

# Comments on the ICRP draft report for consultation: “Radiation Detriment Calculation Methodology”

*Joint comments from the Dutch National Institute for Public Health and the Environment (RIVM) and the Dutch Authority for Nuclear Safety and Radiation Protection (ANVS)*

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This document provides the joint comments of RIVM and ANVS on the draft publication on “Radiation Detriment Calculation Methodology” performed by the National Institute for Public Health and the Environment (RIVM). It is structured as follows:

- Part 1: General opinion and remarks
- Part 2: Specific and detailed remarks
- Part 3: Annex: verification of results

As part of this review, RIVM created an Excel tool (*RADICAL.xlsm*<sup>2</sup>) to verify the calculations presented in this draft ICRP publication. Results of this verification study are presented in the Annex of this review (part 3). The Excel tool is available for ICRP Task Group 102 for validation purposes.

## Part 1. General opinion and remarks

We welcome ICRP’s efforts to produce a historical overview of the calculation of radiation detriment combined with a detailed description of its current calculation methodology. We often have felt the need for such a document in our professional careers and expect it to be valuable to the radiation-protection community. It provides a good overview of past research and assumptions regarding radiation detriment. And, although it does not present new results, it clearly indicates the fields of research where refinement of the modelling could be achieved.

We hope that the comments given below will be useful to the authors in making corrections and further improvements to the draft report.

Section 5.5 of the draft report mentions that ‘There is no simple way to express the multidimensional nature of detriment, and it will be necessary to improve its presentation in the future so that the make-up of radiation detriment becomes more comprehensible to non-specialists’ (Lines 1404-1406). RIVM and ANVS acknowledge this fact and welcome the current report as an important step towards such increased transparency. For example, the graphical representation such as presented in Figure 3.1 is very helpful in understanding the steps and quantities involved in the calculation of the detriment. Our main comment concerns the report’s contribution to comprehensibility of the concept of detriment for non-specialists: it is our view that the report could be more accessible, without losing technical correctness. A few examples to illustrate this:

- (1) Chapter 2 presents an overview of the historical evolution of the quantity ‘radiation detriment’. This evolution is mainly presented as a brief summary of previous publications and risk-related coefficients without explicitly putting them into historical context. This

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<sup>2</sup> [Radiation Detriment from Incidence Calculations](#) (RIVM, 2020)

chapter would gain added value if it were to explain the main conceptual reasons for changes between consecutive ICRP publications. This would demonstrate more clearly how detriment evolved into the quantity as it is defined nowadays (Chapter 3). Perhaps an illustration or infographic (as Fig. 3.1) could be helpful to visualize the timeline of this evolution.

- (2) We understand that, in the historical overview, ICRP uses the terminology from the publications that are cited. However, the use of different terms for similar or related quantities throughout the report is at times confusing, e.g., risk factor<sup>3</sup> (Table 2.1) versus risk-of-induction (Table 2.2) versus probability of fatal cancer (Table 2.3), versus nominal risk coefficient (Table 3.5), with values presented in units of both  $10^{-4} \text{ Sv}^{-1}$  and  $10^{-2} \text{ Sv}^{-1}$ . Additionally, the term risk coefficient is also used for the excess risk (either ERR or EAR), see e.g., Lines 680 and 686/687 on page 25. The index of harm (page 9, Line 346 and page 10 Line 369) is closely related to the life-loss detriment in  $\gamma \cdot \text{Sv}^{-1}$  (page 9, Line 355), but the difference is not described clearly (see part 2 of this document). Another example is the use of fatality rate<sup>4</sup> (Line 393, page 11) as an alternative for the lethality fraction  $k$ , written as both a fraction (Line 393) and a percentage (Line 400). Note that the parameter “Severity of cure” in Table 2.2 is yet another parameter that represents the lethality of a certain cancer. Finally, the use of man-years and person-years are both used in this draft document. Hence, nomenclature of risk-related quantities and their units could be harmonized throughout the document to make it more readable. If this is, however, unwanted for the reason to stay close to the nomenclature used in the original ICRP Publications (26, 27, 45, 60 and 103), several explanatory remarks or a table of (nearly) equivalent technical terms could be added to increase the readability of this draft report.
- (3) The use of dose in Gy and Sv is not always clear, especially in Chapter 2. It could at times be stated more explicitly whether it concerns an organ/tissue absorbed dose, dose equivalent, equivalent dose or an effective dose.
- (4) As described in the technical part of this document below, several small inconsistencies, missing elements and explanations in the methodology (Chapter 3) could lead to confusion and partly inhibit a straightforward verification of the (nominal) risk calculations on which the detriment values are based.

To verify whether we have fully understood the draft report we attempted to reproduce the (majority of the) results in Chapter 3. To this end, an Excel tool (*RADICAL.xlsm*, available for ICRP Task Group 102 for validation purposes) was created, using as input the incidence- and mortality-rate data listed in Tables A.4.10 through A.4.17 of ICRP Publication 103. This numerical verification has led to several technical issues and findings with respect to content, as will be discussed in parts 2 and 3 of this document. Based on that, we propose several changes to Chapter 3, which may increase the comprehensibility of the methodology even further, by which it becomes more accessible to a broad(er) radiation-protection community.

We observe that the scope of the report does not include clear guidance on how to apply the radiation-detriment values in real-life exposure scenarios or situations. For example, we know from experience the detriment and effective dose are frequently misused to determine individual risks (see below for a more detailed remark related to page 7, paragraph 7 below). Explicit guidance on where and when the detriment can be used, and where it should not be used, could be useful. Such guidance could also elaborate on the (practical) applicability of the radiation detriment with respect

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<sup>3</sup> “Factor” would indicate that the resulting unit is dimensionless, whereas it actually carries a dimension:  $\text{Gy}^{-1}$  or  $\text{Sv}^{-1}$ .

<sup>4</sup> “Rate” would indicate a unit of e.g.  $\gamma^{-1}$ , whereas in fact the quantity concerns a dimensionless fraction. We are aware that fatality rate is commonly used in epidemiology. Technically speaking, this is not correct.

to variability amongst individuals (e.g., sex, age) and populations<sup>5</sup>, as well as on its use in the scope of regulatory control of sources of ionizing radiation (e.g., exemption and clearance). Limitations in use could for instance be discussed in view of the uncertainties described in Chapter 4 and the potential evolution in Chapter 5. This would increase the document's contribution to increased transparency of the concept of detriment and its applications

Finally, we recommend that the purpose of the report is specified more explicitly, (for instance in the introduction).

In summary, RIVM and ANVS conclude that the current draft ICRP report is a valuable document in the comprehension of the complex, multidimensional concept of radiation detriment which could serve as a reference work to the radiation-protection community. It will be an excellent extension of the ICRP (draft) report on "The use of the effective dose as a radiological protection quantity". We believe that this draft publication could be improved to gain more transparency and to shed more light on the applicability and limitations of the detriment quantity in realistic situations.

