Therapeutic Uses of the Radioactive Isotope*

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Introduction

Therapeutic uses of the radioactive isotope can be devided in 3 groups, i.e.

1) Brachytherapy,

2) Multicurie teletherapy and

3) Internal use of naked radioisotopes.

By utilizing their radioactivity, radioisotopes can be well adapted as effective means to radiation therapy. From the beginning of the 20th century, natural radioactive substances, like radium, have been widely used for the purpose of the treatment of cancer and other diseases, and have been giving pretty good effects. In the present case of artificial radioisotopes, their applicable fields are not the same with radium, but reach far out to such broader extents, and larger amounts with varieties almost unthinkable with radium. New fields were also cultivated for application of radioisotopes directly into human body, and thereby to bring out desirable therapeutic effects.

I. Brachytherapy

Main radioisotopes used for brachytherapy are shown briefly in Table 1. And further, using such isotope as Cs-137 or Ir-192, which emits only gamma rays of weak energy, it is very easy to protect the gamma rays to the operator, doctor or nurse.

A. Co-60

Its half-life being of 5.3 years, appling should be based on the calculation, that its monthly decay will be about 1%, and 12% by the year, and in 3 years the decay will be approximately 33%, that is one third. This certainly may appear as a disadvantage, when compared with radium having long life (T=1922 years). But these calculation are simple, and in another hands Co-60 has many advantages than radium. These are:

1. The gamma rays of Co-60 are very strong and homogenous in their energy, and also its intensity is 1.7 times stronger than radium. This characteristic gives better therapeutic effects than radium dose, and further with less side effects.

2. As radium emits strong beta rays (3.0 MeV), so radium is needed an expensive container of platinum, to get pure gamma rays for treatment. But Co-60, according to its weak energy of beta rays (0.3MeV), an aluminum tube or stainless steel sheath would be suffice in clinical application to remove the beta rays. Thus price of containers for Co-60 is extremely lower than the price of radium container.

3. Cobalt has a nature to be attracted to the magnet, even when packed in stainless steel container. So it can be handled with great ease by using electro-magnetical instrument for operation. General speaking Co-60 is applied with much more safety than radium is.

4. Since Co-60 has a stable property in metallic form, Co-60 is applicable to broader

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field than radium, and can be made any desired strength, and moreover can be made into any form, such as beads, pellets etc.

Considering all of these points that have given above, Co-60 can be said to posses a number of superior merits, much in excess of those held by radium.

B. Cs-137

Cs-137 has a half-life of 30 years that is long enough to be out of worring about its decay during several years. Its gamma rays is of 0.66 MeV, about the same with the average energy of 1 MeV x-rays, and much lower than that of radium or Co-60.

The strength of gamma rays of Cs-137 is 3.9 R/hour per 1 mCi at 1 cm, which is about the half of radium's, and is about one third of Co-60's. Beta rays of Cs-137 is of 0.52 MeV, somewhat stronger than Co-60's, but very much weaker than radium's. So removal of beta rays of Cs-137 by filtering is also simple and easy. Cesium as an element is unstable, but can be stabled as oxide or chloride melted into glass. Rods of Cs-137 glass are put into stainless steel sheathes as tubes or needles for using.

C. Ta-182

The half-life of Tantalum-182 is of only 115 days, which is not a long one. Being a metal itself of flexible and stable nature, it is well adapted in clinical practice. Gamma rays of 0.334-1.454 MeV and beta rays of 0.51 MeV are approximately the same to these of Co-60. The strength of the gamma rays is 6 R/hour per 1 mCi at 1 cm, which is a little weaker than that of radium's. Using polyethylen tubing as container, wire or pin of Ta-182 are mostly applied in the afterloading technique.

D. Ir-192

The half-life of Iridium-192 is of 74.4 days, which is much more shorter than Ta-182. Being weak energy of gamma rays, 0.3 and 0.6 MeV, safe-handling for the user can be obtained easily. In the same way by Ta-182, wire or pin of Ir-192 are mostly used in technics of the afterloading.

E. Au-198

The half-life of Au-198 is 2.68 days and it radiates gamma rays of 0.418 MeV and beta rays of 0.963 MeV. The strength of the gamma rays being 5.8 R/hour per 1 mCi at 1 cm. Gold is a stable metal, but because of the stronger energy of the beta rays it is practically used with a coat of platinum. Due to its short half-life of Au-198, Au-198 grains can be used in clinical practice as radon-seeds. Radon-seeds are short cut of gold capillaries containing 1 mCi of radon gas, and are very usefull for interstitial application to cancer and the allied diseases. Because of the weak intensity of gamma rays and its short half-life, Au-198 grain of 4.8 mCi

Table 1. Radioisotopes used for brachytherapy as gamma rays sources

Isotope	Half life	Gamma rays (at 1 cm)		Beta rays Energy(MeV)	Container
		Energy(MeV)	Ir(R/h-mCi)		
^{226}Ra	1,620 y.	0.3~2.4	8.4	1.0~3.4	Pt. tube, needle
^{60}Co*	5.3 y.	1.33, 1.17	13.5	0.3	Stainless steel tube, needle, beads
^{137}Cs	30 y.	0.66	3.9	0.8	Glass tube, needle
^{182}Ta*	115 d.	0.1~1.5	6.8	0.5	Wire Pin
^{192}Ir*	74.5 d.	0.3~0.6	4.8	0.7	Wire Pin
^{198}Au*	2.68 d.	0.62	2.3	0.95	Grain

Isotopes with *mark are metal itself.

