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A Brief Review of Researches Related to Radiation Emergency Medicine at Fudan University, China

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Institute of Radiation Medicine (IRM), Fudan University originated from Shanghai Institute of Industrial Hygiene which was founded by the Ministry of Health, P. R. China, in 1962. From 1985 to 2000, it was placed under the management of the former Shanghai Medical University, and it was transferred to Fudan University as the former Shanghai Medical University was merged in 2000.

In the past nearly 50 years, both fundamental and applied researches on the dose–response relationships of ionizing radiation, prevention, diagnosis, treatment of radiation injury and other related subjects were comprehensively conducted in the IRM, and a lot of fruitful results have been achieved. In this review, the main research results associated with radiation emergency medicine in the IRM were briefly introduced and summarized into the following aspects: Prediction of radiological impacts due to nuclear or radiological terrorism events, Dose estimation, Decorporation of intake radionuclides, Treatment of radiation injury.

1. Predict radiological impacts due to nuclear or radiological terrorism events

In case of nuclear accident or radiological terrorism event, predicting its radiological impacts on the environment and public in advance is essential to carry out the corresponding emergency response. For fast and more directly perceived understanding of the impacts due to nuclear or radiological terrorism events in city areas, a new software system entitled with SHERSA was developed in the IRM, Fudan University in 2010[1].

In the prediction system, the impacts of three scenarios of events including spreading radioactive materials, dirty bomb attack, explosion or arson attacks on the radiation facilities can be predicted. The Gaussian diffusion model was employed to predict the spread and deposition of radioactive pollutants, both the internal and external doses can be estimated for the representative person. Through integrating of the computing system and Mapinfo GIS®, the predicted results including the accumulative dose of public, distributions of airborne and surface contaminants can be visually displayed on the electronic maps of a city, as shown in Figure 1. For comparisons of the prediction results, the similar software Hotspot®[2] was also used to predict the same scenarios of events. The results showed that the predicted results were well consistent with each other. The deviation between the new system and the Hotspot® was less than 150 m for predicted isoplethic curves of dose rate downwind. The new software system can predict not only the dose, but also the real-time distributions of airborne and surface contaminants in an electronic map. It is thought that the new software system is of the practical value in predicting the radiological impacts due to nuclear or

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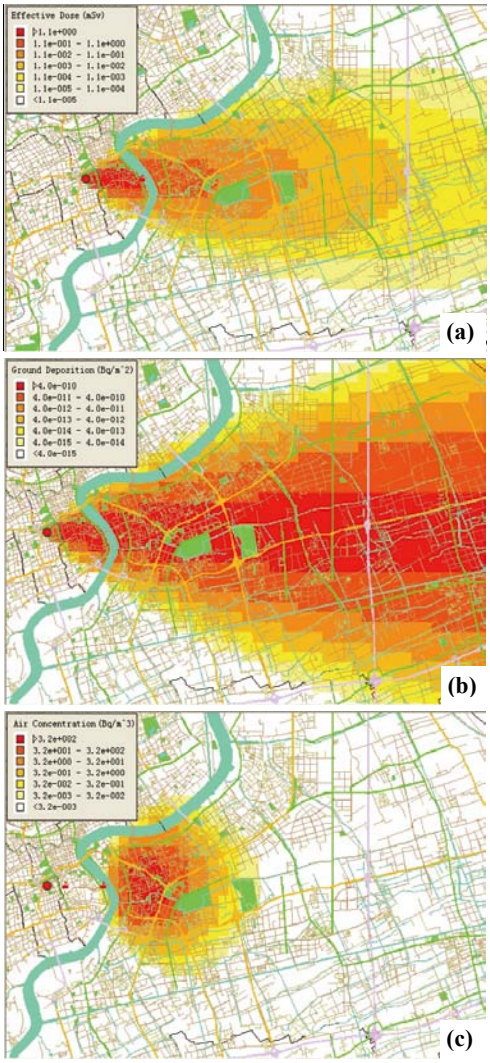

Fig. 1. Predicted results for a case of dirty bomb attack. (a) accumulative dose, (b) surface contamination, (c) airborne concentrations in 1 h.

radiological terrorism events in city areas.