In the next sections (parts 2 and 3) we provide more detailed comments on several technical and editorial issues we encountered in the draft report.

## Part 2. Specific and detailed remarks

Detailed comments are given below per section, where possible. Any specific, textual changes suggested in this part are highlighted in boldface.

### General

The document often uses the expression "cancer site". Is this the same as "cancer type"? If so, isn't cancer type clearer, and if not, please define "cancer site".

### Executive summary

► Page 5, para (g), lines 195-197: "Considering the variation of cancer risk with sex and age, it is advisable to calculate lifetime risks separately for sexes and selected ages (age groups) and average them in the last stage to obtain a nominal value."

The interpretation of this sentence is not clear to the reader who has not read the full report: it could be interpreted in at least two ways. One interpretation is that ICRP intends to say that averaging over ages and sexes should be done after the last step of the procedure followed in ICRP 103, i.e. after a total nominal risk (averaged over reference populations, but separate for age groups and per sex) has been calculated. A second interpretation is that averaging over population, ages and sexes should all be done in the same final step. Replacing 'them' with '**these estimates**' could resolve the issue.

### Section 1. Introduction

► Page 7, para 7, Lines 271-275: "... or to assess risks in retrospective situations for exposures of identified individuals. However, it should be noticed that there are significant differences in risk between sexes and in respect of age at exposure. For the estimation of the likely consequences of an exposure of a given individual or population, it is preferable to use specific data relating to the exposed individuals when they are available."

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<sup>5</sup> Especially since the nominal risk coefficients – on which the established detriment values are based – do not include cancer-incidence and mortality data of all world populations.

This paragraph can be read to imply that detriment can be used to obtain accurate risk assessments on the level of the individual exposed in a specified situation. We suggest a modification of this paragraph to emphasize that detriment is a concept for use at the level of groups, and that at the individual level it can at best give a qualitative estimate for risk. This is a consequence of the fact that effective dose is defined for this use. In fact, in the draft ICRP report on “The use of the effective dose as a radiological protection quantity” we can read that:

“It is important to recognize that while E is a risk-related construct for use in radiation protection, particularly in planning and optimizing protection for workers and members of the public, it does not provide estimates of dose to specific individuals”.

This comment is related to our general recommendation that some guidance on the use of radiation detriment be included in the report (part 1 of this document).

Furthermore, as stated in this paragraph, differences between sexes are significant. In radiation protection, why is the choice made to average over both sexes rather than using two values for detriment? Or more conservatively (and addressing the issue that information on gender in exposed groups may not always be available), why not assume the most sensitive gender?

## Section 2. History of radiation detriment calculation

► Page 8, para 11, Lines 316 through 320: “Based on data ...to be  $25 \times 10^{-4} \text{ Sv}^{-1}$ .”

This part discusses female breast cancer for which a risk factor of  $25 \times 10^{-4} \text{ Sv}^{-1}$  is mentioned, as also listed in Table 2.1. However, this value already is the average over men ( $\approx 0 \text{ Sv}^{-1}$ ) and women ( $50 \times 10^{-4} \text{ Sv}^{-1}$ ), as described in para 36 of ICRP Publication 27. The average over both sexes is stated para 12 of the current draft report, but we suggest to mention this earlier when the term ‘risk factor’ is first introduced (Line 304).

► Page 9, Lines 331 and 332: Table 2.1 and its caption

“...for nominal mortality risk coefficients” → “...for nominal **cancer**-mortality risk coefficients” (i.e., for *fatal cancer*)

Moreover, the caption or an additional footnote could mention that these organ/tissue values are sex- and age-averaged risk values per unit dose equivalent here.

► Page 9, para 14, Lines 342 and 343: “... at a rate of  $10^{-4} \text{ rem}^{-1}$ , with ...”

This value could be explained better, in relation to the total cancer-mortality coefficient of  $125 \times 10^{-4} \text{ Sv}^{-1}$  mentioned earlier in Table 2.1. To our knowledge, on average (men/women), 78% of all fatal cancers is actually expressed due to latency, taking into account the age distribution of the population. This results in an *effective* risk factor<sup>6</sup> of  $0.78 \times 125 \times 10^{-4} \text{ Sv}^{-1} = 98 \times 10^{-4} \text{ Sv}^{-1} \approx 10^{-4} \text{ rem}^{-1}$  as is shown on page 13 of ICRP Publication 27.

Moreover, we understand that the quoted text uses the unit rem. Including a conversion of this result to Sv would be helpful for many readers (see part 1 of this document).

► Page 9, para 14, Lines 341 through 347

The concept of the *index of harm* from ICRP Publication 27 is first mentioned in the last sentence of this paragraph, but not clearly defined here. However, this done explicitly in para 16 dealing with the hereditary effects (ICRP Publication 45). We suggest to include the definition to the beginning of para 14 (as the second sentence): “**The index of harm for ionising radiation is defined as the number of years lost per 1000 worker-years for a given annual dose from occupational exposure.**” Then, after the sentence “*It is concluded that ... occupational exposures*” the resulting index of harm, with a value of 0.3, could be given for an annual dose of 2 mSv (i.e. an average occupational

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<sup>6</sup> ‘...rate ...’, as mentioned in the report, may not be the best way to refer to this value

dose rate of 2 mSv/y), to make values comparable to those mentioned in paras 16 and 17 (page 10). Note that the index of harm is thus closely related to the life-loss detriment, the product of risk factor and mean loss of life expectancy (para 15), but they are not exactly the same.

► Page 9, para 15, Lines 348 through 357

*“The resultant ... in males”* (Lines 355 and 356). Based on the previous remark (concerning para 14), the sentence could be extended as: **“The resultant life-loss detriment, defined as the product of risk factor and mean loss of life expectancy, from all cancer induction was on average  $0.25 \text{ y.Sv}^{-1}$  (i.e.,  $16 \text{ y} \times (1.26+0.29) \times 10^{-2} \text{ Sv}^{-1}$ ),  $0.3 \text{ y.Sv}^{-1}$  in females and  $0.2 \text{ y.Sv}^{-1}$  in males”**.

Additionally, the weighting concept in Table 2.2 could be addressed here in more detail. In the current draft, Table 2.2 is only referred to, but not explained. This concept is actually very similar to the weighting scheme used in ICRP Publication 60, which may deserve some attention in this historical overview.

► Page 10, Lines 358 and 359: Table 2.2 and its caption

The caption or an additional footnote could mention that these organ/tissue values are sex- and age-averaged risk values per unit dose equivalent here (same comment as for Table 2.1).

Furthermore, we notice that the weighting concept in Table 2.2 is not described. This could briefly be done in para 15 (see previous comment).

