NEW DIRECTIONS OF CLINICAL ACTIVITIES IN THE DEPARTMENT OF RADIOLOGY IN THE POSTGENOME ERA

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Abstract: Cloning of all human genome has been completed in 2000 with the beginning of 21st century close at hand, and the full-scale post-genome era has come at last. The department of radiology that should take an important role in medical medicine was one of the few departments that had not taken part in the human genome projects that can be the fundamental plan of life. Of course, there are some human genomes sequenced by researchers of radiobiology or of basic medicine of radiation, however, they are exceptional. As the contrary to the proverb, "You will win every battle, if you know your enemy and yourself," radiologists in the past have entrusted it to physicians in other departments, and they have had little interest in the outcomes of such researches. We have completed cloning of four novel human genomes that can be related with cancer or radiosensitivity, and reported them in articles. We would like to consider the new idea, clinical activities in the department of radiology should play an active part in the era of postgenome. Here we are not concerned with the future prospective of radiology in departments related with IT, such as telemedicine, as we are not in a position to mention it.

Key words: Postgenome era, Department of radiology, IVR, Gene therapy, Regeneration medicine

CLINICAL ACTIVITIES IN THE DEPARTMENT OF RADIOLOGY BASED ON GENETIC INFORMATION IN THE ERA OF POSTGENOME

1. Genes related with radiosensitivity

Several kinds of genes related with the homologue in microorganisms like E. coli, the replication and the repair of DNA, the higher-order structure of DNA, nucleic acid metabolism, membrane, cell cycle, apoptosis, and others have been reported as genes related with ionizing radiosensitivity. Considering that there were novel RNA helicase and BRCA-3 also in genes we handled, at least hundreds of such genes can be reported when the function of every human genome is made clear following the advancement of the analysis of SNPS planned in the West and in our country. It will take more than 10 years until all functions, such as cross talks of every cascade, of every gene related with ionizing radiosensitivity are completely cleared. Then, how radiologists in our country should utilize the information of human genome in actual clinical activities? It is an important issue to consider since a lot of radiologists have had no interest in the information of human genomes.

a. In the field of diagnostic imaging

In diagnostic imaging, advanced computers that integrate imaging information, and the common use of Ultrasound (US), MRI, or nuclear medicine have reduced the role of diagnosis with ionizing radiation compared with that in 20 years ago. Addition to it, technical advancement has also contributed to avoiding the increment of medical exposure dose. However, the medical exposure level in our country is still as twice as that in the West, and the rate of CT per population is the highest in the world owing to significantly lowered price of X-ray CT, which is equipped also in hospitals of practitioners. ICRP has not set the restriction on dose with the reason the medical exposure dose is not enough risky to abandon its great advantages. However, when all human genomes related with radiosensitivity are made clear, the medical exposure dose can be restricted considering various risks that can come up depending on a level of radiosensitivity, although the problem of how to protect the ultimate privacy of individual genetic information still remains. The medical exposure dose has been controlled in the U.S. from the consideration in the aspect of medical economy, and such aspect will be considered in our country as well hereafter. Few cases with late effects, such as carcinogenesis or complication caused by the diagnostic imaging, have been reported except cases with skin ulcer caused by too long fluoroscopic time during the interventional radiology. US will be applied into wider range of diseases since three-dimensional diagnostic imaging is being realized soon, although, the use of MRI might be reexamined because the effect of electromagnetic has
More concretely, for patients with a high radiosensitivity, the use of ionizing radiation might be restricted in diagnosis of diseases that can be accurately diagnosed with alternative diagnostic modalities like US, nuclear medicine, MRI, or the combination use of an endoscope and US for luminal organs that will be developed in the future. The establishment of diagnostic strategies that view not only radiosensitivity but high incident rate diseases for each patient is desired in diagnostic imaging that targets areas including affected organs proved as a polygenic disease. That is to say, it is important to conduct examinations under recognition of the balance of advantages, such as early detection or understanding of conditions, and disadvantages, such as higher risk of causing diseases by periodic examinations. Such a viewpoint seems not to have been reflected in Gamuts' strategies in diagnostic imaging. A manual for diagnosis should be prepared urgently by concentrating all wisdom in the department of radiology. Although the guideline is being prepared at the Japanese College of Radiology, such a viewpoint seems not to be contained in it. It is urgently required to establish a committee in the Japan Radiological Society that takes responsibility in preparing a guideline for diagnostic imaging based on the information or functions of the human genomes.

