La classification des effets sanitaires radio-induits

Congrès national de radioprotection SFRP

Session 8 : évolution des recommandations de la CIPR

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ICRP INTERNATIONAL COMMISSION ON RADIOLOGICAL PROTECTION

Plan de la présentation

1. Objectifs du système de radioprotection
2. Questions posées par l'évolution des connaissances scientifiques
3. Objectifs du groupe de travail 123 de la CIPR
4. Perspectives

Objectifs du système de radioprotection

Le système de radioprotection établi par la CIPR vise à gérer et contrôler les expositions aux rayonnements ionisants de façon à :

1. Prévenir l'occurrence des réactions tissulaires (effets déterministes) ;
2. Réduire aussi bas que raisonnablement possible le risque d'incidence d'effets stochastiques.

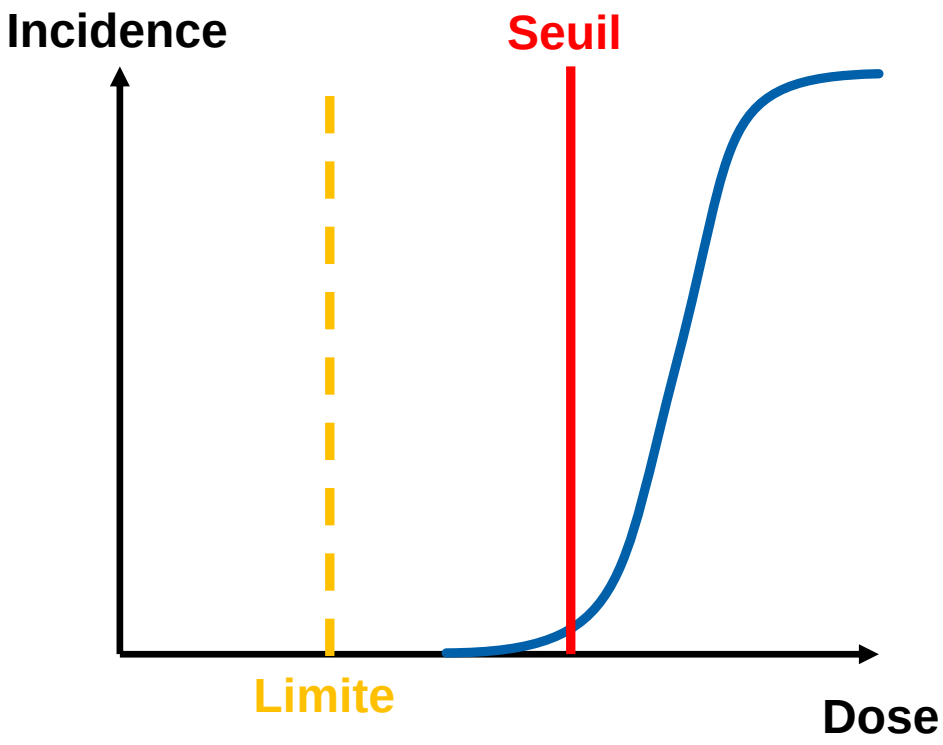
Réactions tissulaires (nocives)

