



UK Health
Security
Agency

Leveraging radiobiology to inform low dose risk assessment

56th meeting of Nuclear & Radiation Studies Board
15 May 2025

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Why does low dose risk assessment remain an area of concern?

- Large populations exposed in medical imaging where there continue to be developments of new modalities and there can be individuals receiving multiple imaging procedures
- New nuclear energy technologies and the contribution of nuclear to net-zero
- Global geopolitical situation and the evolving threat landscape

Some problems with leveraging radiobiological research

Primary scientific literature reports in detail on small specific, incremental advances

- The need to integrate findings – eg UNSCEAR 2020/2021, Biological mechanisms relevant for the inference of cancer risks from low-dose and low-dose-rate radiation; ongoing evaluations of circulatory disease risk, effects on the nervous system and effects on the eye

Model systems utilised in studies can be very specific

- The need to generalise across many, many experimental models

Exposure protocols can be quite varied (and of differing robustness)

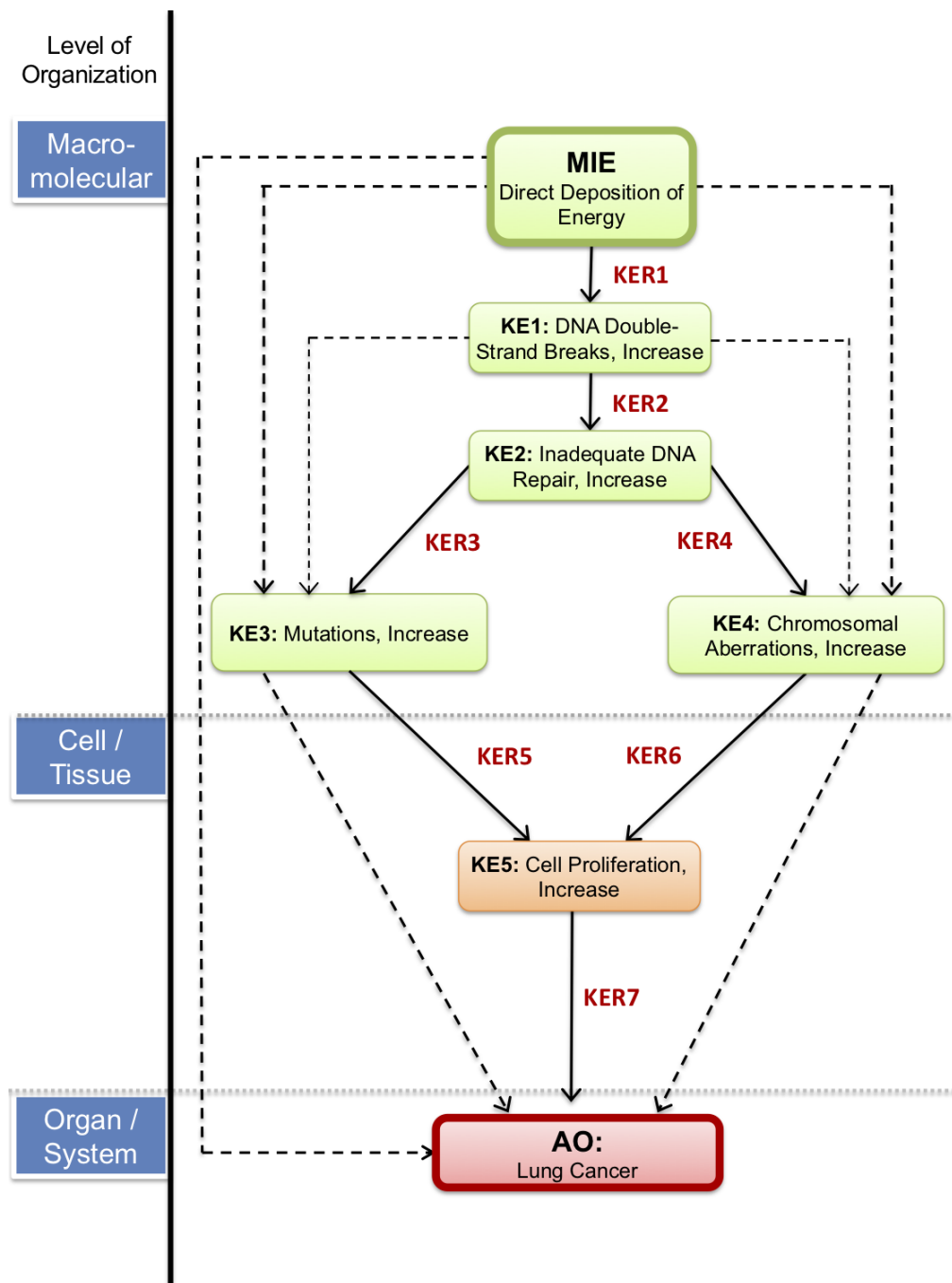
- The need to be clear on the human exposure system to be modelled – eg Medical, generally acute low doses; Occupational, generally chronic and episodic low doses; Public natural background, dominated by chronic alpha particle exposure of the lungs (radon)