Table 2. Survival rate of cancer of the tongue treated with implantation of Ra-needles

Stage	No. of cases	Survived more than	
		3 years	5 years
Stage Ⅰ	22	20 (91%)	19 (86%)
Stage Ⅱ	49	42 (86%)	37 (76%)
Stage Ⅲ	22	12 (55%)	11 (50%)
Stage Ⅳ	97	19 (20%)	14 (14%)
Total	190	93 (49%)	81 (43%)

in each will equal to radon-seeds of 1 mCi.

From our experience cure rate of cancer of the tongue treated with Ra-needling is shown briefly in the Table 2. 5 years cure rate on the total cases is 42%, and on the operable case (stage I and II) is 75%, about 3 times higher than those treated with radical operation.

Recent advance in this field is the afterloading technique. After-loading is very profitable not only to obtain exact irradiation, but also to handle it quite safely.

Ⅱ. Mulitcurie Teletherapy

Recently 1000~3000 Curie of Co-60 has been commonly used as the source of teletherapy. As specific activity of Co-60 being rapidly highing up, sources of 160-360 Curie per g in specific activity are used widely. Therefore diameter of the source should be 1~1.5cm, and the half-shadow decreased apparrently, and with the advance of equipment in its accuracy, effectiveness of multicurie teletherapy showed remarkable progress.

Among supervoltage radiation therapy, the tele-cobalt-therapy is most widely used, because of rather cheeper price and having reasonable property of gamma rays in their energy and homogenity.

The beneficial points of supervoltage radiation therapy are as the followings;

1. decrease of the skin reaction according to small absorbtion in superficial tissues,
2. homogenous irradiation in every tissue without the shadow,
3. higher depth dose depends upon strong penetration,
4. slightness of side scattering,
5. possibility of exact irradiation due to accuracy of the equipment, and decrease of half shadow, which can be obtained using smaller sized source.

From our experience comparison between conventional x-rays and tele-cobalt therapy was made, and some of the results in survival rate are shown in Table 3-5, and in Fig.1-3,

Table 3. Survival rate of irradiated patients with cancer of the larynx, classified according to the stages

(A) Co-60 teletherapy

Stage	No. of cases	Survived more than				
		1 year	2 years	3 years	4 years	5 years
Ⅰ	23	23 (100%)	21 (91%)	20 (87%)	20 (87%)	20 (87%)
Ⅱ	98	73 (74%)	59 (60%)	52 (53%)	46 (47%)	44 (45%)
Ⅲ-Ⅳ	57	30 (53%)	21 (37%)	18 (32%)	17 (30%)	17 (30%)
Total	178	126 (71%)	101 (57%)	90 (51%)	83 (47%)	81 (46%)

(B) Conventional X-ray therapy

Stage	No. of cases	Survived more than				
		1 year	2 years	3 years	4 years	5 years
I	8	7 (88%)	7 (88%)	6 (75%)	5 (62%)	5 (62%)
II	38	16 (42%)	13 (34%)	13 (34%)	12 (32%)	10 (26%)
III-IV	16	5 (31%)	3 (19%)	2 (13%)	2 (13%)	2 (13%)
Total	62	28 (45%)	23 (38%)	21 (34%)	19 (31%)	17 (27%)

(C) Radium therapy by modified Harmer's method

Stage	No. of cases	Survived more than				
		1 year	2 years	3 years	4 years	5 years
I	56	56 (100%)	56 (100%)	56 (100%)	54 (97%)	51 (91%)
II	24	23 (96%)	22 (92%)	21 (87%)	21 (87%)	21 (87%)
III-IV	7	4 (57%)	3 (43%)	2 (29%)	1 (14%)	1 (14%)
Total	87	83 (96%)	81 (93%)	79 (91%)	76 (88%)	73 (84%)

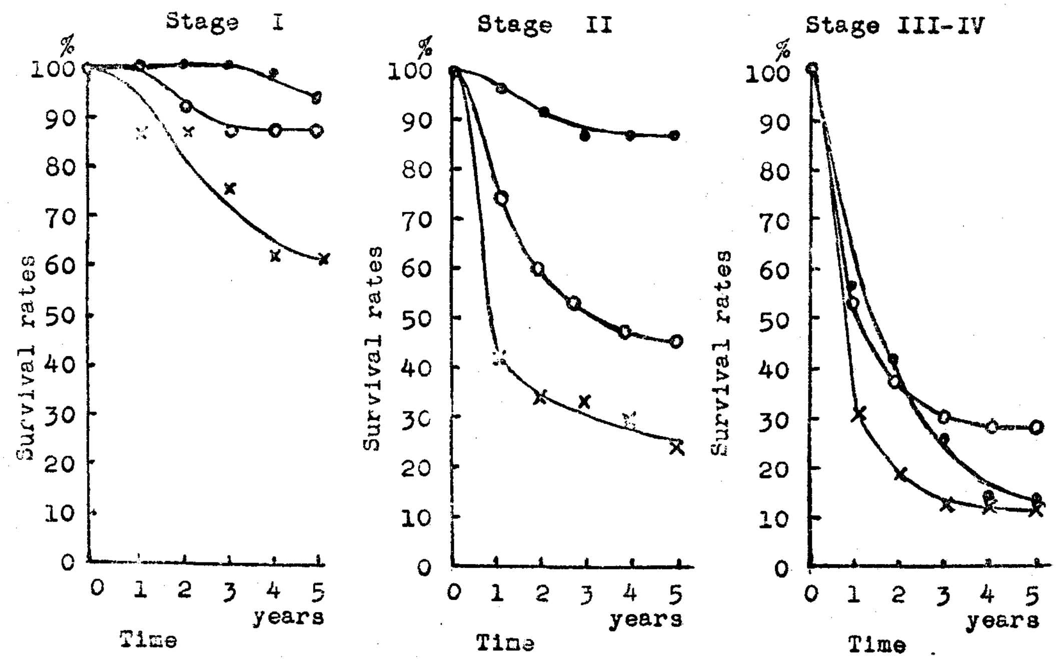

Fig. 1. Survival rates of irradiated patients with cancer of the larynx classified according to the stages.

