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European astronaut radiation related cancer risk assessment using dosimetric calculations of organ dose equivalents

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Abstract

An illustrative sample mission of a Mars swing-by mission lasting one calendar year was chosen to highlight the application of European risk assessment software to cancer (all solid cancer plus leukaemia) risks from radiation exposures in space quantified with organ dose equivalent rates from model calculations based on the quantity Radiation Attributed Decrease of Survival (RADS). The relevant dose equivalent to the colon for radiation exposures from this Mars swing-by mission were found to vary between 198 and 482 mSv. These doses depend on sex and the two other factors investigated here of: solar activity phase (maximum or minimum); and the choice of space radiation quality factor used in the calculations of dose equivalent. Such doses received at typical astronaut ages around 40 years old will result in: the probability of surviving until retirement age (65 years) being reduced by a range from 0.38% (95%CI: 0.29; 0.49) to 1.29% (95%CI: 1.06; 1.56); and the probability of surviving cancer free until retirement age being reduced by a range from 0.78% (95%CI: 0.59; 0.99) to 2.63% (95%CI: 2.16; 3.18). As expected from the features of the models applied to quantify the general dosimetric and radiation epidemiology parameters, the cancer incidence risks in terms of surviving cancer free, are higher than the cancer mortality risks in terms of surviving, the risks for females are higher than for males, and the risks at solar minimum are higher than at solar maximum.

Keywords: Astronaut risk assessment; Epidemiology; Dosimetric methodology; Radiation attributed decrease of survival; Radiation related cancer risks

1 Introduction

Space agency-specific operational standards for crew dose and risk assessment of ionizing radiation exposures for the International Space Station (ISS) have been reported separately in this issue [1]. Up to now, the European Space Agency (ESA) has adopted an operation limit based on a career dose limit for the radiation protection of astronauts [2]. Like other ISS partner space agencies, ESA is currently evaluating different approaches for assessing and communicating the detrimental health risks related to ionizing radiation exposure in space. A recent position paper on

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research plans in Europe for radiation hazard assessments in space, recommended the development of European space radiation risk models to better characterize the radiation risks to astronauts (Walsh et al. [3]). Consistent with this recommendation and with the Radiation Protection Initiative for Astronauts at ESA Medical Operations and Space Medicine (HRA-OM), an ESA/European space radiation risk module for astronauts was developed, verified, and documented (Walsh et al. [4]). Although the risk module described does not yet reflect the current ESA operational standard of practice, it is an important element in further considerations for human missions to low Earth orbit and beyond for exploratory missions such as those calculated here for a proposed hypothetical space mission. The risk module is based on a novel approach for dealing with stochastic effects of radiation exposure that is particularly suitable for the radiation health risk assessment of astronauts. The quantity, Radiation Attributed Decrease of Survival (RADS), representing the cumulative decrease in the unknown survival curve (or cancer-free survival curve) at a certain attained age, due to the radiation exposure at an earlier age, forms the basis for this new approach, Ulanowski et al. [5,6]. The application of RADS completely removes the requirement of survival curve input needed in the calculation of other types of cumulative radiation risks currently applied by space agencies. This RADS based risk approach is also simpler than other radiation lifetime risk measures currently applied by space agencies [1], and relies much less, than current methodologies, on detrimental health information drawn from the general population, which are not a good representation for atypically healthy, non-smoking and carefully health monitored astronauts. Evaluations of deterministic effects of radiation exposure and the dependence of such effects on dose thresholds for tissue reactions are outside the scope of this methodology.

Previous work for ESA [4] was based on estimated mission doses. The further work reported here advances the developed health risk assessment framework with a collaboration with dosimetry experts from the German Aerospace Center (Deutsches Zentrum für Luft- und Raumfahrt, DLR) who provided organ dose equivalent calculations for exposures in space. It is now possible to include dosimetric results based on converting mission doses to the organ at risk dose equivalents that are required as input in the space radiation risk module. An initial sample mission was chosen to be a Mars swing-by mission to illustrate this ongoing work with the application of the space radiation risk module to cancer risk related to model-derived calculations of colon organ dose equivalent. The effects on the cancer risk: of the dosimetric conditions under solar maxima and solar minima; and on chosen assumptions related to which space radiation quality factors are included in the dosimetry calculations, have also been investigated here.