Integration of findings

Potential value of adverse outcome pathway (AOP), and related approaches (see NCRP Report No. 186 – Approaches for Integrating Information from Radiation Biology and Epidemiology to Enhance Low-Dose Health Risk Assessment (2020))

- OECD maintains the AOP system, most relate to chemical hazards but growing numbers of AOPs being developed for radiation health endpoints - <https://aopwiki.org/>
- Currently 28 listed if search 'radiation'
- Cover multiple health endpoints/effects, eg specific cancers such as lung cancer, acute myeloid leukaemia; non-cancer outcomes such as cataract, memory and learning impairment; intermediate endpoints/effects such as induction of chromosomal aberrations

Graphic outlining lung cancer AOP



<https://aopwiki.org/aops/272>

Graphic outlining cataract AOP

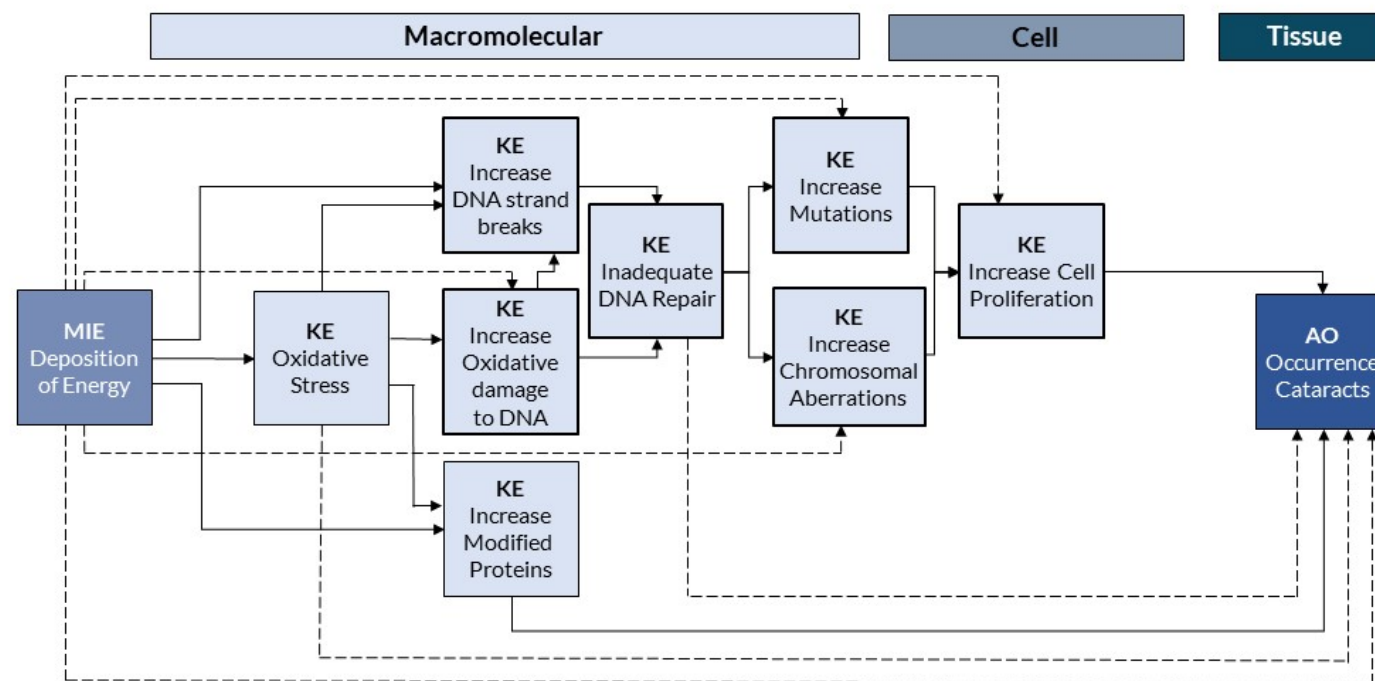
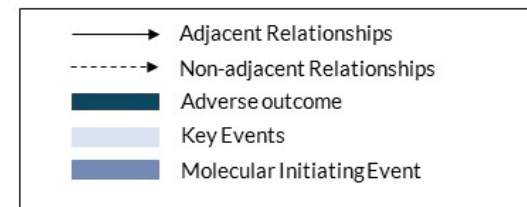
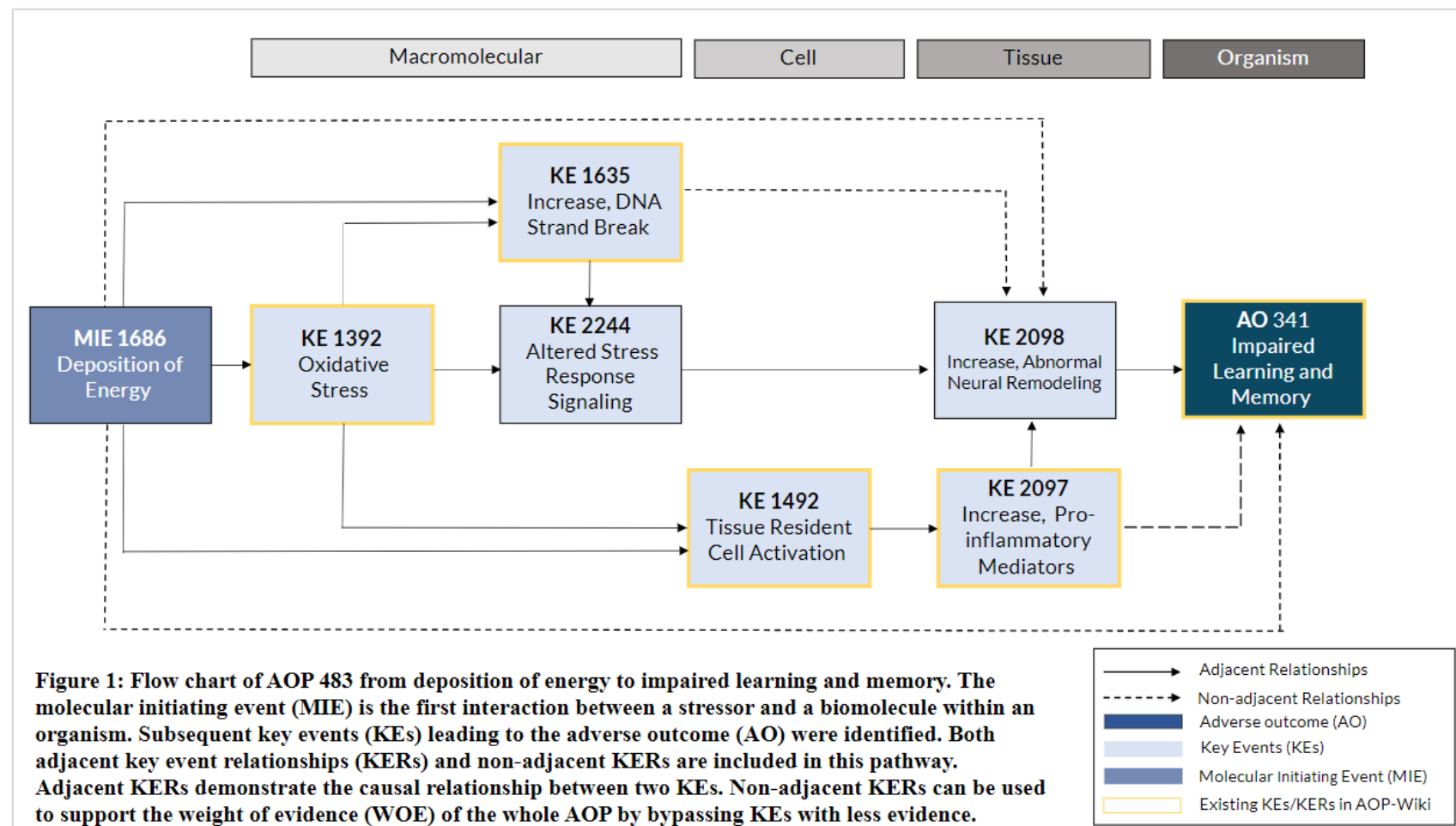


