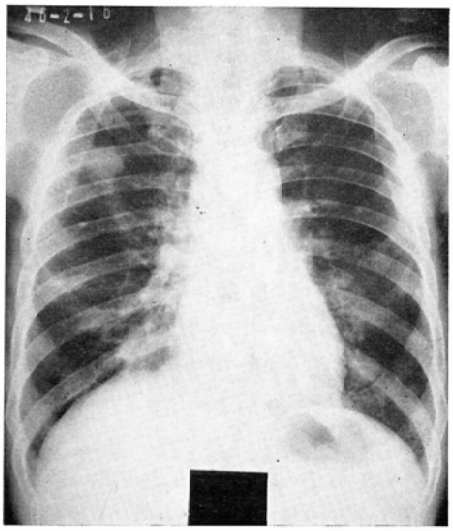


Fig. 25. The metastasis to the lung.

e. Gastric deformity; Following irradiation, indentation of the upper part of the corpus on the greater curvature side probably due to esophageal contraction is noted in 4 cases. In 2 of these cases (Case 8, 9) cancerous infiltration into the lower portion of cardia is revealed by autopsy. In 2 other cases, cicatrical contraction is probably responsible for the deformity. One of these cases is shown in Fig. 26.

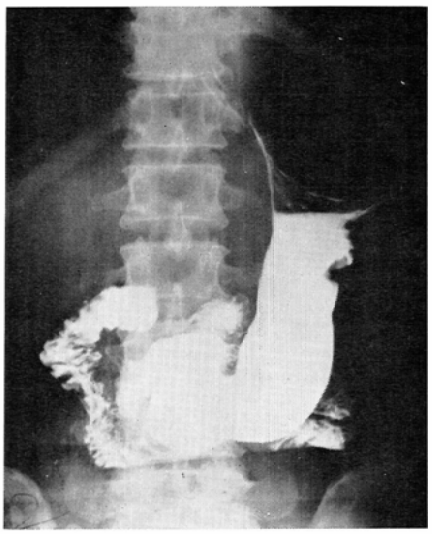


Fig. 26. Deformity of the upper part of the corpus on the greater curvature side.

f. ECG change; In all cases, ECG is obtained before, during and after irradiation. In 3 cases, ECG changes are found before irradiation (atrial fibrillation, bundle branch block, ischemic heart disease). No aggravation is noted after irradiation. In one case with normal findings before irradiation, occasional extrasystoles are noted after irradiation. This case is irradiated at the mid thoracic esophagus (Im) with 10,000 rads. The ECG changes are minimal.

5. Subjective symptoms:

Before, during and following completion of irradiation, changes in subjective symptoms such as dysphagia, sensations of partial obstruction, chest pain, cough and sputum production are surveyed. In 16 of 20 cases, dysphagia was noted before irradiation. After 4,000 to 6,000 rads, marked improvement is noted in about one-half of the cases. At the end of irradiation, only 4 cases have complaints. The sensation of partial obstruction is noted more frequently than dysphagia and practically everyone complained of it. While this decreases along with the disappearance dysphagia, more than one-half of subjects still complained of it at the end of irradiation. Complaints of cough and sputum production tended to increase during irradiation. Fig. 27 summarizes the changes in these subjective symptoms.

6. Endoscopic findings and biopsy results:

Endoscopy and biopsy are conducted in 10 of 20 cases before, during and after irradiation, to study the macroscopic and histologic changes secondary to irradiation. Biopsy before irradiation revealed squamous cell carcinoma in 9 cases and leiomyosarcoma (Case 11) in 1.

Endoscopy following irradiation with 6,000 rads frequently revealed marked shrinkage of cancer lesion (72%), especially in the markedly elevated type. In excavated type and elevated and infiltrative type, the mucosa surrounding the tumor is swollen and bled easily. Ulceration remained in 3 of 7. In the type of stenosis due to a circumferencial lesion, poor distensibility is still present. Biopsy revealed abundant necrotic, with partially degenerated cancer cells and inflammatory findings.

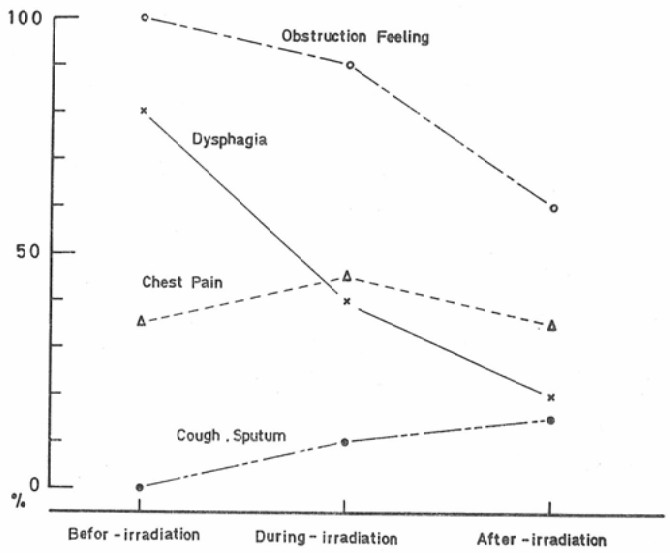


Fig. 27. The changes in subjective symptoms.

