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Climate change and its relation with non-melanoma skin cancers

Rubén D Piacentini, Lara Della Ceca and Adriana Ipiña

Abstract

Climate change is affecting both the environment and the human behaviour. One significant impact is related to health, as detailed in the IPCC 2014 report. In the present work, and as a contribution to this commemorative special issue to Prof Dr Jan van der Leun, we present results of the squamous (SCC) and basal-cell carcinoma (BCC) incidence change in relation to the ambient temperature increase. This increase is produced by the global warming, mainly induced by anthropogenic atmospheric emissions of greenhouse gases. We have broadened a previous work made by van der Leun et al. (PPS, 2008, 7, 730-733), by analysing the effective carcinogenicity of UV dose, for the period 2000-2200 and four climate change scenarios (called RCP2.6, RCP4.5, RCP6.0 and RCP8.5). The corresponding percentage increases of the incidence of SCC for 2100 are: 5.8, 10.4, 13.8 and 21.4 %, and for 2200: 4.3, 12.1, 19.0 and 40.5 %. In a similar way, the percentage increases of the incidence of BCC for 2100 are: 2.8, 4.9, 6.5 and 9.9 % and for 2200: 2.0, 5.8, 8.9 and 18.2 %. We report the SCC and BCC percentage effective incidence results as a function of time, for the whole 21st century and we extended the analysis to the 22nd century, since people possibly affected (like the Z and T generations, born at the beginning of this century) will have a life expectancy extending up to the final decades of the present century and even to the first ones of the next century.

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Climate change and its relation with non-melanoma skin cancers

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Climate change is affecting both the environment and the human behaviour. One significant impact is related to health, as detailed in the IPCC 2014 report. In the present work, and as a contribution to this commemorative special issue to Prof Dr Jan van der Leun, we present results of the squamous (SCC) and basal-cell carcinoma (BCC) incidence change in relation to the ambient temperature increase. This increase is produced by the global warming, mainly induced by anthropogenic atmospheric emissions of greenhouse gases. We have broadened a previous work made by van der Leun et al. (PPS, 2008, 7, 730-733), by analysing the effective carcinogenicity of UV dose, for the period 2000-2200 and four climate change scenarios (called RCP2.6, RCP4.5, RCP6.0 and RCP8.5). The corresponding percentage increases of the incidence of SCC for 2100 are: 5.8, 10.4, 13.8 and 21.4 %, and for 2200: 4.3, 12.1, 19.0 and 40.5 %. In a similar way, the percentage increases of the incidence of BCC for 2100 are: 2.8, 4.9, 6.5 and 9.9 % and for 2200: 2.0, 5.8, 8.9 and 18.2 %. We report the SCC and BCC percentage effective incidence results as a function of time, for the whole 21st century and we extended the analysis to the 22nd century, since people possibly affected (like the Z and T generations, born at the beginning of this century) will have a life expectancy extending up to the final decades of the present century and even to the first ones of the next century.

Introduction

The climate is changing rapidly, mainly in the last decades, as it was presented in the last Intergovernmental Panel on Climate Change (IPCC) Report[1]. The temperature increase trend in the last century was of around 0.6°C/century[2], and different projection predict that, temperature changes, with respect to its value in the year 2000, will be between 0.9 and 3.5°C by the end of the present century (2100), and between 0.75 and 6.3°C, by the end of the next century (2200).The different values correspond to the mean of a large number of climate change models, based on diverse scenarios that can be considered as: optimistic (assuming a large effort made by

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humanity to reduce greenhouse gases, GHG, responsible for global warming[1], technically called RCP2.6, for Representative Concentration Pathways), low intermediate (RCP4.5), high intermediate (RCP6.0) and pessimistic (RCP8.5).These four RCPx were selected by IPCC for its Assessment Report 5 (AR5), where the *x* value represents the *radiative forcing,* -a net balance of incoming and outgoing radiation on the atmosphere-, which depends on the cumulative emissions of GHGs from all sources by the year 2100 (see for example the IPCC web site: http://sedac.ipcc-data.org/ddc/ar5_scenario_process/RCPs.html).