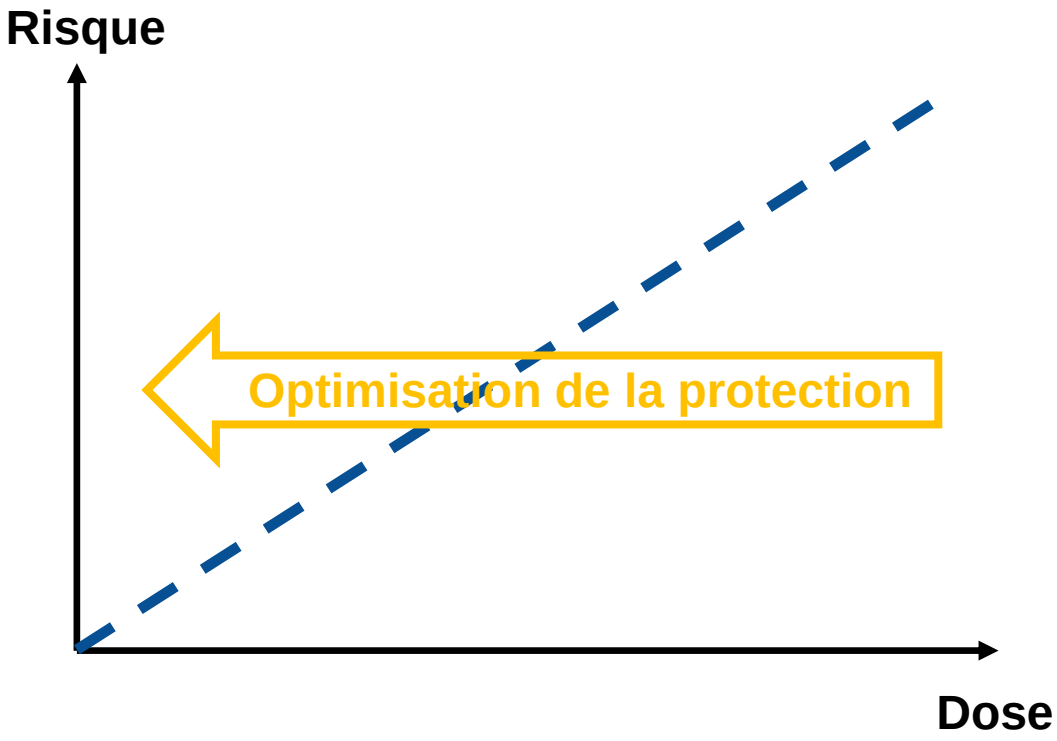
Les réactions tissulaires sont liées à l'élimination/dysfonctionnement de cellules à la suite de fortes doses. Elles sont caractérisées par un seuil et une augmentation de la sévérité de l'effet avec la dose.

Effets stochastiques

Les effets stochastiques, cancers et effets héréditaires, résultent du dommage d'une cellule unique. La fréquence de l'événement croit avec la dose, mais pas la sévérité. A des fins de protection, il n'y a pas de seuil (relation linéaire sans seuil).

Objectifs du système de radioprotection





Threshold dose for tissue reactions : dose estimated to result in only 1% incidence of tissue reactions.

The process of determining what level of protection and safety makes exposures and the probability and magnitude of potential exposures as low as reasonably achievable economic and societal factors being taken into account.

Questions posées par l'évolution des connaissances scientifiques

'**The classification of harmful radiation-induced health effects** into 'stochastic effects' (cancer and heritable diseases) and 'harmful tissue reactions' for protection purposes **should be revisited to ensure that it remains fit for purpose**. For example, for protection purposes, it may be useful to distinguish between severe and other tissue reactions, or between short-term and long-term health effects. Some health effects may not fit well into either category (e.g., **cataract, diseases of the circulatory system**). Whatever classification is adopted, it will be necessary to assess the impact on the management of radiological risks in terms of the tolerability of risks and putting them into perspective with other risks. Any reclassification will not affect the fundamental requirements to prevent severe tissue reactions (using organ/tissue doses) and optimise protection against effects at low doses and low dose rates, principally cancer (using effective dose)'.

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Memorandum

Keeping the ICRP recommendations fit for purpose

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Questions posées par l'évolution des connaissances scientifiques

