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Letter To The Editor

Comments on "Radiation induced breast cancer risk in BRCA mutation carriers from low-dose radiological exposures: a systematic review"

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This letter is regarding the article by Colin *et al.*, entitled "Radiation induced breast cancer risk in BRCA mutation carriers from low-dose radiological exposures: a systematic review", published in *Radioprotection* (Colin *et al.*, 2017). The authors claim that based on the review they performed on 11 studies which included many types of radiological breast exposures, an association between the risk of breast cancer (BC) and low cumulative X-ray doses below the age of 30 was found. The authors concluded that 1) the risk of radiation induced breast cancers in BRCA mutation carriers depends on women's age at exposure, and 2) mammography or any repeated X-ray exposures of breast should be limited and used very cautiously in these mutation carriers.

The reason for the increased concerns regarding X-ray imaging in BRCA mutation carriers is that such patients have deficiencies in DNA double-strand break (DSB) repair, and so may face increased risk of cancer based on the somatic mutation model of cancer. However, DNA damage does occur due to endogenous causes and such damage is much higher than the DNA damage caused by low levels of radiation such as from diagnostic X-ray exposures. Also, the increased damage from low-dose radiation would boost defenses such as antioxidants and DNA repair enzymes which would result in reduced DNA damage from endogenous causes, with the ultimate result being reduced net DNA damage. In addition, low-dose radiation also boosts the immune system and so would eliminate the cancer cells more effectively, reducing the cancer risk. Thus, there is no radiobiological reason for the cancer concerns regarding diagnostic X-ray procedures.

There is also no consistent evidence to support the cancer concerns regarding the X-rays, as indicated by the authors' review of the literature. A review of the epidemiological studies used by Colin *et al.* showed that 1) The findings are inconsistent between the studies and so do not allow any firm conclusions. Moreover, in some cases such as the study conducted by Goldfrank *et al.* (2006), the association with breast cancer was positive only for BRCA1 with an OR of 1.08. 2) The heterogeneity of the types of diagnostic procedures in these studies makes the comparison of the findings of different studies very complicated. For example, while in 7 studies the procedure was either mammography or chest radiography, Pijpe *et al.*'s study included computed tomography (Pijpe *et al.*, 2012). It is worth noting that considering the Table 3 in the paper authored by Colin *et al.*, if they limit the exposures to only radiography (to reduce the heterogeneity and to make the comparison of the studies more accurate), currently positive marked association with breast cancer would become negative. 3) Interestingly, in one of the papers reviewed by Colin *et al.* (John *et al.*, 2013), the OR was not increased for 6 or more chest X-rays, while it was elevated for BRCA2 mutation carriers with 3–5 diagnostic chest X-rays. 4). As indicated in some of these epidemiological reports (e.g., Andrieu *et al.* (2006)), recall bias could have affected the findings.

The number of natural mutations is significantly larger than those created by low-dose ionizing radiation. If low-dose radiation is a hazard, one would expect that the natural mutations would propagate cancer at a rate larger than observed. Since this does not occur, the DNA repair mechanisms and human immune system must function efficiently to remove both naturally occurring abnormalities and those caused by low-doses of ionizing radiation. Although this is a very qualitative argument, the rate of natural mutations suggests that the DNA repair mechanisms should mitigate the detrimental effects of low-dose ionizing radiation observed by Colin *et al.* In summary, there is no radiobiological reason for the cancer concerns due to X-ray scans and there is no consistent epidemiological evidence to support the concerns.

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