Invited Paper

Definitions and outlook targeting x-ray exposure of patients in diagnostic imaging

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ABSTRACT

Computer tomography (CT) is vital and currently irreplaceable in diagnostic radiology. But CT operates with ionizing radiation which may cause cancer or non-cancer diseases in humans. The degree of radiation impact depends on the dose administered by an investigation. And this is the core issue: Even CT exams executed *lege artis*, administer doses to patients which by magnitude are far beyond the level of hitherto known doses of conventional film-screen techniques. Patients undergoing one or multiple CT examinations, digital angiographies or interventions will be exposed to effective doses between roughly several mSv and several 100 mSv depending on type and frequency of the diagnostic investigations. From the radiation protection point of view, there is therefore the worldwide problem of formulating firm rules for the control of these high-dose investigations, as dose limits can not be established for reasons of the medical benefit. This makes the difference compared with radiation protection for occupationally exposed persons. What remains is "software", namely "justification" and "optimization". Justification requires balancing the interests between the health benefit and the potential harm of an exam which has to be responsibly executed by the physician himself; therefore the radiologists' associations are in the duty to prepare practicable rules for justification. Optimization again needs a cooperative solution, and that is the establishment of reference doses for diagnostic examinations, to be checked by the technical service of the producers' companies. Experts and authorities have been aware of the high-dose dilemma in diagnostic imaging since long. It is time for the reflection of active solutions and their implementation into practice.

Keywords: Diagnostic radiology, X-rays, computer-tomography, patient exposure, effective dose, organ dose, RBE, radiation accidents.

1. INTRODUCTION

Worldwide, more than three billion medical X-ray images annually are currently administered in diagnostic radiology aiming to serve for early recognition and prevention of diseases[1]. Radiological examinations help to improve health or, in acute cases, even save life. However, the ionizing radiation involved is in principle biologically negative; its application to humans may be associated with a non-negligible risk to induce cancer. X-rays have officially been classified as "carcinogen" by the World Health Organization, WHO[2] and other organizations. The carcinogenic impact has long been evidenced at high dose levels. At low dose levels, epidemiologic evidence of the radiogenic cancer risk is missing. In this dose range the principle of "justification", based on the linear-no-threshold (LNT) model of the dose-risk relationship[3], is almost the only tool which can support physicians in deciding whether or not an x-ray exam should be administered. Before CT conquered medical diagnostics, the low effective dose to a patient from plain-film imaging ranged between 0.01 mSv (chest x-ray) up to mSv. Nowadays the high-dose to patient from CT examinations range between a few mSv and several 10 mSv of effective dose, for a single examination. In course of a diagnostic investigation with follow-up controls quite a number of such examinations may be necessary associated with an accumulation of the respective effective doses. This results in high cumulative effective doses for individual patients, beyond belief for people from radiation protection in the nuclear field or at work places with radiation sources. Due to the complexity of this comparison between benefit and harm, it is impossible for the practical radiologist to think of justification in each case. Rather, radiologists' associations have to enter at this point and have to establish practicable rules of justification for the

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various categories of X-ray examinations. A problem of similar complexity is optimization, and to my knowledge the best possible way has been the establishment and introduction of "diagnostic reference dose values" which distinguish good from bad radiological practices and good from bad radiological equipment. Again here, the realization is a matter of cooperative action, in which the radiologists' societies and the equipment producers are in the duty.

BEIR Report VII assigns effective doses below 100 mSv to the low-dose category[4]. Physicians administering and patients undergoing X-ray examinations may have difficulty to interpret the magnitude of exposure administered and the related potential risk; both need quantitative information. However, due to the so far limited achievements of epidemiological and radiobiological sciences the knowledge on dose-risk relationship for carcinogenesis at low doses (and dose rates) is still poor. Since there is no clear evidence available neither for biological effects nor for quantified cancer risk of humans at low doses, the present paper will relate typical current patient exposures to the exposure data achieved from natural and especially from other man-made radiation sources which themselves are considered hazardous or carcinogenic, although preferentially at enhanced dose levels.

The paper reflects on the need of potential networking in radiation protection, on concepts to be debated to link exposure at workplace and in medicine. In parallel, concerted efforts should be established, actually and in future, to reduce number of CT examinations and exposures to an utmost necessary level, and introduce novel technology.