► Page 10, para 16: *“For hereditary effects, the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) 1982 report estimated years of life impaired or lost to be 0.63 years per person·Gy of genetically significant radiation at equilibrium after continuous exposure.”*

The meaning of *“at equilibrium”* in this sentence is not immediately clear. Adding the explanation given by UNSCEAR would address this – *“under continuous radiation exposure ( $10^{-2} \text{ Gy/generation}$ ), the population will reach a new equilibrium with respect to the incidence of these diseases”*. (To help the reader interpret this statement, information on the duration of a human generation would be useful). In addition, a definition of genetically significant radiation would be helpful. Finally, the current phrasing suggests that effects occur after exposure has ended. We recommend that the sentence is rewritten as *“...per person·Gy of genetically significant radiation at equilibrium **under** continuous exposure”*

► Page 12, Lines 407 through 413: Table 2.3 and its caption/footnotes

The fifth column label *“Relative non-fatal contribution (2-k)”* is incorrect! In fact, 2-k is the **total** contribution, i.e., fatal + non-fatal, as is explained in para 21. The label could be changed e.g. **“Relative total contribution, including non-fatal, (2-k)”**.

Also, the caption or an additional footnote could mention that these organ/tissue values are sex- and age-averaged risk values per unit equivalent dose (not dose equivalent as in Tables 2.1 and 2.2). The Sv in the total, summed detriment (i.e.  $725.3 \times 10^{-4} \text{ Sv}^{-1}$ ) refers to the effective dose *E*.

► Page 12, para 21, Lines 422 through 426

Here it could be mentioned that the applied weighting scheme of ICRP Publication 60 is similar to that in ICRP Publication 45, with the weighting factor for non-fatal cancer being *k*, the lethality fraction, which compares well with the parameter *“Severity of cure”* in Table 2.2.

In these lines, *F* appears used to denote an absolute number of fatal cancers in a specific tissue, whereas in Table 2.3 the same symbol is used for the probability of fatal cancer. Change *F* in paragraph 12 to a different symbol to avoid ambiguity, or change the text to *“Thus, if in a given tissue there were **F** fatal cancers **per 10,000 persons per Sv**”* for consistency. Moreover, in the expression for the total weighted detriment no reference to the expected number of years of life lost from fatal cancer is made.

### Section 3. Calculation of radiation detriment

► It would be helpful to number the equations in this section.

► Page 14, para 27, Line 454 "... and geographical regions for ..."

What is meant here is that risk estimates are averaged over populations, so we suggest "... and geographical regions (**i.e., populations**) for ..."

► Page 14, para 28, Lines 459 and 460

"... Gy is used as the **absorbed** dose unit ... and Sv is used **as the equivalent or effective dose unit** for the ..."

► Page 14, para 29, Line 463: "... and for the two reference populations"

At this point in the text the reference populations have not yet been mentioned, so we suggest: "... and for two reference populations as defined in 3.1.1.1 and 3.1.1.2 ...".

► Page 15, para 32, Lines 498 through 501, section 3.1.1.3 (survival functions)

The calculation of the survival functions is not described. A short definition would help the reader to understand this quantity before it is used in the calculation of the lifetime baseline risk (LBR) in section 3.1.1.4. Moreover, the *all-cause* survival curves as plotted in Figure 3.2 are not the functions used in the risk integration of the REIC<sup>7</sup>. We suggest to add the following sentences:

**"The all-cause survival function is the probability to be alive at age  $a$  and is calculated as**

$$S(a) = \exp\left[-\int_0^a \mu(x) dx\right] \approx \prod_{n=0}^a (1 - \mu(n)),$$

**where  $\mu$  is the age dependent all-cause mortality rate ( $y^{-1}$ ) and the product on the right-hand side of the equation is the Kaplan-Meier estimator. The all-cause survival function  $S(a|a_{\min})$  is the *conditional* probability of a person, alive at age  $a_{\min}$ , to be alive at age  $a \geq a_{\min}$ , and is calculated as**

$$S(a|a_{\min}) = S(a)/S(a_{\min}) = \exp\left[-\int_{a_{\min}}^a \mu(x) dx\right] \approx \prod_{n=a_{\min}}^a (1 - \mu(n)).$$

**The age-dependent mortality rates, and thus the survival functions, are population and sex-specific."**

A reference to Vaeth and Pierce (*Environ. Health Perspect.* 87, pp. 83-94, 1990) could be made for more information.

► Page 16, para 33, Lines 506 through 511

The cancer incidence rates  $\mu_i$  are different for each specific cancer site. To be in line with the equations in section 3.1.3, we suggest to add a subscript " $c$ ". Furthermore, the explicit dependence on sex by use of parameter  $s$  is only used in this equation, and is dropped in the equations in section 3.1.3. As is already mentioned that incidence and mortality rates are sex-specific, this parameter can be dropped from the LBR-equation as well. We suggest to represent the equation as follows:

$$LBR_c(a_{\min}) = \int_{a_{\min}}^{a_{\max}} \mu_{ic}(a) S(a|a_{\min}) da, \text{ which would now be in line with the additional paragraph}$$

suggested in our previous comment and with the equations in section 3.1.3. There would be no need to explain  $S(a|a_{\min})$  anymore, as reference can be made to its definition as suggested above.

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<sup>7</sup> The REIC makes use of the cancer-free survival functions defined in para 46.

► Page 18/19, para 37, Lines 549 through 551: “The ERR/Gy ...respectively”

It is not very clear from this sentence that Figs. 3.6 and 3.7 are the average values over men and women. That is, these curves are plotted for sex-averaged values of  $\beta = 0.465 \text{ Gy}^{-1}$  (ERR) and  $51.5 \times 10^{-4} \text{ y}^{-1} \text{ Gy}^{-1}$  (EAR).

► Page 20, Lines 569 through 572, Table 3.2

Categories “All solid” and “Other” should be explained in some more detail (in a footnote perhaps). See part 3 of this document for more details on this issue. The same holds for Table 3.3.

► Page 21, Lines 574 through 578, Table 3.3 (concerning breast-cancer coefficients)

Our verification study with *RADICAL.xlsm* led to the observation that the EAR-risk parameterization for breast cancer differs from that used for other solid cancers. Our conclusion is that, if one uses the equation in para 37 of the draft ICRP report for breast cancer as well, then not only coefficient  $\alpha_2$  changes at the age of 50 y, but also the (pre)factor  $\beta$ . The correct values for  $\beta$  then are **25.4** for  $a \leq 50 \text{ y}$  and **10.9** for  $a > 50 \text{ y}$  (both values in units of  $10^{-4} \text{ y}^{-1} \text{ Gy}^{-1}$ ). We refer to part 3 of this document for a detailed derivation of these values.

Not only should the table be updated, section 3.1.2.1 should also elaborate on this issue, as was done in the supplementary material of reference (Zhang *et al*, 2020) [Lines 1599-1601, under references].