It is well known that non-melanoma skin cancers (NMSC): squamous cell carcinoma (SCC) and basal cell carcinoma (BCC) are mainly caused by UV solar exposure[3]. In a previous work[4], it was demonstrated that ambient temperature can also act as an effect modifier of these types of skin cancers. In the present work, the analysis of van der Leun et al[4], considered as a reference, is extended in time and type of NMSC, to determine the temperature influence on the human skin exposed to the solar radiation. We present graphical representations of the effective carcinogenicity of UV dose (or exposure) and NMSC effective incidence changes, in the present and next centuries.

Data and results

Temperature change data

The mean global (Earth) air temperature is the most important variable for the analysis of the climate change. Consequently, the World Meteorological Organization (WMO) and the United Nations Environment Program (UNEP) created the Intergovernmental Panel on Climate Change, a group of hundreds of high level specialists that collect worldwide information about this variable and its consequences on the global warming[1,5].

Figure 1 describes the time dependent behavior of the global air temperature change for the period 2000-2200, for four different RCPx scenarios, as described in the Introduction. It can be seen that in all of them the temperature will increase with respect to the value corresponding to the year 2000. However, there are large differences between them at the end of the present century (year 2100) and even more at the end of the next century (year 2200). For the four scenarios, the corresponding values in 2100, are: *1.0, 1.75, 2.31*and *3.5 °C* and in 2200, are: *0.75, 2.04, 3.13* and *6.33 °C*, respectively. The only temperature change that has a maximum (at year 2075) is the one corresponding to the optimistic RCP2.6 scenario.

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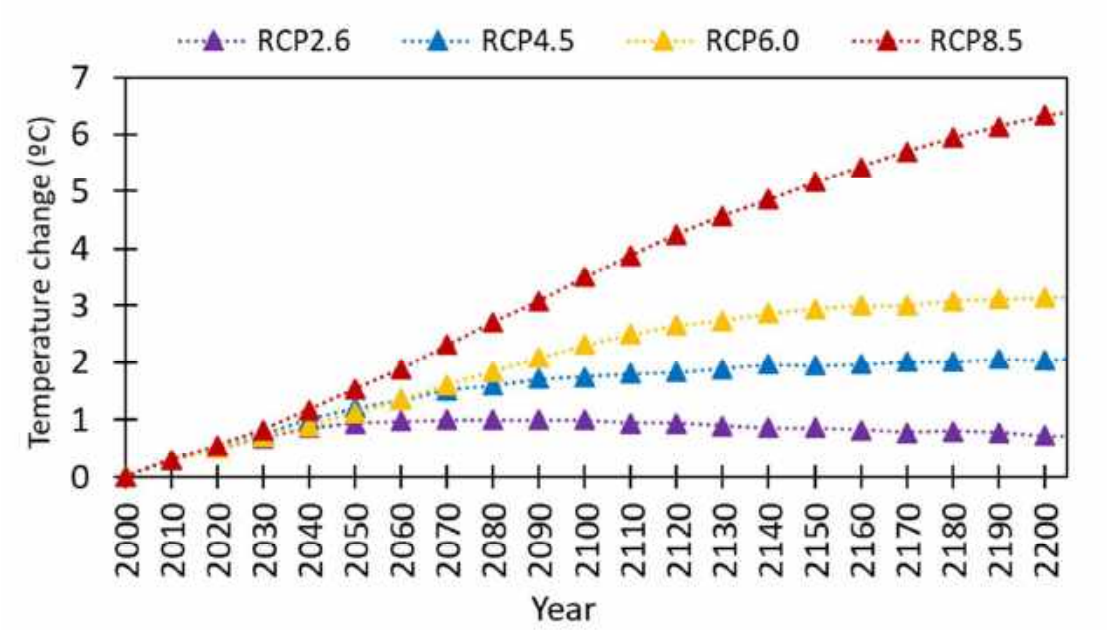

Fig. 1. Mean global air temperature change for the period 2000-2200, for four different scenarios of energetic atmospheric balance directly related to greenhouse gases emissions: RCP2.6 (violet), RCP4.5 (blue), RCP6.0 (yellow)and RCP8.5 (red). Source: IPCC Working Group 1 Report[1], adapted from Figure 12.43.