2. X-RAY EXPOSURE OF PATIENTS

A comparison of mean annual effective dose per citizen of different countries from diagnostic X-ray imaging is difficult since a common protocol has been lacking. Health-care level I countries in Europe, such as Luxembourg, Belgium and Germany have reported mean annual effective doses of about 1.8 mSv to 2 mSv per head of the population, for a year early in the second millennium[5-9]. The United Kingdom, by contrast, reports a mean annual effective dose of 0.4 mSv per head of its population, even for 2008[10]; this is considered due to both a lower frequency of X-ray examinations per head of population and generally lower doses administered per examination in the UK.

More recent US numbers have therefore been expected with great interest, for comparison. Linton and Mettler have published 57 million CT examinations for the year 2000[11]. For 2005[12] or 2006[13], 60 million CT examinations have been reported, with a mean annual effective dose of 3.2 mSv per head of the population which is surprisingly high, since 0.5 or 0.6 mSv have been reported for the twenty-five years before[14]. Individual effective doses of US patients were found in literature to range between 2 and 20 mSv, for a single CT depending on the type of examination. More than one CT scan has been reported, even on the same day, at most patients undergoing abdominal or pelvic CT examinations[15]. At least three scans were administered to 30% of all CT patients, more than five scans to 7%, and nine or more scans to 4%[16]. Even higher CT frequencies up to more than 100 for individual patients are reported for 2007 which study includes a 20 years retrospective consideration[17]. These figures may give rise to very high effective doses of 10 mSv to several 100 mSv individually.

Corresponding Japanese data on patient exposure have for long time not really shown-up in English-language publications. More recently, a mean annual effective dose of 2.3 mSv per caput has been published in an English abstract dealing exclusively with CT[18], which dose value has actually to be backed-up by about 1.4 mSv due to conventional radiology. In total, this will sum-up to a mean annual effective dose per caput of about 3.7 mSv valid for the year 2000. An increase rate of about 12% annually has been reported in CT examinations[19]. Extrapolating by 12% increase per year to the year 2006, the mean annual effective dose per caput in Japan should have reached and probably exceeded 6 mSv, the exposure of nuclear medicine not yet included. It is moreover unclear whether or not angiography and interventions have been included in the Japanese CT data given in[18]. For Japan and the year 2000, the number of CT scanners in operation has been reported to be 87.8 per million populations[18], which would stand for about 11,000 CT units.

All dose numbers given here refer to effective dose, which is an organ risk-weighted dose quantity. Due to its definition as a weighted average, the quantity effective dose can lead to a deception if single organs are irradiated. Organ doses taken separately may reach higher equivalent doses of up to 1000 mSv and more such as for skin, for instance in case of cardio-interventions. Such doses may cause skin injuries and potential risk for deeper lying organs. It would appear that a significant number of cardiologists are not aware that skin injuries may occur or even dermal necrosis can be caused their investigations. The total number of reported severe injuries worldwide so far has been reported to be 100-200, or probably far over 200 when all degrees of skin injuries are included[20]. Many of severe skin injuries in the past have been caused in the "High Level Fluoroscopy Mode" for exceptionally high contrast resolution, where skin doses of 1000 mSv per minute have been observed[21].

As for paediatric CT examinations, recent US estimates indicate CT studies to be between 6% and 11% on children of the total number of CT examinations, which means 3 to 7 million paediatric CT examinations in around 2006[22]. The frequent examination practice in paediatric radiology using adult CT settings for new-borns and infants may result in large doses to children; four fifth of CT studies of children is said to have not been operated by paediatric radiologists[11]. A single neonatal abdominal CT scan may under these conditions expose an infant to an effective dose of up to about 20 mSv[22]. It has been observed that paediatric CT practice can differ in exposure up to a factor 10 and more between different clinics[23]. These figures appear of considerable concern due to the long-term consequences since children are considered more sensitive to ionizing radiation than adults and have a longer life expectancy for cancer development[24].

3. MEDICAL VERSUS OCCUPATIONAL, PUBLIC AND INCIDENTAL EXPOSURE

Figure 1 compares the variation width of effective doses per patient and X-ray examination with annual dose limits valid for (a) occupationally exposed persons and (b) members of the public, from ICRP recommendations[3] and national legislation Radiation workers are controlled such that their effective dose is well kept below the annual limit of 20 mSv. Another dose limit is recommended by ICRP for members of the public to be 1 mSv per year at work places, applying to the sum of the relevant effective doses from external exposures in the specified time period and the committed effective dose from intakes of radio nuclides in the same period[3]. The observance of these limits should prevent harm from man's health caused by ionizing radiation.