► Page 22/23, para 39, Lines 587 through 593

The modelling details for leukaemia – here and elsewhere in the report - are described very briefly. It remains unclear throughout this report what exactly is done to obtain the corresponding risk estimates. This deserves more attention, possibly as part of an Annex.

► Page 23, para 41, Lines 599 through 603: “It should be ... recognised”

This is not very clear. A reference to the section or paras A113 (and possibly to B126) in ICRP Publication 103 as well as a reference to Puskin *et al*. (Health Phys. 63, pp. 579-580, 1992) could help the reader to understand this.

► Pages 23/24, paras 43 through 49, Lines 614 through 660, section 3.1.3.1 (method of calculation)

Para 43: It would be helpful to explain why the REIC method is chosen as the risk quantity for detriment calculations, and not the LAR or ELR methods.

Para 44: To avoid confusion, we suggest the cancer-free survival to be written as  $S_{cf}(a|e, d)$ , to distinguish it from the (normal, unmodified) all-cause survival  $S(a|a_{min})$  (note: same for survival function in para 46). A plot of  $S_{cf}(a|e, d)$  at doses of for instance  $d=0, 0.1$  and  $0.5 \text{ Gy}$  and of  $S(a|a_{min})$  would be insightful to see the difference between these survival functions and the modifying effect of ionizing radiation.

Para 45: Using the incidence rates as presented, we suggest to rewrite and include the REIC estimates as follows:

$$REIC_c(e, d) = \int_{e+L}^{a_{max}} \mu_{ic}(a) ERR_{ic}(a|e, d) S_{cf}(a|e, d) da, \text{ and}$$

$$REIC_c(e, d) = \int_{e+L}^{a_{max}} EAR_{ic}(a|e, d) S_{cf}(a|e, d) da .$$

Para 46: The all-cancer incidence rates,  $\mu_{iac}(n|e, d)$ , depend on the excess relative risk

$ERR_{iac}(n|e, d)$  or excess absolute risk  $EAR_{iac}(n|e, d)$  for “all cancer”. However, Tables 3.2 and

3.3 do not provide the corresponding parameter values. It could be mentioned that the coefficients for “all solid” can be used as a substitute.

Para 46: in the calculations in the document, specify that the time step used is one year.

► Pages 23-27, Lines 694 through 711, Figures 3.8 through 3.11

Our verification study using *RADICAL.xlsm* led us to conclude that Figures 3.8 through 3.11 are most likely based on a risk integral using a radiation-modified survival function  $S(a|e,d)$  whose

underlying Kaplan-Meier products contain the rates  $\mu(n|e,d) = \mu(n) + ERR_{iac}(n|e,d) \times \mu_{iac}(n)$

or  $\mu(n|e,d) = \mu(n) + EAR_{iac}(n|e,d)$ , which are *not adjusted* for extra cancer incidence rates

(Zhang *et al*, 2020, supplementary material, equations (8) and (9)). If this is indeed the case, the net difference of baseline rates,  $\mu_{iac}(n) - \mu_{mac}(n)$ , for ‘all cancer’ has not been included in the

evolution of the survival function within the risk integral. This would be in contrast to the adjusted and radiation-modified rates given between Lines 636 and 637 for the cancer-free survival

$S_{cf}(a|e,d)$ . As the dose  $d$  is only 0.1 Gy for these calculations, the modifying effect of radiation on

these unadjusted rates remains small and thus  $\mu(n|e,d) \approx \mu(n)$ . Therefore, the resulting survival

function would approach the normal survival function  $S(a|e)$  based on the all-cause mortality rates

$\mu(n)$ . Effectively, and as observed in our verification study, the curves in Figures 3.8 through 3.11

then correspond to those from the *unadjusted* Lifetime Attributable Risk (LAR) model instead of

from the adjusted REIC-type model described in Section 3.1.3.1. We refer to part 3 of this document for more details and graphs. We recommend the ICRP to check this and to update these figures if

these findings are true.

► Page 27, para 54 Lines 713 through 717

It would be insightful to include the integral or summation equation on the age-averaging procedure, as is presented in the supplementary material of reference Zhang (2020), and to explain that the (population) weights for each *single* age/year within a 5-year age bin equals  $1/5 * (\# \text{ persons in the 5-year age bin} / \text{total } \# \text{ males or females in the population under consideration})$ .

► Page 28, Figure 3.12

Please state the source of these data in the caption (Line 719). A table with the numerical values in an Annex would also be useful for anyone trying to reproduce the results in this draft ICRP report.

► Page 29, Lines 727 through 728, Table 3.4

For Table 3.4, the choice is made to average over both sexes and to present the results for the two reference populations (Euro-American and Asian) and the two risk models (ERR and EAR). In Table 3.5, however, nominal risk coefficients are shown for both sexes and thus averaging was performed over both populations instead. It is not possible to derive the values in Table 3.5 with those in Table 3.4 using the risk-transfer weights provided in Section 3.1.4/Table 3.1 (and the DDREF). This does not benefit the transparency of the Publication. We suggest to extend Table 3.4 by providing *only* the age (at exposure)-averaged lifetime excess risk values, as also described in Section 3.1.3.3. The number of columns would then double (Euro-American males and females, Asian males and females for ERR and EAR-based risk models), unless of course Table 3.4 would be constructed in two parts, one for the ERR-based model and one for the EAR-based model. In part 3 of this document we constructed these tables based on the output of *RADICAL.xlsm*.



► Page 29, para 56, Lines 734 and 735 (including Table 3.1): “Weights of 0.5 ... and lung”  
The choice for a weight of 0.5 for most cancers is not explained. Is this because there is no scientific information on these values (with the exception of breast, thyroid, skin and lung)? It would be helpful to explain the reason of this choice.

► Page 29, para 60, Lines 750 through 755  
Since ERR- and EAR-based models were not available, the exact procedure for treating leukaemia in the radiation detriment remains unclear. As mentioned earlier in this document, the modelling details for leukaemia deserve some more attention.

► Page 30, para 67, Lines 794 and 795:  
We suggest to add the text in boldface:  
“... nominal risk (**Section 3.1.7**) of 12 per 10,000 per Gy. These values were applied to both males and females, **as seen in Table 3.5.**”

► Page 35, para 76, Lines 855 through 859: “ $q_{\min}$  is a judgement-based ... thyroid.”  
Based on what judgement was the value of  $q_{\min}$  selected?

► Page 35, para 78, Lines 865 through 872  
Here it is unclear how the ‘cancer-free survival’  $S_c(a|e,d)$  is defined. A reference is made to Section 3.1.3.3, but this may be confusing, since there the cancer-free survival is based on the “all-cancer” incidence and mortality rates. A clear definition of  $S_c(a|e,d)$  would therefore be helpful. Is it based on rates  $\mu(n|e,d) = \mu(n) - \mu_{mc}(n) + \mu_{ic}(n|e,d)$ , with  $\mu_{mc}(n)$  being the sex- and age-dependent mortality rates for cancer type  $c$ ?  
Furthermore, ICRP could explain in more detail why values of  $LLE_c(e,d)$  are divided by  $REIC_c(e,d)$ .