ICRP Publication 118

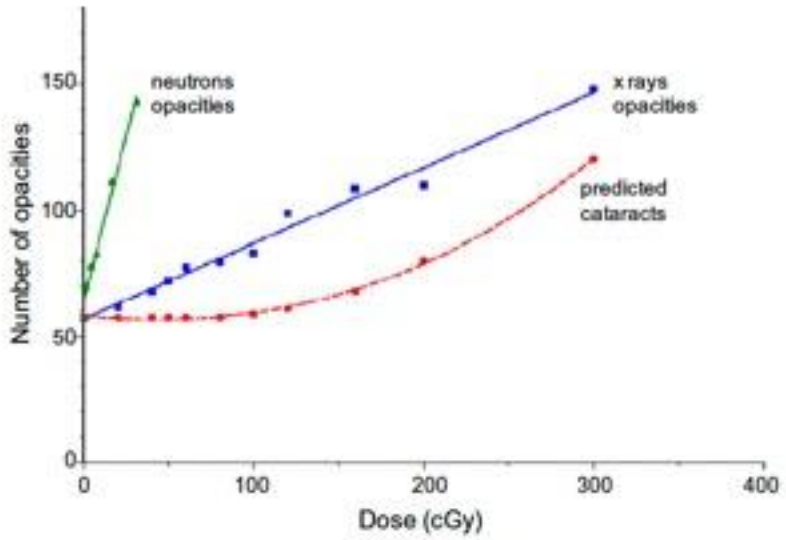
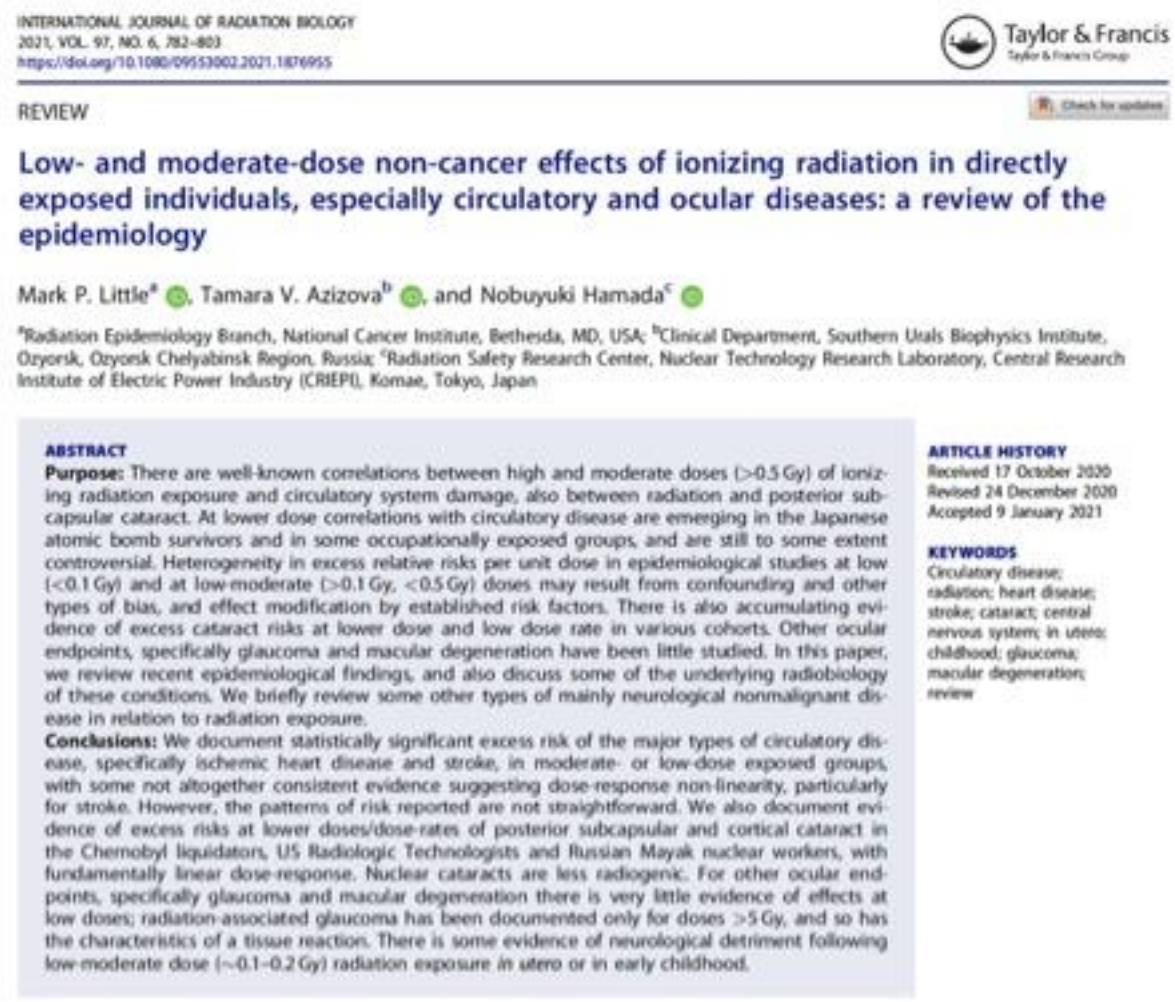


Fig. 2.8. Number of opacities in the murine lens as a function of 250-kVp x rays or 14-MeV neutrons, taken from Di Paola et al. (1978). The dashed line (added by the present authors) represents the shape of a curve for x rays that would be predicted for cataracts, if a cataract results from the accumulated damage to many lens cells i.e. the fusing of multiple opacities.