Endoscopy after irradiation with 8,000–10,000 rads revealed only scar tissue in elevated types but in 3 cases described above with friability. In the cases of circumferencial stenosis, recovery of distensibility is noted. On histological examination of the biopsy specimen, no cancer cells are detected at all in most of the cases, only leaving necrosis, cicatrized connective tissue and inflammatory cells. As a representative case, changes in the histological picture in Case 13 are shown in Fig. 19.

7. Pathoanatomical findings:

Among 20 cases, autopsy is carried out in 3 cases who died during hospitalization (Case 8, 9, 11). The effects of irradiation can not be definitely determined on pathohistologic examination. Common findings are described. In all cases, marked infiltration or metastasis of the tumor is noted around the aorta and bronchi, from the distal end of the lesion to fornix or lesser curvature of the stomach, in the lymph nodes along the lesser curvature, bilateral diaphragmatic, and subclavian lymph nodes indicating widespread invasion beyond the field of irradiation. In Case 8, mild fibrinous adhesions are noted between the pericardium and epicardium. In Case 11, esophagopericardial fistula had developed, along with purulent pericarditis. In each case, the submucosal and muscular layers within the irradiated field contained islands of tumor cells.

Discussion

1. Method of irradiation:

a. Irradiation field; Since supine position appears to be the most stable and reproducible position for irradiation, the material of the back of the treatment couch is prepared with polyester film of 0.1 mm thickness, to remove most of the influence of build up. When treatment of esophageal cancer was started using conformation field irradiation, the isodose curves within a phantom shown in Fig. 8 are constructed for each method of irradiation. As the result of this study, irradiation in

the "Y" configuration with the two anterior and single posterior fields is adopted. Three fields appeared to be adequate since it is quite troublesome in practical application to use more conformation fields in many patients. When the single anterior and two posterior fields are used, the frame of the treatment couch enters the irradiation field, and the dose at this portion decreases by about 30%. Placing the patient at the end of the treatment couch to aboid the frame effect causes instability in positioning. With the use of this method of irradiation, the spinal cord is undesirably irradiated from the back. With the use of 10 MV X-rays, spinal cord is subjected to about 30% of the dose at the lesion when the single anterior and two posterior fields are used, while the corresponding value was 47% using the two anterior and single posterior fields. In other words, when 10,000 rads is given on the lesion, 3,000 rads in the former of 4,700 rads in the latter is delivered to the spinal cord. Therefore the two anterior and single posterior fields are used.

b. Range of irradiation; Ackerman[1] found metastasis of the carcinoma of the middle third of esophagus to abdominal lymph nodes in 24.8% of cases. Similar metastasis was found in 42.4% of carcinoma of the lower third of the esophagus. As was stated before, in a sense of palliative treatment to improve stenosis condition and alleviate subjective symptoms, limits of irradiation are decided 1 cm above and below the edge of the lesion demonstrated by X-ray and at least 5 mm from the basal esophageal line laterally. However, survival period longer than expectation is obtained, and additional irradiation to the lower esophagus and gastric fornix is required. It therefore appeared that this field of irradiation should be enlarged superiorly and inferiorly.

Side effects are unexpectedly mild and the field of irradiation may be enlarged, in which case the total dose to the lesion should be 6,000–8,000 rads as described below. In our department, all cases of carcinoma of the esophagus are currently under this form of treatment.

c. Penumbra of the field; The penumbra peculiar to Linac has been already reported.[8] Penumbra of fractionated multi-leaf collimator is discussed. Since each piece of the multi-leaf collimator moves around the circle with the center at the focus, the end agrees with the direction of radiation beam to minimize the penumbra. In our cobalt-60 unit, simplified multi-leaf collimator may be attached for irradiation. Comparison of the penumbra at the position of the isocenter between two kinds of apparatus revealed the source size of 3 mm in Linac and distance between the focal spot and the distal end of the collimator 470 mm. With the use of cobalt-60 unit, the size of the source was 15 mm, and distance from the radiation source to the distal end of the collimator 410 mm. As is anticipated, the penumbra is smaller in Linac (Fig. 14). The effect of conformation field size is more advantageous in Linac.

d. Irradiated volume in body; The purpose of using conformation fields is to minimize the volume dose, creating a volume of maximum dose with a shape conforming to the volume to be irradiated, and minimizing the amount of irradiation given to surrounding areas. The conformation method used by Takahashi et al.[12] serves this purpose best. However, this apparatus is complicated, hard to handle and expensive.