2. Dose Estimation

2.1. Physical dosimetry

In case of radiation accidents, fast and accurate estimations of the external and/or internal doses of relevant personnel are very important for conducting early stages of medical treatment. Even though several dose calculation codes have been implanted as subroutines in the frequently used software systems, such as RASCAL[3], SPEEDI/WSPEEDI[4], RADOS 3.0[5], however, those systems were mainly developed for predicting the radiological impacts due to large-scale spread of radioactive materials. Both the gamma dose rate and airborne activity predicted by the systems are relatively rough due to the large scale of diffusion calculation, and the reference person is generally assumed to be uniformly exposed. Therefore, it is thought that those computer codes are not suitable for accurate estimations of personal doses

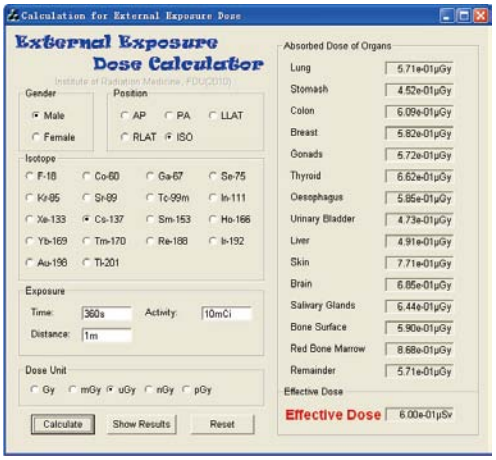

Fig. 2. Schematic diagram of the external dose calculator interface.

in cases of commonly encountered radiation accidents, such as the accidental exposure due to the loss of radioactive sources or strayed into strong radiation fields.

For fast and more accurate estimation of external doses due to the accidental exposure to solid radioactive sources, a new set of software was developed in the IRM, Fudan University in 2010[6]. Figure 2 shows a schematic diagram of the calculation interface. At present, both the organ/tissue dose and the effective dose can be calculated for a reference person (male or female) exposed to any of the 26 radioactive isotopes at any distance and any exposed time. Five kinds of external irradiation modes (AP, PA, LLAT, RLAT, ISO) recommended by International Commission on Radiological Protection (ICRP)[7] were all considered in the dose estimation. The voxel models for male and female developed by Rensselaer Polytechnic Institute[8] and the Monte Carlo particle transport code MCNPX[9] were employed for calculating the doses of organs or tissues exposed to a certain amount (unit) of known particles including both gamma and beta radiation, the air-attenuating effect was also considered. Based on a large number of simulations, a set of database on the doses of organ/tissue exposed to 26 kinds of radioisotopes at different conditions was built and embedded into the software for fast calculations. Simulation results showed that both the organ/tissue dose and the effective dose calculated with the new software are comparable to those with other estimation methods[10].

2.2. Biological dosimetry

Diagnoses of acute radiation syndrome (ARS) are generally based on clinical and laboratory data. Among the assays for biological dosimetry, the chromosomal aberration analysis from cultured circulating lymphocytes is the most widely accepted and reliable one. It is still considered to be the "gold standard" of biological dosimetry by now. In the early 1970s, the dose–response relationships of radiation-induced chromosome aberration and micronucleus formation in human lymphocytes were well established

in the IRM[11], and they had been successfully applied to the dose estimation in a case of ^{60}Co exposure accident happened in 1980. The frequency of dicentrics plus centric rings (Dic+R) was 89%, and the dose was estimated to be 4.78 (4.53-4.88) Gy which was well consistent with the results of physical dosimetric estimation, and the victim was diagnosed as severe hematopoietic type of ARS[12]. Lymphocyte chromosome aberrations were examined in the 12 years follow-up. The results showed that the incidences of Dir+R reduced with logarithmic regression (r=–0.9895), while the number of cells with stable aberrations remained practically unchanged and showing a tendency to increase[13].

