NECA National Evidence-based Healthcare Collaborating Agency

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The Evidence

Safe and Efficient Use of Radiotherapy Equipment from the Health Care Perspectives

Introduction

The highest cause of death among Korean is cancer and has been for the last ten years. Based on the National Cancer Registration and Statistics in Korea up to now, the incidence rate of cancer among people in Korea has continuously increased since 1999 when the compilation of the nation-wide statistics for cancer occurrences began. Thus, anti-cancer treatments using radiotherapy equipment has also been on the rise. It is understood that about half of all cancer patients receive radiotherapy in developed countries, while 30% of all cancer patients undergo radiotherapy in Korea.

With respect to radiotherapy, the rate of lethal accidents to patients is rather low, but therapeutic radiation deals with very high levels of radiation. Excessive irradiation leads to radiation-induced injuries and insufficient irradiation causes failure of tumor control, leading to decrease in his or her span of life. In reality, owing to the fact that radiation treatment is divided into numerous steps and has systematic characteristics of various experts working together in mutual cooperation, radiotherapy has a large potential of developing an accident or error diversely caused by a defect of a device or equipment, inadequacy of procedure or protocol, manipulation mistake, error in communication or transmission of essential information, and unsatisfactory independent check-up. Furthermore, more and more sophisticated and complex equipment for radiotherapy, coincided with steady advancements of radiotherapy technologies, increases the possibility of having an accident caused by carelessness in education and training of proficient manpower, possessing expert knowledge on equipment, and in quality assurance for new devices.

The aspect that radiotherapy is largely carried out by utilization of external equipment, this study attempts to consider the safe and efficient use and management of radiotherapy equipment from the health care perspecitve.

This issue paper is written based on the research results performed by the National Evidence-based Healthcare Collaborating Agency(NECA).
The full texts of the research report is available from the website of NECA (www.neca.re.kr).

Radiotherapy equipments are subject to regulations by the Ministry of Food and Drug Safety and Nuclear Safety Commission, pursuant to the provisions of the Medical Devices Act and Nuclear Safety Act.

Examination of domestic and foreign management system and recommendations relating to radiotherapy equipment

Ⅰ. The premarketing phase

□ Approval and registration for radiotherapy equipment

The approval authorities of Japan, U.S.A., U.K. and Korea provide approval and registration of radiotherapy equipment. Each country has a classification system for grading medical devices based on the risk level. Both Japan and Korea have a classification system with four classes of grading. Medical devices for radiotherapy correspond to Class III.

Japan has established a classification system with 4 device classes and another special classification attributable to device characteristics (Medical devices specially designated for the maintenance and installation/or medical devices for installation and management). Medical devices for radiotherapy are subject to the medical device classification for installation and management. There are 3 U.S.A. regulatory classifications for medical devices, and radiotherapy devices belong to Class II. Medical devices in the U.K. are subject to classification into 4 classes (Class I, IIa, IIb and III) and radiotherapy equipments belong to Class IIb.

Regulations and management system for approval and registration of medical devices come to term with global regulatory harmonization and their provisions among countries mentioned above are largely not dissimilar. However, unlike other countries, radiotherapy equipments are subject to approval by two regulatory agencies, pursuant to the provisions of the Safe Medical Devices Act and Nuclear Safety Act, in Korea. Approval and management regulations for radiotherapy equipments and responsible agencies for each country are shown in Table 1.

<Table 1> Comparisons of approval and management regulations for radiotherapy equipments for each country

Classification	Korea		Japan	U.S.A.	U.K.
Applicable Law	Medical devices Law	Nuclear Safety Act[1] (provisions for approval relating to devices, facilities and manpower)	Pharmaceutical Affairs Law	FD&C Act - Drugs and Devices - Electronic Product Radiation Control	MDR2000 (Medical Devices Regulations 2000)
Responsible agent	Ministry of Food and Drug Safety[2]	Nuclear Safety & Security Commission	Ministry of Health, Labor & Welfare (Application through PMDA)	Food and Drug Administration (FDA)	Medicines and Healthcare products Regulatory Agency (MHRA)

1) Article 5, Nuclear Safety Act: Radioisotope and radiation emitting devices
- Design Approval (Manufacturer or importer): Submitting of device design data, safety evaluation data, and quality assurance plan for production.
- Approval for use (Production/sales/user): Documents of safety analysis report, quality assurance plan, radiation safety report and safety management regulation are submitted, and the guidelines for the approval of production/utilization facilities.