○ Co-60 teletherapy, × Conventional X-rays, ● Radium, interstitial.

Table 4. Survival rates of irradiated patients with cancer of the pharynx.

(A) Co-60 teletherapy.

Site	No. of cases	Survived more than				
		1 year	2 years	3 years	4 years	5 years
Epipharynx	21	11 (52%)	6 (29%)	4 (19%)	3 (14%)	3 (14%)
Mesopharynx	19	13 (68%)	10 (53%)	8 (42%)	8 (42%)	8 (42%)
Hypopharynx	23	5 (22%)	3 (13%)	3 (13%)	3 (13%)	3 (13%)
Total	63	29 (46%)	19 (30%)	15 (24%)	14 (22%)	14 (22%)

(B) Conventional X-ray therapy.

Site	No. of cases	Survived more than				
		1 year	2 years	3 years	4 years	5 years
Epipharynx	9	4 (44%)	2 (22%)	1 (11%)	1 (11%)	1 (11%)
Mesopharynx	9	5 (55%)	3 (33%)	3 (33%)	2 (22%)	2 (22%)
Hypopharynx	11	2 (18%)	1 (9%)	1 (9%)	0 (0%)	0 (0%)
Total	29	11 (38%)	6 (21%)	5 (17%)	3 (10%)	3 (10%)

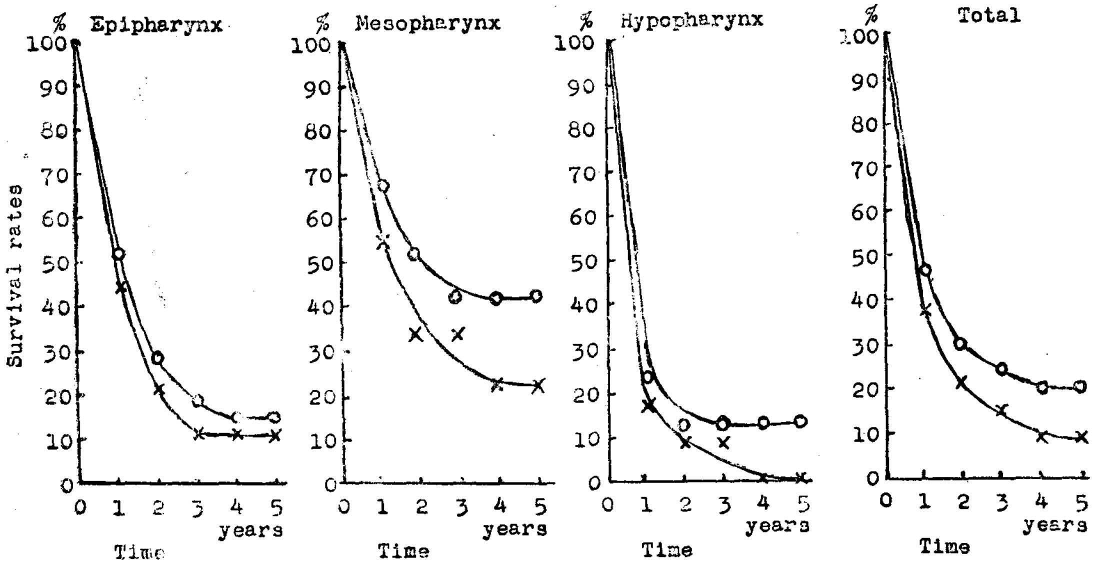

Fig. 2. Survival rates of irradiated patients with cancer of the pharynx.

○ Co-60 teletherapy, × Conventional X-rays.

Table 5. Survival rates of irradiated patients with cancer of the lung.

(A) Co-60 teletherapy.

Stage	No. of	Survived more than				
		1 year	2 years	3 years	4 years	5 years
I - II	49	17 (35%)	11 (22%)	9 (18%)	7 (14%)	6 (12%)
III - IV	56	19 (34%)	10 (18%)	6 (11%)	3 (5%)	2 (4%)
Total	105	36 (34%)	21 (20%)	15 (14%)	10 (10%)	8 (8%)

(B) Conventional X-ray therapy.