'De nouvelles information sur la détection et la classification des cataractes tendent à indiquer que les changements observés tôt au niveau du cristallin seraient de nature déterministe (seuil clairement apparent), alors que les changements observés sur le long terme seraient de nature stochastique'.

Questions posées par l'évolution des connaissances scientifiques



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REVIEW

Low- and moderate-dose non-cancer effects of ionizing radiation in directly exposed individuals, especially circulatory and ocular diseases: a review of the epidemiology

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ABSTRACT

Purpose: There are well-known correlations between high and moderate doses (>0.5 Gy) of ionizing radiation exposure and circulatory system damage, also between radiation and posterior subcapsular cataract. At lower dose correlations with circulatory disease are emerging in the Japanese atomic bomb survivors and in some occupationally exposed groups, and are still to some extent controversial. Heterogeneity in excess relative risks per unit dose in epidemiological studies at low (<0.1 Gy) and at low-moderate (>0.1 Gy, <0.5 Gy) doses may result from confounding and other types of bias, and effect modification by established risk factors. There is also accumulating evidence of excess cataract risks at lower dose and low dose rate in various cohorts. Other ocular endpoints, specifically glaucoma and macular degeneration have been little studied. In this paper, we review recent epidemiological findings, and also discuss some of the underlying radiobiology of these conditions. We briefly review some other types of mainly neurological nonmalignant disease in relation to radiation exposure.

Conclusions: We document statistically significant excess risk of the major types of circulatory disease, specifically ischemic heart disease and stroke, in moderate- or low-dose exposed groups, with some not altogether consistent evidence suggesting dose-response non-linearity, particularly for stroke. However, the patterns of risk reported are not straightforward. We also document evidence of excess risks at lower doses/dose-rates of posterior subcapsular and cortical cataract in the Chernobyl liquidators, US Radiologic Technologists and Russian Mayak nuclear workers, with fundamentally linear dose-response. Nuclear cataracts are less radiogenic. For other ocular endpoints, specifically glaucoma and macular degeneration there is very little evidence of effects at low doses; radiation-associated glaucoma has been documented only for doses >5 Gy, and so has the characteristics of a tissue reaction. There is some evidence of neurological detriment following low-moderate dose (~0.1–0.2 Gy) radiation exposure *in utero* or in early childhood.

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Circulatory disease; radiation; heart disease; stroke; cataract; central nervous system; in utero; childhood; glaucoma; macular degeneration; review

'Conclusions: les auteurs ont identifié un excès de risque significative pour les principaux types de maladies de l'appareil circulatoire, en particulier les cardiopathies ischémique, pour des groupes exposés à des doses moyennes ou faibles'.

Questions posées par l'évolution des connaissances scientifiques

'L'analyse de 15 098 publications a permis d'identifier 93 études qui suggèrent un **risque modéré, mais significatif** de 2,3 à 3,9 décès pour 100 personnes exposées à un Gy. Ces résultats auront potentiellement des implications pour les patients, ainsi que pour les décideurs impliqués dans la gestion des risques d'exposition aux rayonnements ionisants pour les travailleurs et le public'.

'Evidence for cardiovascular disease will soon need to be added to the existing list of radiation induced health risks'. (A. Auvinen)

RESEARCH

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Check for updates

Ionising radiation and cardiovascular disease: systematic review and meta-analysis

Mark P Little,[1] Tamara V Azizova,[2] David B Richardson,[3] Soile Tapio,[4] Marie-Odile Bernier,[5] Michaela Kreuzer,[6] Francis A Cucinotta,[7] Dimitry Bazyka,[8] Vadim Chumak,[8] Victor K Ivanov,[9] Lene H S Veiga,[1] Alicia Livinski,[10] Kossi Abalo,[11,12] Lydia B Zablotska,[13] Andrew J Einstein,[14] Nobuyuki Hamada[15]

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ABSTRACT

OBJECTIVE

To systematically review and perform a meta-analysis of radiation associated risks of cardiovascular disease in all groups exposed to radiation with individual radiation dose estimates.