► Page 35, para 79, Lines 873 through 879 (also applies to Table 3.6)  
The use of symbol  $l$  for the ‘relative years of cancer-free life lost’ is not compatible with the corresponding notation in ICRP Publication 60, where the similar quantity was written as  $l/\bar{l}$ . Note that this finding also holds for Table 3.6 (page 34) and the equation for the radiation detriment (Lines 886-887).

► Page 35, para 81, Lines 885 through 887:  
First, the notation of quantities within the detriment equation here is different from that in ICRP Publication 103, see e.g. Table A.4.1 of ICRP-103 (page 179). Besides quantity  $l$  (see previous remark), also the lethality (fraction) has a different symbol:  $q$  in ICRP-103 versus  $k$  in the draft ICRP report. It would be advisable to mention this in the current draft report to avoid confusion.  
Second, ICRP could describe the similarity with the detriment equation in ICRP Publication 60 as well as emphasize the main differences, i.e., incidence- versus mortality-based; incorporation of  $q_{\min}$ .

#### Section 4. Sensitivity Analyses

► Page 38, para 89, Line 951  
Differences between Asian and Euro-American populations are investigated, giving information about the sensitivity of risk estimates to differences between these populations. Please explain why other populations (in particular African populations) are not included. If this is due to a lack of data, please state that this is the reason

► Page 39, para 92, Lines 988 and 989: “For lung cancer, the detriment for females appears to be higher than for males.”

Does ICRP expect this to reflect differences in smoking behavior?

► Page 40 onwards, all figures with three bars:

On screen, the quality of the figures is fine. When printed, the “dashed” bar does not show. We do not know whether this is related to a specific printer or whether it is a general problem.

► Page 44, Lines 1064 through 1067: Table 4.1

“Standard detriment” is in units of “cases per 10,000 persons per Sv”, which should be mentioned in the caption of Table 4.1 (or, alternatively, in the second column of the table).

► Page 45, para 98, line 1087 “relative years of cancer-free life lost (*l*)”

The notation is inconsistent with that on page 12 (related to ICRP Publication 60), where *l* is used for the expected *absolute* number of years of life lost (This also applies to Table 3.6 and Section 3.2.3).

► Page 48, Lines 1143 through 1147: Table 4.2

“Standard detriment” is in units of “cases per 10,000 persons per Sv”, which should be mentioned in the caption of Table 4.2 (or, alternatively, in the second column of the table).

► Pages 48 and 49, Lines 1149 through 1192, Section 4.3: Summary of sensitivity analysis

The authors give an overview of the impact parameters have on radiation detriment. This section would have been more informative if additional information on the uncertainty (and their origin – for example, when considering different ages at exposure, what is known about the mechanisms leading to differences) in these parameters would have been given, too, where applicable.

## **Section 5. Potential evolution**

We applaud that it is considered to adopt the DALY as a means to estimate the quality of life. The DALY is a well-established method of accounting for health detriment, and it would be very favourable to make the system of radiation protection more compatible with the DALY approach. In addition, it would be beneficial if there could be some discussion on whether (or: under which circumstances) the DALY or the QALY (quality adjusted life year, often used by WHO) is the best method to account for the illness induced loss of quality of life.

***Part 3 (verification of results) starts on the next page.***

### Part 3. Annex: verification of results

Based on the description in chapter 3 of the draft report, a macro-enabled Excel tool, *RADICAL.xlsm*, was created to reproduce the figures in this chapter as well as the values listed in Table 3.4.

#### ► Default settings for evaluations in RADICAL

The following default<sup>8</sup> parameters were chosen for calculations in this annex:

Calculation method:	adjusted REIC (see below), as described in draft report
Dose:	0.1 Gy (note: risk values are scaled to: # cases per 100 per Gy)
Survival-interpolation:	Halfway bin (midpoint integration)
Include 85-89 age bin?	No
Weighting of sexes in pop.?	No

The survival-interpolation method determines how the risk integral (for REIC, LAR or ELR) is calculated. Since the survival is calculated at the start and end of each one-year age bin, the integral can be calculated in different ways. For the verification analysis, the survival is evaluated halfway the one-year age bins (at age 0.5, 1.5, 2.5, ... years) by linear interpolation (i.e., midpoint rule). Incidence and mortality rates from ICRP-103 (Tables A.4.10 through A.4.17) were used and assumed to be constant within each 5-year age bin for which they are given.

Calculation of the age-averaged lifetime excess risk is explained very briefly in lines 723 through 725. Based on this description, we assumed that the 85+ age bin was not included in the age-averaging procedure and therefore our default analysis did not include it. Furthermore, values in “Table 3.4” of this verification analysis were based on sex-weights of 0.5 (i.e. unweighted mean of genders). Actual fractions/weights of males and females in the respective populations deviate slightly from 0.5, but this was not taken into account here.

#### ► REIC versus LAR and the adjustment for extra cancer incidence rates

The REIC is the standard method and is based on the all-cause mortality rates, *adjusted* for extra cancer incidence rates and *modified* by radiation action, as described in Section 3.1.3.1 of the draft report. Hence, it is based on the (conditional) cancer-free survival function  $S_{cf}(a|e, d)$  calculated by the Kaplan-Meier method using *net* rates of  $\mu(n|e, d) = \mu(n) - \mu_{mac}(n) + \mu_{iac}(n|e, d)$ . The LAR method deviates from the REIC method only by the term related to radiation modification in the survival function, which is absent in LAR. The LAR method is therefore based on the adjusted but unmodified cancer-free survival  $S_{cf}(a|e)$ , applying net *baseline* rates of  $\mu(n) - \mu_{mac}(n) + \mu_{iac}(n)$ . For small radiation doses of the order of 0.1 Gy or smaller, the modifying effect of radiation on the survival is small or negligible, and thus  $S_{cf}(a|e, d) \approx S_{cf}(a|e)$ . The adjusted REIC and LAR methods are thus virtually identical for such small doses, with differences of at most a few percent (Zhang *et al*, 2020).

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<sup>8</sup> In *RADICAL.xlsm* these input entries can easily be changed for additional calculations. The survival-interpolation method can also be set to StartOfBin (left-rule integration) and EndOfBin (right-rule integration), weighting of the 85+ age bin can be included (even though risk values are 0 in this bin due to the imposed lag time of 5 years) and the actual fractions of sexes in both populations can be used to obtain the values in Table 3.4 (i.e., weighted mean). Calculation methods in *RADICAL* include the adjusted REIC- and unadjusted LAR-type models.