Stage	No. of cases	Survived more than				
		1 year	2 years	3 years	4 years	5 years
I - II	35	10 (29%)	5 (14%)	4 (11%)	3 (9%)	2 (6%)
III - IV	29	6 (20%)	2 (6%)	1 (3%)	0 (0)	0 (0)
Total	64	16 (25%)	7 (11%)	5 (8%)	3 (5%)	2 (3%)

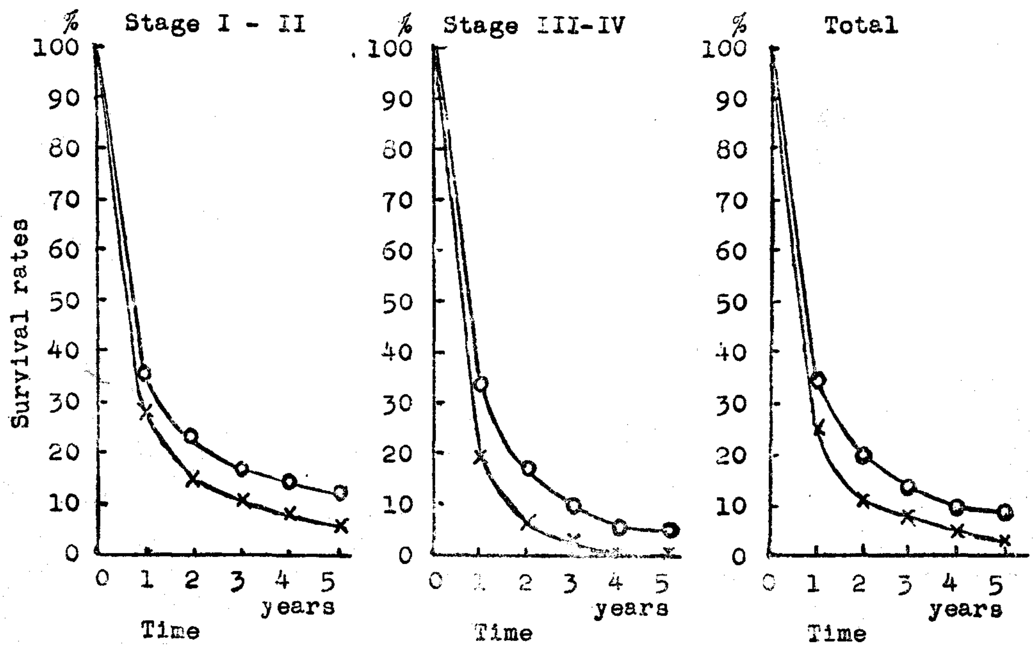

Fig. 3. Survival rates of irradiated patients with cancer of the lung.

○ Co-60 teletherapy, × Conventional X-rays.

It is clear that about 10% level-up in 5 years survival rate is obtained in tele-cobalt-therapy, and it is more evident in advanced cases. And in early stage cases results of Ra-therapy is still more excellent compared to telecobalt, so we should not be forgotten the brachytherapy.

Ⅲ. Internal Application of Radioisotopes

As radioactive isotopes are taken directly into the human body by injection or ingestion, therapeutic effects will increase in accordance with the degree of the affinity between the isotope and the selective tissue or organ that is the objective of the therapy. Such treatment often need to take considerably large amounts of isotope, and moreover that isotope itself possessed strong radioactivity special caution should be paid throughout the administration.

A. General notice to be taken

1. Half-life. As isotope is often used in large quantities special notice must be taken of its half-life. For internal administration isotopes of 12 hours to 15 days are mostly considered suitable. But if the half-life is too short, therapeutic effects will diminish due to the sudden decreasing of the activity. On the other hand if an isotope with a long half-life is administered, the patient will have to receive from inside the radiation for a long period of time, which will cause various radiation injuries. To come down to 10 % of the initial activity, it takes about 4 times of the half-life period. Beside there is a limit to the usefulness of isotopes according to the length of half-life. Therefore one must constantly keep in mind the possibility of a long lived concomitant being present.

2. Chemical property. The chemical property of an element and its composition should be well known, since in the production of many isotopes considerable amounts of radioactivity due to trace of impurities are frequently present. The separation of the desired element must be capable of being effected. It is difficult to eliminate categorically the possibilities of their future use since with the advent of isotopes themselves the necessity of improving our state of knowledge concerning the chemistry of the rarer elements had been recognized. For the time being, however, we must restrict ourselves pretty generally to the use in therapy of those elements whose chemistry is either relatively simple or well understood.

3. Biological behavior. The biological behavior of the material to be used should be well established since its distribution in the body, its rate of excretion, and its effectiveness from a viewpoint of localization are intimately tied up with such behavior. From the physical half-life and the biological half-life of the body or organ, the effective half-life, which acts actually there, will be calculated from the formula:

$$T\ eff=\frac{T\times Tb}{T+Tb}$$

Some isotopes, such as $^{24}NaCl$, $^{3}H_2O$ etc., distribute relatively homogenous through the whole body. On the other hand, another isotopes have special affinity to selective organs or tissues. For examples, there are special affinity between following groups:

I-131 and thyroid gland, Ca-45, 47, Sr-85, 89, 90 and bone or teeth, Fe-55, 59 and hemoglobin of erythrocytes. Distribution of P-32 in the body is very complicated. As for inorganic salt, Ca.phosphate, its uptake in bone and teeth is very high, and as for organic compounds, nucleoprotein, it is collected to the nuclei of body cells, and further it is taken as phospholipid in liver and other organs. Thus, if we know the uptake rate of the isotope to the objective organ (C), the tissue dosage of beta rays (D_β) and gamma rays (D_γ) is determined roughly from the equation:

$$D_\beta=73.8\,E_\beta TC\ \text{(rads)}$$

$$D_\gamma=1.44t.I_\gamma.10^{-3}gC\ \text{(R)}$$

where E_β=mean energy of beta rays (MeV)