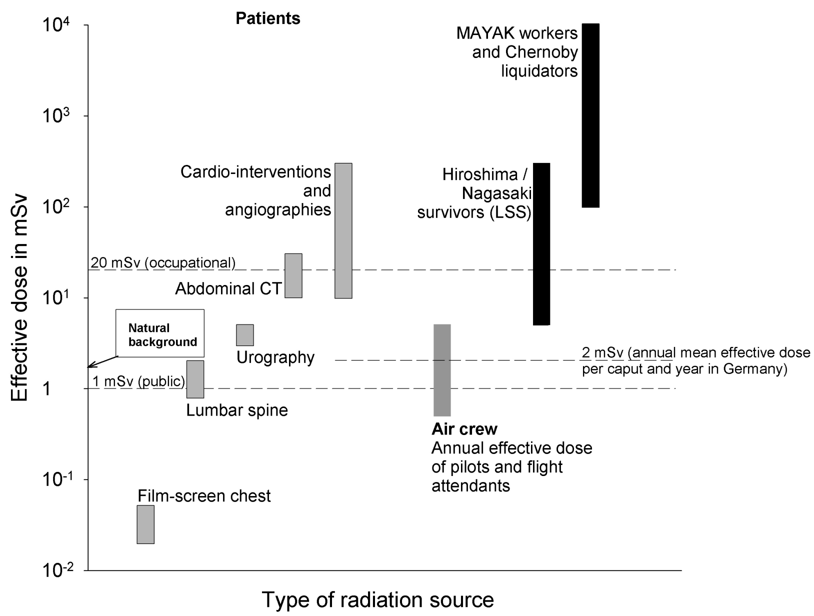

Figure 1: Comparison of exposure data of individual patients from medical X-rays versus exposure data of pilots and flight attendants, atomic bomb survivors, Chernobyl liquidators and early nuclear workers of PO Mayak. The annual dose limits marked in the figure due to ICRP recommendations[3] and national ordinances, are given for members of the public and radiation workers, hence not for patients. Annual background radiation per head of population is about 2 - 3 mSv, averaged worldwide[3]; higher effective doses from background are reported to be up to 10 mSv annually by terrestrial radiation[4], and more by radon[25].

By contrast, ionizing radiation in medical imaging is intentionally administered; it should help to preserve or improve human health. For this reason, no upper dose limits exist for patients' exposure. Radiation protection in medicine is governed by principles, i.e. the ethical justification of an examination, the optimization of equipment and procedures, and the ALARA principle[3]. These principles are expected to be adhered strictly by each radiologist, for each patient and for each X-ray examination, although these principles are difficult to accomplish in practice. Their quantification and control is a still persisting issue. It is worth pointing out from figure 1, that the effective dose of one single adult chest CT of about 5 mSv will be equivalent to a sequence of several 100 conventional plain-film chest examinations administered to the same patient.

The following figures on effective dose hold for occupationally exposed persons, and are presented here for comparison. The German Radiation Protection Register reports a mean annual effective dose for about 315,000 radiation workers (at a terrestrial working environment) to be 0.13 mSv per person as monitored in 2006[26]. In contrast, pilots and flight attendants of commercial airlines are expected to reach higher effective doses annually originating from cosmic radiation at flight altitudes[27]. It is again the German Radiation Protection Register that reports a mean annual effective dose of 2.2 mSv per crew member in 2006 (min 0.5 mSv; max 8 mSv) determined from a cohort of roughly 35,000 persons monitored[26]. Having this mean effective dose of 2.2 mSv in mind, a single head CT of 5 mSv administered to a crew member will refer to more than two years flight time exposure, a thorough abdominal CT may be up to roughly 10 years flight time exposure.

The effective doses to atomic bomb survivors and Chernobyl liquidators, for comparison, cover a range between several mSv and several hundred mSv[28], which dose range clearly matches some of the nowadays administered effective doses to patients originating from diagnostic procedures. Reporting on the doses of the exposed atomic bomb survivor, Brenner and Hall[28] point out that a substantial proportion of the 25,000 survivors received effective doses of less than 50 mSv, which is the dose equivalent of a number of abdominal or cardio CT scans. They report that a significant increase in the overall risk of cancer was recorded for the subgroup of atom bomb survivors who received low doses in the 5 to 50 mSv range. "There is direct evidence from epidemiologic studies that the organ doses corresponding to an extended CT study (two or three scans) result in an increased risk of cancer" and "the evidence is reasonably convincing for adults and more convincing for children"[28]. Hence, repeated CT examinations, angiography and interventional radiology are dealing with doses for which carcinogenic risk can not be excluded and may epidemiologically be quantifiable, in future.

