The Korean Journal of Nuclear Medicine
Vol. 19, No. 1, May, 1985

RADIOIODINE TREATMENT OF THYROID CANCER; RESULTS OF 88 CASES

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Radioiodine treatment is one of the effective therapeutic approaches to thyroid cancer although its indication is limited. This report summarizes the results of radioidine treatment at the National Cancer Center Hospital, Tokyo, with some references to the indication.

Selection of Patients for Radioiodine Treatment

Initial procedures before radioiodine treatment usually start with total thyroidectomy followed by several steps as indicated in Fig. 1. After the surgery, scintigrams are taken with a test dose of radioiodine at the range of 1mCi to 10 mCi and patients are selected for radioiodine treatment on the basis of their scintigrams. In some cases, metastatic lesions may become positive on the scintigrams after ablation of thyroidal bed with 100 mCi of I^{131}.

In practice, however, scintigrams are also taken after therapeutic dose, which gives us better images and new information about additional lesions may be obtained. However, accumulations on the radioiodine scintigrams are not always metastases. Therefore, precise judgment of radioiodine scintigrams is very important.

For example, the salivary glands, breasts, stomach, intestine, liver, urinary bladder, and oral

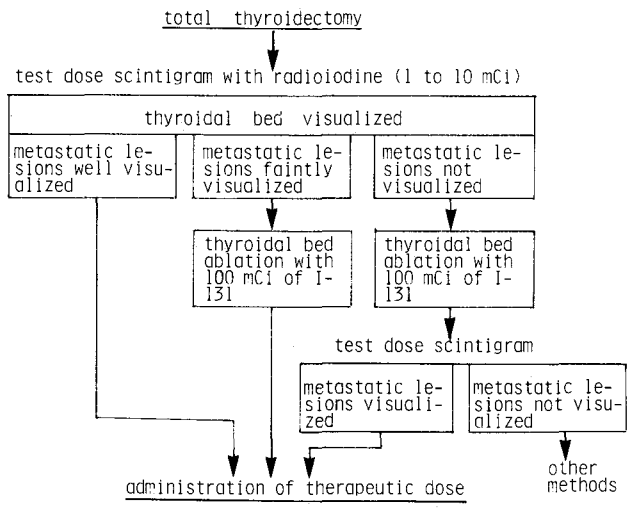


Fig. 1. Procedure of radioiodine treatment.

area have been known to be the area of non-specific accumulations. Besides these non-specific accumulations, there are some other confusing findings which I have experienced. These are a simple asymmetrical accumulation of I^{131} in the parotid gland, a hot spot due to a running nose, a temporary stasis of saliva at the mid portion of the esophagus (Figs. 2a and b), and a hot spot due to rings contaminated with sweat. Furthermore, I experienced one case which presented a hot spot on the left hip which corresponded to the area of old trauma. He had strongly hit this area about 20 years ago, and even at present, 4 years after this test, there is no sign of metasis.

As mentioned here, we have to be aware of these non-specific accumulations in selecting the patients for radioiodine therapy.

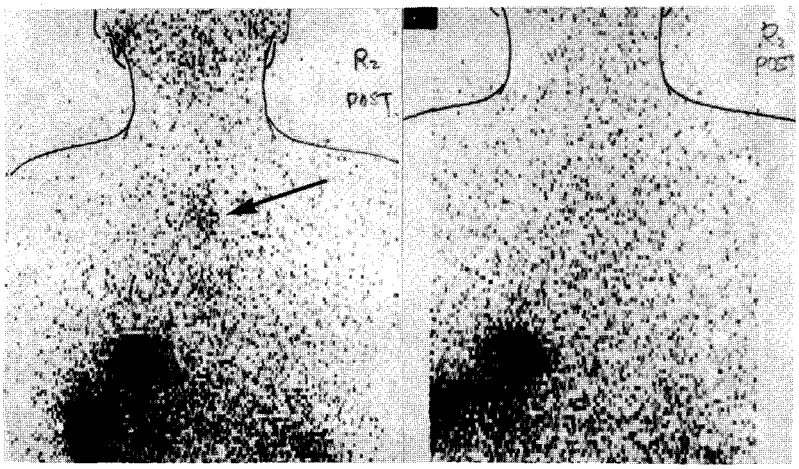
Materials and Results

Since 1962 administration of a large dose of I^{131} was performed to 88 patients.