I_γ=intensity of gamma rays(R/hour per mCi at 1 cm)

Table 6. Diseases effective to the treatment with internal administration of radioisotopes and the methods

Disease	Methods	Radioisotope	Dose
Chronic leukemia Polycythemia vera	Intravenous injection	$Na_2H^{32}PO_4$ $^{24}NaCl$ ^{198}Au-colloid	3~ 5 mCi 1~30 mCi 1~30 mCi } several times
Hyperthyroidismus Struma maligna	Oral administration	^{131}I	3~ 15 mCi 1~3 times 30~100 mCi several times
Carcinomatous effusion	Intra-cavital injection	^{198}Au-colloid Pleura Peritoneum ^{177}Lu-colloid Pleura Peritoneum	30~ 70 mCi 50~100 mCi 30~ 50 mCi 50~ 70 mCi } several times
Metastatic carcinoma	Intra-tumoral injection	$Cr^{32}PO_4$ $^{90}YCl_2$-colloid	10~ 15 μCi per g tissue

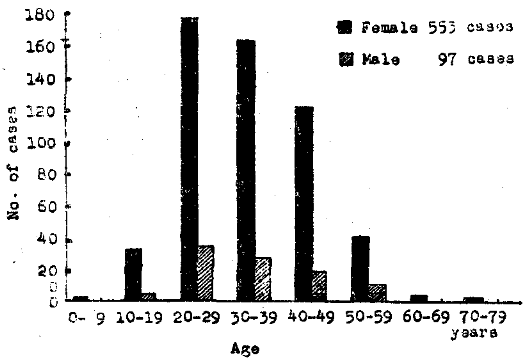

Fig. 4. Age and sex of the hyperthyroidism.

Half-life=T (days)=t (hours)

g is the factor relating to the size of organ.

4. Toxicity. If the element under condition is toxic, specific activity becomes important in keeping the dosage of material within usual limits. For example, Y-90 as produced by an n-γ reaction of Y-89 in the pile does not represent a satisfactory isotope for therapeutic use since this element is extremely toxic and specific activities are not high enough to allow its use when made by this reaction. However, the same isotope may be obtained by beta decay from Sr-90 with subsequent seperation in a resin-exchange column and in this manner carrier-free, or nearly so, material may be obtained and hence used in non-toxic state.

5. Safe handling. For the internal use of radio-isotope in the treatment, fairly large amounts should be given, cautions are necessary to prevent the contamination by all means. Patients, who are given therapeutic dose of radioisotopes internally, will excrete the isotope in their secreting fluids and excretions, mostly in urine and feces. So we should have special sink and toilet connected with special waste disposal units in the ward for isotope treatment.

B. Main radioisotopes used to internal administration for treatment.

The radioisotopes used to internal administration for treatment are rather limited, and can be briefly summarized in Table 6. From our experience some results will be shown in the followings.

Treatment of the hyperthyroidism with radioactive Iodine-^{131}I.

The effectiveness of ^{131}I on therapy of the hyperthyroidism had been well known for a long time. Therapeutic dose of ^{131}I in cases of the hyperthyroidism will be determined from the following formula.

$$D\beta+\gamma=15\frac{U.A}{M}T=120\frac{UA}{M}\cdot\frac{Teff}{8}(\text{rads})$$

Where U=uptake rate of ^{131}I in the thyroid,
M=weight of the thyroid,
A=administration dose.

As Teff=6 days: $D\beta+\gamma=90\frac{UA}{M}(\text{rads})$

$$A=\frac{D}{90}\cdot\frac{M}{U}(\text{mCi})$$

As to irradiate 10000 rad: A=110 M/U
As to irradiate 7000 rad: A=880 M/U
As the first trial of treatment, our intended dose was usually 7000 rad.

650 cases of the hyperthyroidism were treated with ingestion of ^{131}I. Female 553 cases(85%), Male 97cases (15%). The age incidence was as follows: 0–9 years 2 cases (0.3%), 10–19years 39 cases (6%), 20–29 years 215 cases (33%), 30–39 years 199 cases (31%), 40–49 years 140 cases (21.5%), 50–59 years 49 cases (7.5%), 60–69 years 6 cases (1%). Though younger patients should be given smaller dose, all patients were treated with ^{131}I, except those pregnant. Side effects of ^{131}I treatment were very few. Main symptoms were very responsive to ^{131}I treatment and their reduction and disappearance occured between a few weeks to few months in most of cases, as shown in Table 7.

Exophthalmos is only one symptom, which is very difficult to cure. I divided the patients with hyperthyroidism in two groups according to the duration between onset of the disease and ^{131}I treatment, namely less than 5 years and more than 5 years. Results of exophthalmos by ^{131}I treatment were as shown in Tab. 8 and the Fig. 6. In early state cases (less than 5 years) disappearance of the exophthalmos was seen in rather high percentage compared to late stage cases. Serum from the blood of patients was taken, and 1ml of the serum was injected

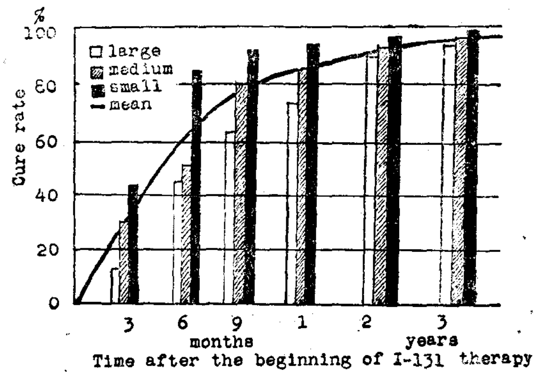

Fig. 5. Disappearance of struma in cases of the hyperthyroidism with I-131 therapy.

