Research on Evaluation of Medical Exposure

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In this just-completed midterm plan at NIRS, the Medical Exposure Research Project (MER-project) has had a mission to investigate the frequencies and doses of Japanese medical radiation uses, both diagnostic and therapeutic. The data are being collected in collaboration with local hospitals and academic societies. These data will be stored in a national database of medical exposure (details for this are under contemplation) and used as scientific and practical purposes for the justification and optimization of radiation protection in medicine. They will also be provided for the UNSCEAR global survey project.

Five studies are being undertaken currently: (i) Estimations of examination frequencies and organ doses in X-ray CT, PET, and PET/CT in collaboration with local hospitals and academic societies; (ii) Organ dose estimations of patients for diagnosis and radiotherapy; (iii) Study of radiobiology in radiation use in medicine; (iv) Development of the method for risk-benefit communications in medicine; and (v) Running an organization (J-RIME: Japan Network for Research and Information on Medical Exposure) for the exchange of information on radiation protection in medicine. Their short descriptions follow.

(1) Estimation of CT and PET doses
CT dose. WAZA-ARI is the web-based open system for the CT dose calculation, which has been developed by Oita University of Nursing and Health Sciences and the Japan Atomic Energy Agency (JAEA). From December 2012, it has been installed in the web server of NIRS, and is available to the public for trial use.

This year, using the improved WAZA-ARI “WAZA-ARIv2”, we investigated CT doses in the NIRS hospital; we inputted the exposure conditions on about 500 CT examinations in cooperation with radiological technologists and calculated organ doses and effective doses. Those doses from devices with auto exposure control (AEC) were compared with doses without the AEC. We also enhanced convenience of use for the functions of exposure conditions and statistical analysis and increased the information of dose coefficients corresponding to more CT scanner models. We held seminars in all over Japan to promote the expanded use of WAZA-ARI in medical settings. The number of registered users was increased to 700 (Fig. 1).

PET dose. A physiologically based pharmacokinetics model (PBPK model) has been used to describe the kinetics of pharmaceuticals physiologically by using physiological parameters such as blood flow, organ volume, etc. in the pharmacokinetics field. For the internal dose estimation for FDG-PET examinations, we have modified and applied the PBPK-model, which can consider the differences among patients who have different body sizes and metabolisms (see the following highlight for details).

(2) Estimation of organ dose in radiotherapy
Recent progresses in radiotherapy can provide benefits to patients with extended survival. On the other hand, the secondary cancer risk by undesired irradiation to non-target healthy tissue is of concern to the survivors.

In 2014, we developed the 3D dose map for estimation of non-target organ doses of the pelvic field using an anthropomorphic phantom and polymer gel dosimeter in radiotherapy for uterine cervical cancer. In 2015, we analyzed the 3D dose distributions of the organs of patients of uterine cervical cancer radiotherapy by using a typical treatment plan, in which irradiation conditions were determined based on the facts of the radiotherapy in the NIRS hospital.
Currently, we have estimated the organ doses of pediatric patients exposed to secondary neutrons after proton therapy using a Monte Carlo simulation code (PHITS); the photon beam line and 5-year-old voxel phantom were modeled (Fig.2). The secondary neutron doses of the non-target tissues were higher so as to be closer to the treatment target. The measurement techniques using an infant physics phantom were also verified to test the possible use of radio-activation of the phantom material for verification of the dose delivery distribution and to assess the doses of heterogeneous body materials (such as bones, muscles and fat) of the proton beam transmission area.

(3) Dose Index Registry

The importance of tracking dose of patients with medical radiation exposure, which is the concept behind the IAEA’s “Smart Card/SmartRadTrack project”, has been acknowledged. We are developing an automatic dose collection system and database for CT examinations, which enables the transfer of DICOM data from devices of different manufacturers into one database (Fig.3). This system can collect CT radiation dose information in large quantities more correctly, compared to conventional questionnaire patterns. This makes it possible to compare the data of one medical institution with those of other medical institutions, so to reduce the variations of CT radiation doses among the institutions.

In 2015, the system became available for data collection from all CT makers. By December 2015, we had connected data acquisition tools to hospital PACS servers or CT devices of 30 medical institutions directly, and collected information on 80,000 CT examinations. These data can be shared among NIRS and cooperative institutions by using the VPN.

(4) Development of the method for risk-benefit communications in medicine

Increasing awareness and knowledge about radiation protection in medicine is necessary to answer the public’s concerns on health risks of low-dose radiation exposure including medical exposure.

Toward that end, we prepared materials explaining a risk assessment/management of radiological examinations. The main contents are global trends of medical exposure, dose assessment of medical exposure in Japan, radiation risk of diagnostic imaging in pediatric patients, improving radiation protection in pediatric imaging, creating better communications between medical staff members and parents of patients, and other related topics. The materials have been delivered into healthcare settings through the training courses hosted by NIRS, such as courses for young radiologists and for medical physicians.

