

REVIEW ARTICLE

The Effects of Medical Radiation: A Few Things Nuclear Cardiologists Must Know

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Abstract

It is important that nuclear cardiologists understand the effects of medical radiation, especially as the use of medical radiation has implications for the public. There are three basic principles regarding the medical use of ionizing radiation, which can be employed by medical practitioners to ensure that they use ionizing radiation appropriately. It is also important to understand the two different types of effects of ionizing radiation; i.e., stochastic and deterministic effects, but the details surrounding these effects are disputed. Clinicians who use ionizing radiation carry a great burden of responsibility because the usage of medical radiation is increasing rapidly, and in developed countries more than half of the public radiation burden is due to medical radiation. Thus, we are responsible not only for the effects of medical radiation on patients, but also on the public as a whole. In addition, medical practitioners should also be aware of the effects of occupational radiation, which are frequently overlooked. These key issues are reviewed briefly in this article.

Keywords: Medical radiation, ICRP, Justification, ALARA, Cataract, Cancer risk

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Ionizing radiation is an essential tool for modern medicine, and its usage is increasing rapidly. Whilst the utility of ionizing radiation is unquestionable, it also has harmful effects. Thus, clinicians must be aware of both the risks and benefits of ionizing radiation. Recently, several papers examining the effects of computed tomography (CT) on cancer risk have attracted public attention (1, 2). In Japan, after the Fukushima nuclear power plant accident there was a flood of conflicting information regarding the effects of radiation from different sources, which has sown confusion among the public.

It is very important for cardiologists to understand the risks and benefits of ionizing radiation because cardiology is one of the medical fields in which ionizing radiation is used most frequently (3). Accordingly, the International Commission on Radiological Protection

(ICRP) published specific guidelines regarding radiological protection in cardiology. In this review, we attempt to answer some basic questions about the medical use of radiation in order to clarify our current knowledge about this topic.

Five basic points to remember

Q: What basic knowledge about radiation do clinicians need to know?

A: The following table lists basic knowledge about radiation (Table 1).

It is not possible to cover all of the listed topics in this short review; thus, we will focus on the most important issues instead.

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Table 1

Effects	Stochastic		Deterministic
Direction	External		Internal
Categories	Public	Occupational	Medical
Principles	Justification	Optimization	Dose limit
Reduction (external radiation)	Distance	Time	Shielding

Principle of Justification

Q: Which of the three principles listed above is the most important?

A: All three are important, but in my opinion “justification” is the most important.

The use of medical radiation carries some risks. According to the linear non-threshold (LNT) theory, which will be discussed later, it is impossible to completely remove the risks associated with radiation. Thus, the use of ionizing radiation is regulated in most countries based on the recommendations of the ICRP. The following three principles regarding the use of radiation are essential.

Justification: The advantages of using ionizing radiation must outweigh the disadvantages.

Optimization: The radiation dose must be kept as low as is reasonably achievable/practicable (ALARA).

Dose limit: Individual dose limits should be set to protect against the risk of radiation.

All three principles are important. However, I consider that “justification” is the most important for two reasons. First, every diagnostic process starts with a decision to perform examinations, and such decisions are closely related to “justification”. Secondly, the other two principles are subject to continuous improvement due to advances in medical techniques and effort of many medical workers. However, “justification” solely depends on clinicians’ decision-making.

To justify the usage of ionizing radiation, the benefits must outweigh the risks. However, how to define “outweigh”? It is necessary to quantify the benefits and risks during the decision-making process, which is very hard because in medical practice the individuals that benefit from the use of ionizing radiation and those that are put at risk by it are usually different. A typical example is cancer screening with positron emission tomography using ^{18}F labeled fluorodeoxyglucose (FDG PET). Roughly 1 in 100 patients that undergo screening FDG PET are found to have cancer (4, 5). Thus, whilst FDG PET is significantly beneficial for the patient whose cancer is detected, it only increases the risks in the other 99 subjects. Do “the needs of the many outweigh the needs of few, or the one (6)” or “the needs of the one outweigh the needs of many (7)”?

