

MELODI workshop on the shape of dose-response curve for cancer

Discussion/questions

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Where are the greatest uncertainties on the shape of the cancer dose-response?

In low dose region, low dose rates, for high LET, dosimetric uncertainties, cancer is NOT one condition, confounding exposures

Which types of investigation are needed to reduce the uncertainty on the cancer dose-response?

- Epidemiological/molecular-biomarker epidemiological (markers still needed)
- Experimental (at many organisation levels)
- Dosimetric (minimal criteria need to be defined)
- Mathematical modelling
- *Interdisciplinary and integrated early*

What populations/exposures for epidemiological investigation?

- Limits to power (1% increase in risk)
- Minimal criteria for good study design needed
- Nested design beneficial for several purposes
- Long lag for results for new cohorts
- Specific populations/situations, including *in utero*

What are the prospects for molecular epidemiology?

- long wait for results (protocols now)
- Populations (with several exposure conditions) (and exptl. Models to understand mechanisms)
- How do we deal with tumour causality (need robust radiation tumour signatures and good data on confounders)
- Need to identify reliable biomarkers of radiation-induced disease
- Good bio-banking required (value of MELODI)

In which areas will experimental work provide useful information for risk assessment?

- Cancer process (will need better animal models and higher dose exposures for p-o-p, improved integration of knowledge from general cancer research)
- Role of non-targeted effects (critical to know importance, esp. for internal emitters and high LET)
- Dose response relationships for cancer relevant end points (controversial & needs research)

Which systems?

- Physical/chemical interactions
- Human (stem) cells (non-uniform ethics in EU countries – MELODI may help)
- Tissue models (require good characterisation, mixed cell cultures may be easier)
- Animals (need good models for several cancer sites and chronic exposures)
- Systems biology as an integrative approach (need for a lot of computing power)

Can we identify low-priority areas for further research effort?

- cell studies with no clear relationship to radiation disease
- modelling of dose response relationships with all cancer sites combined
- ? further traditional radon epidemiological studies (*varying opinions*)

What about internal emitters?

- big differences from external exposures but are very important in radiation protection
- Improved dosimetry/biokinetics required
- Chemical form/toxicity will be important
- each radionuclide is different
- requires discussion to identify priority radionuclide/form (value of MELODI and integrated approach likely to yield results in a reasonable time)

What about tissue sensitivities?

- radiation weighting factors have poor **scientific basis**
- particularly for **high LET**
- possible variation in radiation weighting factors/RBE for different tissues

Infrastructures required

- Exposure facilities (some potential for international collaboration)
- Data/bio-sample storage/sharing infrastructures (? link to STORE)
- Strengthen availability of expertise in pathology and other areas

Has anything been overlooked?