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# Pre-Operative Irradiation Therapy for Cancer

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## 癌の術前照射法

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癌の外科侵襲に先立つて放射線の術前照射を行い癌細胞の発育転移を抑制しおき、次いで之を摘出して癌の手術成績の向上を計り、更に手術適応の拡大を狙つて「癌の手術に当つては術前照射を行いましよう」と提唱して来た。

担癌個体に関する著者の放射線生物学的研究の結論から放射線照射は主癌のみに与え、担癌個体の臨床諸症を勘案しつゝ皮膚表面量凡そ 3,000r を目標に照射し、放射線照射による個体の抗癌態勢の確立を確認したる時期即ち私の研究並に経験からは照射終了後1~2週間の間隔をおいて手術的侵襲を加えるのである。本論文に於ては私の担癌個体に於ける生物学的研究成果を紹介しその術式を解説し、癌の治療は放射線治療を枢軸として一貫して行われるべきことを提唱し、今日迄種々杞憂された術前照射の害は全く見られざるのみならず着々著効を収めつゝあり。

### Summary

This is an introduction to a new technique by pre-operative application of intensive irradiation to cancer in order to destroy the cancer focus, surgical intervention and thorough post-operative irradiation after sufficient removal of lymphatic glands.

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#### 1. Foreword

It is a well known fact that in recent years the surgical treatment of cancer has gradually begun to produce favorable results. However, since this depends greatly on early

detection and early surgical treatment, many scholars do not necessarily feel certain that surgical treatment has progressed.

This author also fully realizes how difficult the treatment of cancer is because there are not a few cases which are fatal and unmanageable according to their type and the site.

The author has sent approximately 120 to 150 gastric cancer patients for surgical intervention yearly during the past few years. A compilation of the post-operative courses shows that there are cases of certain types or cases beyond certain degrees of advancement for which hope of survival for even half a year could not be considered possible about ten or twenty years ago, but are now able to live for one to two years or may be longer. No matter how we may attempt to minimize the results, we must admit that more than fifty percent of the total cases have shown definite results of progress. What is the reason for the favorable results? Why during a long period of time has not a recurrence occurred? Where were these cancer cells during this period of inactivity? These are problems that are always thought about and are yet left unsolved. At any rate, it is believed to be of utmost importance to determine clinically by analysis the cause for the satisfactory results. To the question as to what has brought about this progress, one must first of all give the improvement in the technics of the surgeon. However, it is evident that the correlation of many factors, such as advancement in anesthetic methods, popularization of blood and other fluid transfusions, application of anti-cancer substances, improvement and abundance of medical supplies and equipment, and improvement of hospital facilities and environments are responsible for the progress. It may be said in short that the progress achieved has been based on the consolidated effects of these factors. This author is one of those who recognizes the recent progress and improvement in cancer surgery.

As a clinical radiologist, this author is always "destined" to take charge of the last stage of cancer patients, and in the end, he make it a rule to review all the treatment methods that most likely have been administered as treatment of cancer to date, but always feel that something is forgotten which fills him with a feeling of regret. This paper is being written in order to state this point frankly and also for the purpose of establishing a further new progressive therapy for cancer.

What is the regrettable point which he has mentioned? That is, the fact that post-operative irradiation which is most effective after surgical intervention is not seriously considered and patients are brought in for radiation therapy after recurrence has been confirmed and they become inoperable. It is most regrettable that this was not done immediately after surgery. Whenever possible or when the author sends patients for surgical operation he explains the effectiveness of post-operative irradiation and advises them to return for this therapy, but as mentioned above, they do not return as they must feel that surgery has cured them of their cancer. Swift is heaven's judgement for even in this era, there is a difference between those who received post-operative irradiation and

those who did not, for those in the latter case develop metastasis and/or recurrence earlier and it is not rare that their condition become aggravated within half a year.

As the methods of treatment for cancer available at present, there are surgical removal and radiological therapy. The author cannot help wondering why these two are not more fully used in combination with one another.

Radiological therapy now enters upon a new era where powerful energies which were not available in the past such as ultra high voltage and radioisotope have become easy to obtain, and with the many improvements and advances made in radiological techniques there is an immense difference.

If, in this era, a patient were not to experience this outstanding effectiveness even once, then the knowledge and experience of the physician should be questioned. It is believed that the present powerful energy is reliable so much that the individual cancer disposition should be considered.