2 Material and methods

The dosimetric methodology applied here is based exclusively on model calculations, and no dosimetric measurements on ESA astronauts, or real-life dosimetric information derived from such measurements, has been included in this methodology, procedures, or results. Mission doses were obtained by multiplying calculated dose rates with the assumed mission duration (one year). The organ dose equivalent rates were calculated for the exposure from galactic cosmic rays (GCR) in near-Earth interplanetary space for a mass shielding distribution derived from the Columbus laboratory of the ISS.

Although the Columbus laboratory is not identical to a spacecraft on a Mars mission, it is also reasonable to assume that the mass shielding of such a vehicle would not be fundamentally different. The ORION crew module, for instance, has a mass of approximately 10000 kg (https://www.nasa.gov/sites/default/files/atoms/files/orion_by_the_numbers_2022.pdf) compared to a mass of about 9000 kg of the Columbus laboratory (https://www.esa.int/esapub/br/br144/br144.pdf). A large advantage of using the Columbus laboratory shielding is the possibility of model validation with experimental data collected at high latitudes in the ISS orbit.

GCR intensity varies through the solar activity cycle due to the modulation of the charged primary particles by the magnetic field in the heliosphere. Lowest intensities occur during solar activity maximum and highest intensities during solar activity minimum; for this work two mission scenarios corresponding to solar minimum and maximum exposure conditions were calculated. Primary GCR nuclei (hydrogen to nickel) as described by the model from Matthiä et al. [7] were transported through a spherical shielding geometry using numerical calculations with the Monte-Carlo framework Geant4 (Agostinelli et al. [8]; Allison et al. [9,10]). A more detailed description of the procedure can be found in Berger et al. [11]. The resulting particle fluence rates inside the shielding geometry were folded with fluence-to-dose conversion coefficients provided by ICRP [12] to obtain organ dose rates and effective dose equivalent rates. The calculations were based on two different sets of radiation quality factors (Q) as published in ICRP report 60 (ICRP [13]) and by NASA (NASA [14]).

The cancer risk assessment methodology has already been fully reported (Walsh et al. [4], see also Hafner et al. [15] and the paper by Hafner and Walsh in this issue [16]) and is based on calculation of a cumulative radiation cancer risk called Radiation Attributable Decrease in Survival (RADS), based on the radiation-attributed hazard, which represents the total integrated excess risks for cancer mortality or incidence, and is conditional on survival until a certain age. In the interests of avoiding redundancy with the previ-

ously published paper fully describing the methodology on which this analysis is based, Walsh et al. [4], while increasing readability and transparency of methodology here, the methodology has been comprehensively summarized in Table 1.

In practical terms, RADS based on radiation related cancer mortality models gives the percentage by which the probability of surviving until e.g., retirement age (65 years) will be reduced, due to an organ dose equivalent received during missions at typical astronaut ages of e.g., around 40 years old. Similarly, RADS based on radiation related cancer incidence models gives the percentage by which the probability of surviving cancer free until retirement age will be reduced, due to an organ dose equivalent received during missions at typical astronaut ages around 40 years.

RADS at an attained age of 65 years old for the outcome all cancer incidence and mortality, based on calculated astronaut colon organ dose equivalent, has been chosen here to illustrate the application of the model-derived estimates of the organ dose equivalent. The calculations were performed analogously to the method described in Walsh et al. [4] and summarized in Table 1 and for a Mars swing-by mission lasting one year in duration and for male and female astronauts on such a mission at age 40 years old. RADS results presented here and in Walsh et al. [4] and in Hafner et al. [15] were calculated with a quality factor of 80 for neutrons relative to gammas in the radiation related excess risk models from the Hiroshima and Nagasaki A-bomb survivors Life Span Study (LSS) (exposed to gammas and neutrons) that go into the RADS calculations. However, in Hafner and Walsh [16] a corresponding quality factor of 10 was applied, as used in all the published risk models contributing to the multi-model inference presented in Hafner and Walsh [16]. Any age at exposure and any later attained age, beyond the latency period for cancer development, may be applied generally in the RADS calculations. However, since the ERR and EAR models (Table 1) from the A-bomb survivors were only fitted to organ dose ranges up to 4Gy, the valid upper dosimetric limit of applicability of RADS in this application is 4 Gy.