In *RADICAL.xlsm*, the REIC method is based on  $S_{cf}(a|e,d)$  as described above and in section 3.1.3.1 in the draft ICRP report (adjusted, and modified by radiation), but the LAR method is based on the normal, all-cause survival function  $S(a|e)$  instead of  $S_{cf}(a|e)$ , i.e., unadjusted<sup>9</sup> and unmodified<sup>10</sup>. This survival function is therefore based only on the all-cause mortality rates  $\mu(n)$ . Reason for this definition of LAR will become apparent when describing the issue related to Figures 3.8 through 3.11 of the draft report (see below). This difference in definition, also investigated by Zhang and coworkers, inherently leads to a larger deviation between REIC- and LAR-based risk values at small doses, of >10% for most cancer types (see Table 1 in Zhang *et al* (2020), fifth column).

► **Figures 3.8 through 3.11**

Based on the default settings, we reproduced Figures 3.8 through 3.11 for “All solid cancer” (cases per 100 persons per Gy). Figure 1 shows the results for the Euro-American, female population for the ERR-type model (a,b) and the EAR-type model (c,d). For both risk models, the curves in Figure 1 deviate by more than 10% from those in the draft report, the curves in Figure 1 resulting in smaller values. If, however, we perform the risk integral using the normal, all-cause survival function  $S(a|e)$  (*unadjusted*<sup>9</sup> LAR-type model), then results appear similar to those in the draft report, as can be seen from Figure 2. We observe a similar difference for the Asian population as well as for males (results not shown). In fact, with reference to equations (8) and (9) of the supplementary material of Zhang *et al* (2020), Figures 3.8-3.11 of the draft ICRP report are most likely based on a survival function  $S(a|e,d)$  which employs unadjusted, radiation-modified rates given by

$$\mu(n|e,d) = \begin{cases} \mu(n) + ERR_{iac}(n|e,d) \times \mu_{iac}(n) & \text{for ERR-based model} \\ \mu(n) + EAR_{iac}(n|e,d) & \text{for EAR-based model} \end{cases}$$

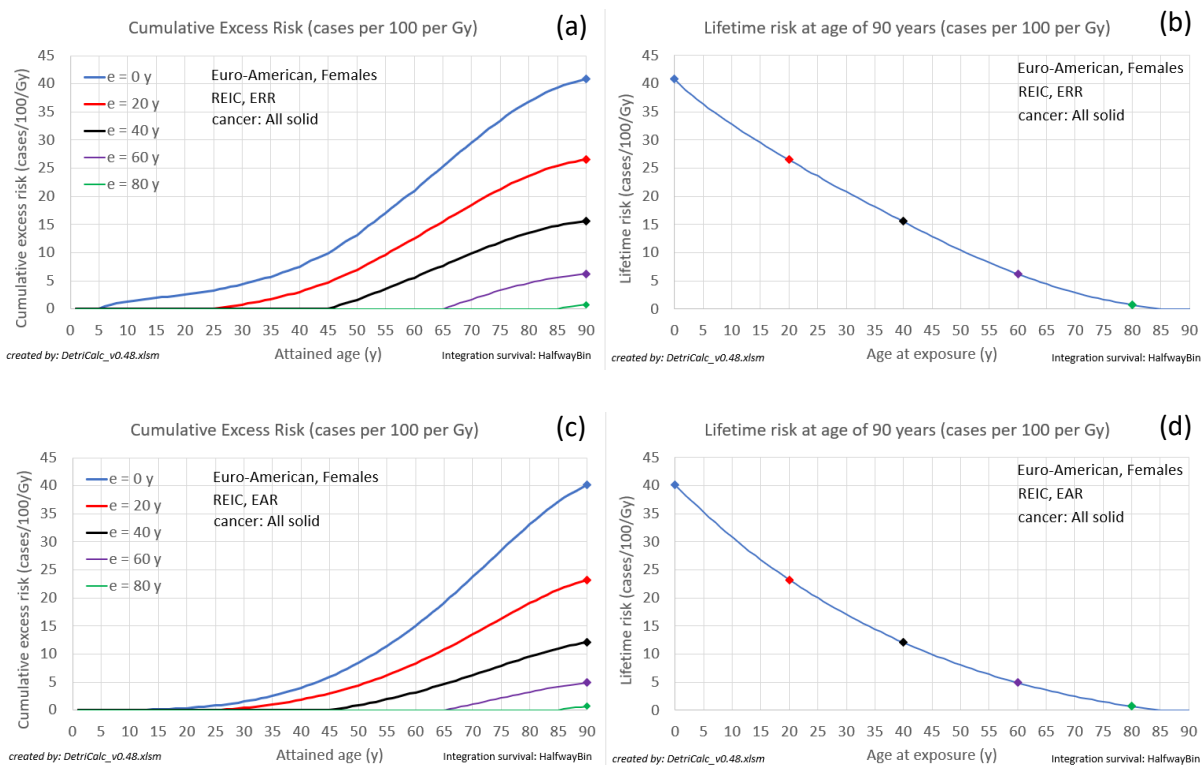
As radiation action at a dose of 0.1 Gy is very small or even negligible, the risk curves would then indeed appear to be based on the unadjusted LAR-type risk model.

Another observation confirming this finding is the fact that, in Figure 3.11 (EAR, all solid cancer), virtually no difference is found between Euro-American and Asian females. Using *RADICAL*, the lifetime excess risk for age-at-exposure = 0 y is 40.1 (cases per 100 per Gy) for Euro-American females and 42.2 for Asian females, a significant difference of over 5% in the default REIC-type model. However, when using the unadjusted LAR-type model these values are 46.9 and 47.1, respectively, a difference of less than 0.5%. Hence, for the unadjusted LAR-type model, not only the absolute risk values show a better correspondence with those in Figure 3.11, but also the difference in risk values between populations.