As a more general figure, the Chernobyl nuclear power plant accident in 1986 has recently been reported responsible for a global collective effective dose of roughly 0.7 million person·Sv[13], once. The medical exposure of humans, in contrast, will generate a global collective effective dose of roughly speaking 5 to 10 million person·Sv, every year, as calculated from the above dose figures.

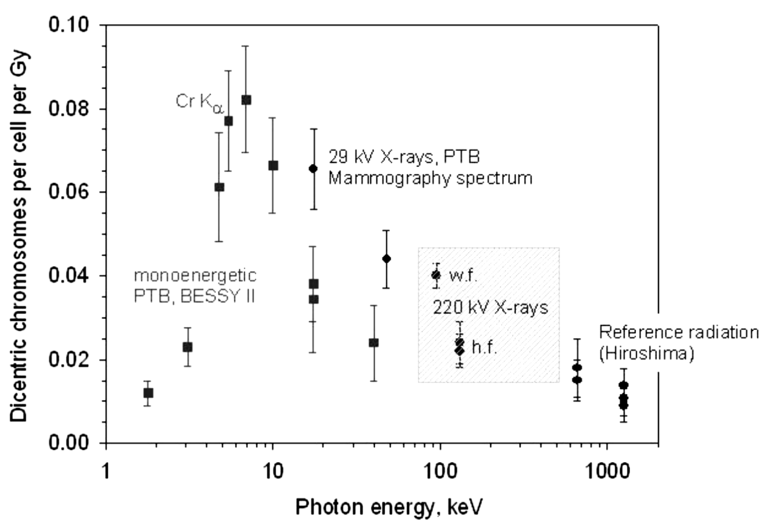

Figure 2. Yield of dicentric chromosome aberrations plotted versus the energy of different monoenergetic synchrotron X-rays (PTB/BESSY II, Berlin) (filled squares) and chromium K_{α} fluorescence X-rays[29], as well as versus the mean energies of different X-ray spectra, respectively the one of ^{60}Co γ-radiation (approximately serving as reference radiation for the Hiroshima/Nagasaki photon spectra) (filled circles)[30, 31]. Note, w.f. stands for weakly filtered, h.f. for heavily filtered X-ray spectra.

4. RELATIVE BIOLOGICAL EFFICIENCY (RBE) OF X-RAYS

Atomic bomb survivors experienced high energy photon spectra peaking above 1 MeV, the energy spectra of cosmic rays at flight levels show maxima around 1 MeV and 100 MeV, while diagnostic X-ray spectra have maxima at about 20 keV (mammography), 50 keV (dental radiology) and around 80 keV (2- and 3-dimensional organ radiography, including CT).

For evaluation whether the biological effectiveness of these different types of sparsely ionizing radiation is comparable and can be described by the same radiation weighting factor, $w_R = 1$, the response of the biological endpoint of exchange-type chromosome aberrations in human lymphocytes has experimentally been considered as typical for RBE evaluation. The in vitro studies have resulted in significant yield differences between the various energies, up to about a factor of 8 between ^{60}Co γ-rays and soft X-rays depending on spectral distribution (Fig. 2)[7, 29-31] and receptor size[32, 33].

Although dicentric chromosomes are not relevant for cancer induction by themselves, the associated RBEs may be taken as a model for the RBEs of the chromosome exchanges and deletions which have a more direct bearing on cancer-prone somatic mutations. ICRU and ICRP recommend constant weighting factors Q = 1 and w_R = 1 for all sparsely ionizing radiations, irrespective of radiation energy and spectral distribution[3]. This recommendation appears justified by the desirable simplification of practical radiation protection and by the missing significant evidence of RBE variations within the presently available epidemiologic risk coefficients for sparsely ionizing radiations. However, ICRP[3] has also expressed that in specific risk estimates, RBE differences should be considered[,34] (see Fig. 2). This could hold for expert opinions or reports when radiation victims claim for financial compensation after radiation injury[3, 35]. The German Supreme Court, in its decision, considers medically non-justified x-ray examinations to represent an intentional bodily injury to be prosecuted; the impact of x-rays to human body is similarly judged as an infection with HIV.