These patients were divided into two groups; one (Group A) is composed of the patients without known metastases, to whom radioiodine was given only to eradicate the thyroidal bed, and the other (Group B) is composed of the patients with metastases. The reason for giving radioiodine to the patients in Group A is based on the expectation that newly developed metastases can be easily detected on the scintigrams if they ever occur.

As shown in Table 1, twenty patients belong to Group A and recurrence occurred in 4. Out of the four, three had radioiodine scintigram tests but none of them had shown accumulations in the recurrent lesions. At present, therefore, I do not ablate the thyroidal bed with radioiodine unless metastases or recurrences become definite.

The real radioiodine treatment was performed to 68 patients in Group B (Table 2) which includes 19 males, age 11-66, and 49 females, age 6-67. In the early days of this treatment, the dosage of radioiodine was less than the dosage given now. The highest dose at one time was 220



a) Before swallowing water. b) After swallowing 300 ml of water.

Fig. 2. A hot spot due to a temporary stasis of saliva at the mid portion of the esophagus. Scintigram was taken a day after administration of I^{131} (3 mCi).

mCi for males and 238 mCi for females. At present, around 180 mCi is usually given at one time in my place.

The results are shown in Table 3. The therapeutic effects were classified into four categories. "Markedly effective" means a complete disappearance or nearly 80% of shrinkage of the lesions. "Effective" means nearly 50% shrinkage of the lesions. "No response" means less than 25% shrinkage of the lesions. The patients who have failed to follow-up or on whom no test has been done are classified as "judgment indefinite". Changes in clinical symptoms such as neurological signs and findings on test dose scintigrams are also taken into consideration for the classification of patients. For example, in the area where X-ray is impossible the appearance of hot spot on repetitive scintigrams is taken as proof of "no response".

As shown in Table 3, 7 out of 11 patients in the "markedly effective" group are alive and 4 have died, three of them from cancer. Of 30 patients in the "effective" group, 19 are alive and 2 of them now show progression of the disease. Death occurred in 11, 9 of them were from cancer. Of 23 patients in the "no response" group, 9 are alive and 2 of them now show progression of the disease. Death occurred in 14, 11 of them were from cancer.

Investigation of Died Cases

In Group B, 31 deaths occurred as a total. About a half of the deaths was from the "no response" group but some were from the "markedly effective" and "effective" groups as shown in Table 3. Twenty-three out of the 31 cases are known to have died of cancer.

As shown in Fig. 3, the grade of expected therapeutic effect was divided into three categories on the basis of scintigram findings; "effect expected", "effect moderately expected", "effect unexpected". Three cases in this figure have similar metastases to the lungs but their scintigram patterns are different.

Table 1. Group A

Number of patients	20
Appearance of metastases	4/20
Scintigram test	3/4
Accumulation in metastatic lesions	0/3

Table 2. Group B

No. of patients			Age	Dosage (mCi)	Frequency
68	Male	19	11 – 66 (av. 39.7)	50 – 220 (av. 138.7)	1 – 4 (av. 1.7)
	Female	49	6 – 67 (av. 43.6)	30 – 238 (av. 136.0)	1 – 5 (av. 2.0)
	Total	68	6 – 67 (av. 42.5)	30 – 238 (av. 136.7)	1 – 5 (av. 1.9)

Table 4 shows therapeutic effects and survival terms of the 23 patients who are known to have died from the progression of thyroid cancer. There are 10 patients in the "effect expected" group; 3 of them had once shown marked effect, 5 showed comparative effect and 2 showed no change at all. The average survival term of this group was 3.3 years.

In the "effect moderately expected" group, there were 8 patients, the therapies of 4 were judged as effective and the remaining four were considered to be unchanged. The average survival term of this group was 3.5 years.

In the "effect unexpected" group, there were 5 patients; all of them showed no effect and gradual progression to death occurred in all. The average survival term was 1.7 years.

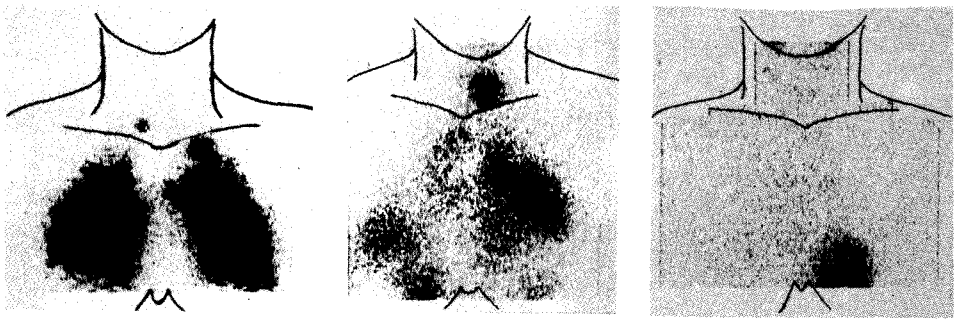


Fig. 3. Three categories concerning the grade of expected therapeutic effect.

