# Brain Tumors, Interventionists, and Radiation: How Real Is the Risk?

Weighing the available evidence on dosimetry, epidemiologic data, and cellular and vascular effects to evaluate risk.

**BY REBECCA M. MARSH, PhD, AND MICHAEL SILOSKY, MS**

In 1998, Finkelstein reported on two interventional cardiologists in Toronto, Ontario, Canada, who were diagnosed with brain cancer.[1] Although there were many plausible explanations, including coincidence, the author noted that the occurrence of brain cancer in two additional cardiologists over the previous 10 years "would confirm the occupational causation theory." Sixteen years later, another publication caught the attention of the interventionist community, in which nine interventionists from around the world, all of whom worked in catheterization labs, developed brain tumors.[2] Four of the tumors were found in the left side of the brain (tumor location was unknown for the other five cases). Interventionists are exposed to more radiation to the left side of their head than the right because of how they stand relative to the patient during procedures. Thus, the authors indicated that the prevalence of left-sided brain tumors further suggested a causative relationship between occupational radiation exposure and brain tumors.

The question of whether brain cancer is an occupational hazard for interventionists remains unanswered. In this article, we discuss the current body of scientific knowledge surrounding this topic, reviewing reported operator doses, epidemiologic studies that have attempted to characterize radiation-induced health effects related to the brain (including their strengths and limitations), and position statements of several national and international groups regarding the risk posed by exposure to low doses of ionizing radiation. We also present a brief discussion of this collective information and its role in radiation safety practices.

## DOSIMETRY

Any discussion of radiation risk requires quantification of the amount of radiation to which a group is typically exposed. A limiting factor in the discussion of risk to interventionists is the large degree of variation in the reported operator dose from fluoroscopy-guided interventional (FGI) procedures. Comparing results from different studies is further confounded by inconsistent use of dose metrics, with studies reporting absorbed dose, effective dose, organ dose, or entrance air kerma.

One review of FGI cardiac catheterization procedures found that reported effective doses ranged from 0.02 to 38 µSv per procedure (ie, percutaneous coronary interventions, ablations, and pacemaker and intracardiac defibrillator implantations).[3] A study of noncardiac procedures found that the estimated effective dose per case ranged from 0.1 to 101 µSv per examination (ie, percutaneous nephrolithotomy, vertebroplasty, orthopedic extremity nailing, biliary tract, head/neck endovascular therapeutic, transjugular intrahepatic portosystemic shunt creation, and endoscopic retrograde cholangiopancreatograph) and that, per procedure, the dose to the operators' brains ranged by orders of magnitude from about 0.1 to 300 µGy.[4]

A wide range of doses to FGI operators continues to be reported. Study findings include an average operator effective dose of 9 µSv for complex endovascular procedures, with a higher effective dose* for fenestrated endovascular aneurysm repairs (20 µSv/procedure),[5] an air kerma of 10.2 µGy per procedure to an operator's unshielded head,[6] a dose of 224 µSv per endovascular procedure,[7] and a 3-month cumulative dose to the head of 2.77 mSv

*Doses are reported here as they appear in each article. The actual dose measurement (effective dose vs entrance air kerma vs organ dose) is sometimes not specified for the studies cited.

without the use of a hanging lead shield and from 0.22 to 1.16 mSv when using a hanging shield.[8] Yet, other studies reported an annual dose of 12 mSv to the brain[9] and a dose rate of approximately 106 mSv per hour, which the authors extrapolated to an annual dose of 146 mSv.[10]

There are a number of reasons to explain this variability, including differences in how physicians perform the same type of procedure (eg, total beam-on time, tube angulation, and use of personal shielding) and differences in equipment, physician workload, and the types of procedures being performed. These studies also used a variety of experimental designs and dosimetry tools, some of which may be questionable[7,10] to accurately measure scattered radiation.

Even if there were more consistency in the ranges of reported dose per procedure, there is still disagreement about the number of procedures a typical interventionist performs each year[11] and how much this workload varies among interventionists. One study found that 26% of interventionists perform more than 700 cases a year,[12] yet studies evaluating operator exposure based on dose per case have assumed a workload of up to 1,000 cases per year.[10] Clearly, the number of cases performed annually will not only depend on how many cases are performed within an institution, but also on the difficulty of the procedure—operators who perform more complicated procedures will likely perform fewer cases, but each case may lead to higher operator exposure compared with less complicated procedures.