There will be very few cases that X-ray CT highly exceeds the latest high-speed MRI in the diagnosis of some sites, such as brain or central nerves where respiratory motion can be ignored. Only the imaginary CT endoscope for three-dimensionally reconstructed bronchies, blood vessels, and intestines requires not US or the latest high-speed MRI but X-ray CT in the diagnosis of trunk and limbs. It is necessary to reconsider diagnosis modalities including digitized radiography, the fluoroscopy of intestines, or angiography, from the viewpoint of the balance of advantages and disadvantages in each case.

b. In the field of radiotherapy

Has the situation in the field of cancer radiotherapy, which once made Prof. E.Hall say "Physics is with us, but Biology is against us." changed? Or is it about to change? How significant the elucidation of the functions of every human genome is? There are only few records of radiotherapy for malignant tumor in patients with high radiosensitivity except some in specific cases, as AT. The response of tumors and the acute reaction of normal tissues are remarked in relation to the genetically determined radiosensitivity. Apoptosis is especially attracting attention recently as a phenomenon that determines the radiosensitivity of tumor cells based on the rate of cell death. However, we are gaining the data that hypoxic state, which is rather an old idea but recently gaining attention again in relation to the clinical prognosis, is an important factor as a determinant of radiosensitivity in human malignant tumor xenografts.

Not a few radiotherapists must have experienced the cases that showed a significantly strong response of skin or mucosa, or bone marrow suppression, while conducting radiotherapy. The predictive assay to examine the sensitivity of normal tissues before conducting radiotherapy is being reported shortly. Besides, Prof. Nakamura and Prof. Nishiya have started the attempts to realize the chemotherapy in so-called tailor-made cancer by predicting sensitivity of tumor itself against chemotherapy at the genetic level. However, the assays at the genetic level have not led to a clinical common view yet even on the sensitivity of the representative gene, p53. Since not only a single gene but polygenes might determine the sensitivity against chemotherapy, many complications can be expected until the cross talk of mutual cascade that related genes are involved in is cleared, and chemotherapy in tailor-made for cancer at the genetic level is realized.

The predictive assay of the sensitivity in three-dimensionally cultivated cancer tissues, mainly of stomach cancer, against chemotherapy has been taken up as a highly advanced medicine in Keio University and Osaka Medical University, and such idea is spreading in our country. Although the former predictive assay of sensitivities in various kinds of two-dimensionally cultivated tissues had been considered as a clinically meaningless assay, there are reports, mainly in our county, that the novel predictive assay has already led to gaining clinical outcomes. On the other hand, the significance of radiotherapy is being admitted more widely than before, and its combination use with chemotherapy tends to be a standard therapy for several kinds of cancers in our country.

We have already applied to the Ethics Committee of Nagoya University School of Medicine for conducting the novel predictive assay in the combination use of chemotherapy and radiotherapy, and we would like to ask for establishing a committee of novel predictive assay also in the Japanese Society for Therapeutic Radiology and Oncology. Since the novel predictive assay that we contrived enables us to assay the sensitivity of normal tissues as well as that of cancer cells, we consider the assay will be also effective in selecting a fractionated time interval and fractionated dose. The outcome of radiotherapy will be improved drastically, if we succeeded in determining the most efficient fractionated time interval and dose or in predicting whether side effects, such as acute reaction or late effects, are slight or not before starting therapy.

Regarding side effects, the correlation between skin ulcer and high radiosensitivity has recently been reported after the treatment with a gamma knife. Although there are many worldwide records of radiation carcinogenesis seen after radiotherapy, there are only a few cases succeeded in elucidating the genetic background. The famous crisis of osteosarcoma in and around the orbita after radiotherapy for retinoblastoma is an exception. It might be necessary to have plenty records of observations of the progress and to prolong the period of observation over ten years. The records of the long-
term observation of secondary cancer seen after the cure of leukemia as well as that of genetic information will enable us to analyze the background of late effects, especially of the secondary cancer, after radiotherapy.