2) Pursuant to the Law of administrative organization (The Enactment No. 11690, 2013.3.23), name has been changed to “the Ministry of Food and Drug Safety.”

Notwithstanding the fact that radiotherapy equipments are a part of health technologies applied to patient treatment, regulations of safety management for patients have not yet been stipulated in Korea.

Ⅱ. The postmarketing phase

□ Safety management

Comprehensive safety managements for facilities, workers and patients are necessary along with the quality assurance for equipments for postmarketing safety management of radiotherapy equipments.

Radiation-emitting medical devices include equipment for radiation therapy and equipment for diagnostic radiation, as most countries have a similar management system for safety control of these medical devices. However, in Korea, the system of postmarketing management of devices for diagnostic radiation and that of devices for radiation therapy are separate.

In an attempt to scrutinize more definitively, the current state of management of radiotherapy equipments, the current situations of safety management of both radiotherapy equipments and diagnostic radiation devices were examined and compared in Table 2.

In Japan, the Ministry of Health, Labor and Welfare manages both diagnostic radiation devices, as well as radiotherapy equipments, pursuant to the Medical Care Act of Japan.

Management of facilities and workers is carried out as stipulated by the Medical Care Act and Basic Safety Standards for protection against ionizing radiation.

Both diagnostic radiation devices and radiotherapy equipments of the U.S.A. are managed by the stipulation of state governments. Some state governments issue license and audits facilities of radiotherapy equipments.

In the U.K., the quality control for devices is being achieved by the mechanism of voluntary management through institutions, such as the Radiological Physics Center (RPC). Medical radiation exposure including patients' safety, along with diagnostic and therapeutic radiation devices, are regulated by the Care Quality Commissions (CQC), as stipulated by the provisions of the Ionising Radiation (Medical Exposure) Regulations 2000 [IR(ME)R]. Safety management of exposure to radiation by workers is regulated by the Health & Safety Executive (HSE), pursuant to the provisions of Ionising Radiation Regulations (IRR) 1999. The European countries, for which the quality control of radiotherapy equipments is obligatory by law, include France, Germany and Norway.

With respect to safety management of diagnostic radiation devices (and special medical devices) in Korea, the safety management of facilities, devices, patients and workers are regulated by the provisions of the Medical Care Act. Pursuant to the stipulations of the Medical Care Act, the quality control of testing laboratories or of special medical devices is regulated by a regulatory agency through the Korean Institute for Accreditation of Medical Image. On the other hand, safety management of radiotherapy equipments is regulated by the Nuclear Safety Commission, in conformity with the provisions of the Nuclear Safety Act. Notwithstanding the fact that radiotherapy equipments are a part of health technologies applied to patients' treatment, regulations of safety management for patients have not yet been stipulated. The quality control of radiotherapy equipments is being carried out by spontaneous management through the Ministry of Food and Safety's quality assurance of dosimetry in radiation treatment.

□ Professional groups in radiotherapy

It is necessary to define the standards and roles of relevant professionals for the quality assurance and safety management of radiotherapy, as specified in the guidelines and regulations. As shown in Table 3, International organizations,

such as IAEA or WHO, have suggested the functions of radiotherapy experts such as a radiation oncologist, medical physicist and radiation therapist, etc. The guidelines are specified by the IR(ME)R2000 in the U.K., and by the specialty board in Japan and the U.S.A. Particularly in Japan, experts of scientific societies relating to radiotherapy gathered together to establish the Quality Assurance Committee for Radiotherapy, and created the guidelines for "safety management system for the prevention of medical accidents in radiotherapy." They also suggested the functions of expert manpower relating to radiotherapy as showed in Table 3.

Various provisions are somewhat stipulated in Korea. Nevertheless, the role of professional groups involved in radiotherapy has merely focused on a few limited duties of handling and quality assurance of these devices. Thus, clear-cut provisions on functions and cooperative efforts in radiotherapy have not been suggested.

Unlike the provisions specified by international organizations or foreign countries, the guidelines on the roles of professionals with a focus on radiotherapy, which were scrutinized by experts in cooperative consultations, are none-existent in Korea.