5. DISCUSSION

Elias Zerhouni, NIH, in his Mansfield Lecture at the 2006 International Society for Magnetic Resonance in Medicine meeting in Seattle, predicted a central role for medical imaging in the 21st century medical research and practice[36]. He predicted radiology move to the forefront of medicine, a trend he expects to continue. His visions may be expected to apply particularly for CT in the near future focussing on wide-band applications in emergency medicine, whole body scans and screening programs. Screening is an important motivation for increased CT use in asymptomatic adults, its utilization growth will arise from virtual CT colonoscopy, CT lung cancer screening, cardiac screening, and whole-body screening. But it should also be noted that a single whole-body CT scan may give rise to an effective dose of several ten mSv. Noteworthy, the effective dose of 10 mSv to a patient from an extended CT examination corresponds to the effective dose of roughly 1000 conventional chest X-ray exams taken with screen-film technique[1].

No doubt, CT and other high-dose digital imaging techniques are of greatest benefit for the patients and physicians and thus a blessing of mankind in general, provided the examinations are ethically justified and properly executed. But the prize for this high diagnostic quality is a high radiation dose to individuals and population. The number of CT units and hence CT examinations will continue to rise for the next future. "Medical imaging has become the largest controllable source of radiation exposure, although it remains unregulated", says Fred Mettler[13, 15]. If we continue to operate CT under present conditions it may be that we might leave a huge risk potential for future generations, from present radiation point of view. We urgently need practicable solutions for justification and optimization. Physicians and their professional associations, industry and its product services, authorities and their scientific consultants, patients and the public should become aware and search for ethical, technical and administrative-legal ways out - otherwise we will probably be compelled to admit to have exaggerated radiation protection in the past.

As for the radiation risk, our present knowledge refers mainly to the consequences of nuclear impact, such as the long-term observation of ten thousands of atomic bomb survivors in Japan (dealing with some five hundred cases of leukaemia and solid cancer, in total), with some hundred thousand radiation workers in nuclear industry[37], and more recently, late effect studies from some 10 thousand radiation workers of the early USSR nuclear facilities like MAYAK (formerly, Chelyabinsk-65, USSR)[38-40]. However, our knowledge is definitely limited, as far as risk of low doses and low dose rates and particularly of X-rays is concerned.

Unlike victims of nuclear accidents and early nuclear workers, diagnostic radiology deals with some billion X-ray examinations respectively patients world-wide, each year. Among them are estimated 10 to 15 percent high-dose CT scans, i.e. about 500 million annually. These numbers are presently rising by roughly 10% each year in countries of high-level healthcare and will probably continue to rise in the near future. As a consequence, corresponding data on individual patients and related X-ray examinations pile-up in clinical departments. Individual data records, related reference dose information and technical data of the X-ray equipment, could serve for the assessment of organ or effective doses and serve for subsequent epidemiological risk estimates, and that directly in the domain of diagnostic X-ray qualities.

6. OUTLOOK ON REDUCTION OF PATIENT EXPOSURE

The exposure of patients could be lowered conventionally by, e.g., compliance with the indication catalogue[41], i.e. the use of alternative techniques such as ultrasound and MRI, a highly ethical indication of the X-ray examination, the clinical optimization of apparatus, techniques and procedures as well as an risk-refined education and training of physicians and technical staff including careful observance of the so-called diagnostic reference levels. In USA, one third of all CT scans are argued not to be justified by medical need[22]. Many radiologists agree that inappropriate or unjustified CT scans are performed because of medico-legal concern and exploitation by profit-driven physicians and commercial imaging providers, said Dr. Michael Brant-Zawadzki, a member of the RSNA's public information advisor's network[42].

The probably only mid-term strategy and thus perhaps some kind of silver bullet to satisfy all parties involved, at least lies in the systematic development of novel dose-saving CT technology[43-51]. Science and industry should, for radiation protection of mankind, jointly work efficiently on reducing the dose demand, e.g. by a factor 10 and more thus approaching dose levels of earlier plain-film examinations. For such examinations no excess cancer risk has recently been reported from a cohort study of more than 100,000 new-borns and infants at the University Children's Medical Hospital in Munich, using individual patient and x-ray data from 1976 to 2003, and applying individual dose assessment and validation against the German Childhood Cancer Registry[52-61]. The risk evaluation of CT scanned new-borns and infants are now under study[62]. Another promising mid-term strategy will be a display of effective dose or organ dose of patient's directly in mSv and on the CT scanner[63].