Considering the matters stated above, it is urgently required to investigate how to determine dose in the radiotherapy for cases with high radiosensitivity by using the novel predictive assay. Although IMRT and three-dimensional conformal radiotherapy, whose applications are under development world-wide, might enable to concentrate dose more in tumor compared with the irradiation in current radiotherapy, the wider field in normal tissues will be irradiated nevertheless the level of dose is low. It is necessary to pay attention to how it effects the risk of radiation induced carcinogenesis with relevance to genetically clarified susceptibility to cancers in the era of postgenome.

c. Others

The exposure dose in an examination of nuclear medicine is ordinarily within the range where the effect can be ignored, but investigations of SNPS at the genetic level might be necessary in the cases with patients with high radiosensitivity when the selectivity against targeted organs is high. To leave plenty of records of unsealed brachytherapy in cases with targeted organs with high selectivity regardless of levels of radiosensitivity will enable to gain useful information for the future. As for the application of various proteins, as the largest fruits of the postgenome era, other experts in nuclear medicine will refer, and we will not mention it here.

In relation to the acute response and late effects stated above, there is a therapy against the effects of exposure. As it can be seen in the recent accident in JOC, bone-marrow transplant or peripheral blood stem cell transplant (PBSCt) is highly effective in the prevention or treatment for bone marrow death, and grafts of regenerated skin might be effective for severe skin injury. However, still there is no effective prevention or therapy for the intestine death, and it has resulted in loosing two lives. We consider the transplant of small intestine from patients with brain death may be the only method until the regeneration of small intestine, the most expected method, is realized.

In exposing with a certain level of dose where it is highly possible to cause the secondary cancer, it is necessary to consider risk of carcinogenesis based on the results of the biopsy of high-risk organs and of the SNPS analysis of genomes related to cancer in organs using DNA chips. When the risk of other radiation effects, especially the late effects such as fibrosis of tissues in important organs, is high, the combination use of hepatocyte growth factor (HGF), whose possibilities have been reported, should be attempted.

2. Cancer associated genes

The relation of oncogenes and cancer suppressor genes with carcinogenesis and progression of cancer, a polygenic disease, has already been investigated widely. There can be about a thousand or more cancer associated genes, considering the fact that some of them were seen also in our cloned genes. The cancer associated genes that make up one percent of all human genomes may cause carcinogenesis by about 10-20 mutations (hits), and a series of such mutations will lead to gaining highly metastastic potentials, or more malignancy. The idea of "field cancerization" has been universally acknowledged in research of carcinogenesis. That is to say, genes with relatively few hits, or genetic changes in the precancerous state that are although pathologically normal, are found in analysis at the genetic level. How we should conduct intensity modulated radiotherapy (IMRT) and three-dimensional conformation radiotherapy (3D-CRT) that can cover wide range of normal tissues with much lower dose, while facing the idea that radiotherapy, which is normally local therapy as well as operations, may promote field cancerization? However, there is no doubt whether these treatments will certainly increase the dose in local tumor, drastically improve the rate of local control of cancers, and reduce the acute toxicities and late sequelae.

On the other hand, whether regions or sites with more than a certain number of hits should be included in the radiation field, and whether such regions or sites have the possibility to cause malignant alteration by conducting radiotherapy, especially IMRT or 3D-CRT, might be issues of discussion. It has been indicated that there is a limit in repairing DNA damage without making any errors in the cases with cancer. From such a viewpoint, the application of radiotherapy in the era of postgenome, especially in pediatric or juvenile cases, might be limited in the cases without any alternative treatment. What kind of and which dose of drugs should be chosen in chemotherapy have been discussed mainly on the aspect of anti-tumor efficacy and of side effects in the acute phase, but it will also be argued on the risk of carcinogenesis in some cancer associated genes in surrounding normal tissues with a certain number of hits in the era of postgenome.

With regard to the highly expected "tailor-made cancer therapy" in predicting clinical efficacy against radiotherapy, the utility has not been proved yet because even opinions on the status of p53 that mutates in cancer tissues in over half of patients with malignant tumor still differ. The functions of p51 and p73 will be clear soon, and they have gradually proved to play important roles in relation to carcinogenesis or sensitivity in some organs. The entire family of p53 might assume the function that has been expected with p53 alone. Other families with such function can be found, when the whole function of the human genome is cleared. It can be a reflection of the fact that more bypasses are prepared for more important cascades in the mechanism of signal transduction. Therefore, it will take more time to establish the tailor-made cancer radiotherapy at the genetic level. Many researchers once proposed models setting only p53 as a central dogma, however, the hypothesis will be reexamined in the postgenome era.

