Hypothesis: Is frequent, commercial jet travel by the general public a risk factor for developing cutaneous melanoma? [version 1; referees: 2 approved, 1 approved with reservations]

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Abstract
Melanoma incidence has been increasing worldwide over the past 50 years and various risk factors have been identified. Interestingly, multiple studies have shown a multifold increased risk of developing melanoma in jet pilots and airline crew. There has also been a dramatic increase in the availability and frequency of jet travel by the general population during this time period. Therefore, it is hypothesized that frequent commercial jet travel may represent an additional risk factor for the development of cutaneous melanoma in susceptible individuals of the general public.
Background
The incidence of cutaneous melanoma in light pigmented individuals worldwide has been steadily increasing over the past 4–5 decades. Sun exposure, including intermittent exposure, is an important environmental risk factor for melanoma, along with history of sunburn, residence in equatorial latitudes and tanning bed usage. Genetic risk factors include red hair, family history of melanoma, dysplastic nevi, lightly pigmented skin, tendency to burn, inability to tan, and DNA repair defects. Phenotypic expressions of gene/environmental interactions are risk factors and include melanocytic nevi (increased total number, multiple atypical [dysplastic], and congenital [particularly large axial lesions with multiple satellites]), ephelides, and personal history of melanoma. Non-solar occupational risk factors have also been shown to be associated with the development of melanoma. Since no specific currently recognized risk factor adequately explains the rapidly increasing incidence among the general population, the identification of new risk factors that could play a role in melanoma prevention is needed.

Studies from many countries have shown a significant increase in the risk of melanoma in commercial and military pilots; these range from approximately 2 to 10 fold. An increased risk has also been shown in some studies of cabin crew. Recently a meta-analysis was published that also showed an increased risk in pilots and cabin crew. Though it is unclear why aircrew have an increased risk of melanoma, one proposed explanation regarding their increased risk has focused on the exposure to cosmic ionizing radiation present at cruising altitudes of 30,000 feet or higher. Currently, commercial jets frequently cruise at an altitude that results in cosmic radiation exposure. In addition, the cosmic radiation exposure is increased with higher altitude flights and long-haul routes. Cosmic ionizing radiation contains multiple particles that can damage DNA. Epidemiologic studies have reported a possible relationship between melanoma and exposure to ionizing radiation in other occupational settings. A recent systematic review regarding cosmic radiation and cancer assessed the role cosmic radiation plays in the development of cancer as compared with other lifestyle factors.

Another proposed explanation for the documented increased risk among pilots is their increased exposure to UV light during flight. Recently an analysis was done and found greater amounts of UVA exposure through the windows of jets. At this time, it is unclear whether increased UVA exposure, cosmic ionizing radiation, circadian rhythm disturbance and/or other undetermined factors are contributing to this increased risk of melanoma in pilots and cabin crew.

Presentation of the hypothesis
It is hypothesized that individuals of the general population who frequently travel by jet plane may also have an increased risk of developing cutaneous melanoma in a similar fashion as pilots and cabin crew. This hypothesized risk factor may play a role in the development of melanoma due to a variety of potentially harmful exposures associated with frequent jet travel that could interact synergistically with other known genetic and environmental risk factors in susceptible individuals. This hypothesis is based on the findings that both pilots and cabin crew, generally healthier than the general public, and with a prevalence of skin cancer risk factors similar to that of the general public, have a dramatically higher risk of melanoma.

Since the late 1950s, commercial jets have begun to cruise at an altitude of 30,000 feet or higher. This major change in the flying altitude of air travel is consistent with the temporal nature of the rapid increase in the incidence of melanoma. During the past 50 years, the availability and frequency of jet travel among the general public have increased dramatically. In addition, with the deregulation of the airline industry in the 1970s, and the resulting decrease in fares, a higher percentage of the overall population began to experience jet travel. An ecologic study found an association between accessibility to air travel and the incidence rate of melanoma.

A widely accepted epidemiologic finding consistent with the proposed hypothesis is that intermittent sun exposure is an independent risk factor for melanoma. The correlation between melanoma incidence and ‘sun holidays’ has been primarily interpreted as secondary to intermittent sun exposure. The proposed hypothesis suggests that the increased risk associated with ‘sun holidays,’ may also be related to jet travel and the resultant exposures associated with jet travel to those vacation destinations. Higher socioeconomic status (SES) is also a risk factor for melanoma development; and higher SES is associated with increased jet travel and ‘sun holidays.’ All findings consistent with the hypothesis.

Testing the hypothesis
A case-control methodology could be utilized to test this hypothesis. One would assess jet travel histories in melanoma patients and comparable controls, controlling for known risk factors such as age, skin type, genetic host factors and sun exposure history. One would obtain assessments of subjects’ jet travel history in terms of frequency, duration of flights and altitude. Assessment of travel routes, season of travel and increased sunspot activity during flights should also be undertaken. It would be necessary to disentangle intermittent sun exposure history from jet travel history.