7. CONCLUSIONS

According to recent literature, the number of CT examinations and collective effective doses in diagnostic radiology has risen highest in Japan and USA which nations have most probably taken over the world-leadership in x-ray administration, among the health-care level I countries[64]. Presently, individual effective doses may reach almost 10 mSv, on an average, per patient and examination (i.e., 1000 mrem in terms of the previous dose units). Multiple CT exams for a patient in the course of a diagnostic or therapeutic follow-up may result into a cumulative effective dose up to 100 mSv and more.

Also angiographic or interventional examinations may administer effective doses of up to 100 mSv and more per patient. The question whether or not these sound exposures will intrinsically bear a significant risk for patients to develop malignancies will continue to be subject of controversial debates within the LNT discussion. Conventional projection radiography uses doses which are 100 to 1000 times less than those mentioned above for CT, angiography and interventions. But even these much smaller doses have been considered a risk, at that time.

Of course, the immediate diagnostic benefit of the new imaging techniques is immense and highly appreciated by radiologists and patients, particularly in case of medical emergency. But reviewing our enormous efforts in medical radiation protection in course of the seventieth and eighties to reduce patient exposure from, e.g., 0.2 to 0.02 mSv per chest examination, the way of today acceptance of radiation exposures boosting up to 10 and 100 mSv per examination appears surprising, at least (Fig. 3).

Today, patients and radiologists accept high-dose CT examinations, or they are not properly informed about the dose magnitude and risk. People even accept media-advertised whole body CT scans interpreted as a valuable tool for preventive medical check-up; there is nobody caring about neither justification nor ethical indication of such diagnostic measure. Radiation has obviously lost its frightening for the public, for radiologists and even for the members of the radiation protection community, at least as far as medicine is concerned.

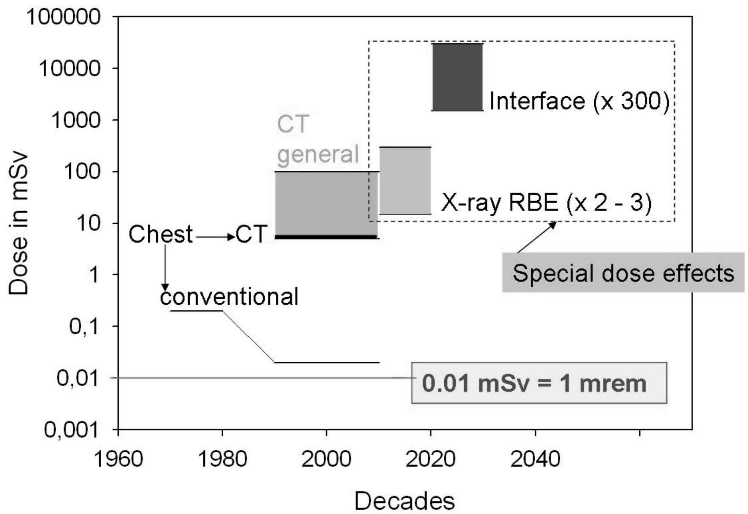

Figure 3: Time-based development of effective dose to patients per X-ray examination originating from plain-film radiographs and CT, between the years 1970 and presence,. The special dose effects refer to (a) potentially higher relative biological effectiveness (RBE)[29-31] and (b) dose enhancement effects as observed, in vitro, in tissue adjacent to metallic surfaces (e.g., contrast media, implants, prosthesis, etc.)[65].

This new tolerance however is not valid for even dramatically lower exposures of the same public, if the radiation originates from other man-made sources: "The public is concerned about nuclear industry and waste problems …. They seem less concerned about increasing radiation doses due to new technologies in medical radiology"[66, 67]. Does the new tolerance comprise current radiation exposures in medicine to be negligible from the risk point of view? Not really, since we must be aware that radiation-induced cancers do typically not show-up before long time after exposure. Major questions also remain unanswered concerning the risk of non-cancer diseases following low level ionizing radiation and concerning non-targeted effects of radiation. Another issue to be debated in radiology could be the term and concept of justification, which is supposed to serve physicians for decision-making and patients as protection umbrella[68].

Of course, the immediate health benefit of an, e.g., emergency patient will first and above all deserve highest priority in radiological diagnostics.

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