Mathematical representation of the non-melanoma skin cancer effective incidences

In order to mathematically represent the non-melanoma skin cancer (SCC and BCC) effective incidence, we follow Slaper et. al[6], who propose a relation between the change in effective carcinogenicity solar UV radiation dose.

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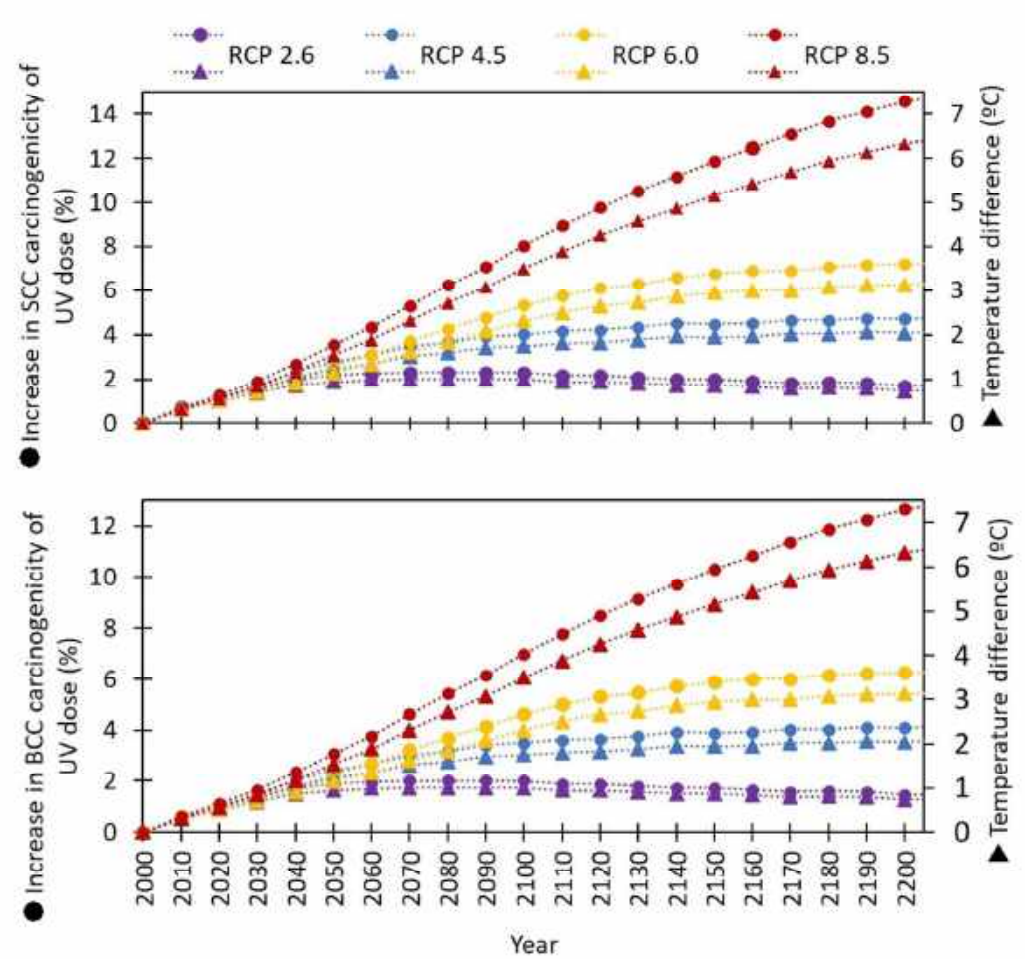

Fig. 2. Increase in non-melanoma skin cancers carcinogenicity of UV dose due to global warming, for the four IPCC scenarios, for the 2000-2200 period, based on Equations (1) and (2).The color code is the same as in Figure 1. Top: SCC, bottom: BCC.