Science cannot answer this question. Assessing the risks and benefits of medical radiation is not merely a question for medical science, but is also social issues such as risk communication, health policy making and culture.

One possible way of measuring the benefit of medical radiation is to assess the change between the management strategies employed before and after such examinations. A previous study revealed that roughly 30% of pediatric CT examinations are unnecessary or can be replaced with examinations that do not involve ionizing radiation (8). Gibbons et al. showed that 25% of nuclear perfusion tests performed at the Mayo Clinic were carried out under inappropriate or uncertain indications (9). These findings suggest that the assessments of the “justification” that are currently performed in daily practice are far from perfect.

Optimization and dose limits

Q: How can nuclear cardiologists optimize the use of radiation?

A: We can optimize radiation doses and protocols and employ DRL.

Even when the justification is assessed appropriately, optimization is required.

Many different methods can be used to optimize the radiation dose. One simple method is to use technetium-labeled agents instead of thallium. In ICRP publication 106, it was stated that 0.14 mSv/MBq is an effective dose for thallium in adults (10). Note, this dose is smaller than that described in ICRP pub 80 (11). As the commonly prescribed thallium dose for stress perfusion scans is 111 MBq, the effective dose delivered during typical thallium study is roughly 16 mSv. Since the effective dose of $^{99\text{m}}\text{Tc}$ MIBI is 9.0×10^{-3} mSv/MBq (11) and the commonly prescribed dose is 1110 MBq, which results in an effective dose of roughly 10 mSv, the use of $^{99\text{m}}\text{Tc}$ MIBI leads to one third reduction in the radiation dose compared with thallium. Recent advanced solid state detector technology allows us to reduce both the radiation dose and the duration of imaging scans without sacrificing image quality (12). In the absence of advanced scanners, choosing stress-only protocols for selected low-risk patients (13) might help to avoid the

unnecessary radiation (14). Even determining the injected dose based on the patient's weight instead of using a fixed dose could result in a significant reduction in the radiation dose (15). Combining these techniques might make it possible to reduce the radiation dose to approximately 1 mSv/patient (16).

Setting dose limits for medical radiation can be harmful to patients. Thus, the "dose limit" principle is not applied to medical radiation. However, many professionals consider that the use of medical radiation should be standardized to some extent. Recently, the concept of diagnostic reference levels (DRLs) was introduced into radiological practice (17, 18). DRLs should not be misunderstood as a dose-limiting tool; instead, they were developed to aid the standardization of the usage of medical radiation. Medical practitioners can perform comparisons of the average doses delivered during 10 to 50 typical daily examinations with the DRLs (19). If the average dose is considerably higher than the DRLs, problems with the scanner settings, imaging protocol, or operator technique should be suspected. Conversely, when the average dose is quite lower than the DRLs, it may indicate poor image quality. Thus, by using DRLs clinicians can review daily procedures and fix any problems (20). For example consider the case of myocardial perfusion scan using ^{201}Tl . First thing to do is to calculate average injected dose of 10~50 routine studies. Then, compare the average with the recommended DRL of ^{201}Tl study. It is not yet published but 180 MBq will be Japanese DRL for ^{201}Tl . (For nuclear medicine, DRLs are defined as activity per exam. For other radiological examinations, DRLs are defined as dose such as mGy/min) If the calculated average is much larger than the 180 MBq, procedure should be evaluated to reduce the injected dose. On the other hand, when the average is much smaller than the 180 MBq, the image quality should be evaluated. If the image quality is good enough, it is OK. However, when the image quality is clearly suboptimal, increasing injected dose can become the option. Japanese DRLs, including that for nuclear medicine, are currently being developed, and the first report will be published this year. Note that DRL for nuclear medicine procedures including myocardial perfusion imaging are defined based on the actual injected dose, not the dose at reference time.