Furthermore, based on the G-banding studies on the chromosome aberrations of bone marrow cells, the acute lymphocytic leukemia (ALL) in the victim was diagnosed 12 years after the radiation accident[14].

Many studies have shown that the dicentric frequency per cell can provide a reliable estimate of the dose in case that the whole body is uniformly exposed to an acute accidental exposure. However, in most of the accidental scenarios, the exposure was normally non-uniform and involved only parts of the human body. This will bring out the difficulty in accurate dose estimations. Through the experiments on the fractionated *in vitro* irradiation to the peripheral blood of healthy volunteers and the *in vivo* studies on patients undergone fractionated and partial-body radiotherapy, the dose-response relationships in the scenario of partial-body irradiation was also established in the IRM, Fudan University based on the contaminated Poisson distribution method[15]. The results showed that our method was feasible in the dose estimation of partial-body irradiation with an exposure larger than 2 Gy[15].

3. Decorporation of intake radionuclides

Once radionuclides enter into the human body, the chelation therapy is recognized as an effective method to increase the excretion of radionuclides and reduce their toxicity to person. At present, diethylenetriaminepentaacetic acid (DTPA) is the only chelating agent clinically used for decorporation of actinides. However, its decoporation efficacy is still low for uranium and strontium, and a number of side effects on persons may also occur. Since the late 1960s, our institute has devoted a lot of effort in the synthesis and testing of new chelating agents, such as pheno-licpolyaminopolycarboxylate derivatives and bisphosphonate sequestering agents, for decorporation of thorium, uranium and strontium.

For decorporation of thorium and uranium, we have synthesized about 20 kinds of chelating agents. We found that the chelating agents of 8102 (CABMIDA), 7601(CBMIDA) and 9501 (BPCBG) were superior to the DTPA for decorporation of thorium and uranium[16-22]. And they were found to be the most effective agents for scavenging superoxide and hydroxyl radicals, inhibiting radiation-induced lipid peroxidation *in vitro*, modifying ^{234}Th induced bone marrow and liver injury *in vivo*, alleviating the uranium induced kidney injury *in vivo* , demonstrating low toxicity at effective injection dosages[23-29]. Moreover, we demonstrated for the first time that the protective effects of 9501 and 7601 against damage induced by ^{234}Th or uranium are mediated by both pronounced removal effectiveness for ^{234}Th or uranium and anti-oxidative action[22]. Recently, the chelating agents, trisodium salts of calcium- and zinc-diethylenetriaminepentaacetate ($CaNa_3$- and $ZnNa_3$-DTPA) we prepared, have been approved by Shanghai Municipal Health Bureau for emergency medical use in China to decorporate actinides.

For decorporation of strontium, we have successfully developed a new decorporation agent named S186 as the strontium-specific chelating agent[30-32]. The S186 is a kind of sodium salts of calcium-acetylpropylamine phosphonate (APAP). In a case test for 4 persons who took ^{90}Sr in due to an internal contaminated accident, the APAP was administered intramuscularly once a day for 3 days, the increased excretion of ^{90}Sr was obvious and no side effects were observed among them[33]. Recently, the S186 has also been approved by Shanghai Municipal Health Bureau for emergency medical use in China.

4. Treatment of radiation injury

Treatment of radiation dermatitis was performed in our institute from 1970s, and we had diagnosed and treated nearly 150 cases of radiation dermatitis by 1987[34-36]. Moreover, we had also treated more than 100 cases of radiation proctitis[37], radiation cystitis[38] and other partial radiation injury due to the radiotherapy by 1997. We found that the alpha-2-macroglobulin was an effective drug for the treatment of radiation injury.

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