or exposure (D_k), for each type of skin cancer (with *k = SCC* or *BCC)* to a given power *(c_k)* and the effective incidence change of NMSC*(S_k)*

$$S_k/S_{o,k} = [D_k/D_{o,k}]^{c_k} \quad (1)$$

Where c_k is equal to 2.5 for SCC and 1.4 for BCC[6] and $D_{o,k}$ and $S_{o,k}$ are values corresponding to the reference year 2000. The exposure is related to ambient temperature change *(ΔT),* as follows

$$D_k = p_k \Delta T + 1 \quad (2)$$

The coefficient p_k is obtained from van der Leun et al[4], based in National Skin Cancer Surveys in USA[7], as: p_{SCC} = *0.023/°C (*or in percentage *2.3 %/°C)* and p_{BCC} = *0.02/°C (*or in percentage *2.0 %/°C).* Value 1 is added to this equation in order to normalize the exposure D_k in year 2000.

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It must be pointed out that equation (1) corresponds to a simplification of the model used by Slaper et. al[6]. This model considers a dynamical analysis of the effects of changing exposures over time by including the dose-dependency of tumor formation and the time/age dependency. In this work, we only consider the dose-dependency, which implies that the calculations of the changes in incidence are associated with a lifetime static increase in temperature (and thus exposure).

Table 1. Changes in global ambient temperature *(ΔT)*, effective solar UV exposure *(D_k)* and effective incidence of NMSC (*S_k)* at the end of the present century (2100) and at the end of the next century (2200) for the four climate change scenarios, for *k = SCC* (upper Table) and for *k = BCC* (lower Table). Equation (2) was used for relative exposure (column 3) with $p_{SCC} = 0.023/°C$ for SCC and with $p_{BCC} = 0.02/°C$ for BCC, and equation (1) was used for relative incidence (column 5). The percentage exposure: $\Delta D_k = 100*[(D_k/D_{o,k}) - 1)]$ % and incidence: $\Delta S_k = 100*[(S_k/S_{o,k}) - 1)]$ %,are given in columns 4 and 6, respectively. Note: The starting year is 2000 with a reference value of 1 for D_{ok} and consequently, for S_{ok}.

Squamous Cell Carcinoma (SCC)					
RCPxscenario	***Temperature change (ΔT in °C)***	D_{SCC}/D_{oSCC}	ΔD_{SCC}(%)	$S_{SCC}/S_{oSCC} = [D_{SCC}/D_{oSCC}]^{2.5}$	ΔS_{SCC}(%)
2100					
RCP2.6	1.00	1.023	2.3	1.058	5.8
RCP4.5	1.75	1.040	4.0	1.104	10.4
RCP6.0	2.31	1.053	5.3	1.138	13.8
RCP8.5	3.50	1.081	8.1	1.214	21.4
2200					
RCP2.6	0.73	1.017	1.7	1.043	4.3
RCP4.5	2.04	1.047	4.7	1.121	12.1
RCP6.0	3.13	1.072	7.2	1.190	19.0
RCP8.5	6.33	1.147	14.7	1.405	40.5

Basal Cell Carcinoma (BCC)					
RCPx scenario	***Temperature change (ΔT in °C)***	D_{BCC}/D_{oBCC}	ΔD_{BCC}(%)	$S_{BCC}/S_{oBCC} = [D_{BCC}/D_{oBCC}]^{1.4}$	ΔS_{BCC}(%)
2100					
RCP2.6	1.00	1.020	2.0	1.028	2.8
RCP4.5	1.75	1.035	3.5	1.049	4.9
RCP6.0	2.31	1.046	4.6	1.065	6.5

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RCP8.5	3.50	1.070	7.0	1.099	9.9
		2200			
RCP2.6	0.73	1.015	1.5	1.020	2.0
RCP4.5	2.04	1.041	4.1	1.058	5.8
RCP6.0	3.13	1.063	6.3	1.089	8.9
RCP8.5	6.33	1.127	12.7	1.182	18.2

Figure 2 represents the time evolution (for the 2000-2200 period) of the change in the carcinogenetically effective dose of skin cancers (SCC and BCC), for the four scenarios, relative to the starting year 2000. We can see that in all scenarios and for all years, the incidence of SCC is larger than that of BCC. Also, for all scenarios up to, approximately 2030, the general trend of the incidence is quite similar, starting to differ significantly by the middle of the present century.