□ **Safety information management such as adverse events reporting**

Pursuant to the provisions of the Pharmaceutical Affairs Law in Japan, the system of management of adverse events and accident reporting relating to radiotherapy (equipment) is handled in accordance with the management of adverse events caused by medical devices. The U.S.A. FDA regulates management of the adverse events caused by medical devices and, at the same time, some american states regulate, by statutory regulations, the management of adverse events and collection of information of these adverse events caused by radiotherapy equipments.

The U.K. is one of those countries in which collections of adverse reaction information in association with radiotherapy are systematically achieved rather well. Adverse events caused by radiation exposure, not by the failure or defect of a device, are regulated by the provisions of IR(ME)R2000, but accident(s) caused by the defect of device(s) are subject to stipulations set by IRR199. However, problems in the performance or safety of these devices are regulated by MDR2002.

Pursuant to the provisions of the Medical Device Act of Korea, the Ministry of Food and Drug Safety collects safety information in cases of adverse events or accidents caused by the defect or problem of devices. Nevertheless, in general, adverse events or accidents caused by exposure to medical radiations have not been managed by any governmental body (Table 4).

<Table 2> Comparative classification of safety management regulations relating to radiation medical devices (diagnostic devices and treatment devices) for each country

	Korea			Japan			U.S.A.		U.K.	
Classification	1) Diagnostic equipment 2) Special medical devices	Treatment devices	RI[1)] (Radioisotope)	Diagnostic devices & Treatment devices		RI[1)]	Diagnostic devices & Treatment devices	RI & gamma stereotactic radiosurgery device, brachythera-py device	Diagnostic devices & Treatment devices	RI[1)]
Applicable Law	Medical Care Act 1) Regulations for safety management of radiation emitting diagnostic devices 2) Regulations for installation and operation of special medical device(s)	1) Nuclear Safety Act (Enforcement law and regulations) etc. 2) Regulations on the technical standards of radiation safety management		1) Article 30, Enforcement regulation, Medical Care Act	2) Regulations on protection against ioniz-ing radiation	Regulations on protection against ionizing radiation	The State Law	NRC (Nuclear Regulatory Commission) Part 35, Medical use of byproduct material	IR(ME)R2000	IRR1999
Content of description	1) Protection for safety management, patients and workers from radiation emitting diagnostic device(s) operated by medical institution(s) 2) Regulations for installation authorization standard (manpower), quality assurance test (type, standard, management item, etc.), etc.	1) Investigation of actual condition(s) & exposure man-agement of workers 2) Specification of maintenance management duties for medical care devices of radiation		Safeguarding of radiation emit-ting devices, regulations for the prevention of workers and patients from radiation expo-sure	Regulations for the limited amount of irradi-ation in facilities and the limit of irradiated dose exposure by workers	Regulations on protection against ionizing radiation	Licensing for facilities for use (Executed by some state), and on-the-field inspection, etc.	Administrative requirement relating to usage and handling of radioisotopes (RI) etc., user licensing, qualification requirement, etc.	Safety management for patients and workers, etc.	Safety management for workers in radiation related occu-pation
Regulatory agency	The Ministry of Health and Welfare (Local government)	1) Nuclear Safety Commission 2) The Ministry of Education and Science Technology		The Ministry of Health, labor and Welfare (Local govern-ment)	The Ministry of Education, Culture, Sports, Science and Technology	The Ministry of Education, Culture, Sports, Science and Technology	State govern-ment (in the Depart-ment of Health)	NRC or state government in contract with NRC	Care Quality Commissions (CQC)	Health & Safety Executive (HSE)
Quality control for devices	1) Test laboratories for registration 2) Korean Institute for Accreditation of Medical Image	The Ministry of Spontaneous management through a project of quality assurance of dosimetry	Ministry of Food and Drug Safety	-			1) Spontaneous management through RPC (radiologi-cal physics center) 2) Some states stipulated the provision for quality assur-ance (QA) of devices as a compulsory regulation		※France: Regulations for the external quality assurance (QA) procedure are included in the Public Health Law. ※Norway: QA program organization within NRPA, Quality control and on-the-field inspection through KVIST	

1) Excluded radioactive pharmaceutical product(s)

<Table 3> Comparisons of defining the roles of professional groups involved in radiotherapy