DESIGN

Systematic review and meta-analysis.

MAIN OUTCOME MEASURES

Excess relative risk per unit dose (Gy), estimated by restricted maximum likelihood methods.

DATA SOURCES

PubMed and Medline, Embase, Scopus, Web of Science Core collection databases.

ELIGIBILITY CRITERIA FOR SELECTING STUDIES

Databases were searched on 6 October 2022, with no limits on date of publication or language. Animal studies and studies without an abstract were excluded.

RESULTS

The meta-analysis yielded 93 relevant studies. Relative risk per Gy increased for all cardiovascular disease (excess relative risk per Gy of 0.11 (95% confidence interval 0.08 to 0.14)) and for the four major subtypes of cardiovascular disease (ischaemic heart disease, other heart disease, cerebrovascular disease, all other cardiovascular disease). However, interstudy heterogeneity was noted (P<0.05 for all endpoints except for other heart disease), possibly resulting from interstudy variation in unmeasured confounders or effect modifiers, which is markedly reduced if attention is restricted to higher quality studies or those at moderate doses (<0.5 Gy) or low dose rates (<5 mGy/h). For ischaemic heart disease and all cardiovascular disease, risks were larger per unit dose for lower dose (inverse dose effect) and for fractionated exposures (inverse dose fractionation effect). Population based excess absolute risks are estimated for a number of national populations (Canada, England and Wales, France, Germany, Japan, USA) and range from 2.33% per Gy (95% confidence interval 1.69% to 2.98%) for England and Wales to 3.66% per Gy (2.65% to 4.68%) for Germany, largely reflecting the underlying rates of cardiovascular disease mortality in these populations. Estimated risk of mortality from cardiovascular disease are generally dominated by cerebrovascular disease (around 0.94-1.26% per Gy), with the next largest contribution from ischaemic heart disease (around 0.30-1.20% per Gy).

CONCLUSIONS

Results provide evidence supporting a causal association between radiation exposure and cardiovascular disease at high dose, and to a lesser extent at low dose, with some indications of differences in risk between acute and chronic exposures, which require further investigation. The observed heterogeneity complicates a causal interpretation of these findings, although this heterogeneity is much reduced if only higher quality studies or those at moderate doses or low dose rates are considered. Studies are needed to assess in more detail modifications of radiation effect by lifestyle and medical risk factors.

SYSTEMATIC REVIEW REGISTRATION

PROSPERO CRD42020202036

WHAT IS ALREADY KNOWN ON THIS TOPIC

Exposure to high dose ionising radiation during radiotherapy can damage the heart

Cardiovascular disease risk in the low dose range (<0.1 Gy), characteristic of doses that patients receive from medical diagnostic exposures or those radiation workers receive from occupational exposures is not well understood

Previous systematic reviews published over a decade ago looked at a much smaller number of studies, mostly with lower dose or lower dose rate exposures

WHAT THIS STUDY ADDS

A systematic review of 15 098 studies yielded 93 informative and largely non-overlapping studies and suggest modest but significantly increased excess lifetime risk of 2.3-3.9 deaths per 100 people exposed to one Gy of radiation

These findings have implications for patients who undergo radiation exposure as part of their medical care, as well as policy makers involved in managing radiation risks to radiation workers and the public

The potential increased risk of radiogenic cardiovascular disease should prompt vigilance to control other modifiable cardiovascular risk factors and extra consideration of cardiovascular disease following radiation exposure

Introduction

Cardiovascular diseases are the leading cause of death worldwide.[1 2] Cardiovascular disease was the underlying cause of death for about a third of the 2.8 million deaths in the USA in 2018: ischaemic heart disease accounted for 42% and stroke for 17% of all cardiovascular disease deaths.[3] Worldwide, ischaemic heart disease ranks first in years of life lost and stroke ranks third. Consistently identified independent risk factors include age, smoking, diabetes mellitus, hypertension, obesity, and increased total and low density lipoprotein or decreased high density lipoprotein cholesterol.[4-6] A heritable genetic

