

## Physicians' exposure to radiation prompt cellular changes that may protect the body from harm

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Cardiologists who perform heart operations using x-ray guided catheters are exposed to ionising radiation at levels two to three times higher per year than those experienced by radiologists. Now, new research has found the first evidence that these constant, high levels of exposure cause changes at cell level that might represent the body's way of protecting itself against the harmful effects of radiation.

The research, published online today in the European Heart Journal, found that among ten interventional cardiologists who were regularly exposed to x-rays for their work, levels of two chemicals rose: one, glutathione, an anti-oxidant that protects against cell damage from oxygen-containing molecules called 'reactive oxygen species' (ROS), and the other, hydrogen peroxide, which indicates the amount of oxidative stress caused by the ROS.

In addition, lymphocyte cells showed increased levels of an enzyme called caspase-3, which is involved in <u>programmed cell death</u> (known as apoptosis) and which indicated an increased susceptibility of these cells (which are part of the body's immune system) to apoptosis.

The authors of the research, led by Dr Eugenio Picano, director of the Institute of Clinical Physiology at the Italian National Research Council (CNR) in Pisa, Italy, believe that these changes indicate that the <u>radiation</u> was inducing potentially harmful changes at the cellular level



(as indicated by the three-fold increase in hydrogen peroxide), but that this in turn prompted a protective response, reflected by an almost twofold increase in the antioxidant glutathione and an increased susceptibility of <u>white blood cells</u> to apoptosis, which could be the body's way of killing off damaged and potentially <u>cancerous cells</u>.

The first author of the study, Dr Gian Luigi Russo, a senior research scientist at the CNR's Institute of Food Sciences in Avellino (Italy), said: "Our findings clearly emphasise for the first time that exposure to a level of radiation, which is considered 'safe' by regulatory standards for interventional cardiologists, can induce a profound biochemical and cellular adaptation whereby increases in the levels of reactive <u>oxygen</u> species in these workers are balanced by an improvement in antioxidant defences. We also observed an increased susceptibility of lymphocytes to apoptosis, which may represent a compensatory mechanism to efficiently remove genetically damaged cells.

"It remains unclear whether these changes are adaptive, beneficial modifications or the harbinger of clinically relevant adverse changes, since increased DNA damage, oxidative stress and apoptotic activity have been involved in the development of a variety of diseases."

Interventional cardiologists are part of a larger population of about 23 million people worldwide (excluding military personnel) who are exposed professionally to ionising radiation. About seven million are medical workers who can be exposed to x-rays (e.g. interventional cardiologist) or to gamma-rays (e.g. workers in nuclear medicine). Over the past 20 years the interventional cardiologists' exposure to radiation has risen as the number of x-ray guided interventions has increased; in the USA cardiac catheterisation procedures have increased from 2.45 million in 1993 to 4.6 million in 2006, with similar trends seen in Europe.



Dr Picano said: "Each procedure involves a large radiation exposure to the patient, which may range from the equivalent of 300 to 5,000 chest xrays and more, with an average dose of 750 chest X-rays for a percutaneous coronary intervention or a cardiac radiofrequency ablation. Interventional cardiologists must work close to the source of x-rays, and this explains why their own professional exposure is three times higher than that of radiologists, and can be equivalent to the dose of 250 chest xrays per head per year. After 30 years of work, this corresponds to a lifetime's increased risk of developing cancer of approximately one in 100, although there is still some uncertainty in these risk estimates."

The researchers compared 10 interventional cardiologists with 10 health workers who were not exposed to radiation. Information on the cardiologists' exposure to radiation was obtained from their radiation badges and their lifetime exposure calculated from these data. The researchers took blood samples in order to test for glutathione, hydrogen peroxide and caspase-3.

Dr Russo concluded: "Our findings have clinical and scientific implications. Interventional cardiologists should make every effort in their daily practice to minimise their exposure, as we know that if there is a radioprotection culture in the catheterisation laboratory, then the same activity can be done with a dose reduction of 90% for doctors, staff and patients. From the scientific perspective, invasive cardiologists today have a unique opportunity to clarify the effects of chronic low dose exposure. A large study, called the Healthy Cath Lab study, is being conducted in Italy to address this question. It is done by interventional cardiologists, with the aim to clarify the cancer and non-cancer effects of chronic low dose radiation exposure.

"A good cardiologist should not be afraid of life-saving radiation, but must be afraid of radiation unawareness and negligence."



In an accompanying editorial [2], Professor Thomas Münzel and Dr Tommaso Gori from the Department of Cardiology at the University Medical Centre of Mainz (Mainz, Germany), point to some of the limitations of the study (its small size, incomplete insight on the mechanisms involved, differences in body mass index and lack of information on other cardiovascular risk factors) but write that despite this, the study is interesting. "While interventionalists were subject to more radiation-induced oxidative stress (or rather, in response to radiation-induced stress), fortunately they developed (partial) counterregulatory antioxidant defences."

They agreed with Dr Russo about the need for both more research and more awareness of protective measures by <u>cardiologists</u>. "In conclusion, more research is necessary, both at the level of basic science to understand the interaction between toxic . . . effects of ionizing radiations and hormesis phenomena, and at the level of epidemiology. While the effects of ionizing radiation remain incompletely understood, it is our responsibility as physicians to take all precautions in reducing any potential hazard to our patients, our colleagues and ourselves. The beauty of modern medical images, the personal sense of self-achievement that follows a complex, prolonged interventional procedure, must be balanced by their costs, clinical utility and risks – not least, that of prolonged operator's exposure to radiations," they write in their editorial.

**More information:** [1] "Cellular adaptive response to chronic radiation exposure in interventional cardiologists". European Heart Journal. <u>doi:10.1093/eurheartj/ehr263</u>

[2] "Biological effects of low-dose radiation: of harm and hormesis." European Heart Journal. <u>doi:10.1093/eurheartj/ehr288</u>



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