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Guidelines on the use of ionising radiation in health research projects

Appendix 2

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General provisions

Any use of ionising radiation from X-ray sources or radioactive substances in biomedical trials will expose the trial subject to radiation.

The risk associated with radiation depends on the size of radiation dose applied. The person who is clinically responsible for a research project can obtain information about the radiation dose of individual procedures from the responsible hospital physicist who, according to rules issued by the Danish Health Authority, must ensure availability of the information.[i] In the event that it is not possible to obtain the information from the responsible hospital physicist, the National Institute of Radiation Protection[ii] may offer assistance.

It is required for certain procedures that the absorbed dose in a certain type of tissue or the medium dose in organs is stated, e.g. skin dose in interventional radiology and the dose in tumours and surrounding tissue in radiotherapy. In case of continued fluoroscopy, the total radiation dose is not known beforehand but should be estimated, and it should be indicated if there is a risk of deterministic damage.

Classification of research projects

The classification below is based on the guidelines from the International Commission on Radiation Protection (ICRP) and the European Commission.[iii],[iv]

Category I: Effective doses less than 0.1 mSv in adults:

This category involves a risk of total stochastic detriment from the radiation exposure for normal subjects of the order of 1 in 1 million or less. This risk may be considered trivial. The research project can therefore be approved even though the benefit is minor and the project might only be expected "to increase our knowledge".

Category IIa: Effective dose range 0.1-1 mSv in adults:

This category involves risks of the order of 1 in 100,000. In order for a research project to be approved, the benefit should be justified by the expectation that the project may provide "increased knowledge and health benefits".

Category IIb: Effective dose range 1-10 mSv in adults:

This category involves risks to the irradiated individual in the order of 1 in 10,000. In order for a research project to be approved, its degree of benefit to society should be somewhat greater in that the project is expected to be "aimed directly at the diagnosis, cure or prevention of disease".

Category III: Effective doses greater than 10 mSv in adults:

Here the risks to the irradiated individual are estimated at greater than 1 in 1000. This is a moderate risk for a single exposure but might be considered as verging on the unacceptable for continued or repeated exposure. To justify investigations in this category, the benefit would have to be "substantial and directly related to the saving of life or the prevention or alleviation of serious disease". Doses should be

kept below the threshold for deterministic effects unless higher doses are necessary for the therapeutic effect.

The table below applies only to adult research participants under 50 years of age. For each of the above categories, the dose figures could be increased by an age-dependent factor for research participants older than 50 years of age. The factor increases with age exceeding 50 years, and a factor of 5 to 10 can be used for the oldest research participants.

In the event that approval is granted for a research project involving the irradiation of children, the corresponding dose figures should be reduced by a factor of 2 (children over the age of 10) or 3 (children under the age of 10) due to an increased risk of damage.

Level of social benefit	**Risk level compared to the benefit**	**Risk category (Stochastic damage – see definitions)**		**Corresponding effective dose range (adults) mSv**
Minor	Trivial	Category I	10^{-6} or less	< 0.1
Intermediate to moderate	Minor to intermediate	Category IIa	Approx. 10^{-5}	0.1 – 1
		Category IIb	Approx. 10^{-4}	1 – 10
Substantial	Moderate	Category III	10^{-3} or more	10 (see note a)
a) To be kept below deterministic thresholds except for therapeutic experiments.				

Information to trial subjects

Information about the risk of radiation exposure must appear clearly from the project description to the research ethics committee and the information to trial subjects. This information must be so extensive that it enables the trial subjects to assess the size of risk.

In most diagnostic procedures, the effective dose can be used as a measure of the likely stochastic radiation damage. To illustrate the size of the effective dose, you can compare it with the background radiation. In Denmark, the average annual background radiation is 3 mSv. A radiation dose of 10 mSv thus corresponds to approx. 3 years' background radiation.

For every Sievert (Sv), the risk of inducing an incurable cancer disease increases by 5% compared to the general population risk. Exposure to a dose of 20 mSv = 0.02 Sv increases the risk by 5% x 0.02 = 0.1%. This risk is added to the general risk of 25% by which a total risk of 25.1% is found.