3 Results

Table 2 illustrates the risks in terms of Radiation Attributable Decrease in Survival (RADS) due to all solid cancer plus leukaemia for calculated radiation exposures from a 1-year Mars swing-by mission for male and female astronauts. The astronauts are assumed to be 40 years old at the start of the mission, and the % RADS values presented here for both cancer incidence and cancer mortality are applicable at an attained age of 65 years.

Table 2 shows that the relevant colon organ dose equivalents for radiation exposures from a 1-year Mars swing-

by mission vary between 198 and 482 mSv, where the doses depend on sex, solar activity phase and choice of radiation quality factor. The Radiation Attributable Decrease in Survival (RADS) due to all solid cancer plus leukaemia from these doses ranged from 0.38% (95%CI: 0.29; 0.49) to 1.29% (95%CI: 1.06; 1.56) for cancer mortality and ranged from 0.78% (95%CI: 0.59; 0.99) to 2.63% (95%CI: 2.16; 3.18) for cancer incidence, also depending on sex, solar activity phase and choice of radiation weighting factor. It can be seen from Table 2 that the risks and organ equivalent doses are lower during dosimetric conditions pertaining to solar maxima than during solar minima. Table 2 also illustrates that the choice of whether to apply either the ICRP 60 (ICRP [13]) or NASA (NASA [14]) radiation weighting factors, Q_{60} or Q_{NASA}, respectively, in the calculations of organ dose equivalents also has an influence on mission organ dose and therefore on mission risk, with the Q_{60} weights resulting in lower colon dose equivalents than the Q_{NASA} weights. The effects of sex (that females have a higher risk than males for the same organ dose), the effects of age attained and age at exposure and differences between mortality and incidence risks were all fully explained in Walsh et al. [4] and Hafner et al. [15] and are as expected from the features of the models applied to quantify the radiation epidemiology parameters.

4 Discussion

Work has been described here on the further developments of a European space radiation risk assessment framework for astronauts and illustrated with an initial sample mission chosen to be a Mars swing-by mission lasting exactly one calendar year in duration and cancer risks were provided. This further work involves a main aspect of extending the previous work with more detailed dosimetric calculations for obtaining the required organ doses for radiation risk assessment. Sample risk assessments have been carried out based on organ dose equivalents calculated for exposures in space. The specific input are the model-based estimates of the organ dose equivalents that were input into the risk assessment software written to apply the quantity RADS. Specifically, these requirements are for the astronaut equivalent organ doses (measured or estimated) to the colon, Red Bone Marrow (RBM), lung and female breast. Such doses have been made available for calculated organ dose equivalent rates per day. The calculations were based on two different sets of radiation quality factors (Q) as published in ICRP report 60 and by NASA and the two dosimetric conditions under solar maxima and solar minima.

Calculations of lifetime attributable risks (LAR) and risk of exposure-induced death or cancer (REID/REIC) quantities (Vaeth and Pierce 1990 [24]), currently applied by space

Table 1

Summary of the methodology on which this analysis is based from Walsh et al. [4]. The all solid cancer incidence ERR and EAR models were re-fitted to the Hiroshima and Nagasaki A-bomb survivors Life Span Study (LSS) data with respect to colon dose and the leukaemia models were also refitted with respect to red bone marrow, RBM, dose. Refitting was necessary to obtain the covariance matrices required for the uncertainty analysis. All fit parameters and covariance matrices are given in [4]. However, to calculate total cancer risks, a common dose scale is required on the space radiation side. For space radiation, the colon doses and the RBM doses will be approximately equal at very high energies for a given fluence. Therefore, as a first order approximation, leukaemia and all solid cancer risks were just summed up. Mortality risks were obtained from the incidence risks by applying an average lethality factor of 0.49. This lethality factor was calculated as weighted mean of the different cancer lethality factors from Table A.4.5 of the ICRP report 103 [23], using the A-bomb survivor cancer case counts as weights.