Table 7. Chief symptoms of hyperthyroidism and the effects of treatment with ^{131}I

Symptoms	No. of cases	Recovered perfectly	Improved	No change
Struma	632 (97%)	612 (97%)	7 (1%)	13 (2%)
Heart beating	578 (89%)	518 (99.5%)	0	1 (0.5%)
Tremor of hands	454 (70%)	453 (99.7%)	1 (0.3%)	0
Tremor of eyelids	369 (57%)	367 (99.4%)	1 (0.3%)	1 (0.3%)
Decrease of body weight	486 (75%)	476 (98%)	10 (2%)	0
Hyperidosis	504 (78%)	504 (100%)	0	0
Exophthalmos	178 (28%)	87 (48%)	40 (22%)	51 (29%)
Nervous symptoms	467 (72%)	415 (89%)	42 (9%)	10 (2%)

Table 8. Effects of ^{131}I-treatment on the exophthalmos of patients with hyperthyroidism divided from duration between onset of the disease and I-131 therapy

Course of the disease	Cure rate at the time from beginning of ^{131}I therapy				
	3 months	6 months	1 year	2 years	3 years
Diffuse type					
less than 5 years	20%	40%	70%	78%	80%
more than 5 years	10%	30%	50%	60%	62%
Nodose type					
less than 5 years	5%	25%	80%	86%	84%
more than 5 years	2%	10%	25%	25%	25%

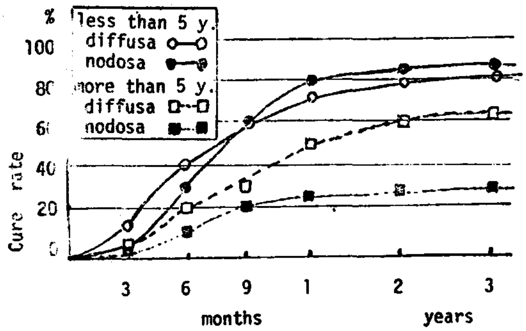

Fig. 6. Curability of exophthalmos in cases of the hyperthyroidism treated with I-131.

into the peritoneum of gold fish. If exophthalmos produced substances (it is said as hormons of the hypophysis) is present in it, exophthalmos will be produced within 1-2 days to the fish. This substances are found only in early stage cases and can not be found in late stage cases. In cases, whose serum contains the exophthalmos producing substances, curability of exophthalmos can be expected, and further, irradiation to the hypophysis of the patient is very effective to cure the exophthalmos.

Electrocardiographic examinations were made on several cases, and some important changes were observed, as shown in the Fig. 7. Tachycardia existing in almost every cases before treatment, and other disorders before treatment disappeared after treatment. However myocardiac injuries were found in certain cases before the treatment and curable, but in some of the other cases they appeared only after the treatment, when they were untraceable in the beginning. It seemed to be rather late appearing signs. As similar late appearing symptoms, there are fall of the hair, exophthalmos, nervous symptoms and others.

Except the exophthalmos curability of the hyperthyroidism by treatment of ^{131}I was very high as shown in Table 10 from our experience. In about 90% of cases perfect cure was obtained. As side effects of ^{131}I treatment, appearance of hypothyroidism should be carefully noticed. From our experience hypothyroidism was seen in 5% in early time after the treatment, which was disappeared spontaneously within 1 year. While chronic hypothyroidism was appeared in about 5% of cases after interval of several years, which is very difficult to cure.

Important notice should be taken on the effective half life, which was scattered in a broad range of values from 2~8 days, indicating the importance of measuring this pattern parameter in order to estimate the dose to be administered (Siehe Fig. 8). Fig. 9 shows the absorbed dose of I-131 in the first trial of the

Table 9. Electrocardiographic changes in cases of the hyperthyroidism treated with ^{131}I.

Electrocardiographic findings	No. of cases	Before the treatment	After the treatment
Myocardial damage	37	20	24
Sinus tachycardia	30	29	8
Sinus bradycardia	3	0	3
Respiratory arrhythmia	3	1	2
Supraventricular extrasystole	2	2	1
Ventricular extrasystole	4	4	1
Atrial fibrillation	2	2	2
Atrioventricular block	4	2	2
W.P.W. syndrome	2	1	1
Pulmonary P.	8	8	2
Mitral P.	2	2	1
Right ventricular load	4	4	0
Myocardial infarction	1	0	1
Total	102	75	48

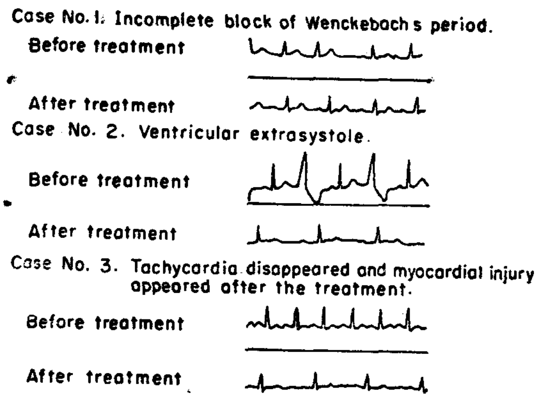

Fig. 7. Electrocardiograms of hyperthyroidism before and after I-131 treatment.