Table 3. Therapeutic Effects in Group B

Markedly effective	11		
alive	7		
died	4	died of cancer	3
		died of other disease	1
Effective	30		
alive	19		
died	11	died of cancer	9
		died of other disease	2
No response	23		
alive	9		
died	14	died of cancer	11
		died of other disease	1
		unclear	2
Judgment indefinite	4		
alive	2		
died	2	died of cancer	1
		unclear	1

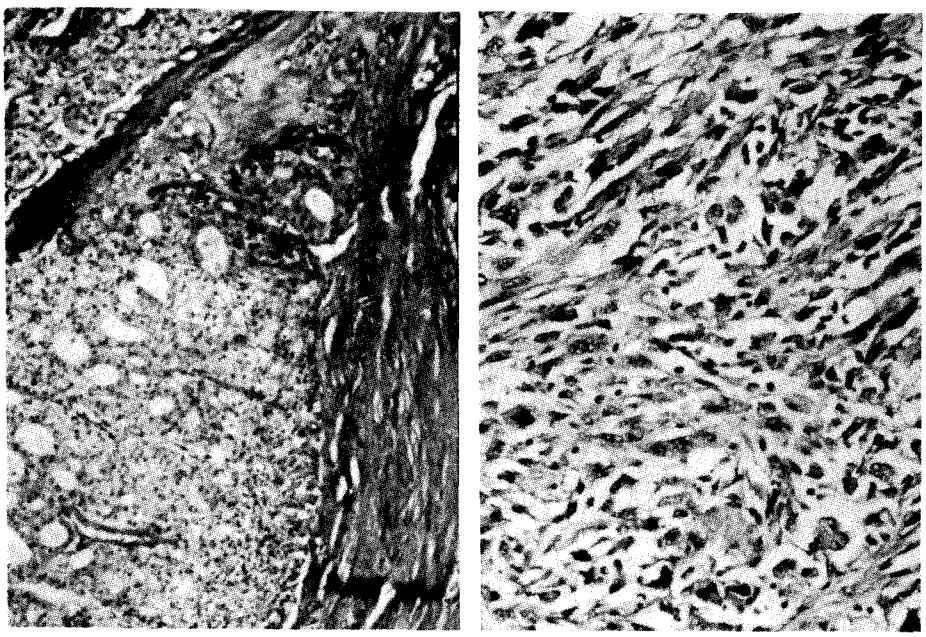
Although it has been pointed out for many years that there might be some connection between radioiodine treatment for thyroid cancer and its anaplastic transformation in the terminal stage, there has been no direct proof.

The results of histological investigation in patients who died from cancer are shown in table 5. As far as the patients whose histological types at their terminal stages were known, are concerned, anaplastic transformation occurred in patients who were classified into the "effect expected" group and "effect moderately expected" groups. However, some others also showed alteration in their histology to some extent.

Fig. 4 shows an example of anaplastic transformation occurred at the terminal stage in one case whose original histology was follicular type.

Table 4. Investigation of Died Cases

Expectancy	No. of patients	Actual therapeutic effect		Survival term	Average survival term
expected	10	markedly effective	3	11 mo – 6 y 9 mo	3.3 y
		effective	5		
		no response	2		
moderately expected	8	effective	4	5 mo – 9 y 3 mo	3.5 y
		no response	4		
unexpected	5	no response	5	9 mo – 3 y 7 mo	1.7 y



(follicular type) (anaplastic type)

Fig. 4. Histological change after radioiodine treatment. See the text.

Table 5. Histological Changes at the Terminal Stage. See the Text.