Questions posées par l'évolution des connaissances scientifiques

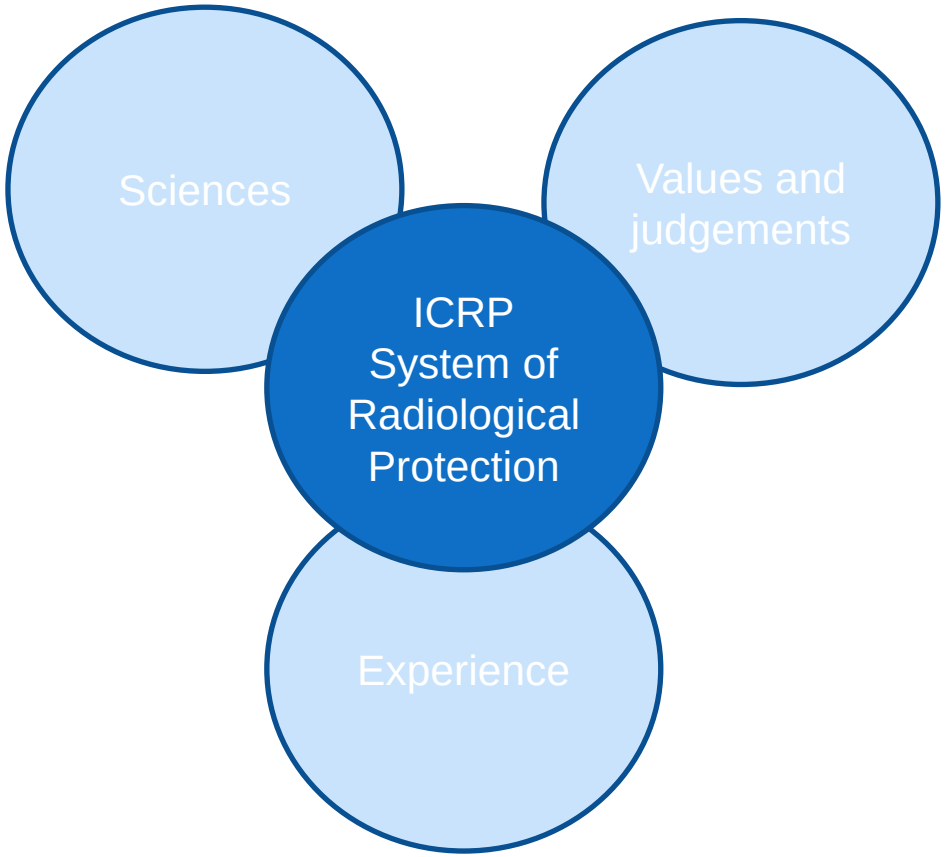
'The mechanism of the induction by radiation of leukaemia and other types of malignancy is not known. Such induction has so far been clearly established after doses of more than 100 rads, but it is unknown whether a threshold dose exists below which no malignancy is produced. If such a threshold dose did exist, there would be no risk of the induction of malignancy, as long as the threshold was not exceeded. **As the existence of a threshold dose in unknown, it has been assumed that even the smallest doses involve a proportionately small risk of malignancies. Also, because of the lack of knowledge of the nature of the dose-effect relationship in the induction of malignancies in man – particularly at those dose levels which are relevant in radiological protection – the Commission sees no practical alternative, for the purposes of radiological protection, to assuming a linear relationship between dose and effect, and that doses act cumulatively**. **The Commission is aware that the assumptions of no threshold and of complete additivity of all doses may be incorrect, but is satisfied that they are unlikely to lead to the underestimation of risks**'. ICRP Publication 9, §7, 1966.

Objectifs du groupe de travail 123 de la CIPR

1. Apporter un éclairage sur la rationalité de la classification actuelle (à partir essentiellement de l'examen des publications de la CIPR) et les principaux objectifs de protection du système de la CIPR,

2. Évaluer les éléments qui vont dans le sens d'une évolution de la classification, à partir d'une analyse de la littérature scientifique,

3. Si une évolution est jugée souhaitable d'un point de vue scientifique, évaluer l'impact sur la gestion pratique du risque radiologique.