treatment. Although our intended dose was 7000 rads, the dose actually absorbed varied widely, 2000-12000 rads, and the mean value was 7300 rads. It was also shown that the patients with subsequent hypothyroidism received much higher absorbed dose over the expected dose than

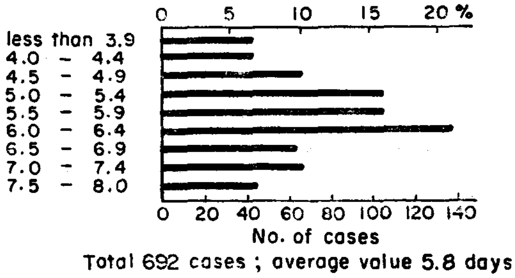

Fig. 8. Effective half-life of I-131 in the thyroid gland of hyperthyroidism.

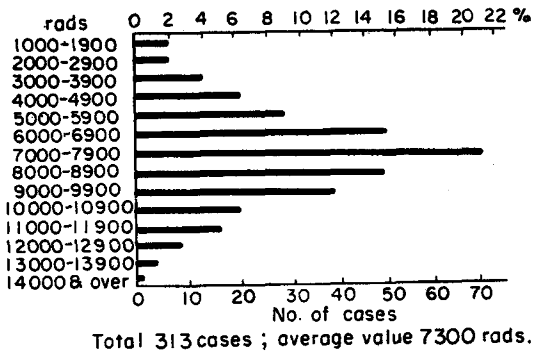

Fig. 9. Absorbed dose(rads) of I-131 in the thyroid gland at the first treatment.

Table 10. Results of treatment of hyperthyroidism with ^{131}I

	Results	1 year	2 years	3 years	5 years
Struma diffusa	Cured perfectly	560 (92%)	423 (97%)	165 (93%)	72 (89%)
	Improved	13 (2%)	9 (2%)	6 (3%)	0
	No effect	2	1	1	0
	Recurrence	2	1	0	0
	Hypothyroidism	30 (4%)	0	0	5 (6%)
	Died	3	1	1	0
	Failed to follow	0	0	5 (3%)	4 (5%)
Struma nodosa	Cured perfectly	30 (75%)	20 (95%)	6 (100%)	4 (100%)
	Improved	6 (15%)	1 (5%)	0	0
	No effect	3 (8%)	0	0	0
	Recurrence	0	0	0	0
	Hypothyroidism	1 (2%)	0	0	0

Table 11. Late effects after I-131 treatment of hyperthyroidism

Diseases	No. of cases
Chronic hypothyroidism	12
Nervous symptoms	4
Struma nodosa(Adenoma, benign)	10
Adenocarcinoma	1

those cured without hypothyroidism.

Cancer of the thyroid gland

In some cases of the thyroid gland, uptake rate of ^{131}I in the tumor shows very high, and hot nodules can be seen in the scintigram. Such cases are mostly histopathologically follicular adenocarcinoma, and can be expected splended effects of ^{131}I treatment giving large amounts of it. Recently combined with thyroidectomy or application of thyroid preparations or TSH-hormone, all kinds of thyroid cancer could be effective to ^{131}I.

Table 12. Results of combined treatment with ^{131}I and others on the cases of malignant struma

Authers	No. of cases	^{131}I given	Thyroid-ectomy	Thyroid-prepar.	TSH	Living	3 year living	5 year living
Kramer 1955 (Royal Marsden)	48	12	11	3	0	5	75%	17%
Russo 1955 U. Oklahoma)	41	13	13	0	1	7	39%	31%
Bejerwates 1956 (U. Michigan)	—	57	31	0	0	33	85%	15%
Maloof 1956 (Mas. Gen. H.)	190	21	15	14	0	13	34%	38%
Sheline 1957 (Montefiole H.)	124	18	15	6	15	8	50%	39%
Halnan 1957 (Univ. London)	123	76	0	14	0	57	78%	22%
Catz 1959 (U.S. Calif.)	44	44	33	0	44	10	55%	34%
Blahd 1959 (U.C.L.A.)	63	26	25	1	25	10	67%	55%
Rose 1963 (A.D. Anderson)	69	69	41	20	5	54	68%	50%

Table 13. Treatment of malignant struma with ^{131}I

Authors	Papillary adeno-ca.	Follicular adeno-ca.	Others	Total
Beierwalts (Michigan U.)	11 : 0 (0%)	5 : 3 (60%)	—	16 : 3 (19%)
Pochin (London U.)	—	7 : 5 (71%)	—	7 : 5 (71%)
Rose, Kelsey (Anderson H.)	10 : 7 (70%)	23 : 19 (83%)	4 : 1 (25%)	37 : 27 (73%)
Yamashita (Keio Univ.)	—	20 : 4 (20%)	—	20 : 4 (20%)
Total	21 : 7 (33%)	55 : 31 (64%)	4 : 1 (25%)	80 : 39 (53%)

In table 12, reports of such treatment are summarized, and it seemed that relatively good results can be obtained with the combined ^{131}I treatments. 5 years survival rates of malignant struma treated with large doses of ^{131}I showed in Table 13 divided from histological findings. It is said that most effective ones are follicular types, but the others are also efficacious.

Treatment of Malignant Disease with Radiocolloids

Application of colloidal radioisotopes is very important in the treatment of cancer and allied diseases. The principal ones of these are $^{32}Cr\ PO_4$, ^{198}Au-colloid, $^{177}LuCl_2$, $^{90}YCl_2$ etc.