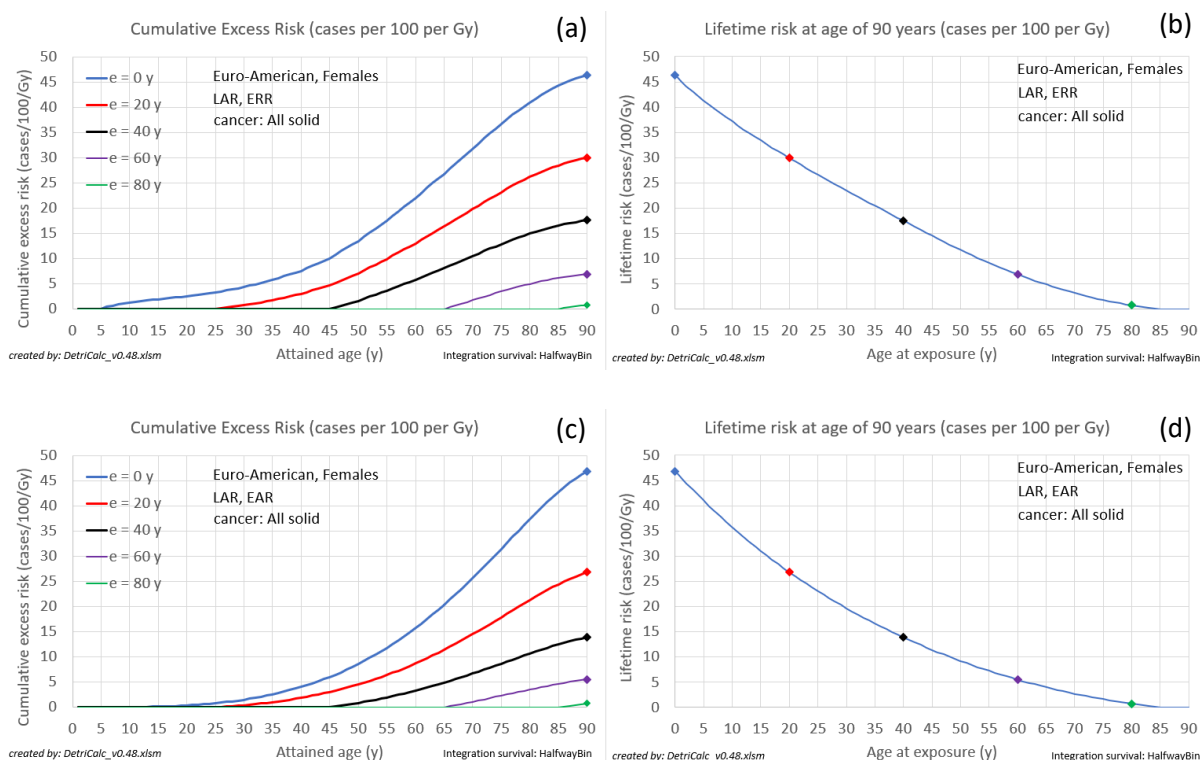
Hence, our conclusion is that the curves in Figures 3.8 through 3.11 are probably not adjusted for extra cancer incidence rates, i.e., by omitting the net difference of (‘all-cancer’) baseline rates  $\mu_{iac}(n) - \mu_{mac}(n)$  as building stones for the survival function in the risk integral.

<sup>9</sup> Not adjusted for extra cancer incidence rates

<sup>10</sup> No radiation-modifying terms.



**Figure 1.** Results of verification study (*adjusted REIC-type model*). Cumulative excess risk at 1 Gy for all solid cancers in Euro-American females by age at exposure  $e$  using an ERR-based model (a) and EAR-based model (c) [compare with Figures 3.8 and 3.10 in draft report]. Also shown is the lifetime excess risk (at 90 years) for all solid cancers after exposure to 1 Gy using an ERR-based model (b) and EAR-based model (d) [compare with Figures 3.9 and 3.11 in draft report].



**Figure 2.** Results of verification study (*unadjusted LAR-type model*). Same as Fig. 1, but here using the risk integral based on the normal, all-cause survival instead of the adjusted REIC-type integral employing the cancer-free survival (used for Fig. 1).

► **Table 3.4**

After these findings related to Figures 3.8 through 3.11, we investigated whether the sex- and age-averaged lifetime excess risks for the whole population, as presented in Table 3.4 of the draft report, were indeed based on the adjusted REIC-method. Using RADICAL with the aforementioned default settings, we determined the lifetime excess risk averaged over the age distributions (Fig. 3.12) of the respective populations as explained in Section 3.1.3.3. Values were first determined for males and females separately, before calculating sex-averaged values (unweighted mean) for the two populations (Euro-American, Asian) in the two risk models (ERR, EAR). These results can be found in Table 1. Absolute and relative differences with the values from Table 3.4 in the draft ICRP report are listed in Table 2.

**Table 1.** Results of verification study (**adjusted REIC-type model**). Age-averaged lifetime excess risk (cases per 100 per Gy) for the whole population of males and females (green cells) and the corresponding sex-averaged values (orange cells). Values are given for various solid cancers, two populations (Euro-American and Asian) and two risk models (ERR and EAR). Sex- and age-averaged values can be compared with those in Table 3.4 of the draft ICRP report. Absolute and relative differences with these values are presented in Table 2.

Cancer type:	Excess Relative Risk model (# cases per 100 persons per Gy)						Excess Absolute Risk Model (# cases per 100 persons per Gy)					
	Euro-American			Asian			Euro-American			Asian		
	Males	Sex-avg. value	Females	Males	Sex-avg. value	Females	Males	Sex-avg. value	Females	Males	Sex-avg. value	Females
	0.500		0.500	0.500		0.500	0.500		0.500	0.500		0.500
Oesophagus	0.28	0.24	0.19	0.56	0.44	0.32	0.15	0.21	0.28	0.15	0.20	0.26
Stomach	0.30	0.27	0.25	1.80	1.65	1.51	1.57	2.00	2.43	1.84	2.37	2.91
Colon	1.91	1.37	0.83	2.60	1.76	0.92	1.36	1.00	0.64	1.60	1.18	0.76
Liver	0.12	0.11	0.10	1.14	0.92	0.70	0.99	0.67	0.34	1.16	0.79	0.41
Lung	1.65	3.04	4.43	1.86	2.71	3.56	1.21	1.66	2.11	1.34	1.82	2.31
Breast	-	-	-	-	-	-	0.00	1.72	3.44	0.00	2.12	4.24
Ovary	0.00	0.28	0.56	0.00	0.15	0.30	0.00	0.19	0.39	0.00	0.23	0.47
Bladder	1.79	1.36	0.92	0.91	0.68	0.44	0.38	0.54	0.70	0.44	0.62	0.80
Thyroid	0.17	0.48	0.80	0.18	0.77	1.36	-	-	-	-	-	-
Other solid	5.72	4.01	2.31	2.88	2.32	1.77	1.79	2.28	2.77	2.09	2.70	3.31
All solid	12.12	15.11	18.09	12.61	13.94	15.27	10.23	13.04	15.85	11.99	15.47	18.95

**Table 2.** Results of verification study (**adjusted REIC-type model**). Difference of sex-and age-averaged lifetime excess risk values in Table 1 with the values presented in Table 3.4 of the draft ICRP report. Both absolute differences (orange cells, verification study *minus* draft ICRP-report) and relative differences (light-blue cells, in %) are tabulated.