Original or early stage	Terminal or late stage		Expectancy of therapeutic effect	
papillary carc.	papillary carc.	2	mod. expected	2
papillary carc.	pap. carc. with squamous cell metaplasia	2	unexpected	2
papillary carc.	anaplastic cell carc.	1	mod. expected	1
follicular carc.	papillary carc.	1	unexpected	1
follicular carc.	anaplastic cell carc.	2	expected	2
follicular & pap. carc.	anaplastic cell carc.	1	expected	1
follicular & trabecular carc.	trabecular carc.	2	expected mod. expected	1 1
?	papillary carc.	1	mod. expected	1
?	trabecular carc.	1	unexpected	1

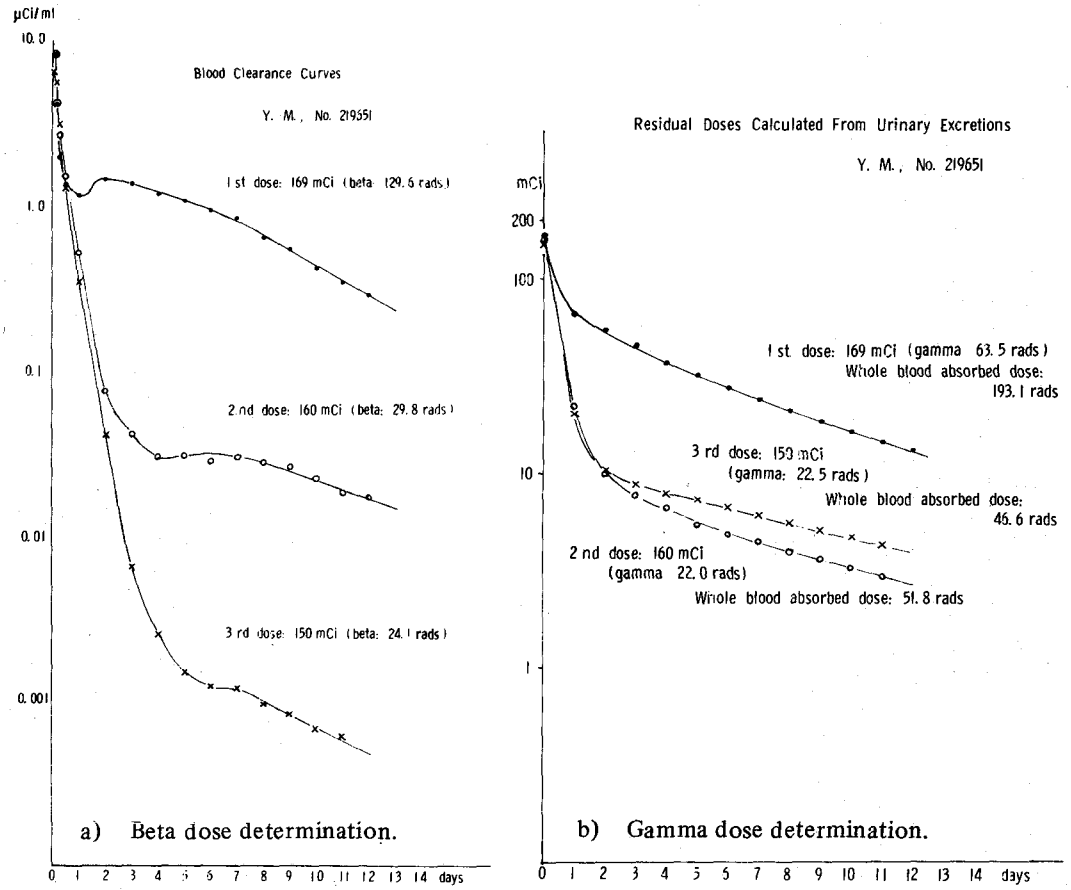


Fig. 5. An example of the estimation of whole blood absorbed dose. See the text.

Whole Blood Absorbed Dose

Since radioiodine therapy results in internal irradiation of the body, the whole blood absorbed dose was calculated as an index to the whole body exposure to radiation. As shown in Fig. 5a, serial blood sampling was done for about 12 days to determine the beta dose. Also, whole urine was collected for nearly 10 days, from which residual radioiodine in the body was claculated to estimate the gamma dose as indicated in Fig. 5b. The sum of the beta dose and gamma dose will be the whole blood absorbed dose.

The Table 6 indicates whole blood absorbed doses in 14 patients together with some other data.

Sequelae of Radioiodine Treatment

In literatures, it has been pointed out that radioiodine treatment might cause undesirable sequelae, such as leukemia, mailignant tumors in other organs, anaplastic transformation as mentioned already, pulmonary fibrosis, bone marrow suppression, etc.

In our study, there were no cases of leukemia, but one case of gastric carcinoma and one case of multiple lipoma in the fat tissue of the abdominal wall were observed. Gastric cancer occurred 15 years after the administration of radioiodine and lipoma occurred 11 years after the dose.

Table 6. Whole Blood Aborbed Doses in 14 Patients.