Stochastic effects

Q: Does medical radiation cause cancer?

A: Medical radiation might increase the risk of cancer. However, such effects are hard to detect

in the range of diagnostic radiation doses.

Radiation has two kinds of biological effects, stochastic and deterministic effects. Stochastic effects are not usually considered to exhibit thresholds. Instead, the probability of their occurrence increases linearly with the dose (the LNT theory). Biologically, radiation-induced carcinogenesis and heritable effects are classified as stochastic effects. However, in humans there is no evidence of heritable effects of radiation; thus, the stochastic effects of radiation essentially refer to radiation-induced carcinogenesis. Fig. 1 illustrates roughly calculated excess cancer risks using detriment-adjusted nominal risk coefficient (10^{-2}Sv^{-1}) from ICRP pub 60 and pub 103 (21).

Recently, several studies have examined the link between medical radiation and the risk of cancer, especially in pediatric patients (1, 2, 22). Medical radiation has recently become a public concern. However, these epidemiological studies must be read very carefully because analyzing the risk of medical radiation is very difficult. Patients who receive medical radiation visit hospitals because they are sick or at least are suspected to be sick. Thus, such patients might be more predisposed to cancer than control subjects, and hence, might develop cancer because they are predisposed to it instead of the effects of medical radiation. Such bias is known as "confounding by indication" or "reverse causality" and removing such bias is very difficult. Thus, we should not treat the findings of the above-mentioned reports as established facts. They are still under debate.

However, there are several established facts that clinicians must know.

1) The cancer risk attributable to medical radiation is too low to detect

According to the LNT theory, even small radiation doses will increase the risk of cancer to some extent. Whilst this is theoretically true, the increase in cancer risk is very small and uncertain when the radiation dose is less than 100 mSv. This uncertainty has led to the proposal of several non-LNT theories such as supra-linearity, linear-quadratic, and hormesis theories (Fig. 2). Fig. 3 shows a famous graph that depicts the linear relationship between the radiation dose and the excess relative risk of colon cancer in atomic bomb survivors (23). This graph shows a clear linear relationship across a "wide" range of doses. The controversy regarding the effects of low-level radiation (Fig. 2) concerns a very "narrow" dosage range (between the arrows in Fig. 3). The data below 100 mSv is very susceptible to statistical noise. To solve this uncertainty, it is necessary

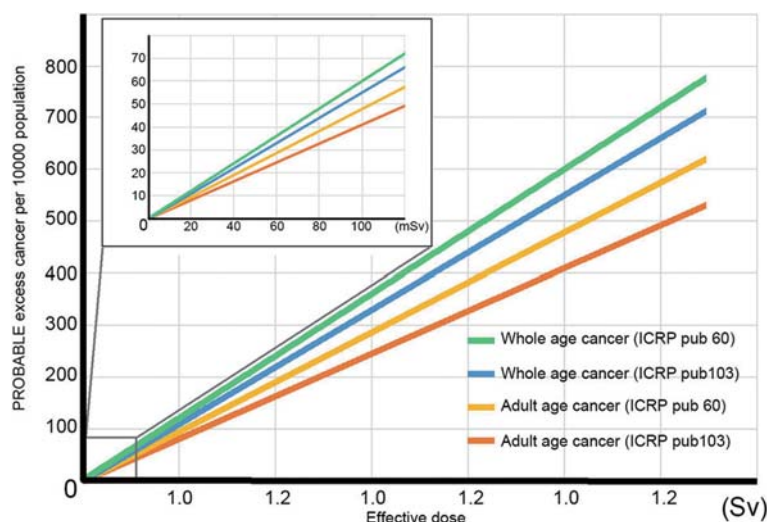


Fig. 1 Rough illustration of excess cancer risk according to radiation dose calculated from the ICRP pub 60 and 103

Note, this is very rough calculation which not accounting ethnic/age/gender/exposed organ difference. This graph gives you only rough idea regarding magnitude of cancer risk increase according to radiation dose in the large population. Do not use it for individual risk assessment.