Table 1 presents the changes in exposure and incidence for a given skin cancer type (BCC or SCC), at the end of the present century (2100) and at end of the following century (2200). Since the delay between exposure changes and incidence changes are not included in this analysis, the 2100 and 2200 increased incidences that are calculated reflect incidences that would occur if the temperature would be stable for a full generation. It can be seen that the behavior is similar to the temperature change (modified by the power c_k). Moreover, Table 1 shows the percentage of the exposure: $\Delta D_k = 100*[(D_k/D_{o,k}) -1)]$ % and of the incidence: $\Delta S_k = 100*[(S_k/S_{o,k}) -1)]$ %, both relative to the corresponding values in the year 2000, for the same scenarios and years.

We would like to point out that, for a given year, not only the temperature value at that moment determines the lifetime effective exposure and consequently, the incidence, but also the changes over time prior to that period. Slaper et al[6] found a time-lapse of about 60 years between the calculated increase in UV and the corresponding increase in incidence, taking into account the Copenhagen amendments to the Montreal protocol[7] related to ozone depletion.

Discussion and conclusion

In the present work, we consider the temperature change as an effect modifier added to solar UV radiation, in relation to carcinogenicity of solar UV exposure and BCC and SCC incidence changes for the present and next century. The four different climate change scenarios considered, go from an optimistic one (RCP2.6), -the only one that considers global temperature will start to decrease by 2075 going to less than 1 °C-, to a pessimistic one, -with increases as high as 6.3 ºC at the end of the 22 century-. This large changes in temperature will

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induce similar increases in the effective carcinogenicity solar UV dose and thus, in the effective NMSC incidences. Consequently, a large effort needs to be made to reduce significantly the actual trend of greenhouse gas emissions, responsible of the global warming[1].

Concerning the initial year 2000 that was chosen for the present analysis, we would like to point out that the global ambient temperature started to increase before that year, particularly, in the initial years of the Industrial revolution (around 1750) and mainly in the last (20) century. Consequently, the total effect of climate change becomes larger than the values determined in the present work. However, we were essentially interested in the future behavior of this important health problem.

Also, we would like to remark that we presented the SCC and BCC percentage incidence results as function of time for the whole 21st century and we extended the analysis to the 22nd century, since people possibly affected (like the Z and *T* generations, born at the beginning of this century) will have a life expectancy extending to the final decades of the present century and even to the next century[10].

Some indirect evidence of an opposite effect (DNA repair and a reduction in skin carcinogenesis) due to temperature increase has been presented. In particular, recently, Lan et al[11] detailed the following main results: a) *UVB induced DNA damage was significantly lower in keratinocytes that were pretreated in an environment with slightly elevated temperature followed by UVB treatment (Heat-UVB) as compared to UVB and UVB radiation followed by exposure to equivalent increase in environmental heat (UVB-Heat) groups*. However, these experiments were made with cultured cells and the present work was based on epidemiological data of the USA National Skin Cancer Surveys, which analyzes a very large number of SCC and BCC incidences in both men and women living in different regions of USA[4,8]. Moreover, keratinocytes in humans and in mice do not evolve in time in the same way. For example, the turnover rate from stem cells to desquamation is 5 times higher (in terms of number of days) in humans than in mice: every 40-56 days in the case of humans[12] and every 8 to 10 days in the case of mice[13]. Keratinocytes are also called basal cells (related to BCC), so the results obtained by Lan et al[11] are only related to this type of cells and not to squamous cells (related to SCC); b) *In the animal model, it was found that Heat-UVB treated mice showed delayed and reduced tumor formation as compared to the UVB and UVB-Heat treated groups*. However, as was detailed in item a), the present analysis was based on epidemiological data obtained from SCC and BCC incidences on humans and, consequently, it is not based on an animal model; c) Item 2.2 Treatment of cells: *2) UVB irradiation only (25 and 50 mJ/cm^2); 3) UVB irradiation followed by heat treatment for 30 min (UVB-Heat); 4) heat treatment for 30 min followed by UVB irradiation (Heat-UVB).* So, only artificial UVB radiation (312 nm peak lamp) was employed and not the whole UV spectrum, as in the case of outdoor exposure considered in the present