In this good era, the two methods of therapy should join forces. The author can not help wondering why this has not been fully realized.

In short, could this be due to the fact that radiologists have little knowledge of surgery while on the other hand, many surgeons are indifferent toward the progress made in the field of radiology? The authors would like to discuss the problem of pre-operative and post-operative irradiation of cancer and propose that it be administered with courage and confidence. In this paper he wishes to present various radiobiological facts and experiences and explain the theoretical basis for the effectiveness of not only post-operative irradiation but also pre-operative irradiation, and thus request the further endeavours of those concerned so as to exterminate "cancer" as soon as possible with the united forces of all medical departments.

## 2. The Theoretical Basis for Advocating the Necessity of Pre-Operative Irradiation for Cancer

### A) Considerations from the basis mechanism of radiobiological action

There is no need to mention that the primary effect of radiation (X-ray, gamma ray etc.) is the destruction of cells, but the secondary biological effect is exerted upon the whole body through the products of destroyed cancer cells (in a broad sense, the so-called Casparische Nekrohormon) which as well known, results in further strengthening of the primary effect.

However, since this secondary biological effect occurs in conjunction with the primary effect according to the Arndt-Schultz Law, in the course of treatment it should be borne in mind that these destroyed products may adversely exert poisonous effects.

The fact we have always experienced in the treatment of inoperable patients in the terminal stage with multiplex metastasis that when the primary cancer focus is irradiated the non-irradiated metastasized cancer foci located in areas quite apart from the primary focus show reduction in size or softening. It is not necessary for the author to mention

this fact because it has been confirmed long ago by his predecessors. The mechanism that is responsible for this is the "shock" which is given to metastasized cancer cells in accordance with the theory on necrohormone, "The destroyed products of cells destroy homogenic cells within the same living body."

What dose this fact suggest to us in regards to pre- and post-operative irradiation of cancer cells?

It is not necessary to mention that in recent years utmost care is being exercised for thorough removal of associated lymphatic glands at the time of operation so as not to leave any cancerous cells but it is very natural that "complete" removal cannot be expected from the theoretical nor technical point of view. Furthermore, nothing can be done about cancer cells which have most likely transferred into lymphatic circulation and blood circulation prior to and during the course of operation, but to leave the matter in the hands of God.

However, it is a well known fact that all possible means have been applied in recent years to cope with this tragedy by using anticancer substances before and after operation. However, this anticancer substance is not by all means selectively effective for cancer cells only.

Hence, the use of necrohormone which is produced from cancer cells is more natural than anti-cancer substance and from the results of studies on cancer disposition which will be mentioned in the following paragraph, the importance of its role can be understood. That is, it is felt there is no comparison to it in effectiveness from the selective and rational point of view. Thus the importance of pre- and post-operative irradiation together with consideration on radiation technique has been established theoretically.

#### B) Kind of abnormality induced due to growth of cancer

It is noteworthy that cancer research which had been chiefly concerned about cancer cells has been expanded to include studies of the individual condition such as cancer disposition. The study has been expanded so as to include studies such as relation of cancer and hormone, problem of cancer and constitution and problem of cancer and metabolism which have made this disease a matter closer to we clinicians.

Our experience concerning these problems is not by any means few in our daily life. For example, although some cancers are extremely small in size, they hardly respond to large dosages of radiation and further gradually grow to show malignant signs even while being treated, while on the other hand, there are cancers of the same type in surprisingly large size which respond well to radiation and completely resolve. This fact can not be explained by considering the cancer cells or radiological energy alone.

What dose this fact suggest?

It is needless to say that this is a condition of an individual with cancer and suggests that the constitution or disposition should be considered. It also explains that even homogenic cancer cells are remarkably different from one another according to their environment.

With an attempt to probe into the condition of an individual with cancer, studies of the body fluid, tissues and metabolism of inorganic salts in the tumor were made and presented in a report under the title of Experimental Study Concerning the Effect of X-ray on Metabolism of Malignant Tumors. It was learned that the abnormal metabolism caused by the occurrence and development of tumor was reinstated to normal metabolic condition with the resolution of the tumor by means of X-ray irradiation, and the following conclusion was reached. It is needless to say that this study covers only a part of metabolism of inorganic salts and it is quite impossible to assume the condition of the whole individual from the result of this study alone, but it is an experimental study in which the selection of metabolism of salts was made as they are most closely related to disposition of sickness and respond sensitively. This selection was made in consideration of the fact that this metabolic "movement" is suggestive of an important "trend" in the individual. The conclusion of the report will be reproduced below and the metabolic trends in individuals with cancers will be discussed.