Classification	Korea	Japan[2]	U.S.A[3]	U.K.	International Organizations	
					IAEA[5]	WHO[6]
Radiation oncologist	*Handling of radiotherapy equipments, performance of dosimetry, quality control. etc. (A specialist in radiology who possesses a special license for handling radioactive isotope)[1-1]	*Accurate application of standard treatment. *Decision on radiation dose(s) *Decision on target volume(s) of tumor(s) *Confirmation of the limits of all radiation doses *Placing a limit on radiation dose(s) on normal tissues *Approval of the process of treatment plan *Final approval for treatment plan	*Prescription for radiation dose(s)*Supervision of treatment process(es) *Responsibility for reporting on treatment results	*Responsibility for the validity of radiation exposure for medical care and that of other aspect of radiation exposure[4-1]	*Clinical diagnosis *Decision on treatment method *Confirmation of target area, and making decision on normal tissues sensitive to radiation *Analysis of preliminary plan *Selection of treatment plan *Simulation of deliberation and verification of treatment plan(s) *Setting up of radiotherapy *Selection of the position of film(s) *Evaluation after treatment *Making of follow-up observations	* Advice about treatment options and consent for treatment *Target and normal tissue delineation *Prescription of radiotherapy *Planning review and approval *Monitoring of treatment *Patient follow-up
Medical physicist	*Participation in handling, dosimetry and quality control of radiotherapy equipments - A master's degree in physics, nuclear engineering or in the related discipline, and four years of on-the-job experience in radiotherapy under a supervision of a specialist in radiology; or a doctorate in such field with practical experience of radiotherapy for two years[1-1]	(Radiotherapy quality control technician) *Obtaining of patient's data *Management of data *Calculation of dose distribution manually or by using a computer *Preparation of treatment plan(s) for each patient *Preparation of documentation for treatment plan *Cooperation for the quality control of radiotherapy in various aspects: treatment devices and devices' QA program for treatment plan *Establishment and execution of quality control plan(s) after equipment failure, and after completion of equipment repair	*Calibration of treatment devices *Decisions and reviews of the distribution of radiation dose(s) for patients in radiotherapy *Responsibility for weekly review of patient's radiation dose *Responsibility for installation and verification following introduction of new device(s) and their maintenance *Responsibility for procedure and regulation making of quality control for radiotherapy equipments *Responsibility for top priority supervision and management for overall QA procedure	*Accurate calibration of radiotherapy device(s) *Providing of beam data for the calculations of all radiation dose(s); Supervision and management for the analysis and measurement of these data *Supervision of radiotherapy plan *Cooperation with a medical doctor in times of reporting of mechanical results by patient(s) *Management of patient's image data *Development, research, education and training of new devices and material(s), *Confirmation of the defect of hardware and software *Auditing for the sake of patient's safety[4-2]	*Verification of target area *Contour forming technology for patients *Computerization of beam data *Analysis of preliminary plan *Selection of treatment plan	*Specifications of equipment used in therapy and imaging *Facilities design including shielding calculation *Commissioning and quality assurance of diagnostic, planning and treatment equipment and software *Dosimetry assurance *Producing and measurement and beam data analysis *Check treatment plans
Radiation therapist	*Handling of ionizing radiation and non-ionizing radiation, test of nuclear medicine using radiation isotope, handling of diagnostic device(s) for medical imagery and equipment of ultrasonographic diagnosis, selection and management functions of radiation device(s), parts and materials[1-2]	*Precision fixation of patient's position and its confirmation *Early detection of device malfunction and breakdown *Understanding of the safety limit of device manipulation *Irradiation after double confirmations on dose administration for each patient *Investigation for the cause in case of having error(s) in the treatment plan: Defect in equipment and material, problem relating to patient, and making decisions on whether there is a mistake by the operator	*Accurate administration of radiation dose, prescribed by radiologic oncologist, to patient *Responsibility of making observations of changes in patient's condition, and of reporting to radiologic oncologist *Responsibility of management on fluctuation or malfunction of measurement devices, and regulations of safe usage *Responsibilities of decision making and reporting of treatment withholding or postponement in times of trouble with radiotherapy equipment(s)	*In charge of planning and execution of radiation treatment *Irradiation of a precise dose onto tumor(s) by using devices *In charge of planning and execution throughout the entire duration of treatment for cancer patient *Explanation to patient(s) about treatment process and adverse events etc. *Making observations and reporting of treatment process[4-2]	(Technician for simulation for deliberation) *Simulation for deliberation of a treatment plan and its verification (Radiotherapy technician) *First day of treatment: setup *Selection of film position *Daily treatment	*Patient's information and support *Simulation *Planning *Producing and checking treatment plans *Data transfer and monitor unit calculations *Daily radiotherapy delivery *Treatment Verification *Monitoring the patient on a daily basis