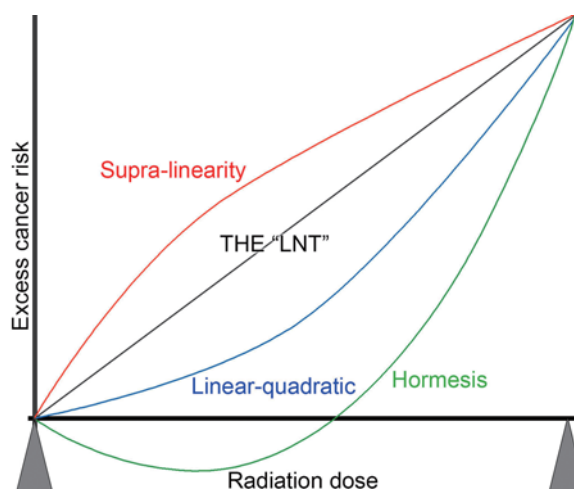


Fig. 2 Illustration of the LNT and other non-LNT theories

Note, this figure focuses on the very narrow range between the arrows shown in fig. 2. The gray arrowheads roughly correspond to the arrows shown in fig. 2.

to perform very large-scale lifetime cohort studies. As shown in Fig. 4 (which is based on data obtained by the National Research Council in 1995 (24)), a cohort size of 80,000 is required to obtain evidence for radiation dose of 50 mGy, which is still higher than the doses used in common nuclear cardiology procedures. Note, this kind of study requires lifetime follow-up to provide definitive evidence, and performing such large-scale lifetime cohort studies is extremely difficult.

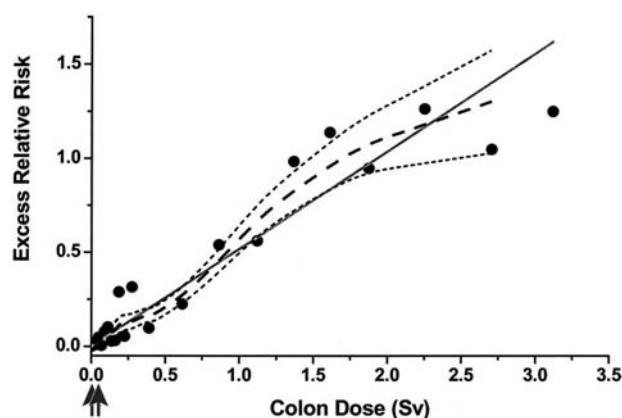


Fig. 3 Relationship between the incidence of colon cancer and radiation dose in atomic bomb survivors (from ref (23), reprinted with permission)

The arrows indicate radiation doses of less than 100 mSv. Note, radiation doses of less than 100 mSv only account for a very small part of the far left of the graph.

2) DNA double-strand breaks (DSB) occur even after the diagnostic use of radiation, but they usually heal

Recent molecular biology techniques have made it possible to easily assess the frequency of DNA DSB in a quantitative manner. γ -H2AX has been used as a marker of the DNA DSB (25) caused by low-dose ionizing radiation and its repair in many studies (Fig. 5). In several CT- or FDG PET-CT-based studies, low-dose medical radiation was shown to induce DNA damage. The DNA damage caused by CT exhibits a dose-damage relationship (26) and typically normal-