(5) J-RIME

For the nation-wide exchange of information on medical exposures, a general meeting of the Japan Network for Research and Information on Medical Exposure (J-RIME) was held in April 2014, and it was decided to establish a Working Group for diagnostic reference levels (DRLs) for each radiation examination.

J-RIME has discussed such topics as how to determine the DRLs of computed tomography, plain radiography, mammography, dental radiography, fluoroscopically-guided interventional procedures and nuclear medicine procedures. These “Japan DRLs 2015” were approved for publication by the J-RIME and its liaison organizations in June 2015 (Fig.4). This was the first attempt to establish national DRLs for radiation imaging in Japan, and it has brought favorable reactions from international bodies.

We have promoted better understanding, expanded use and deeper permeation of DRLs in medical settings in cooperation with J-RIME and its liaison organizations. We prepared standard manuals to explain DRLs for optimization of protection. They were authorized as official documents of J-RIME and delivered to healthcare workers through liaison societies of J-RIME as well as to the public via the J-RIME homepage.
Physiologically-based pharmacokinetic model for calculating internal doses in $^{18}$F-FDG examinations

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Introduction
In nuclear medicine, positron emission tomography (PET) as well as other conventional imaging methods are well-established and performed as very useful methods in diagnoses for patients. Among the radiopharmaceuticals used in PET, $^{18}$F-fluoro-deoxy-glucose ($^{18}$F-FDG) is a typical and widely used compound. The medical exposures of patients in $^{18}$F-FDG examinations can be calculated based on the International Commission on Radiological Protection (ICRP) Publication 106 [1] in which the biokinetic data for the radiopharmaceutical and conversion factors of the organ doses (mGy) and effective doses (mSv) to the injected activities (MBq) of patients of 1, 5, 10, and 15 years of age and adult patients are shown in the publication tables. To determine these biokinetic parameters, compartment models have been used for calculating the cumulated activities in source organs. The compartment model can phenomenologically explain the kinetics of radiopharmaceuticals inside the body by setting the combination of organ or ideal compartments and movements of radiopharmaceuticals among them. On the other hand, a physiologically based pharmacokinetics model (PBPK model) has also been used to describe the kinetics of pharmaceuticals physiologically by using physiological parameters such as blood flow, organ volume, etc. in the pharmacokinetics field. The PBPK model is more realistic and provides better consideration for the physiological differences among individuals compared to the compartment models. In this study, the PBPK model was applied to estimate internal doses of the patients in $^{18}$F-FDG examinations to consider the differences among patients.

Methods
In the PBPK model, the main organs are combined with blood flow lines among them. The parameters used in the model are organ volumes, blood flow rates, pharmaceutical concentrations, and partition coefficients of blood to organs as the physiological data for calculating the kinetics of the radiopharmaceuticals. However, the whole body PBPK model including all main organs is complicated and needs all parameter values determined (Fig.1). For the practical simplification in the dose calculation, the model was simplified (Fig.2) with source organs of $^{18}$F-FDG by referring to the ICRP publication data.
The time dependencies of the pharmaceutical concentrations in organs after injection can be described as a set of simultaneous differential equations. The concentrations of the pharmaceuticals were calculated by using a program implementing the Runge-Kutta method in the Linux system. Physiological parameters of blood flow rates and volumes were determined by referring to data in the literature and papers on physiology. The rest of them were roughly assumed by considering the kinetics in the body.

Results and discussion

The results of time dependencies of the concentrations and amounts of the activities of radiopharmaceuticals in organs depended on the settings of the physiological parameters in the PBPK model. Considering the characteristics of the $^{18}$F-FDG radiopharmaceutical, some of the parameters were modified. By adjusting the parameters, concentrations of these organs were changed and the curves were reproduced to some degree (Fig. 3).

The PBPK model has many physiological parameters and flexibility to fit the pharmacokinetics in the physiological conditions and anatomical components of the individual patient. For the same person, the differences of kinetics of radiopharmaceuticals depend not on the blood flow rate or organ volumes, but on the metabolisms of organs corresponding to the kinds of the nuclide and chemical forms. For the FDG kinetics, some parameters of the PBPK model were modified, and distribution patterns in organs showed differences compared to general conditions. Further consideration and remodeling of the movement and metabolism of the pharmaceuticals inside organs is necessary to reconstruct the kinetics of $^{18}$F-FDG more accurately.

Adjusting parameters, in principle, the differences of patient body sizes and physiological conditions should be considered in the calculations not only for absorbed fractions of mathematical or voxel phantoms, but also the biokinetics of radiopharmaceuticals for dose estimations.

References