#### Research Project

Experimental Study Concerning the Effects of X-ray on Metabolism of Malignant Tumor.

Part 1. The effects of X-ray on metabolism of salts in malignant tumor

Part 2. The effects of X-ray irradiation of tumor of organic tissue respiration and glycolysis in rabbit with sarcoma, and effects of potassium and calcium on sarcoma tissue respiration and glycolysis in rabbit

(In this experiment transplantable sarcoma in Kato strain rabbit was used and the study was conducted at the Kumamoto University Medical School Medical Radiology Department (The former Kumamoto Medical College Physical Therapy Department) during the period from 1935 to 1937.) It was reported in the Kumamoto Igakkai Zasshi (Journal of the Kumamoto Medical Society, Volume 15, No. 9, September 1939).

Based on the result of the above experiments, the author made the following conclusion in respect to metabolism of salts (potassium and calcium) in individuals with tumors and/or malignant tumors, and the effects of X-ray irradiation.

1) A very close relationship exists between the amount of potassium and calcium contained in tumor tissue and development of tumor. That is,

- a) While the potassium content in a rapidly growing malignant tumor tissue is very large, the amount of calcium content is very small. Therefore, potassium/calcium indicates a large value.
- b) While the potassium content within softening regressive tissue decreases the amount of calcium increases. Therefore, the potassium/calcium value is small.
- c) When X-ray irradiation is carried out, the potassium content decreases and the calcium content increases remarkably. Thus, presents a potassium/calcium value contrary to the case of rapidly growing tumor.
- d) As a remote effect of X-ray irradiation, the potassium content within non-

irradiated tumor shows a transient decrease and the calcium content increases, but again reverts to the former metabolic condition of malignant tumor.

- e) The aforementioned abnormal metabolism of salts within tumor is in complete concurrence with metabolism of the special "energy" of tumor and its histological findings.
- 2) It is obvious that transplantation of tumor induces abnormal metabolism of salts within the individual. That is,
    - a) The potassium content in serum increases while the calcium content decreases.
    - b) Both the potassium and calcium contents in the whole blood decrease.
    - c) Both the potassium and calcium contents in the organs decrease.
    - d) Both the potassium and calcium contents in urine increase.
    - e) Definite evidence of interference is noted between fluctuation in the contents in the body fluid and visceral organs and that of the contents in the tumor tissue.
  - 3) When X-ray irradiation is applied to the tumor, abnormal metabolism of salts caused by the occurrence of tumor is corrected in conformity with the process of healing and resolution. That is,
    - a) The potassium content in serum decreases while the calcium content increases.
    - b) The potassium and calcium contents in the whole blood increase.
    - c) The potassium content in the organic tissue increases or shows a tendency to increase with the lapse of time as compared to after transplantation and is restored to its original value. The calcium content shows a remarkable increase.
    - d) The potassium content in urine shows a tendency of slight increase while the calcium content slightly decreases.

Further, an experimental study was conducted to learn the effects of X-ray irradiation to tumor of the organic tissue respiration and glycolysis in rabbit with sarcoma, and effects of potassium and calcium on sarcoma tissue respiration and glycolysis in rabbit and the following conclusions were reached.

The results of aforementioned experiment are summarized and comparison made with the results of metabolism of salts in rabbit with transplanted sarcoma reported earlier.

- 1) The tissue respiration and glycolysis of the liver and spleen of rabbit with transplantable sarcoma are definitely affected by the occurrence of tumor.
- 2) The tissue respiration and glycolysis of the liver and spleen are reduced due to the development and proliferation of tumor.
- 3) When the tumor is reduced in size or healed by means of X-ray irradiation, the tissue respiration and glycolysis of the liver and spleen are elevated and restored.
- 4) The resolution of "energy" metabolism of the aforementioned organic tissues is in conformity with increase, decrease and/or resolution of potassium and calcium contents within these organic tissues.

5) Potassium and calcium exert definite influence upon "energy" metabolism of malignant tumor.