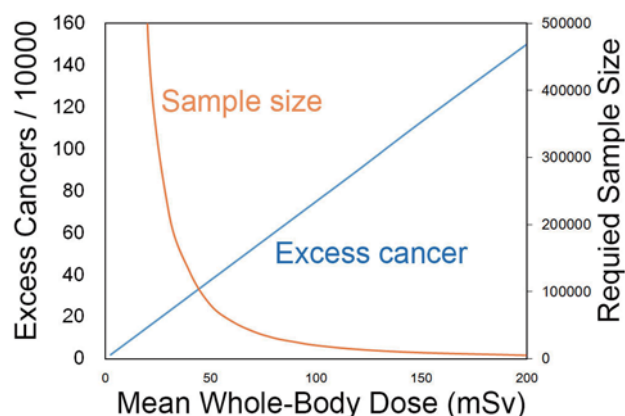


Fig. 4 Relationships between radiation dose, the expected excess cancer cases, and the required sample size for detecting an increased cancer risk

Note, as the radiation dose decreases, the number of excess cancer cases falls linearly, but the required sample size increases exponentially.

izes at 24 hr after the irradiation (27). Few studies have examined the effects of DNA damage induced by nuclear medicine procedures, especially that caused by diagnostic procedures. A study from Germany demonstrated that the DNA damage induced by FDG PET-CT involves a tri-phasic period of DNA damage and repair, which lasts for over an after the injection of FDG (28). In FDG-PET CT, the radiation from the CT causes two to three times more DNA damage than the FDG itself.

Deterministic effects

Q: Can medical radiation cause severe deterministic effects?

A: Yes, of course.

Deterministic effects have dose thresholds, below which no effects are observed. Usually, the thresholds for deterministic effects are considered to be relatively high; thus, these effects tend to be overlooked, even by medical professionals.

Radiation can have various deterministic effects (Fig. 6) (3, 21, 29, 30). Among the various deterministic effects of radiation, most major effects relate to the skin or the lens of the eye. Skin reactions are the most important problem in cardiology because the majority of acute skin injuries are caused by interventional procedures. It is generally considered that marked skin reactions occur when the absorbed skin dose is greater than 2 Gy, and clinically important skin reactions occur when the absorbed skin dose is greater than 5 Gy (30). However, these thresholds are often exceeded during nuclear cardiology procedures. Koenig reported that among 73 reported skin injuries, 59 (80%) were due to cardiology-related procedures, mainly angiography and other interventions (31). It should be noted that these

threshold values are for people with average radiation sensitivity, which can vary markedly between patients. Thus, during fluoroscopy clinicians must follow the ALARA concept and monitor their patients carefully.

Radiation-induced cataracts might be the most overlooked deterministic effect. In the early stages, the effects of radiation on the lens typically present as posterior lens opacity (32). As radiation-induced cataracts exhibit a low dose threshold and a long latency period, taking precautions against cataract is important not only for patients but also medical workers. Old textbooks have described threshold values for lens opacity of 2–8 Gy (2 Gy for lens opacity after a single acute exposure, and 8 Gy for visual impairment after chronic radiation exposure) (33, 34). However, a recent report has suggested a markedly lower threshold value of 0.5 Gy (35).

In clinical practice, the effective dose employed during nuclear cardiology is lower than the threshold values described above; thus, no specific precautions against such deterministic effects are required. However, as many nuclear cardiologists also act as/with interventionalists, nuclear cardiologists should be aware of such effects.

Our responsibilities

Q: How great is our responsibility to the public?

A: Huge.

There are various natural sources of radiation. For example, internal inhalation (e.g., radon), ingestion (e.g., potassium), external cosmic rays, and terrestrial sources are all common natural sources of radiation.

Fig. 7 shows various sources of the public radiation burden and the amounts of radiation each source contributes. According to the UNSCEAR 2008 report (36), roughly 20% of the public radiation burden is due to medical radiation. However, this is the worldwide average and so the contribution of medical radiation might be even higher in developed countries. As shown in fig. 7, medical radiation is a major source of public radiation in both the US (roughly 50%) (37) and Japan (over 60%) (38). Thus, medical practitioners have a huge responsibility to the public. In the US, the total effective dose per person due to nuclear medicine is 0.77 mSv/year, which represents 12% of the total dose. The NRC specifically analyzed nuclear cardiology procedures and found that 10% of the total public radiation burden is due to nuclear cardiology procedures. In Japan, there have not been any specific analyses of the effects of nuclear cardiology procedures, but it was reported that nuclear medicine contributes a radiation