No. of patients:	14
Dosage:	120 – 220 mCi (average: 178.3 mCi)
Urinary excretion:	
0 – 24 hr:	35.5 – 84.7% (average: 62.7%)
24 – 48 hr:	2.0 – 26.0% (average: 12.2%)
Residual dose at 48 hr:	9.8 – 81.1 mCi (average: 37.2 mCi)
Whole blood absorbed dose:	51.1 – 354.6 rad (average: 147.0 rad) 82.4 rad per 100 mCi

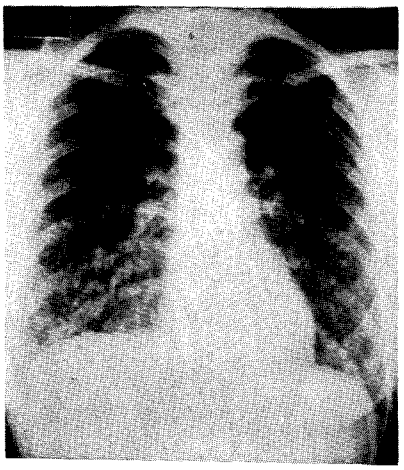


Fig. 6. Before radioiodine treatment.

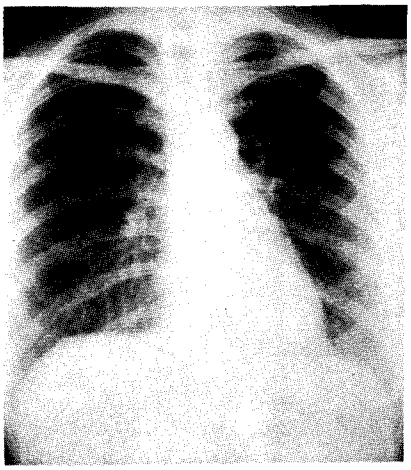


Fig. 7. After radioiodine treatment.

One Representative Case

The case to be presented here is the longest survivor (female) without any sign of recurrence at present. After total thyroidectomy and right side neck dissection, she started receiving therapeutic doses of radioiodine for multiple metastases to the bilateral lungs and the left cervical lymph nodes in 1965 at the age of 29 (Fig. 6). The dose reached 350 mCi as a total within 2 years and all lesions once disappeared on the X-ray film (Fig. 7) as well as on palpation. As seen in Fig. 8, however, a coin lesion did later develop in the right lung, which disappeared 3 months after raising the dosage of triiodothyronine from 62.5 ug per day to 75 ug per day as seen in Fig. 9. Now, she is completely well and enjoying her life.

Fig. 8. Recurrent lesion in the right lung.

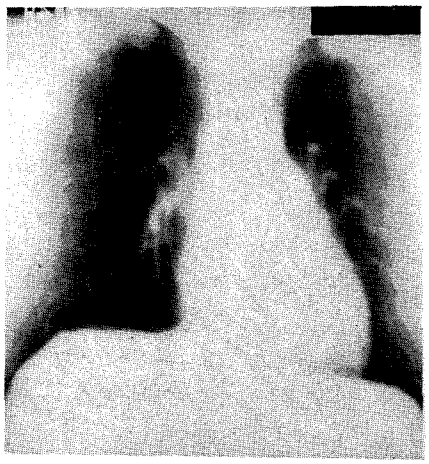


Fig. 9. The recurrent lesion in Fig. 8 disappeared after.

Summary

The results of radioiodine treatment of 88 patients are reported. As in the case presented above, careful follow-up with continuous administration of adequate amount of thyroid hormone is very important. To check whether recurrent lesions have appeared or not, scintigrams with test dose of I^{131}, usually 1 to 10 mCi, are taken in general. However, it is important that there is a fact that administration of much larger dose (30 to 100 mCi) of I^{131} may result in presenting additional lesions on the scintigrams. Recently, clinical usefulness of serum thyroglobulin determination has been mentioned in literatures from the standpoint of follow-up study of patients after radioiodine treatment. Although this technique seems to be valuable, we have to be aware of the possibility of fluctuation of data which may occur in connection with administration of thyroid hormone.

Finally, I would like to say that radioiodine treatment is an effective method for thyroid cancer if patients are adequately selected. However, radioiodine treatment itself is sometimes not enough from the standpoint of radiation dose to the lesions. In such cases, we should not hesitate to consider combination therapy with other modalities. Therefore, in order to overcome this undesirable disease, cooperation between nuclear medicine specialists and other oncologists, such as radiotherapists, is necessary.