3. Other genes related with life-style related disease

It is questioned whether many of the life-style related diseases are monogenic diseases, but it will also be clear as the elucidation of the function of the genome progresses.
The most expected contents in the era of post-genome, whether SNPS that is related with the life-style related disease can be induced or increased by ionizing radiation or in electromagnetic field, will be investigated hereafter. When a high risk can be expected by conducting radiotherapy in the life-style related diseases in important organs, the use of gene therapy should be considered as an alternative therapy.

FUNCTIONAL IMAGING BASED ON GENETIC INFORMATION IN THE POST-GENOME ERA

1. The analysis of the images of the magnetoencephalogram or IMRI has recently enabled us to grasp the functions of the brain, and related various interesting phenomena are being obtained from it. By using PET with it, information at the molecular level can be available now. Even the correlation between the mechanism of neuro-transmission in specific areas in the brain and diseases has been a target of the analysis. To combine enhancement and restriction in specific areas will make clear the mechanisms of schizophrenia, depression, actism, or even abnormal behavior. It is significant that the function of the brain can be elucidated not by invasive methods used in the past but by a non-invasive method now, and it will also be effective in assayng the correlation between the function of genome and a wide range of diseases. The investigation combining the new method and the former research at the molecular level using brain specimens is expected. It will make clear the role of the genesis of various genomes and epigenetic phenomenon in the function of the brain or spirit.

2. To have the image of mind can be highly expected since the function of spirit is being clarified now. Although it is not directly connected with radiological diagnosis, the information of the mind will be useful for diagnosing patients with cancer who are always attended with anxiety and pain. Although various methods to scale the anxiety or pain, such as WHO scale have already been developed and are used clinically, the more objective and reproductible information from the image of the mind will be useful for assessing the efficacy of each therapy. This field will be advanced since 21st century will be the age of the mind rather than the age of matter.

GENOMIC PHARMACEUTICALS

The application of the genome or its products structure based drug design has already been progressed in the nuclear medicine centered on the receptor. However, if the fact that individual lives with a lot of specific SNPS is premised before gaining complete elucidation of all cross talks of the cascade of many genome functions, a question of how widely the drug in the future can be applied still remains. If there are only a few monogenic diseases, the analysis of the patterns of genesis of the genome in specific tissues will be useful for designing drugs. Moreover, genome information will also be useful for predicting the main action and side effects of drugs. While the drugs associated with cancer are desired in the clinical activities in the department of radiology, the drugs to overcome side effects or complications of radiotherapy or chemotherapy can also be realized.

GENE THERAPY AND IVR

Gene therapy has been used not only for malignant tumor but also for other diseases, such as congenital dysbolism or cardiovascular system malfunction in our country. Since radiologists will have many more occasions to diagnose patients who have experienced gene therapy, it is necessary to have knowledge of them at least. There might be only a few radiologists who take up gene therapy as a main therapy in Japan. However, the way to cure arteriosclerosis obliterans (ASO) that has been researched actively in the department of radiology, especially in the group of intervention radiology (IVR), has been the target of gene therapy or regeneration medicine, and it has shown good results.

On the other hand, some strategies against malignant tumors, such as the introduction of wild type p53, have once been temporarily effective by using with radiotherapy or chemotherapy, however, it is doubted whether they will finally improve the long term outcome. There is a limit to cure with local therapy since patients with progressive cancer or recurrent cancer have been targets so far, and it is still difficult to cope only with the introduction of a single gene. Although attempts to introduce cocktail genes have been progressed, it is still difficult to have a safe and effective image with the therapies for solid cancer since the targeting, mentioned below, is difficult and some cases resulted in death from the side effects have already been reported. The efficacy of gene therapy alone against solid cancer can be little expected also from the viewpoints of gene dosage or gene concentration gradient. The gene therapy should be applied into diseases with the gene distribution in blood vessel that do not require targeting, such as congenital metabolism disorder, cardiomyuscular system malfunction, leukemia, or progressive malignant lymphoma, considering the balance of the risks and advantages.