When a rectangular field is used in the irradiation of esophagus, unnecessary tissue occupies a large part of the volume. With the use of the conformation field, irradiation of the unnecessary portions may be aboided. This is especially advantageous for lower esophagus with large curvature. In the

studies of Rider et al.,[10] 3 year survival rate appears to be better in cases with small volume of irradiation. When irradiation is carried out from three fields using conformation collimator, the volume exposed to the maximum dose is only 50–70% of the corresponding volume upon irradiation of three rectangular fields.

e. Dose at the lesion; In carcinoma of the esophagus, in order to estimate the dose at the lesion accurately, differences in the distribution due to heterogeneous substances such as lung and bone should be taken into consideration. It is fall into trouble to calculate these differences in each cases, but the correction of dose may be neglected because of very small value for high energy X-rays. Since an error is naturally expected between the estimated dose in the therapeutic plan and actual dose at the lesion, the calculated value and the dose within the esophagus measured by fine glass rod dosimeter were compared. The maximum error was ± 3%. The calculated value therefore may be used with considerable accuracy.

2. Therapeutic results:

Before practicing this form of treatment, scarcely any palliative radiation therapy for esophageal cancer had been carried out, so that it is impossible to compare the therapeutic results. In surgical treatment as well as radiation therapy, the results are influenced by the selection of patients, so that the superiority or inferiority of the results cannot be discussed based on minor differences. However, the report by Bauer et al.[2] probably indicates general results. Bauer et al. summarized the results of high energy radiation therapy in 1319 cases collected from 25 reports in the literature. The 6 month survival rate was 71%, and 1 year survival rate was 20%, according to this report. In the results of our studies based on 20 cases, the corresponding results are 83 and 28%, indicating a considerably favorable result. With surgical treatment, the best results were obtained by Nakayama et al.,[6] utilizing preoperative irradiation. Their 5 year survival rate was 15.8%. Generally, it seems that figures between 3.3 and 9%[3][4] were obtained. The best results with radiation therapy were the 5 year survival rate of 21% by Watson.[14] The previously mentioned reports by Bauer et al. were more generally acceptable. However, in our department, a broad standard for patient selection is used. Except for those who died before irradiation, all patients are treated. The treatment is therefore believed to be successful. The use of as small a radiation field as possible also means the lack of consideration for the metastasis any distance from the lesion. The influence of such situation on long term result should be clarified by future study. Even if an excellent result was obtained in survival rate of 6 months or 1 year, decrease of the rate of survival due to such metastasis is naturally expected.

3. Side effects:

The purpose of using a conformation fields for irradiation in the present study is to keep the radiation beam to the minimum requirement, alleviating the unnecessary or harmful load to the patient. Through giving sufficient dose on the lesion, restoration of esophageal function is attempted, for the purpose of prolongation of life. Among 20 cases, pulmonary fibrosis and pneumonitis due to irradiation is noted in 1 case of carcinoma of the cervical esophagus, and another case in which such involvement occured due to overlapping of the field of irradiation owing to an additional course of irradiation. Such involvement is not detected in any other cases in the X-ray pictures.

In a few cases, mediastinal pleurisy and ECG changes are noted, but all these with 10 MV X-rays, it is possible to decrease side effect outside of the target of irradiation. Since 8,000–10,000 rads are delivered to the lesion, cicatrical stenosis naturally occurs as the result. This is seen in 4 of 20 cases. In 3 of these cases (Case 10, 13, 14), 10,000 rads was given. In 1 case (Case 19), 8,000 rads was given. As the dose increases, esophageal stenosis probably occurs more frequently. Since this treatment is aimed at the improvement of cancerous stenosis, 10,000 rads appears to be rather excessive. In the treatment of esophageal cancer, besides concentric atrophy leading to stenosis, atrophy in the axial direction results in shortening of the esophagus. Occasionally this involves stomach, appearing as the indentation of the greater curvature of upper corpus. In 4 of 20 cases, such findings are noted. In 2 of these cases (Case 8, 9), autopsy reveal cancerous infiltration into the stomach. Such findings should be carefully evaluated.

