Dose and risk assessments for clinical trials involving exposure to ionising radiation

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Introduction

Well designed clinical trials play an important role in clinical research. Many clinical trials involve irradiation of volunteer trial participants, often using X-ray or nuclear medicine imaging to assess pharmaceutical or surgical interventions. It is ethically important that research ethics committees and individual volunteers understand risks of medical research exposures.

International and national landscape for medical research dose and risk assessments

Helsinki Declaration, ICRP, EC

- Declaration of Helsinki protects human subjects participating in research, requiring risk/benefit analysis and informed consent.
- ICRP emphasize need to guarantee research ethics committee easy access to radiological protection advice.
- EC 'Medical Exposures' Directive requires dose constraints or target doses for each research project.

UK implementation

- Ionising Radiation Medical Exposure Regulations (IRMER) apply to all medical exposures.
- Clinical Trials Regulations require informed consent and expected benefit to outweigh/justify risks to participants.
- National Research Ethics Service requires MPE assessment if study involves exposure to ionising radiation.

Medical physics expert contributions to UK clinical trials

Lead MPE role

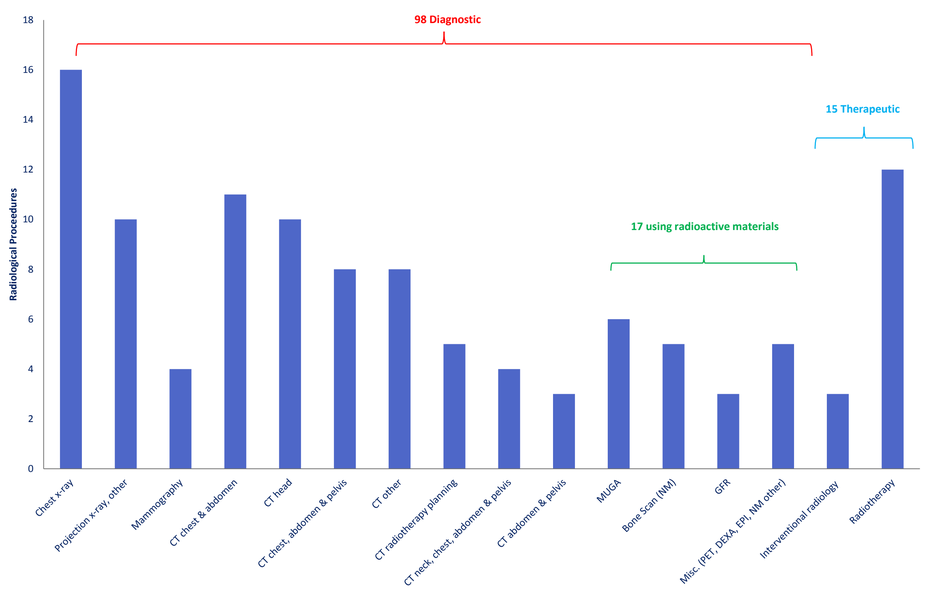
- Provides advice to Research Ethics Committee through electronic smart form:
  - Calculates total research protocol dose and element potentially additional to normal clinical practice.
  - Estimates risks to participants, taking into account population irradiated.
- May recommend revision of explanations of risk in protocol and participant information sheet.

Local MPE responsibilities

- Local MPE role is distinct from Lead MPE.
- Advises employer on local IRMER compliance for trial:
  - Reviews local applicability of Lead MPE dose assessment, establishing dose constraint / target dose for site.
  - IRMER requires MPE involvement in all medical exposures, including research exposures, for optimisation.
- Provides advice on other radiation safety requirements, particularly for trials involving radioisotopes.

Experiences with 56 consecutive research protocols referred for MPE assessment

Radiological procedures in trial protocols



Problems encountered

- **Some research protocols unclear** as to what exposures will be performed, and whether or not they are normal clinical practice.
- **Some draft protocols require correction** of misleading assertions by others (not MPEs) about radiation dose/risk.
- **Reconciliation of differences requires careful judgement**. Guidance recommends basing dose assessments on national diagnostic reference levels (derived from mean dose distributions) where available. However lead MPE is also expected to indicate maximum dose to participants, taking account of variations in procedures and normal practice at participating UK sites.
- **Dose calculations for non-standard procedures** may be complex.
- **Standard risk coefficients may be inappropriate for specific cohort.** Risk assessments should take into account factors such as age, latent period for stochastic effects and patient prognosis.

Conclusions

Dose and risk assessments are an essential element of the research ethics process for clinical trials involving exposure to radiation. Lead and local MPE roles are distinct, though complementary. Their task is made more difficult if research protocols are unclear. Risk assessments should take into account research participant characteristics, notably their age and patient clinical prognosis.

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