1-1) Technical standards for safety management of radiation in medical field Article 9. 1-2) Enforcement regulations relating to medical technicians Article 2. 2) Establishment of the system of safety management for the prevention of accident(s) in radiotherapy (the Guidelines for radiotherapy by the Quality Control Committee) 3) AAPM Report no.46 Comprehensive QA for Radiation Oncology. 4-1) IR(ME)R2000 (Regulations of ionizing radiation in medical exposure). 4-2) Careers of NHS & IPEM 5) IAEA-TECDOC-1040 Design and implementation of a radiotherapy program: Clinical, medical physics, radiation protection and safety aspects. 6) Radiotherapy Risk Profile, WHO/IER/PSP/2008.12

<Table 4> Comparisons of systems for management of adverse events relating to radiotherapy and incident reporting systems

Classification	Korea	Japan	U.S.A.	U.K.
Applicable law	Article 31, Medical Device Act Provisions for the management of safety information such as adverse events of medical device Article 5 1) Medical device operator[1]: During operation of such device(s), case(s) of death, or of developing or possibly developing serious adverse reaction(s) should be reported to the Minister of Food and Drug Safety (MFDS), and their records must be maintained. Practitioner, patient or user of medical device(s) may report to the Minister of MFDS) or medical device operator 2) Manufacturer/Importer/Repairman/Distributor: must recover device(s) of quality defect, and report to the Minister of MFDS after establishment of the recovery plan ※Installation of "Monitoring Center for Safety Information of Medical Device(s)" in medical centers. Ten (10) medical centers were selected in 2012 ※In the Nuclear Safety Act, incidents refer to accident(s) following radiation exposure, excessive exposure to radiation by worker(s), and do not come from adverse events following equipment defect or usage. Also, accident(s) must be reported then to the Nuclear Safety Commission	Article 77, the Pharmaceutical Affairs Law 1) Medical care institution (hospital), its founders, and medical care related personnel 2) Manufacturer and distributor ※In the Regulations on protection against ionizing radiation, accident(s) are not mishaps caused by neither device defect nor device usage, but denote misfortunes caused by radiation exposure, excessive radiation exposure by workers. These accidents are reported then to the Ministry of Education, Culture, Sports, Science and Technology	1) 21 CFR Part 80313 MDR (Medical Device Reporting) - Manufacturer, Distributor, and User - MedWatch program is activated 2) State Law	1) IR(ME)R2000 - Reported in cases where incidents are caused by excessive exposure to medical radiation, and not by breakdown or defect of equipment 2) IRR1999 - Reported to HSE in cases where incidents are caused by equipment defect 3) MDR2002 - Reported when there are problems about device performance or safety
Governmental agency to report	The Ministry of Food and Drug Safety	The Ministry of Health, Labor and Welfare	1) FDA 2) State government	1) CQC 2) HSE 3) MHRA

1) Medical device operator(s): Manufacturer, importer, repairman, distributor or lessor of medical devices, and medical institution founder(s) pursuant to the provisions of the Medical Care Act, and animal hospital founder in conformity with the Veterinarian Act.

Conclusion and policy suggestion

From this study, the safe and efficient utilization and management measures for radiotherapy equipment, from the health care perspectives are suggested as follows.

It is necessary for product approval procedure to be integrated and improved in the step prior to marketing of radiotherapy equipments. Manufacturers/distributors of radiotherapy equipments must obtain a approval from the Nuclear Safety Commission and a medical device approval from the Ministry of Food and Drug Safety successively in order to attain authorization for marketing. However, owing to overlapping of the submitted data, improving the process of approval procedure seems imminent.

In the postmarketing phase, the safety management measures focusing on patient safety are required. Presently, safety management, conducted in conformity with the provisions stipulated by the Nuclear Safety Act, places emphasis on safety management of radiation utilization facilities and workers. Thus, supplementary revisions of regulations and current system focusing on patient safety are necessary.

Furthermore, in an effort to secure the fundamentals of quality control and safety management for radiotherapy, the roles and standards for professionals relating to radiotherapy must be defined.

Moreover, it is necessary to prepare a management system for adverse events and incidents generated in the process of radiotherapy, in addition to adverse events due to a defect or problem of radiotherapy equipments.

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