PET Centre
Centre for Addiction and Mental Health
and University of Toronto

Guidelines for Informed Consent Statements

These guidelines are for informed consent statements for PET research projects involving radiation exposure for research purposes and not for the medical benefit of the subject. They apply to adults (18 year old or older). This document covers only to those aspects of the informed consent which are directly related to the use of radionuclides and which are not covered explicitly in the Code of Conduct for Research Involving Humans (MRC, NSERC, SSHRC, 1996) (1).

Requirements

- The research protocol must state the dosage of any radionuclide to the research subjects as well as any additional radiation exposure from other radiological procedures (X-ray, CT or nuclear medicine scans) performed for research purposes.

- The consent form must specify the radiotracer to be administered and the route of administration (almost always intravenous injection).

- The consent form should state that the radiation doses are within the guidelines of the PET Centre and applicable regulatory limits.

- The research protocol must state that the radiation exposure to be received by participating in the study is for research purposes and in the case of patients that it is not medically indicated for the benefit of the subject.

- The consent form must accurately reflect the source of radiation exposure and radiation doses to be received by the subjects participating in the study.

- The consent form must contain an accurate statement of the risks associated with the administered radioactivity.

- The consent form must include a statement that women of child bearing age may not participate in research involving radiation if they are or could be pregnant at the time of the study.

Radiation Doses Guidelines

The PET Centre annual limit for the effective radiation dose to the whole body allowed for research subjects is 20 mSv per year (1 Sv = 100 rem). This limit is recommended value in the guidelines issued by the AECB Group of Medical Advisers (2) and is also the proposed new annual limit for occupational exposure (AECB 1991; ICRP 1991).

Only under exceptional circumstances will higher doses be allowed in normal volunteers. This annual limit also reflects the current practice around the world for PET research studies. In the United States, the FDA regulatory limit is 50 mSv (5 rem) per annum for the whole body which is the occupational limit (3).

Risk estimates

Risks estimates for radiation are difficult to estimate because most of the radiation exposures that humans receive are very close to the natural background level. The average radiation dose from a PET scan or other diagnostic nuclear medicine procedures is about 4.5 mSv. The whole body radiation dose from natural sources is about 3 (2–4) mSv per annum. It is therefore very difficult to distinguish the effects of low doses of administered radioactivity from those from normal natural levels. The current risk estimates for radiation have been derived mainly from epidemiology studies of medical patients and the Japanese survivors from the atomic bombs in 1945. Epidemiological studies have not demonstrated definite adverse health effects in individuals exposed to small doses (<100 mSv) delivered in a period of many years. Thus, while there is convincing scientific evidence and general agreement on the deleterious effects of high acute doses of radiation, there is much less agreement on the effects of "low-dose" radiation (< 50 mSv / yr). The current radiation protection standards are based on the assumption that any radiation dose, no matter how small, may result in detrimental health effects such as cancer and hereditary genetic damage. The Biological Effects of Ionizing Radiation Committee V (BEIR V) has estimated that the risk of cancer death is 0.008% per mSv for doses received rapidly and might be 2–4 times less than that for doses received over a long period of time. The risk is assumed to increase linearly with the radiation dose received with no-threshold. These risks estimates are an average for all ages, males and females, and all forms of cancer. There is a great deal of uncertainty associated with this estimate. It is based on plausible assumptions, but is an estimate nevertheless. It is not based on measurements or observations. It is also considered a conservative estimate since it does include biological mechanisms such as cell repair following radiation injury. Until the health effects are established for the dose range used for PET studies, including the possibility of zero health effects, the PET Centre uses the BEIR V estimate of cancer induction as the basis of risk estimate for the human subjects. Hall recommends a value of 0.04% / mSv for nuclear medicine studies (4).

In order to allow research subjects to make an informed decision about their willingness to accept the radiation risks from their participation in a study, the risk must be presented in meaningful terms. The common approach is to use risk comparison to explain to the subjects by how much radiation exposure might increase my chances of cancer death over their lifetime.

The current death rate from cancer in Canada is approximately 20%. Thus, assuming the maximal dose of 20 mSv, the linear, no-threshold model would predict a risk increase from 20% to 20.08%. It is generally felt that this type of risk estimate is not very meaningful. Other approaches have been used.

One way is to look at the number of "days lost" out of a population due to early death from separate causes and to derive an average Loss of Life Expectancy (LLE) due to those causes (5):

Health Risk	Loss of Life Expectancy
Smoking 20 cigarettes per day	6 years
Overweight (15%)	2 years
All accidents	200 days
All natural hazards	7 days
Single exposure to 10 mSv	1.5 day

Adapted from BL Cohen, 1991.