Main equations

Equation	Definition	Choices applied
$RADS(a|e,D,g,RBE) = 1 - \exp(-H(a|e,D,g,RBE))$	Radiation Attributed Decrease of Survival (RADS)	Ulanowski et al. [5,6]
$H(a|e,D,g,RBE) = \int_{e+l}^{a} h_s(u,e,D_c,g,RBE)du + \int_{e+l}^{a} h_L(u,e,D_m,g,RBE)du$	Hazard for all solid cancer plus leukaemia	Walsh et al. [4].
$h_S(a,e,D_c,g,RBE) = \frac{wERR_S(D_c,a,e,g,RBE)m_S(a)+(1-w)EAR_S(D_c,a,e,g,RBE)/10,000}{DDREF}$	Hazard term under the integral for all solid cancer incidence	Walsh et al. [4].
$h_L(a,e,D_m,g,RBE) = \frac{wERR_L(D_m,a,e,RBE)m_L(a)+(1-w)EAR_L(D_m,a,e,g,RBE)/10,000}{DDREF}$	Hazard term under the integral for leukaemia incidence	Walsh et al. [4].
$ERR_S(D_c,a,e,g,RBE) = \beta D_c \mu_s(e,a,g) f_S(RBE)$	Excess Relative Risk model for all solid cancer incidence	Grant et al. (2017) [17]
$EAR_S(D_c,a,e,g,RBE) = \beta D_c \mu_s(e,a,g) f_S(RBE)$	Excess Absolute Risk model for all solid cancer incidence	Walsh et al. (2019b) [18]
$ERR_L(D_m,e,a,RBE) = (\beta f_{L1}(RBE)D_m + \delta f_{L2}(RBE)D_m^2)\mu_{L1}(e,a)$	Excess Relative Risk model for all leukaemia incidence	Hsu et al. (2013) [19]
$EAR_L(D_m,e,a,g,RBE) = (\beta f_{L1}(RBE)D_m + \delta f_{L2}(RBE)D_m^2)\mu_{L2}(e,a,g)$	Excess Absolute Risk model for all leukaemia incidence	Hsu et al. (2013) [19]
$m_S(a), m_L(a)$	Population age-specific cancer incidence rates for all solid cancer (S) or leukaemia (L)	Combined for 8 European countries (2008–2012), Bray et al. 2017 [20]
$f_S(RBE) = \exp(\alpha(RBE-10))$	Model for risk ratio variation with RBE for all solid cancer	Hafner et al. (2021) [15]
$f_{L1/L2}(RBE) = \exp(\alpha(RBE-10)^2)$	Model for risk ratio variation with RBE for leukaemia	Hafner et al. (2021) [15]

Definition of input parameters

Parameter	Definition	Choices applied
a	Attained age	65 years
e	Age at exposure	40 years
g	Sex	Males or females

RBE	Relative Biological Effectiveness of neutrons (LSS)	80, Cordova and Cullings (2019) [21]
D_c, D_m	LSS colon dose, LSS red bone marrow dose	Colon dose equivalent at solar max or min. (Table 2)
l	Minimum latency period	5 years for all solid cancer, 2 years for leukaemia, WHO 2013 [22]
DDREF	Dose and Dose Rate Effectiveness Factor	1
w	Weight: relative contributions of ERR and EAR models	0.5, ICRP 103 (2007) [23]
β, δ	Linear and quadratic dose risk coefficient	Walsh et al. [4]
$\mu_s(e,a,g), \mu_{L1}(e,a), \mu_{L2}(e,a,g)$	Modifying functions	Grant et al. (2017) [17], Walsh et al. (2019b) [18], Hsu et al. (2013) [19]
α	Fit parameter of the model for risk ratio variation with RBE	Hafner et al. (2021) [15]

Table 2

Radiation Attributable Decrease in Survival (RADS) due to all solid cancer plus leukaemia for radiation exposures from a one-year duration Mars swing-by mission for male and female astronauts. The astronauts are assumed to be 40 years old at the start of the mission, and the RADS values presented here for both cancer incidence and cancer mortality are applicable at an attained age of 65 years. A Dose and Dose Rate Effectiveness Factor (DDREF) of unity was applied in the software for all cancer and equal weighting was given to the additive and multiplicative dose response models in the risk calculations (Table 1). The radiation quality factors, Q_{60} or Q_{NASA} are from ICRP 60 (ICRP [13]) or NASA [14] respectively and applied to the model through fluence-to-dose conversion coefficients (ICRP [12]).