Figure 1. Visual representation depicting the AOP leading from the deposition of energy to cataracts. Both adjacent KERs and non-adjacent KERs are included in this pathway. Adjacent KERs demonstrate the causal relationship between two KEs. Non-adjacent KERs can be used to support the weight of evidence (WOE) of the whole AOP by bypassing KEs with less evidence.



<https://aopwiki.org/aops/478>

Graphic outlining learning and memory impairment AOP



<https://aopwiki.org/aops/483>

Potential benefits

- Identification of intermediate 'key events' between exposure and observable health outcome – can provide biomarkers/bio-indicators for use in epidemiology or health screening
- Mechanistic understanding can inform risk projection from where epidemiology 'ends' to real-life exposure levels
- Quantitative AOPs could inform quantitative risk assessment

Protection of the population or the individual?

- Current ICRP System of protection is clearly a population-based system
- Much interest (especially in diagnostic imaging) on ‘individualisation’ – stratification by age, sex...
- ICRP has two Task groups in this area, TG111 assessing the evidence and TG128 considering future application
 - What are the factors that modify risk of radiation-associated health outcomes?

Benefits of better understanding of risk modifiers

- Informs on transfer of risk across populations with differing underlying rates of specific diseases
- Will assist with decisions on value of individualisation/stratification in radiation protection
- The biomarkers/indicators identified through radiobiology/AOP approaches could be used in health screening

Multidisciplinary and trans-national working

- Well established research 'platforms' in Europe such as MELODI, EURADOS, EURAMED (funded by modest subscription)
- Develop and maintain strategic research agendas (community-led prioritisation)
- EU funded *Pianoforte Partnership* – a five year, 29M Euro funding, has run three open calls for research. Covers all sub-disciplines and encourages multi-disciplinarity. <https://pianoforte-partnership.eu/>

To conclude

- Improved low dose and low dose rate risk assessment is needed and is feasible
- There is value in integration between epidemiology and radiobiology (and ways to achieve that)
- There is value in multidisciplinary working
- Judgements will be needed on dose-risk relationships for the 'emerging' non-cancer outcomes to inform protection strategies and approaches
- Judgements also required on benefits of stratification/individualisation

Thanks for listening – simon.bouffler@ukhsa.gov.uk