In addition, the current quantification of dose to the brain does not take into account the protective benefits of the skull. One study acknowledged that measurements made at the skin surface provide a conservative value of dose to the brain.[9] This is caused by the brain being located farther from the source of radiation and by the attenuation provided by the skull, which absorbs approximately 40% of scattered radiation.[13]

Limiting the discussion to exposure to the head, one could take a conservative approach and assume that a busy interventionist performs 1,000 procedures per year. Based on this and using the previously mentioned values, one could use the data reported as dose per case to posit that the typical entrance dose to the head is 10.2 mGy per year and that, due to the range in reported values, the calculated annual effective dose varies considerably, from estimates of 9 to 224 mSv.[5,7] Ultimately, a review of the literature does not yield a clear picture of typical operator exposure during these FGI procedures.

## EPIDEMIOLOGIC DATA

In addition to the difficulties in accurately quantifying dose to the interventionist, there is another difficulty in assigning risk to an operator's exposure. The fact remains that very little is known about how human tissues respond to low levels of radiation. Most of what is known comes from epidemiologic studies[14]; however, interpretation of epidemiologic data is problematic, as this is limited by effects such as reverse causation and confounding by indication.[14,15] Many studies also lack information about individual dosimetry and lifetime estimated dose, have follow-up times that may be too short to follow workers until cancer is more likely to occur, and lack information for more complicated procedures or procedures performed with modern equipment.[11] A review of eight major cohort studies involving medical radiation workers showed mixed results.[11] Some studies found no increase in mortality, including cancer mortality,[15] whereas others found a slight increase in the incidence of breast cancer.[16] Other studies found an increased risk of leukemia to varying degrees, and findings for other solid tumors were not consistent.[11] Increased incidence of brain cancer has been seen in children who received therapeutic x-rays in the 1940s and 1950s,[17] but the exposures (average, 1.5 Gy) were much higher than those seen in an occupational setting. Survivors of the bombing of Hiroshima showed a slightly elevated risk of developing brain cancer,[18] but those data are derived from a severely malnourished Japanese population after years of war and may have limited applicability to a healthy interventionist. Some studies have reported an increased incidence of brain cancer in physicians, although these studies had very small sample sizes of six[19] and three subjects, respectively.[20]

More recent data reported by Rougin et al also have limitations.[21] The original report of nine interventionists who developed brain malignancies has been updated and now includes information about 31 current or former interventionists from around the world. Twenty-two of the 26 cases for which lesion location is known were on the left side of the brain. Rougin et al stated that the observed prevalence of left-sided brain tumors "cannot be explained by coincidence," but they also noted that their observations must be interpreted with caution.[8] The most significant limitation of the study is that the information is based on self-reported data, which inherently introduces bias.[21]

When considering these case studies, it is interesting to note that an increased incidence of gliomas has been found in other groups, including engineers, surveyors,[22,23] veterinarians,[24] artists,[20] department store workers, waitresses, salespeople, and farmers.[25] There were conflicting findings regarding the increased risk of glioma among teachers.[22,23] Additionally, it has been suggested that left-side brain tumors may be diagnosed earlier because symptoms appear earlier, and some tumors occur more frequently on the left side of the brain among the general population.[26] All of this opens the possibility that brain cancer risk may be affected by factors other than ionizing radiation.

## CELLULAR EFFECTS

Cellular studies have provided some additional information about the effects of radiation, but data are limited. Some studies have demonstrated an adaptive response to low doses of radiation, showing that exposure to very low amounts of radiation protects against subsequent larger exposures.[27] On the other hand, studies have also shown that some detrimental cellular responses are stronger at low doses than higher doses.[27] Regardless of the limited information about the effect of radiation on cellular processes, the relationship between many of these cellular processes and disease outcomes is still unknown.

## VASCULAR EFFECTS

Another concern is interventionists' risk of radiation-induced vascular disease. The high rate of cardiovascular disease and its strong dependence on lifestyle factors make it difficult to identify which cases are caused by radiation. Some cite this as a reason to use caution against claiming a causal effect between exposure to low doses and radiation and increased risk for vascular disease.[28] Multiple studies have failed to demonstrate increased risk of circulatory disease after exposure to low levels of radiation,[14,29-33] including a study of 146,022 radiologic technologists,[30,31] which may have been confounded by the healthy worker effect, survival bias, and response and participation bias.[14] Recent data on atomic bomb survivors suggest that the observed increase in cardiovascular mortality was likely due to radiation-induced renal failure rather than direct vascular damage.[14] Of note, although still important in discussing whole-body exposures, the exposure to an interventionist's kidneys is insignificant if lead is worn appropriately.