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study. Also, the laboratory treatment of the cells was done applying UVB radiation in a different time interval than the heat treatment. So, the corresponding results cannot be extrapolated to outdoors conditions. Moreover, the model with rats achieved results with a very large standard deviation (SD) from week 16 and, consequently, it is difficult to extend this conclusion to environmental conditions. Beyond the biological aspect, this work is not considering all the photochemistry triggered by UVA radiation, which also affects the aminoacids present in the human skin. Moreover, the work presents a conclusion about the UVB + heat, considering temperatures within the range 38-43 °C, that are rarely reached in nature (only in some very hot regions of the world).

In addition to these arguments, the present results, obtained from an ecological approach, could also be a consequence of changes in exposure behavior in relation to higher temperatures.

We would like to point out that the results of van der Leun et al[4], considered as inputs in the present study, were based on two independent databases, those of men and women affected by NMSC, exposed to solar radiation and ambient temperature in a wide range of latitudes and altitudes[8].

Conflict of interest statement

There are no conflicts to declare.

Acknowledgements and remembering Jan van der Leun

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Rubén D Piacentini would like to remember Jan van der Leun, an exceptional person and scientist that made a significant contribution to the Science of ozone, solar UV radiation and biological effects. I had the opportunity to meet Jan when I participated as a Reviewer, at the Meeting with the Authors of the UNEP Assessment 2002 *Environmental Effects of Ozone Depletion and its Interaction with Climate Change*, done at Park city, USA, in September 2002. This assessment was done pursuant to Article 6 of the Montreal Protocol on Substances that deplete the Ozone layer and it was prepared under the auspices of the United Nations

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Environment Programme (UNEP). Jan van der Leun, in collaboration with Xiaoyan Tang and Manfred Tevini were Co-chaimans of this 2002 Assessment (http://ozone.unep.org/en/Assessment_Panels/EEAP//eeap-report2002.pdf). They made a very interesting introduction to this Assessment, where they wrote: "The induction of skin cancer by solar UV radiation is likely to increase with global warming." I was interested in the subject and based on the analysis of the Skin Cancer US National Surveysdone by Scotto et al[6], I developed[14] a mathematical function that allows the correlation between the incidence of non-melanoma skin cancers (NMSC)in Caucasian population, and the Northern Hemisphere latitudinal location of cities and regions where the survey was conducted. However, a large fluctuation of the data points was evident, suggesting that another variable influenced the NMSC. We started to exchange information on this research subject with Jan and Frank de Gruijl, who published with Jan the basic article on *Climate change and skin cancer*[15]. Once we were convinced that there was a well-defined correlation between NMSC (SCC and BCC) incidence and temperature change, -for men as well as for women-, we started to prepare the publication. At that time, I suggested the Organizing Committee of the 21st World Congress of Dermatology, held at Buenos Aires, Argentina in 2007, to invite Jan van der Leun to give a Plenary Conferenceon Climate change and skin cancer. It was a real success, with several thousand of attendants. Finally, the work was published in 2008[4] and later on, it was includedin Volume 2 of the IPCC, Working Group 2 report: *Impacts, Adaptation and Vulnerability*[5] to show one of the impacts of climate change on human health.

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The increase in ambient temperature due to climate change is expected to affect the carcinogenicity of squamous cell carcinoma (SCC) and basal cell carcinoma (BCC).