For healthy trial subjects, the risk of detrimental effects can be explained by an increased risk of dying from cancer. In Denmark, this risk is 25%, and an effective dose of 20 mSv increases this risk by 0.02 [Sv] A 5 [% per Sv] = 0.1% to 25.1%.

In irradiation involving risks of deterministic damage, e.g. continued X-ray fluoroscopy, the trail subject should be informed thereof.

Definitions

Medical exposure

Included in medical exposure are all X-ray investigations, nuclear medical examinations and radiation therapy that are part of the project.

Radiation damage and risks

Ionising radiation causes stochastic and deterministic damage. Stochastic damage covers cancer and genetic damage, and the risk of stochastic damage is the sum of the risk of cancer and of genetic damage. In high radiation doses, the individual cells suffer deterministic damage. The radiation dose must exceed a certain threshold before the damage is significant, and the extent of damage increases with the radiation dose.

Radiation dose in trial subjects

In X-ray and nuclear medical investigations, the radiation dose in trial subjects is stated by the effective dose in mSv (milliSievert). In the use of radiation therapy and irradiation that may cause deterministic damage, the absorbed dose for the irradiated tissue area is stated.

Effective dose

The effective dose is a calculated weighted mean value of the radiation dose for the research participant's tissue and organs. The calculation is further described in the Danish Health Authority's Executive Order no. 823 of 31 October 1997 on Dose Thresholds for Ionising Radiation.1

Background radiation

Human beings are exposed to ionising radiation every day, for example because we are surrounded by naturally occurring radioactive elements. The most significant contributors to the background radiation is the ionising radiation from outer space and the naturally occurring radioactive elements such as Potassium 40, Radium, Radon and Thorium in our bodies and our surroundings. The radiation dose from the background radiation is accumulated year after year throughout life. The background radiation varies from place to place, depending on the subsoil and the design and condition of the houses we live in.

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[i] Executive order no. 975 of 16 December 1998 on Medical X-ray Installations for Investigation of Patients (Danish title: Bekendtgørelse nr. 975 af 16. december 1998 om medicinske røntgenanlæg til undersøgelse af patienter)

Executive order no. 954 of 23 October 2000 on the Use of Open Radioactive Sources in Hospitals, Laboratories, etc. (Danish title: Bekendtgørelse nr. 954 af 23. oktober 2000 om anvendelse af åbne radioaktive kilder på sygehuse, laboratorier mv.)

Executive order no. 48 of 25 January 1999 on Electron Accelerators in Patient Treatment using Energies from 1 MeV up to 50 MeV (Danish title: Bekendtgørelse nr. 48 af 25. januar 1999 om elektronacceleratorer til patientbehandling med energier fra 1 MeV til og med 50 MeV)

Executive Order no. 765 of 6 October 1999 on X-ray Therapy Equipment in Patient Treatment (Danish title: Bekendtgørelse nr. 765 af 6. oktober 1999 om røntgenterapiapparater til patientbehandling)

Executive Order no. 663 of 16 August 1999 on Bigger Dental X-ray Installations (Danish title: Bekendtgørelse nr. 663 af 16. august 1999 om større dentalrøntgenanlæg)

Executive order no. 209 of 6 April 1999 on Dental X-ray Installations for Intraoral Imaging using Voltages of 70 kV or Lower (Danish title: Bekendtgørelse nr. 209 af 6. april 1999 om dentalrøntgenanlæg til intraorale optagelser med spændinger til og med 70 kV)

Executive Order no. 985 of 11 July 2007 on Closed Radioactive Sources (Danish title: Bekendtgørelse nr. 985 af 11. juli 2007 om lukkede radioaktive kilder)

[ii] National Institute of Radiation Protection, see www.sis.dk.

[iii] Radiological protection in Biomedical Research. ICRP Publication 62, Annals of the ICRP, Oxford Pergamon Press, 1992.

[iv] Guidance on medical exposures in medical and biomedical research, Radiation protection 99, European Commission.