The problem in gene therapy is how to introduce genes into targeted genes of targeted organs efficiently. Some means to improve the efficiency of gene introduction have already developed by a maker in our country, but a method to improve selectivity against targeted cells has not been established yet. Unexpectedly, IVR is the best method at present as a means of surgical or non-surgical gene delivery. If new vectors including liposomes are developed to facilitate the targeting, and if they are recognized as a safe therapy, they will be widely used as interventions for life-style related diseases or genetic diseases. It will be necessary, as a part of IVR, to have measures to establish a committee or an organization to prepare the manual of gene delivery in gene therapy for various kinds of diseases. Especially we, the members of the department of Radiology whose modalities often induce the genetic injuries, may be requested to cope with gene therapy more actively.

IVR AND TRANSPLANTATION MEDICINE

Another important clinical activity can be realized with
IVR. That is the follow up after and the assessment of success or failure of the transplantation of the deep seated organs from brain-death cases or from regenerative organs. For examples, these are important to confirm whether the blood flow to the transplanted organs is enough or not in the transplantation, and to grasp which type of mononuclear cells are infiltrating into the transplanted organs. These information can be readily obtained by the IVR methodologies, and the experts on transplantation can predict the degree of rejection and the need of change in immunosuppressants. More recently Graft versus Host Disease (GVHD) reaction against various organs such as skin, although the whole immunological mechanisms of local tumors during mini-transplantation, that is, slight chemotherapy or TBI with peripheral blood stem cell transplantation (PBSCCT) followed by the combination of immunosuppressants, has not revealed yet. It is obvious that IVR may play an important role in this field because this treatment for cancer requires the slight GVHD and utilizes GVT, very potent reactive reaction against cancer. On the other hand, there is another possibility for ASO to be cured by gene therapy may be promising. There is a report that the transplantation of mesenchymal stem cells (MSC) is useful for ASO.

**PREVENTIVE MEDICINE USING HUMAN GENOME INFORMATION IN THE POSTGENOME ERA**

The analysis of SNPs targeting several kinds of life-style related diseases as a gene therapy has progressed. However, many problems in the system of management of individual information have been pointed out at the same time, and there is a concern on whether an adequate system that takes responsibility for the most private matter, the management of genetic information, can be prepared or not. There is almost no control in the management of individual information, such as medical information, in university hospitals or in public institutions. There are also some doubts on whether the analysis of SNPs can be conducted widely under such conditions. Although the so-called tailor-made medicine against several cases of diseases or life-style related diseases is permitted topically or methodologically at present, it is unavoidable to have some defects until the cross talks between cascades stated before is completely cleared. Therefore, the gene therapy is rather expected in preventive medicine.

For the early detection of various diseases, the information of genome is very meaningful, however, it is extremely private matter and so there may be arguments on who to manage it, that is, nation, hospitals, companies or individuals? Such discussions should be promoted among people and these preventive medicine based on genomic information might have to be initiated after nation-wide agreement. These kinds of processes should be proceeded very carefully since the outcomes of scientific progress in the 20th century have not always been considered as agreeable ones for human beings. Although the guideline for research or clinical activities related with human genomes has already been published, it will be tested whether this point of view is carefully reflected in it or not.

**REGENERATION MEDICINE AND RADIATION MEDICINE**

Worldwide researchers are in fierce competition for realizing regenerated organs or regeneration medicine using MSC in various organs including ES or bone marrow.

Although radiologists are out of such competition, they, especially the group of IVR will be able to realize an epoch making research, if they urgently come to grip with it. As noted above, the authors are in progress on the research for the transplantation of regenerative organs or gene therapy that may be needed especially for the high risk cases of severe radiation injuries of critical organs. Already we have succeeded in making several stratified regenerative mucosa such as bronchus. If regenerative bowel mucosa is available, it may be very useful for the cases of radiation bowel death to whom almost no treatment has been established. Especially the transplantation of regenerative tissues or cells to the liver or spleen must be very practical procedures for the members of IVR. In the stage of regenerative medicine, IVR may offer the most effective methodologies irrespective of vascular or non-vascular.

**THE EDUCATION IN THE DEPARTMENT OF RADIOLOGY TO SURVIVE IN THE POSTGENOME ERA**

The education in the department of radiology for interns or graduates has tended to be focused much on clinical applications compared to other departments because of a lack of clinical human power in image diagnosis or in radiotherapy. Molecular biology has been educated as a material for thesis in some medical office of radiology or as an avocation research for instructors. However, such educational situations in the department of radiology that gives much effort on the diagnosis of malignant diseases should be changed, considering the facts that forms and functions are determined by the expression of genes in specific tissues after the process of genesis and differentiation and that malignant tumors are a polygene disease.