Cancer type:	Excess Relative Risk model (absolute difference in # cases per 100 persons per Gy, and relative difference)				Excess Absolute Risk Model (absolute difference in # cases per 100 persons per Gy, and relative difference)			
	Euro-American		Asian		Euro-American		Asian	
	Sex-avg. value	Rel. diff.	Sex-avg. value	Rel. diff.	Sex-avg. value	Rel. diff.	Sex-avg. value	Rel. diff.
Oesophagus	0.00	0%	0.01	2%	-0.01	-2%	0.00	0%
Stomach	0.00	1%	0.04	3%	-0.08	-4%	-0.01	0%
Colon	0.03	2%	0.03	2%	-0.01	-1%	-0.02	-2%
Liver	0.00	2%	0.02	3%	0.00	0%	-0.01	-2%
Lung	-0.01	0%	0.11	4%	-0.11	-6%	-0.02	-1%
Breast	-		-		-0.32	-16%	-0.33	-13%
Ovary	0.00	1%	0.01	8%	-0.01	-3%	0.00	1%
Bladder	0.02	1%	0.02	2%	-0.06	-9%	-0.01	-2%
Thyroid	-0.01	-1%	0.04	6%	-		-	
Other solid	0.06	2%	0.03	2%	-0.08	-3%	-0.01	0%
All solid	0.25	2%	0.57	4%	-0.33	-2%	0.15	1%

As can be seen, for most cancer types the differences are small, in the order of only a few percent. However, for breast cancer differences >10% are found. Based on our previous findings for the Figs. 3.8-11, our initial idea was that this was related to the use of the *unadjusted* LAR method. Indeed, the use of the unadjusted LAR method does solve this finding. Relative differences for breast cancer reduce then from about 13-16% (adjusted REIC, see Table 2) to only 3-4% (unadjusted LAR).

However, when turning to the supplementary material of Zhang *et al* (2020), we discovered the real reason for these larger relative differences. In fact, for breast cancer, a different parametrization is used for the EAR model, which is not clearly mentioned in the draft ICRP report. The model is based on a pooled analysis by Preston *et al* (2002) and reads:

$$EAR_{\text{breast cancer}}(a|e, d) = \mathbf{10}d \times \begin{cases} \exp[-0.05(e - \mathbf{25}) + 3.5 \ln[a/\mathbf{50}]] & \text{for } a \leq 50 \\ \exp[-0.05(e - \mathbf{25}) + 1.0 \ln[a/\mathbf{50}]] & \text{for } a > 50 \end{cases}$$

where the values in boldface deviate from those in the equation of the excess risk and Table 3.3 ( $\beta$  value for breast cancer) in Section 3.1.2.1 of the draft ICRP report.<sup>11</sup> Note that this parametrization can still be expressed by the equation presented in Section 3.1.2.1, i.e., by

$$EAR_{\text{breast cancer}}(a|e, d) = \beta \times d \times \exp[\alpha_1((e - 30)/10) + \alpha_2 \ln[a/70]],$$

with  $\alpha_1 = \ln[1 - 0.39] = -0.494 \approx -0.5$ ,  $\alpha_2 = 3.5$  for  $a \leq 50$  and  $\alpha_2 = 1.0$  for  $a > 50$ , and

$$\beta = 10 \exp[5\alpha_1/10 + \alpha_2 \ln[70/50]] = \begin{cases} 10 \exp[-5 \times 0.494/10 + 3.5 \ln[70/50]] = 25.4, & a \leq 50 \\ 10 \exp[-5 \times 0.494/10 + 1.0 \ln[70/50]] = 10.9, & a > 50 \end{cases}$$

with  $\beta$  expressed in units of  $10^{-4} \text{ y}^{-1} \text{ Gy}^{-1}$ . For breast cancer, the latter value of 10.9 for  $a > 50$  y is mentioned in Table 3.3 of the draft ICRP report, but the value of 25.4 for  $a \leq 50$  is missing, which caused the actual difference between our reproduced, sex- and age-averaged values with those from Table 3.4. A recalculation using the adjusted REIC model with the updated value of  $\beta = 25.4$  for  $a \leq 50$  y then also yields results similar to those in Table 3.4 of the draft ICRP report: 1.97 cases per 100 per Gy for the Euro-American population (3% smaller than corresponding value in Table 3.4) and 2.42 cases per 100 per Gy for the Asian population (1% smaller than corresponding value in Table 3.4).

Finally, with the updated model for breast cancer, we repeated the assessment of the values in Table 3.4 using the unadjusted LAR-type model. Then, for each cancer type (including breast cancer), differences >10% are found with respect to the values in Table 3.4 of the draft ICRP report, confirming the 'adjusted REIC-methodology' basis of these values.

In summary, we conclude that, despite our earlier observations concerning Figures 3.8-3.11, the values in Table 3.4 of the draft ICRP report are indeed based on the adjusted REIC-type model for all cancer-types. For breast cancer, however, we conclude that the value of  $\beta$  in Table 3.3 should be updated from 10.9 to: "25.4 for  $a \leq 50$  and 10.9 for  $a > 50$ ". We suggest the ICRP to check this and to update Table 3.3 if our findings are true.

<sup>11</sup> The rounded value of -0.05 in this equation is  $\alpha_1/10$ .

### ► Additional findings

*Other solid cancer:* In ICRP-103 and the draft ICRP report, category 'other solid' is defined as the 14 remainder tissues: adrenals, extra-thoracic region, gall bladder, heart, kidneys, lymphatic nodes, muscle, oral mucosa, pancreas, prostate, small intestine, spleen, thymus, uterus/cervix (see e.g. footnote b of table 3.1). Incidence rates for these 'other solid cancers' are not explicitly provided in tables A4.10 through A.4.17 of ICRP-103. We therefore determined these incidence rates by subtracting the cancer incidence rates of {Stomach, Colon, Liver, Lung, Breast, Ovary, Bladder, Thyroid} from the 'All solid' cancer incidence rates. The fact that we obtain sex- and age-averaged risk results similar to those in table 3.4 of the draft document (see tables 1 and 2, 1-4% difference) implies that the same procedure was followed by the ICRP. If this is indeed the case, then bone and skin cancers cannot be included in the 'All solid' category. If bone and skin cancer would be included in 'all solid', then obviously 'other solid' - as calculated above - would include these types of cancers as well. However, this would be in contrast with the aforementioned definition by the ICRP of the category 'other solid' where bone and skin cancer are *not* included. The exclusion of bone and skin cancer from 'all solid' should then be made explicit and therefore we suggest ICRP to define the categories of groups of cancers in more detail to avoid confusion.

*All cancer:* Related to the previous finding for 'other solid', we observed that if we subtract 'All solid' and 'Leukaemia' cancer incidence or mortality rates from 'All cancer' incidence or mortality rates, the difference is not (close to) 0. This could of course be related to bone and skin cancer, but we also found that, using tables A4.10 through A.4.17 of ICRP-103, the resulting subtraction is actually negative. This only occurs for Euro-American males and females though, for the Asian population no negative values are obtained.

### ► References

Preston, D.L., Mattsson, A., Holmberg, E., et al., 2002. Radiation effects on breast cancer risk: a pooled analysis of eight cohorts. *Radiat. Res.* 158, 220–235.

Zhang, W., Laurier, D., Cléro, E., et al., 2020. Sensitivity analysis of parameters and methodological choices used in calculation of radiation detriment for solid cancer. *Int. J. Radiat. Biol.* DOI: 10.1080/09553002.2020.1708499.