Sex; radiation weighting factor applied	Colon dose equivalent at solar minimum (mSv)	All solid cancer and Leukaemia INCIDENCE risk RADS (%) (95% CI)	All solid cancer and Leukaemia MORTALITY risk RADS (%) (95% CI)	Colon dose equivalent at solar maximum (mSv)	All solid cancer and Leukaemia INCIDENCE risk RADS (%) (95% CI)	All solid cancer and Leukaemia MORTALITY risk RADS (%) (95% CI)
Male, Q_{60}	393	1.54 (1.16;1.97)	0.76 (0.57;0.97)	198	0.78 (0.59;0.99)	0.38 (0.29;0.49)
Male; Q_{NASA}	482	1.88 (1.45;2.41)	0.92 (0.71;1.18)	242	0.95 (0.73;1.22)	0.47 (0.36;0.60)
Female; Q_{60}	396	2.18 (1.78;2.65)	1.07 (0.87;1.30)	199	1.10 (0.90;1.34)	0.54 (0.44;0.66)
Female; Q_{NASA}	478	2.63 (2.16;3.18)	1.29 (1.06;1.56)	240	1.33 (1.09;1.61)	0.65 (0.53;0.79)

agencies, require as input: age-specific cancer rates in the general population to multiply the ERR models (Table 1) and survival curves calculated from all cause mortality rates and, for cancer free survival curves, age-specific cancer rates in the general population (i.e., cancer rates in the general population need to be applied twice). The application of RADS in the risk assessment has the advantage of completely removing the requirement of survival curve input needed for LAR, REID and REIC, while still requiring just one application of the age-specific cancer rates in the general population. This renders the RADS approach to be simpler than other radiation lifetime risk measure methodologies currently applied by space agencies, with fewer sources of uncertainty, and to be much less reliant, than current methodologies, on detrimental health information drawn from the general population, which are not a good representation for atypically healthy, non-smoking and carefully health monitored astronauts. Therefore, RADS is particularly suitable for application in astronaut radiation risk assessments. However, the assumption that population based cancer rates will stay constant into the future is still required, and the degree of suitability of such rates for the application to a healthy astronaut population still unknown, and these are limitations. It is shown that a one year Mars swing-by mission with colon dose equivalents varying between198 and 482 mSv, received at typical astronaut mission ages of around 40 years old will result in: the probability of surviving until retirement age (65 years) being reduced by a range from 0.38% (95%CI: 0.29; 0.49) to 1.29% (95%CI: 1.06; 1.56); the probability of surviving cancer free until retirement age being reduced by a range from 0.78% (95%CI: 0.59; 0.99) to 2.63% (95%CI: 2.16; 3.18).