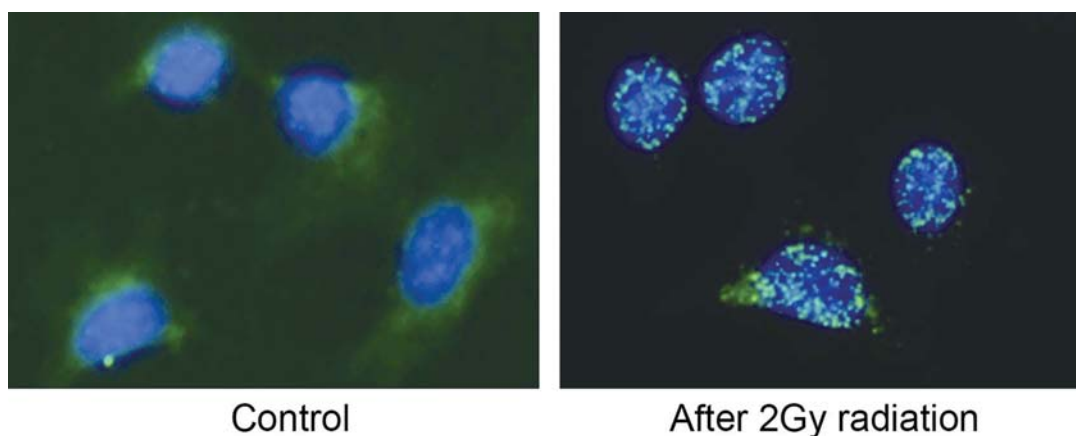


Fig. 5 Image showing γ -H2AX foci (green dots) at sites of DNA DSB
Note, the greater number of foci observed after irradiation with 2 Gy compared with that seen in the control. (Personal data)

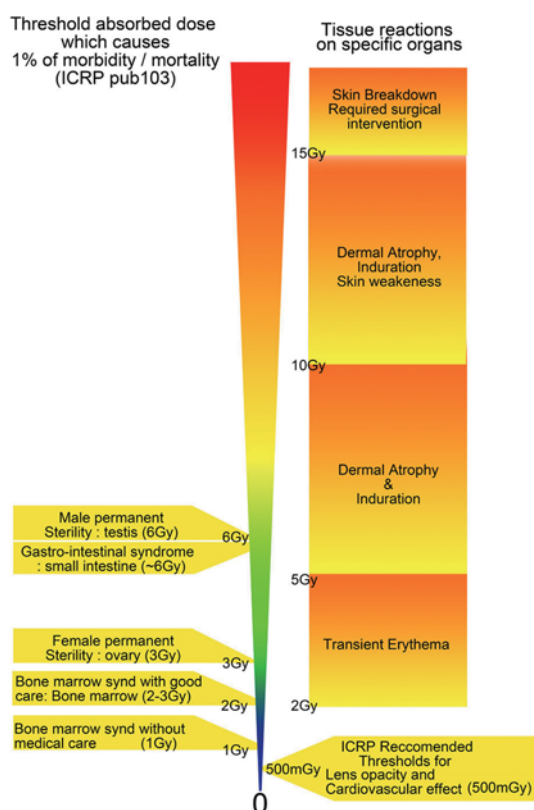


Fig. 6 Relationship between typical deterministic effect and radiation dose

Sources: (3, 21, 29, 30)

Left side is projected threshold estimates from ICRP pub 103. Threshold was defined as absorbed dose for 1% incidences of morbidity and mortality. Right side is effect on specific organs.