6) When the added concentration of potassium salt drops to a certain low level it accelerates glycolysis of malignant tumor tissue. In contrary, calcium salt in that case reduces this action. When the added concentrations of potassium and calcium salts reach certain high degrees, both potassium and calcium reduce glycolysis.

7) Potassium and calcium salts do not have marked effects on the tissue respiration of malignant tumor.

As observed from the results of the experimental studies mentioned above the occurrence and development of tumor cause an abnormality in metabolism. This should be considered to be a favorable condition for the development or metastasis of tumor. When this tumor is irradiated with X-ray on the other hand, with its resolution the above abnormal metabolism is not only corrected so as to recover normalcy but as shown from the above example, it provides anti-cancer action by inhibition of development and reduction in size of the metastatic tumor. Accordingly, it is reasoned that this study is an important item in the research on the healing mechanism of tumor and disposition for tumor.

It is needless to say that the essence that brought about this anti-cancer condition is the appearance of the secondary biological action of necrohormone of cancer cells. If the fact that such complicated factors exist in the irradiation of cancer focus and that these factors act through the living body and work to the advantage of man against cancer cells are understood, the author feels that he is not alone in believing that there is hope in treatment for cancer.

#### C) Observations on radiological therapy for inoperable cancer patients

Early discovery and early treatment are the ideal methods of treatment for cancer and the results are naturally satisfactory. However, because of the characteristic of cancer the realization of this ideal cannot be brought about by physical efforts alone. As a matter of fact, this author has keenly felt that some sort of "luck" is involved.

Therefore, there are actually many cases who are too far advanced and that is the reason why importance and great hope are attached to radiological therapy as the conclusive method of treatment.

What is the ideal of radiological therapy? It is needless to say that this is nothing more than how to administer large doses to cancer focus without disturbing the other organs. It must be remembered that necrohormone of cancer must always be kept in an anticancer state.

With the recent development of ultra high pressure apparatuses and radioisotopes, it is possible to readily obtain powerful energy, but however powerful or effective these energies may be, cancer cannot be expected to be completely cured by radiological therapy alone. Also it should be kept in mind that utilization of these powerful energies may result in the remedy being worse than the evil it was supposed to correct. This is the reason why the author warned earlier that necrohormone is in agreement with the Arndt-



Schutlz law.

In short, the point is how to utilize effectively these powerful energies. The responsibility of radiological therapeutic technique will be of great importance in the future.

The "destiny" of the radiologist who is in pursuit of cancer cells which recur or metastasize one after another is a very pitiful one. The mind of the radiologist who has to fight along with the cancer patient to the last is filled with miseries of a dying man. He has various strategies against cancer, but as yet a good method has not been found. However, one cannot deny that upon obtaining these powerful energies the results have shown magnificent progress. Based on these results, this author has been wondering since more than a few years ago why "pre-operative" irradiation is not being administered, and whenever he recommended post-operative irradiation, he also stressed the effects of necrohormone and emphasized the pre-operative irradiation method.

The fact is that people have not paid much attention to his case, but the author cannot remain silent any longer and wishes to present his views.

### 3. Clinical Significance of Pre-Operative Irradiation in Cancer Patient.

Since the above facts are well known it is not necessary from the theoretical basis of radiobiological action to state that with pre-operative irradiation to the primary cancer focus and metastasized lymphatic glands, the development of cancer cells can be inhibited and their metastasis prevented, which proves very favorable to the patient. What is the reason, then, that this has been hardly attempted to date?

First, the author shall explain a few reasons that he has learned of:

a) It has been said that surgical intervention of the region once irradiated becomes very difficult due to adhesion and changes in blood vessels and connective tissue caused by irradiation.

However, further investigation revealed that such difficulty was experienced in a thyroid cancer case which had been previously administered radiation under the erroneous diagnosis of Basedow's disease and also in a case who underwent extraction of the irradiated cervical lymphatic gland.

This author has had experience in treating two inoperable gastric cancer cases which were later able to undergo surgery as the masses had almost resolved and became reduced in size due to X-ray irradiation; one lived for three years after receiving total gastrectomy while the other died of perforation of the sutured site four months after the operation. One month and a half had elapsed since both two cases had been irradiated, but no difficulty was encountered at the time of surgical intervention.

b) Bleeding is presented as a problem, but the fact is that there is not much to it.

c) It is feared that a skin disorder will develop resulting in roentgen ulcer, but this problem can be easily avoided at present. There are the points that the author has heard given as reasons, but there is no counter-evidence which maintains that pre-operative radiation should not be given and the facts speak for themselves in that these opinions are

not worthy of notice.