Chromium Phosphate, $^{32}Cr\ PO_4$

Colloidal suspesion of $^{32}CrPO_4$ was injected into the tumor or in the surrounding area at the dose of 10~15mCi per 1 g of tissue to be distributed homogenously. In most of cases decrease of the tumor was observed, and in histopathological examinaitons degenerative changes, such as pyknosis, vacuolar degeneration, giant cell formation etc., began to appear after 2 weeks and in the third week increasing of necrosis and fibrosis in surrounding became evident. Clinical experience showed that the tumors were gradually shrinking, and in the best cases the tumors disappeared perfectly as is shown in the Table 14.

Radioactive gold, ^{198}Au-colloid

Sterilized colloidal solution of ^{198}Au for medical use can be easily obtained. The most effective applications are intracavitary injection for carcinomatous effusions of the pleura or peritoneum. Adequate dose for pleural cavity is 30~70mCi, and for the abdominal cavity 50~100 mCi. The treatment is repeated several times at the interval of 2~4 weeks. In some cases good results were obtained as prolongation of life with remarkable clinical palliation, as shown in Table 15. One year remission in 10%, and 3 years remission in 7%.

Radioactive lutecium, $^{177}LuCl_3$

^{177}Lu is obtained by neutron bombardment of natural Lu in the pile, and has half-life of 6.7 days, emitting beta rays of 0.495~0.17 MeV and gamma rays of 0.112~0.318 MeV. $^{177}LuCl_3$ as solution can be rendered into colloidal states connected with protein and others. Because of the adequate half-life and the chemical properties ^{177}Lu is gradually used widely, and is obtained good results treatment of cardinomatous effusions, giving 30~100 mCi. Results of our clinical experience are summarrized briefly in

Table 14. Effects of intratumoral injection of colloidal $^{32}CrPO_4$

Histological findings	No. of cases	Decreased in size	Disappeared
Adenocarcinoma	9	9 (100%)	4 (44%)
Squamous cell carcnioma	19	19 (100%)	10 (53%)
Carcinoma simplex	24	21 (87%)	6 (25%)
Total	52	49 (94%)	20 (38%)

Table 15. Results ef treatment of the carcinomatous effusions of pleural and peritoneal cavities with colloidal ^{198}Au or ^{177}Lu

Isotope	Location	No. of cases	Little effect	Effective and lived more than				
				3 mon.	6 mon.	1 year	3 years	5 years
^{198}Au	Pleural cavity	60	21 (35%)	39 (65%)	24 (40%)	9 (15%)	5 (12%)	2 (11%)
	Periton. cavity	65	44 (68%)	21 (32%)	12 (19%)	3 (5%)	1 (2%)	1 (3%)
	Total	125	65 (52%)	10 (48%)	36 (29%)	12 (10%)	6 (7%)	3 (7%)
^{177}Lu	Pleural cavity	12	2 (17%)	10 (83%)	6 (50%)	2 (17%)	1 (8%)	—
	Periton. cavity	8	4 (50%)	4 (50%)	2 (25%)	1 (13%)	0	—
	Total	20	6 (30%)	14 (70%)	8 (40%)	3 (15%)	1 (5%)	—

Table 16. Results of ^{198} Au-treatment on pleural and peritoneal effusions divided from primary sites of the carcinoma

Primary site	No. of cases	Pleural cavity	Peritoneal cavity	Total
Ca. of breast	49	49 : 34 (70%)	—	49 : 34 (70%)
Malig. endometriom.	7	7 : 3 (43%)	—	7 : 3 (43%)
Ca. of ovary	30	—	30 : 15 (50%)	30 : 15 (50%)
Ca. of stomach	25	—	25 : 3 (12%)	25 : 3 (12%)
Ca. of liver	5	—	5 : 2 (13%)	5 : 2 (13%)
Ca. of uterus	2	—	2 : 0 (0%)	2 : 0 (0%)
Others	7	4 : 2 (50%)	3 : 1 (33%)	7 : 3 (43%)
Total	125	60 : 39 (65%)	65 : 21 (33%)	125 : 60(48%)

Table 15.

$^{90}YCl_2$ Radioactive yttrium

Carrier-free $^{90}YCl_2$ is separated by milching apparatus of $^{90}SrCl_2$ solution using positive ion-exchange resin by washing with 5% ammonium citrate solution at any time when it needs. $^{90}YCl_2$ has a half-life of 2.68 days, emitting only a beta rays of 2.24 MeV in its energy. $^{90}YCl_2$ has a similar property as ^{177}Lu chloride and can be used as colloidal solution in clinically.

Radioactive gallium, ^{67}Ga-citrate

^{67}Ga has a half-life of 3.24 days, emitting only gamma rays of 0.1~0.39 MeV in their energy. Gallium is not only one of the bone-seaker, but also has a tendency to be gathered in some of the tumor, when it was given as citrate. According to adequate half-life its therapeutic use is expected, but the clinical experience has not been performed.

Conclusion

Therapeutic uses of the radioactive isotope are briefly explained from our experiences. Necessary use of large amounts of radioactive isotopes special cautions should be needed for handling of them, and special medical care should be paid for the patients treated with them. But extremely exellent results are obtained already in various fields, and it is not exaggeration to say that new fields of the treatment are still promised to be cultivated by many splendid investigators in the near future.

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