Of course it must be controversial how the time and manpower can be ensured in the department of radiology where the clinical tasks are overwhelmingly a lot. The appropriate training or recruitment of young Radiologist must be critical for the Radiologists to survive in such an era of integrated medicine. Therefore, JRS or JASTRO should recommend that the leaders to encourage young doctors to learn molecular biology or medicine during their postgraduate course. Although we have heard that JRS and JASTRO recommend such action, only a few clinical members of these societies are active in the medicine related to the genome information. These is an amazing gap between the department of Radiology and other departments in this sense. We would like to propose a stepwise project in the concrete
curriculums for obtaining enough research grants or funds for the younger members by not only attending very short period of training courses at annual conferences but also spending several years to do research or training along this line.

**ADDITION: RADIOLOGY IN THE ERA OF POST-GENOME**

As we stated before, E.Hall once said “Physics is with us, but biology is against us” as for the cancer therapy. However, it is obvious that each progress has been supported the diagnosis in radiology. Not only classical radiobiology but advanced molecular biology is required to have more progress in the present situation of radiology. The development in recent information technology, such as image information processing or information forwarding to remote areas is remarkable. Radiologists are highly expected to be in charge of conflating biology and physical engineering. The issues in the disclosure of information and notification are attracting as much public attention as never before. The responsibility for the idleness can be looked closely into now when the responsibility to results is strictly required. The responsibility for explanation, and accountability can also be required in this age of disclosure of publication. Namely, we radiologists might have to give effort to realize to have urgent approach by predicting each risk in each case and by checking the latest genome information while taking such responsibility into account. The education in terms of the department of radiology for students before and after graduation needs to be reexamined urgently.

To take the matter of electromagnetic effects as an example, it has still been disputed while a lot of devices that generate high electromagnet are used in radiological clinical activities. We hope the effects will be researched also in our country and the consequences will be gained soon.

Active approaches against late effects, especially against secondary cancer, seem not to be conducted in worldwide radiotherapy. That is to say, the problem of the secondary cancer might not have seriously considered at the time when advanced chemotherapy has realized a cure for leukemia. Even now, the leader of ASTRO sadly responds against a question about the risk of secondary cancer in radiotherapy, as if he does not want to answer it. It would soon be revealed which sub-population has the highest risk of secondary cancer, and lack of which gene mutations associated with a relatively low risk. We considered it was better to develop a means to prevent the secondary cancer actively, and we are now conducting basic research of some substances as a chemoprevention keeping our pace with clinical research in the U.S.

We conclude the article with the hope of radiologists, especially those in our country, realizing great dreams in the new era of post-genome.

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要旨：ゲノムプロジェクトには世界的に完全に立ち後手の放射線療法があるが、2万5千から4万と言われるヒトゲノムの内、4つの新規ゲノムをクローニングした我々の視点から、ポストゲノム時代の放射線療法の新機軸という新しい概念を紹介したい。既に世界各国で、国家、公的機関あるいは企業がゲノムの機能解析に新しい視点をもつその解析を始っているが、全てのゲノムの機能、それを含むカスタード、更にそのクロストークなどの解明により、全ての病態あるいは生体内の活性性が明らかとなるまでには10年以上必要であろう。しかしそのまでの間に、放射線感受性や発癌、生活習慣病などに関連したゲノム上のSNPsなどの解析が進み、個人のプライバシーであるゲノム情報が発症のリスクを予想する上でも、重要となる。画像診断の予防医学における意義を、このような情報をしっかり管理し踏まった上で、発症リスクを増加させることなく、早期に確実に発見するということに経り、再検討する必要がある。また高精度放射線治療においても、発癌から悪性進展への過程がField cancerizationという形での広がりがある中で、また重複癌が増加する中で、治療範囲の設定を具体的にどのように進め、どの治療をどのタイミングで併用するのか、また経過観察の必要性が示唆されよう。遺伝子レベルでのオーダーメイド治療の実現までもう少し時間が必要だが、我々は新たな試みを始めている。一方、現在進められている遺伝子治療や再生医学においてもIVRの方法論は大きい役立つ。更に被曝後医療においても再生医学あるいは移植医療が重要となる。このように最新の分子生物学遺伝子情報と物理工学の統合融合こそが21世紀ポストゲノム時代の放射線療法に必要とされている。