Objectifs du groupe de travail 123 de la CIPR

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Perspectives

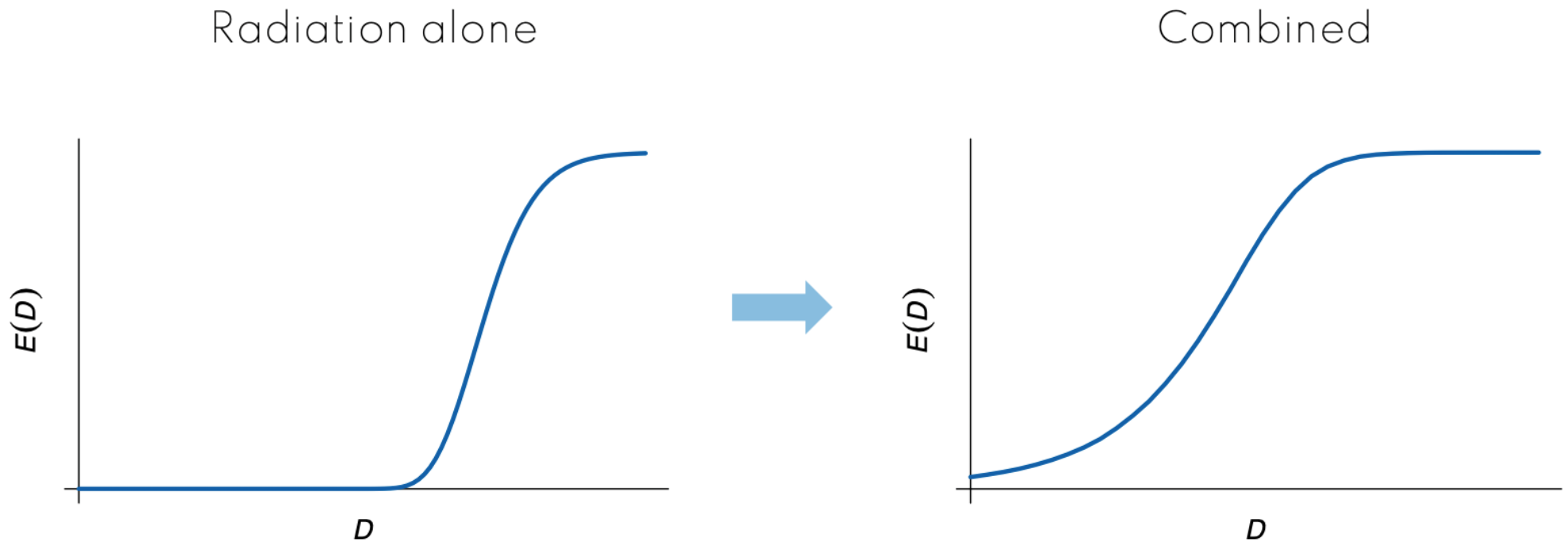
La classification actuelle ne reflète pas parfaitement les connaissances scientifiques, mais elle est adaptée à la gestion de la protection radiologique. Doit on changer d'approche et considérer par exemple :

1. Effet sanitaire induit uniquement par les rayonnements et géré avec le seuil ;

2. Maladies multifactorielles gérées par la LNT. Le terme d'effet radio-induit n'est alors pas correct - les dommages induits par les rayonnements s'ajoutent à ceux résultant d'autres facteurs de risque (environnement, mode de vie, patrimoine génétique, etc.).

La méthodologie AOP (Adverse Outcome Pathway) peut potentiellement apporter des éclairages utiles.

Perspectives



Extrait d'une présentation de N. Ban (Japon, NRA, Réunion du TG119).

Perspectives

Le TG123 s'est réuni à 2 reprises et organisera sa première réunion en présentiel les 4 et 5 juillet prochains.

Session dédiée à l'occasion du Symposium de Vancouver à Tokyo en novembre 2023.

Projet de rapport prévu à l'horizon 2025/2026 pour une publication en 2027.

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