Implications of the hypothesis
It is hypothesized that frequent commercial jet travel by the general public may increase the risk of developing melanoma due to various harmful exposures associated with frequent jet travel. This melanoma and jet travel hypothesis has potential for reducing melanoma-associated morbidity and mortality and warrants properly designed analytic epidemiologic evaluation to assess the validity of this hypothesis. In addition, if demonstrated to be a risk factor, evaluation of the underlying mechanisms behind this increased risk may lead to the expansion of basic science research of etiologic factors of melanoma and of cancer in general.

Competing interests
No competing interests were disclosed.

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Open Peer Review

Gabriella Fabbrocini
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The hypothesis put forward by the author is interesting, yet hard to prove. It is extremely difficult to separate the weight of individual exposures: the cosmic radiation at high altitudes and that related to sun exposure of the trip. The bibliography is extensive and still valid. Considering the bases from which originates the article, or the increased incidence of melanoma in the last decades and the multifactoriality, it might be interesting to start the case control study that the author sets out to accomplish. It would be necessary to consider some essential factors, including the frequency of air travel, the duration of the flight, altitude, intermittent sun exposure of patients during their trip.

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Competing Interests: No competing interests were disclosed.

Robyn Lucas
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The authors raise the hypothesis that commercial jet travel by the general public may increase the risk of developing cutaneous melanoma through increased exposure to cosmic radiation or UVA radiation. Previous studies have shown an increased risk of melanoma in flight crews and pilots. The hypothesis in relation to UVA seems unlikely, given that most air travellers are well-clothed. The hypothesis in relation to cosmic radiation needs stronger evidence of the measured levels within aircraft. The author proposes a case-control study, but this seems unlikely to provide valid results - the most likely explanation of an increased risk of melanoma in flight crews and pilots is higher sun exposure at the locations that they fly to, especially of the intermittent high dose pattern that confers particular risk of melanoma. However sun exposure is poorly reported (as would be the measure of exposure in a case-control study) while air travel likely to be well-reported (and able to be validated). It will be impossible to clearly separate these "exposures". There is likely to be a very high correlation between a history of air travel and of sunny holidays in people with melanoma, such that a history of air travel is a proxy for high dose intermittent sun
exposure. Findings resulting from such a study are highly likely to be spurious associations. It is an interesting hypothesis - a start would be to measure levels of cosmic radiation inside passenger aircraft, more clearly make the link between cosmic radiation and melanoma, and assess the body sites affected in cabin crew and pilots who develop melanoma.

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

**Competing Interests:** No competing interests were disclosed.

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Desiree Ratner  
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The hypothesis, “Is frequent, commercial jet travel by the general public a risk factor for developing cutaneous melanoma?”, provides an interesting perspective on possible reasons for the increasing incidence of melanoma worldwide. The author cites multiple studies documenting a significant increase in melanoma risk among commercial and military pilots as well as cabin crew. Possible reasons for this increase include exposure to cosmic ionizing radiation at cruising altitudes of 30,000 feet or higher, particularly on long haul routes, as well as increased exposure to UV light during flight. Given that a significant portion of the world’s population now takes advantage of the increased availability and frequency of jet travel, it is possible that the increased incidence of melanoma may be, in part, due to increased exposure to cosmic rays and/or UV exposure during high altitude jet travel.

The author suggests that a case-control methodology be used to test his hypothesis, by assessing jet travel histories in melanoma patients and comparable controls, controlling for known risk factors such as age, skin type, and exposure history. It would be necessary to look at frequency of air travel, duration of flights, and altitude, and to disentangle patients’ intermittent sun exposure history from their jet travel history. If the hypothesis that frequent commercial jet travel represents an additional risk factor for developing cutaneous melanoma proves to be true, not only will it be necessary to look at the mechanisms behind this increased risk, but it will also be necessary to develop appropriate screening and preventive measures to decrease the morbidity and mortality to the greatest degree possible from air travel associated melanoma.

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

**Competing Interests:** No competing interests were disclosed.
Reader Comment 01 Sep 2015

Ian Burgess, Medical Entomology Centre, UK

With regard to aircrew engaged in commercial intercontinental services it should be noted that the general rostering arrangements are that they have a number of rest days between flights. In the case of crews travelling to warmer parts of the world it has certainly been the case historically that a good proportion of those “off” days were spent lounging around the hotel swimming pool, with associated exposure to higher levels of UV. Surely this must be a factor if there is detected higher incidence of radiation associated carcinomas in all grades of aircrew rather than just flight crew, who would be the only ones exposed directly to UV through cabin windows.

Competing Interests: No competing interests