Another approach is to look at the relative risk of "one in a million" chances of dying from common activities:

Activity	Risk
Smoking 1.4 cigarette	Lung cancer
Eating 40 tbls of peanut butter	Cancer
Driving 70 km in a car	Fatal accident
Flying 4,000 km in a jet	Fatal accident
Canoeing for 6 min	Fatal accident
Receiving 0.1 mSv of radiation	Cancer

Another widely used approach is to compare the risks of radiation to those of smoking and driving as done by Hall is his radiobiology textbook (4).

Comparison to a limited number of transatlantic flights is also not acceptable. The dose received from cosmic radiation during a flight from Toronto to Europe is only about 50 μSv.

Unacceptable comparisons are those to chest X-rays. The whole body dose equivalent from routine chest radiography is about 0.05 mSv. Medical radiation gives an average exposure across the population of 0.63 mSv / yr which causes a LLE of 6.2 days (5). However, this average (collective US population exposure / total US population) cannot be equated with a single radiographic procedure. Typical doses for individual radiographic examinations vary greatly: 0.05 mSv for chest X-ray, 1.4 mSv for abdominal examinations, 4.4 mSv for intravenous urograms and 4–8 mSv for barium meals / enemas (UK data from (6)). Doses from typical head CT scans are about 2 mSv and for body CT scans 6–16 mSv (7).

However, the typical radiation dose from PET studies, about 5 mSv, is similar to those of most diagnostic nuclear medicine procedures (8). This comparison is useful in reassuring subjects that the amount of radioactivity administered for PET studies are inline with typical medical procedures.

Women of Child-Bearing Age

The PET Centre does not routinely require pregnancy testing in all women of child bearing age prior to a PET scan. However if there is any doubt that a subject might not be reliable, it is the investigator responsibility to determine the pregnancy status of that subject.

Acceptable Wording

In order to provide uniformity in the wording of radiation related statements on consent forms or information sheets among projects carried out at the PET Centre, the following statements of risk must be used.

In the information section of the consent form (fill in the blanks with the appropriate item):

> "To study … with PET, we will inject a small quantity of a radioactive substance, called <radiolabeled compound>, through an intravenous line placed in your forearm. A PET study will require about <…> hours of your time, including preparation and scanning time. You will also receive a small amount of radiation from a brief transmission scan to measure how much radiation is absorbed by your brain and the bones of your skull. The radiation dose to the you during a PET scan is comparable to other nuclear medicine scans and represents a very low risk. The total radiation dose from the study is <…> which is well within the guidelines for this type of study and close to the amount of radiation received from natural sources during one year (3 mSv). The potential long-term risk from the radiation dose you will receive is uncertain, but these doses have never been associated with any definite adverse effects. Thus the risk to you, if any, is estimated to be slight."
>
> "If you are or could be pregnant at the time of the PET scan, you should not participate in the study."

In the consent section of the consent form:

> "If I am a woman of child bearing age, I confirm that I am not or could not be pregnant at the time of the PET scan."

For long term studies involving multiple scans, a statement similar to the following one should be included:

> "If at any time time during this study, there is a possibility that I could have become pregnant, I will inform the investigator and will not undergo further PET scanning."

References

1. Tri-Council Working Group. Code of conduct for research involving humans. Ottawa: MRC, NSERC and SSHRC, 1996 (Draft document).
2. GMA AECB. Guidelines for research on human subjects using radionuclides. Ottawa: Group of Medical Advisors, Atomic Energy Control Board, 1993.
3. Food and Drug Administration HHS. Radioactive drugs for certain research use. Washington, DC: FDA, 1993.
4. Hall EJ. Radiobiology for the radiologist. (4th ed.) Philadelphia: JB Lippincott Co, 1994.
5. Cohen BL. Catalog of risks extended and updated. Health Physics 1991;61(3):317-335.
6. Shrimpton P, Wall B, Jones D, et al. A national survey of dose to patients undergoing a selection of routine X-ray examinations in English hospitals. Didcot, Chilton: National Radiological Protection Board, 1986.
7. Huda W, Sandison G, Lee T. Patient doses from computed tomography in Manitoba from 1977 to 1987. Br J Radiol 1989;62:138-144.
8. Huda W, Sandison GA. Estimates of the effective dose equivalent, H_E, in positron emission tomography studies. Eur J Nucl Med 1990;17:116-120.