Note, determining fixed threshold for skin reaction is very hard because of inter/intra-individual variation and variation.

dose of 0.034 mSv/person/year, which represents 0.85% of the total annual radiation dose in Japan. Due to the low number of nuclear cardiology procedures performed in Japan, the contribution of nuclear cardiology

to the total public radiation burden might not exceed 0.5%.

Occupational radiation risk for cardiologists

Q: Do we have to worry about the effects of occupational radiation?

A: Clinicians should not worry excessively, but precautions should be taken, especially eye protection.

Considering the weak effects of medical radiation, the increase in cancer risk due to occupational radiation is quite low. According to a survey conducted at our hospital (unpublished data), the radiation dose delivered during oncological FDG PET procedures is around 0.5 to 2.0 μ Sv per patient in most cases. It is unlikely that the radiation dose during nuclear cardiology procedures is markedly different.

However, it is very important to note that interventionalists receive much larger doses during procedures, and hence, can be affected by minor deterministic effects. As noted, the dose threshold for lens opacity is much lower than was previously thought, and it was reported that interventional cardiologists and associated staff exhibit a higher incidence of cataracts (39, 40). Therefore, such staff are strongly recommended to wear eye protection during cardiac angiography, especially when performing interventions. I also strongly suggest that cardiologists should carefully observe their associate staff to prevent unnecessary radiation exposure.

Take home messages

Instead of writing a long conclusion, I want to provide some brief take home messages.

Always remember the principle of justification.

Even when the usage of medical radiation is

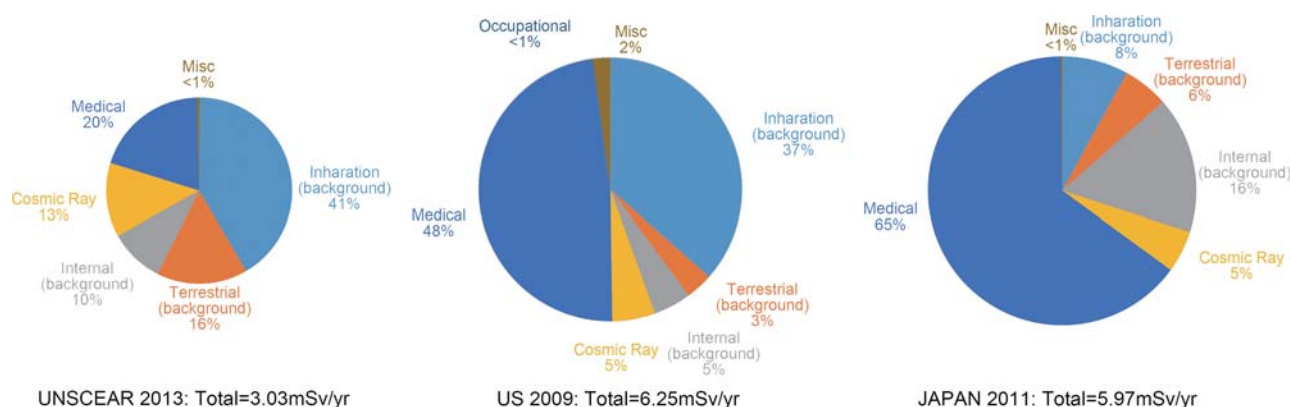


Fig. 7 Sources of public radiation worldwide (UNSCEAR 2013) and in the US (2009) and Japan (2011)

All of the sources that account for less than 1% of the total radiation burden (such as occupational radiation, nuclear power, nuclear weapons, etc.) are labelled "Misc". Note, therapeutic radiation is not included in this figure.

justified, the procedure must be optimized.

- # The contribution of medical radiation to cancer risk is under continuous debate.
- # Medical radiation can damage DNA, but such damage is usually repaired.
- # Do not forget deterministic effects; they are very important for cardiologists.
- # If you do not want to develop cataracts after retirement, wear eye protection today.
- # Clinicians are responsible not only for their patients, but also for public.

"Failure (of knowing) is not an option" (41)

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Conflicts of Interest

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