Should Interventionalists Be Screened for Genetic Mutations That May Impair Their Ability to Repair DNA Damage from Radiation Exposure?

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Contemporary research has taught us a great deal about both the mechanism of chronic radiation exposure's close relationship with cancer and the implications of this mechanism for individuals. We know that x-rays and other forms of ionizing radiation can cause DNA breakage and other forms of molecular damage (eg, nucleotide substitution and sugar ribose alterations). In turn, these molecular insults can result in acquired mutations that affect gene function and protein expression. Importantly, the duration and intensity of radiation exposure tracks with the extent of DNA damage. In flight crews, for instance, greater flight distances and higher altitudes are associated with increased risk of chromosomal translocations (1). In the case of certain types of genes, for example, tumour suppressor genes, which restrict cell growth through various methods; oncogenes, which have the potential to drive uncontrolled cell proliferation; and DNA repair genes, which fix DNA damage before cell division takes place, such mutations can ultimately lead to cancer (2).

Are some of us at more risk than others when it comes to occupational radiation exposure? Although ionizing radiation and other carcinogens cause acquired mutations, the DNA repair and tumor suppressor genes that normally serve to mitigate the impact of these mutations are endogenous and inherited (2). It therefore follows that individuals with inherited mutations that compromise these repair mechanisms could be at increased risk of radiation-induced cancer. Indeed, recent work supports this notion. In a 2017 study, El-Sayed et al (3) used flow cytometry to quantify the perioperative expression of DNA damage and repair markers (γ-H2AX and pATM) in vascular surgeons who performed fluoroscopy-guided aortic interventions. Following a standardized amount of radiation exposure, some surgeons exhibited a notably greater number of DNA breaks than others, a finding perhaps reflective of interindividual variability with regard to DNA damage susceptibility.

Can we use this knowledge about interindividual differences to minimize risk to interventionalists and technologists?

One feasible risk reduction method would be the development of a prescreening procedure for inherited mutations that would predispose individuals to radiation-induced cancer. The first step would be to account for family cancer history and to identify high-risk populations. Some of this is simple population genetics. The Ashkenazi Jewish population, for instance, has a 2% chance of carrying a *BRCA* germ line mutation that predisposes to impaired P53-mediated DNA (4), the consequence of which manifests as increased risk of breast, ovarian, peritoneal, and prostate cancers (4). Interestingly, concern has been raised regarding the potentially carcinogenic effects of low-dose ionizing radiation from annual or even biannual mammograms in *BRCA1/2* mutation carriers. However, if we are concerned about biannual low-dose mammography radiation breast cancer induction, should we not be concerned about the much higher daily doses received by an interventionalist who carries *BRCA1/2* mutations?

A follow-up step may be to offer potentially at-risk interventionalists and trainees access to genetic screening for germline mutations (likely including mutation types in *BRCA1*, *BRCA2*, and *MLH1*, among others) that increase susceptibility to radiation-induced DNA damage. Certainly, screening for specific mutations is a well-established and increasingly affordable practice in the context of patients with family histories positive for breast, ovarian, and colorectal cancers. The intent of such a screening process would be to provide an objective estimate of the risk an individual might incur by pursuing a career in interventional radiology and to allow them to make informed decisions on the basis of that knowledge. The choice of what to do if the inability to repair DNA were identified would be completely up to the individual. Perhaps an early trainee could choose to pursue a career based more on interventional imaging using magnetic resonance imaging or ultrasonography, whereas an

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established interventionist may heighten their adherence to lead barrier-based risk reduction methods or reduce the number of high-exposure procedures they perform each year. Of course, the potential ethical ramifications of such screening would have to be considered carefully. For one, the test results would need to be strictly confidential to safeguard against any possible discrimination, however well meaning, that might ensue from their dissemination. Screening would have to be performed strictly in the context of appropriate counseling and informed interpretation. Finally, participation in screening would have to be purely optional, with the choice to know more about their genetic risk profile left up to each individual.

Recently there have seen scattered reports of neoplasms and posterior chamber cataracts in some of our senior interventional colleagues (5). In light of this, we should acknowledge the limitations of current, lead barrier-based risk reduction methods and act proactively to identify new approaches that let us practice our profession more safely. In the view of the present authors, an excellent first step would be a baseline cross-sectional analysis of cancer incidence and cancer risk factors within the 6,000 members of the Society of Interventional Radiology. This could be followed by the establishment of a longitudinal health study in the vein of the Johns Hopkins Precursors study, which has followed the health of Hopkins Medical School graduates since 1948. These data would help us to hold an informed conversation on this critical topic and make better plans for our future.

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