4. Alleviation of subjective symptoms:

One of the purposes of this treatment consists of alleviation of subjective symptoms. As stated before, marked improvement is noted in dysphagia, the most important symptom, in 75% of cases. Sensation of partial obstruction is noted in about one half of cases. The improvement was not as good as with dysphagia. Chest pain, cough and sputum increased along with irradiation. At the end of irradiation, these symptoms is restored the same as before irradiation. Irradiation appears to aggravate these symptoms.

This treatment markedly improved dysphagia, the most important symptom, and side effects were rather mild. This treatment may therefore be considered a success. However, subjective symptoms could not be completely reversed. Further modes of treatment are necessary.

5. Endoscopic, biopsy and autopsy findings:

Besides X-ray studies, observation carried out through fiberesophagoscope with photography and biopsy proved to be quite useful in diagnosis and evaluation of treatment. One disadvantage is that it is not possible to examine the distal side of the stenotic lesion. Even when spread of cancer to the lower part of esophagus and upper part of the corpus in the X-ray picture after treatment is suspected, it is not possible to examine the portion beyond the portion of stenosis. Since the danger of perforation accompanies biopsy, a limitation is seen in the diagnostic ability. In the histological diagnosis of biopsy specimen after irradiation of 8,000–10,000 rads, no cancer cells are noted in most of the cases. However, histological examination at autopsy revealed cancer lesion in some part.

6. Improvement of irradiation method:

In the beginning, 10,000 rads were given to the lesion. As stated before, it is rather difficult to eliminate cancer cells completely. Stenosis is induced rather frequently due to cicatrical contraction. Additional radiation therapy may be necessary in cases with spread of cancer to the lower or upper part of the esophagus.

When stenosis extended more than 10 cm, metastasis to lymph nodes is expected. For these reasons, it is attributed that 10,000 rads is not necessary for symptomatic treatment. The total dose to the lesion should rather be reduced to expand the field of irradiation above and below the lesion, and the fornix should also be irradiated to attempt to prolong life. Consequently, the field of irradiation is extended above and below the lesion at present, using total dose of, 6000–8,000 rads.

Conclusion

In cases of maligant tumor of the esophagus (19 cases of carcinoma and 1 case of leiomyosarcoma) mainly with the range of stenosis more than 10 cm, Y-type irradiation is conducted from two anterior fields and single posterior field with 10 MV X-rays utilizing a conformation collimator (range of irradiation is 1 cm above and below the abnormal lesion in X-ray, and at least 5 mm from the basal esophageal line in the lateral direction) in an attempt to improve dysphagia, and other subjective symptoms, leading to prolongation of life. The following conclusions are obtained.

1. The volume exposed to the lesion with the conformation field using a fractionated multileaf collimator is decreases about 50–70% of the volume using a rectangular field under the same conditions.

2. Comparison of the calculated dose to the lesion and the value actually measured with fine glass rod dosimeter inserted into the esophageal lumen reveal a difference less than ± 3%.

3. The one year survival rate of 18 cases was 28%, average length of survival 8.4 months, survival of one-half of the patients 7 months, median survival 7 months, the longest survival 15 months and shortest survival 4 months. The longest survival of patients currently living is 20 months. The high energy X-rays treatment technic with conformation field thus appears to be effective in patients with advanced esophageal cancer.

4. As the side effect of irradiation, radiation penumonitis or fibrosis is seen on chest X-ray in 2 cases. Cicatrical stenosis due to irradiation is seen in 4 cases. In 3 of these cases, dose at the lesion reached 10,000 rads. In 1 case, 8,000 rads are given. Other side effects are mild.

5. Due to the esophageal atrophy in the axial direction, indentation of the upper part of corpus is occasionally noted on the greater curvature. However, in 2 of 4 cases with such findings, spread of cancer to the upper part of the corpus is responsible.

6. This method is effective in the improvement of subjective symptoms. Dysphagia markedly have been improved in 75%. However, sensation of partial obstruction still remain after irradiation in about 1/2 of cases.

7. Observation and biopsy through fiveresophagoscope is useful in diagnosis and evaluation of therapeutic effect but useless in the examination of the distal end of the stenosis.

8. By biopsy under fiveresophagoscope, the existence of cancer cells have been disappeared in 50, 80 and 100% of each cases with the radiation dose of 6,000, 8,000 and 10,000 rads respectively. By autopsy, the remain of cancer cells are observed in 3 cases treated with 10,000 rads.

9. Among 3 autopsy cases, extension from the primary lesion towards oral side is noted in 1 case, and extension to the distal side is noted in 3, invading upper part of corpus.

10. As above the results, the dose to the lesion of 6,000–8,000 rads are most adequate amount. And it is necessary to attempt the radiation therapy with the field extended upward and downward from the visible cancer lesion and also to the upper part of the stomach.

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