A 50-year follow-up study showed no increase in the rate of heart disease in tuberculosis patients who had received doses of approximately 1 Gy to the heart.[32] The International Commission on Radiological Protection states that the threshold for circulatory disease may be as low as 500 mGy to the heart or brain. The National Council on Radiation Protection and Measurements has concluded that there is no evidence of increased risk after heart doses below 5 Gy. Although it would be unwise to look at this information as conclusive evidence that radiation exposure has no effect on vasculature, international organizations have concluded that data are insufficient to identify a causal relationship between low levels of radiation exposure and increased cardiovascular mortality.[14,33,34]

Over a century of research has guided occupational dose limits for those who work with radiation. Despite these efforts, there are still many unknowns. The American Association of Physicists in Medicine has adopted a position statement that emphasizes that at acute doses below 50 mSv and cumulative doses over short periods of time below 100 mSv, any risk is "too low to be detectable and may be nonexistent."[35] Other organizations have taken a similar stance.[36,37] Another assumption that is starting to be challenged is the linear "no-threshold" model of radiation risk.[14,36] This is especially important, because a linear relationship is implicitly assumed in any estimate of excess relative risk,[38] as well as in the estimate of population risks provided by the BEIR VII report.[39] Currently, an interventionist's radiation exposure is limited to a total effective dose of 50 mSv per year.[40] If workers are receiving over four times this annual dose limit, as some data might suggest, then there is a cause for concern. However, other studies suggest that interventionists receive doses that are substantially below 50 mSv annually, in which case, there is little to indicate that there is any increased risk from this occupational exposure.

## CONCLUSION

It is apparent that there is substantial disagreement between position statements made by several professional organizations regarding radiation exposure and risk and claims made by the authors of studies who assert that the doses received by interventionists over a protracted period of time are a likely cause of brain malignancies. Claims that there are adverse health effects associated with even small amounts of radiation can be found throughout the medical literature and the public media. However, rigorous scientific scrutiny of the available data shows that the effect of low doses of ionizing radiation is unclear. Further, opinions on this topic may be fragmented by subspecialty, with physicians and physicist groups sometimes drawing different conclusions about radiation risk.

It is important to recognize that the effects of these opinions, whether correct or incorrect, can have real consequences on the course of clinical care for patients and in assessing one's own occupational risk. As an example, in a 2012 study of 615 health care professionals who had worked in cardiac cath labs and responded to a survey about radiation protection measures and health issues, 10.6% of respondents stopped working in the cardiac cath lab environment due to concerns about radiation exposure.[41] However, only 2.2% of respondents had ever been diagnosed with cancer—a lower incidence than in the general population. This suggests that professional decisions were made based on fear rather than fact.

We would like to emphasize that we are not trying to claim that there is absolutely no risk associated with the radiation exposure that interventionists encounter. However, we argue that investigations into these matters should be conducted with attention to detail regarding experimental design, dosimetry, and statistical analysis, with these data objectively evaluated. Additionally, new reports that reference previous studies should fully disclose the limitations of the previous work upon which their studies are based.

Little et al emphasize the importance of understanding the uncertainties associated with even the highest-quality epidemiologic studies.[28] According to the National Council on Radiation Protection and Measurements, "epidemiological uncertainties ... weaken the evidence for concluding that a radiation risk has been detected at very low doses."[14] These limitations must be entertained when interpreting studies that address risks of low levels of radiation.

Finally, it has been stated that science can never prove the nonexistence of risk, as "statistical variation will be consistent with a small effect that cannot be excluded."[28] On the other hand, the absence of statistical significance does not mean that a small risk does not exist. This is the foundation of the complexity in quantifying the risk associated with exposure to small amounts of radiation—they are consistent with nonsignificant increases in risk but also with the absence of risk.[28] ■


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**Rebecca M. Marsh, PhD**
University of Colorado School of Medicine
Aurora, Colorado
rebecca.marsh@ucdenver.edu
*Disclosures: None.*

**Michael Silosky, MS**
University of Colorado School of Medicine
Aurora, Colorado
michael.silosky@ucdenver.edu
*Disclosures: None.*