The author does not know whether or not these points were considered problematic, but the fact that 25 years ago Professor Ando of Gynecology Department, Keio University, had already devised and introduced large dosage mid-operative and post-operative close irradiation of X-ray by inserting a tube into the body cavity and achieved excellent results has constantly occupied a place in his mind. As in the present when powerful energy is easily obtainable it is not necessary to depend upon close irradiation. However, he cannot help but pay his respects to the far-sight of Professor Ando, who hoped to make further advancement in treatment for cancer through close team work of surgical intervention and radiation therapy. It is also well known that Professor Nakayama of Chiba University is an authority in this field and that he has already actually put this method to practice. The author has not heard many sound arguments against pre-operative irradiation to date. As powerful energy is easily obtainable at present, the problem of suitability of applying radiation to the body for operation should be discarded as a groundless apprehension of the past.

Consequently, it is easily understood from the above theoretical basis that with sufficient dose of radiation obtained by improving the technique for irradiation, necro-hormone which is the product of destroyed "cancer cells" mentioned earlier is produced in accordance with the reduction in size and resolution of cancer, and this necrohormone demonstrates a so-called secondary biological action as it is contained in the body fluid and circulates within the body which causes the cancer accelerating condition to change to an anti-cancer condition.

Accordingly, not only the cancer cells located in the irradiated site but also both the cells attempting to infiltrate and expand into the surrounding tissues and those that are about to spread widely by metastasis are inhibited by necrohormone. As surgical intervention will be carried out under this anti-cancer condition, favorable therapeutic results can be expected.

What is further important is the problem of the metastatic lymphatic glands which are confirmed in the course of surgery. In such case, sufficient and precise post-operative irradiation should be performed in accordance with the surgical findings. From this point of view, pre-operative irradiation should no longer be referred to as a new method, but should be included as a measure for routine cancer operations.

#### 4. Practice of Pre-Operative Irradiation

It is believed most convenient for the understanding of this method to consider what technique should be taken when putting this method into practice.

First, if a diagnosis of cancer is made, the selection of the appropriate therapeutic apparatus, that is, either deep therapeutic X-ray or radioisotope, to be used is determined by the site of cancer and the condition of the individual.

Next, as the dose and field to be irradiated pre-operatively should be determined in

consideration of surgical intervention, discussion should be made with the surgeon.

In order to avoid the occurrence of skin disorders and to apply deep irradiation in sufficient amounts the author plans to use  $Co^{60}$  gamma ray and is installing necessary facilities for this, but the method being practiced for the present is the use of a 200 KVP X-ray apparatus and body cavity tube.

It goes without saying that the selection of the site to be irradiated and the dose of radiation to be administered should be determined based on the primary cancer focus and applied in a dose of sufficient amount. In pre-operative irradiation, consideration should be made so as to administer a certain amount of radiation to the surrounding tissue with the purpose of inhibiting metastasis. Therefore, it is necessary to make the decision in consideration of the lymphatic glands distribution and protection for the skin against surgical wounds. At present, it is believed that the purpose of preoperative irradiation can be sufficiently achieved by administering a dose of 500 to 1000 r (Skin dose 2000~3000 r) to the focus which is the dose presently being administered by this writer. The next important problem is to decide how many days after irradiation surgical intervention should be introduced. It is of no avail if surgery is performed too shortly after irradiation while on the other hand, if performed too long after irradiation satisfactory results may not be obtained due to the lack in radiation effect. That is, the determination of the number of days following pre-operative irradiation before surgery should be discussed from various viewpoints, but the author decided upon the policy that operation should be performed as soon as possible after it is confirmed that the tumor has been obviously reduced in size and its consistency has decreased. In other words, at this time, destruction of cancer cells have definitely begun within the primary cancer focus by the effects of radiation and necrohormones have gradually increased and began to demonstrate their effectiveness.

As a means to determine this time more scientifically, the author is making a study on the fluctuation of NPN in blood as an index.