It is fully acknowledged that the mission characteristics will influence the crew doses received and this sample Mars mission applied here is just for the purpose of illustrating how this prototype risk assessment software, based on RADS, could be applied for Humans Space flight and the European Space Agency. Other scenarios for mission characteristics can also be implemented. However at this stage, given the ongoing nature of the work in refining the calculations of the organ dose equivalent estimates, it was considered inappropriate to provide more extensive risk calculations, as these will all need to be repeated when dosimetric model calculations progress and improve even further. In fact, the new risk assessment software may be applied to any calculated organ dose equivalent for any type of exploratory missions or eventually even to actual crew organ dose equivalents, including ISS missions. However RAD calculations require astronaut organ dose equivalents after quality factor application to be comparable to the neutron-corrected organ doses from the LSS In other words, organ dose equivalents provided must be directly applied to the risks per unit organ weighted dose (i.e., gamma organ dose + RBE of neutrons relative to gammas * neutron organ dose) from the Hiroshima and Nagasaki A-bomb LSS, that are implemented in the ESA risk assessment software [4]. Here, a 1-year exposure has been assumed. For missions lasting longer than 1-year, the ERR and EAR risk models (see Table 1) may be applied at several ages at exposure and summed in the RADS calculations, but a limitation is that these ERR and EAR risk models come from the analyses of acutely exposed LSS members, although any choice of DDREF (see Table 1), as a simple method for accounting for dose-rate effects, is included in the methodology. However, the current methodology does not further differentiate to a more sophisticated degree, other than by just being capable of applying any DDREF value (a feature not demonstrated here), between risks associated with a solar particle event delivering a large dose in a few minutes and risks from a Galactic cosmic ray dose delivered over a year. This is because, based on current radiation epidemiology and space dosimetric considerations, it will only become clear with future research efforts how to achieve this aim. Furthermore, the software can be applied to sum RADS over several separate missions, e.g., a sum of risks for ages at exposure 35, 41 and 55 years from exposures accrued on 3 separate missions, but this feature was not demonstrated here.

A recent U.S. National Academies of Sciences, Engineering, and Medicine report (NA [25]), details recommendations given to NASA to change risk assessment. In particular, 3 recommendations from this report appear important for consideration by ESA in their further development of risk assessment software: a) recommendation 2: " In the near future, NASA should re-examine whether to use risk of exposure-induced death (REID) or other metrics, or a combination of metrics, ..." b) recommendation 3: "To inform astronauts about their radiation risk, NASA should provide all astronauts with an individual radiation risk assessment ...." c) recommendation 4:, "NASA should communicate a comprehensive picture of an individual astronaut's cancer risks due to radiation exposure .…..." Based on these recommendations it can be asserted that the work for ESA presented in Walsh et al. [4] and in the work presented here contribute substantially towards fulfilling these U.S. National Academy recommendations to NASA. RADS may be graphically interpreted, without the use of equations, and communicated to the astronauts as the unknown probability of surviving until retirement age (65 years) being reduced by a specified percentage or range of percentages due to the exposure. RADS may be included into operational procedures by space agencies by judicious choices related to which ages at exposure and which ages attained (e.g., retirement and/or some choice of old age beyond retirement) are applied.

The usefulness of the RADS metric and its particular suitability for space applications has been shown here and in the

previous work cited here, and an extension of this previous work has been presented separately to include Multi-Model Inference (MMI), also incorporating multi-method inference, into RADS calculations based on estimated doses (in the paper by Hafner and Walsh – this issue [16]). Future work could aim to combine the expert dosimetry calculation reported here with the MMI methodology reported by Hafner and Walsh [16] in this special issue. Future work will also involve including dosimetric uncertainties, summing up organ-specific cancer risks using organ/tissue doses for each of the specific cancer types and the use of appropriately generalized/anonymised actual crew exposure data.

5 Conclusion

This study presented the application of the European risk assessment software to a one-year Mars flyby mission, considering the modelled primary organ dose equivalent rates from numerical simulations. These organ dose equivalents for radiation exposure on this example Mars flyby mission depend on sex, phase of solar activity, and choice of radiation quality factors, and range from 198 to 482 mSv. RADS is considered, by the authors, to be more suitable for astronaut risk assessment than other risk metrics because survival curve input is not required making the metric therefore less dependent on detrimental health information drawn from the general population. For the example mission, the probability of surviving until retirement age (65 years) for a typical 40 year old astronaut was found to be reduced by a range from 0.38% (95%CI: 0.29; 0.49) to 1.29% (95%CI: 1.06; 1.56); and the probability of surviving cancer free until retirement age to be reduced by a range from 0.78% (95%CI: 0.59; 0.99) to 2.63% (95%CI: 2.16; 3.18). The work presented here contributed substantially towards fulfilling the recent recommendations from the National Academy recommendations to NASA.

Data Availability Statement

No patient or astronaut data has been used in this paper.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Disclaimer

In this work, no actual dosimetric data on real astronauts has been used or nor has any information derived from such actual dosimetric measurements been used.

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