From past experience, the so-called time suitable for operation mentioned above is one or two weeks after completion of irradiation (there is individual difference in the speed of size reduction and resolution of the tumor), but on the average, it is felt the most appropriate time is about 10 days after irradiation. However, strictly speaking, the concrete policy should be decided upon after consultation with the surgeon on each case as aforementioned. Furthermore, it is needless to mention that before determination is made thorough consideration should be given to the results of various biochemical test, blood tests and examinations of the heart, liver, kidneys and other organs.

The author believes that with the wide practicing of pre-operative irradiation methods in the future the important problems involved, that is, the problems of radiation dose and determination of the time of operation, can be settled on their own accord through mid- and post-operative findings and its subsequent course.

The author's opinion that surgery should be performed one to two weeks after irradiation has its grounds. The reduction in size of the tumor naturally becomes the primary

objective for clinicians, but this author further estimated this time in consideration of the results of detailed review of his experimental research with respect to the effects of X-ray irradiation on metabolism of malignant tumor and his clinical experience. That is, the abnormal metabolism caused by transplantation of tumor brings about remarkable changes, restoration to the original value and recovery of normal metabolism in one to two weeks due to X-ray irradiation of the tumor. Particularly, the recovery of metabolism is remarkable in the organic tissue and it is observed that the tissue respiration of these organic tissues recover so as to even exceed the original value in 10 days after completion of irradiation.

Based on this fact, the author makes an estimate to decide the time for operation, determines a concrete schedule and sends the patient for surgical intervention. From its subsequent course he is confident that this method is correct from the clinical point of view.

In summarizing this once again, the time of operation should be determined upon considering the reduction in size of the cancer and appearance of secondary biological effect. As for post-operative irradiation, a sufficient and necessary dose should be administered in accordance with the instructions of the surgeon based on surgical findings, doing away with the unscientific method of the past whereby radiation was administered as extensively as possible depending on instinct.

## 5. Conclusion

Irradiation is the last "resort" at present for those cancer patients that are inoperable, and/or beyond the help of drugs. This author who has treated such cancer patients for more than 20 years has always wondered if there were not any means to relieve them. However, there has not been anything to be done but to commit them to the healing power of nature.

After all, as "death" is the unavoidable "destiny" for all living beings, the radiologist must also abide with this "destiny".

However, as aforementioned, in reviewing the past therapeutic courses of cancer patients who have depended upon this last resort, it is found that there are points that we, as clinicians, must reconsider. There have been numerous cases in which early detection was missed. There have been successful extirpations for which post-operative irradiation have been neglected and delays in treatment due to erroneous diagnoses. These are all the responsibility of the physician.

This author feels that there should be a method whereby a patient may undergo operation with hope and free of anxiety even though his condition may be too far advanced.

When anti-cancer substance first appeared, the author immediately thought of pre-operative irradiation before anything else. However, from his experience he could not emphasize its application as strongly as he does now in consideration of skin disorders which are caused by the 200 KVP apparatus.

Nevertheless, as aforementioned, since the results of cancer operations have definitely progressed and powerful energy is easily obtainable, this writer believes that "pre-operative irradiation" is the best method available at present. He has discussed the matter with surgeons on every occasion he has had, but it does not seem to meet fully with their approval. Therefore, he has frequently considered about building an operating room and ward of his own, and seek the cooperation of a competent surgeon in order to employ the combined efforts of surgery and radiation, but he has been confronted with financial difficulties and is unable to realize the plan.

Since the main problem in effecting achievements in cancer therapy is to obtain powerful energy, this author purchased a tube which can be inserted into the body cavity the year before last and was able to obtain better therapeutic result. This year, he has decided to install a cobalt<sup>60</sup> radioisotope apparatus. This apparatus will add power to the body cavity tube and 200 KVP X-ray therapeutic apparatus he has at present with these he hopes to be able to send patients to surgical hospitals after administering to them "pre-operative radiation" based on his past experience. Following the operation he is looking forward to administering post-operative radiation in accordance with the instructions of the surgeon based on the surgical findings.

The author earnestly hopes that all readers will devote more interest toward this problem and further cooperate in the treatment of "cancer". He has introduced in these pages the "cancer". He has introduced in these pages the "Theoretical basis of pre-operative irradiation" based on his experience along with the results of his experiment. This paper is concluded with the firm conviction that this theory will be substantiated by facts in the future.