

# OCCUPATIONAL RISKS OF CHRONIC LOW DOSE RADIATION EXPOSURE IN CARDIAC CATHETERISATION LABORATORY: THE ITALIAN HEALTHY CATH LAB STUDY

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**Disclosure:** Produced on behalf of the Healthy Cath Lab (HCL) Study Group of the Italian Society of Invasive Cardiology (GISE).

**Citation:** EMJ Int Cardiol. 2013;1,50-58.

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## ABSTRACT

Contemporary interventional cardiologists have an exposure per person, per year, two to ten times higher than that of diagnostic radiologists. Cumulative doses after 30 years of working life are in the range of 50 to 200 mSv, with a projected professional lifetime attributable excess cancer risk in the order of magnitude of 1 in 100. Of special concern, the left side of the operator is more exposed (30% to 100%) than the right side, and less protected parts of the body (e.g. head and hands) can receive equivalent doses between 5 and 50 mSv per year.

Focused studies are clearly needed to define the occupational health risk of accumulated radiation exposure in catheterisation laboratories, particularly in respect of potential risk for circulatory diseases (i.e. heart disease and strokes) and effects on the cognitive function. This paper describes the rationale of the ongoing Healthy Cath Lab (HCL) Study, designed by interventional cardiologists, for interventional cardiologists. The Italian HCL project is a case-control study that will include a cohort of 500 highly exposed subjects (interventional cardiologists, nurses, and technicians working in the cath lab >3 years) and a 'best match' control group of 500 unexposed subjects. All aspects of in-room personnel radiation exposure (e.g. standard safety precautions, workload), as well the health status of each participant, will be investigated by using a web survey. In order to overcome the inherent limitations of the epidemiological approach, the relationship between radiation exposures and the risk of health effects will also be evaluated through 'early warning' signs, which are easy to measure and are capable to identify long-term risk for subsequent clinically overt disease. Examples of surrogate endpoints include chromosome aberrations analysis for cancer risk, carotid intima-media thickness and telomere shortening for atherosclerosis, and olfactory dysfunction for neurodegenerative disorders.

The HCL project will contribute in the defining of the potential occupational health effects of radiation exposure in cath lab, as well as strengthening 'the culture of safety' in the cath lab.

**Keywords:** Radiation exposure, personnel, health risk, biomarkers, Healthy Cath Lab Study.

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## INTRODUCTION

The use of radiation in medical diagnosis in Western societies is the largest man-made source of radiation exposure,<sup>1,3</sup> especially for the growing use of computed tomography and interventional cardiology. Over the last 20 years, the number of interventional cardiovascular procedures has increased rapidly. In Europe, arteriography and interventions were 350,000 in 1993 and >1 million in 2001.<sup>4</sup> On average, a left ventriculography and coronary angiography correspond to a patient radiation exposure of about 300 chest X-rays; and a percutaneous coronary intervention (PCI) or a cardiac radiofrequency ablation to 750 chest X-rays (range:350-2350).<sup>5</sup> In adult cardiology, interventional cardiology procedures account for 12% of examinations, and 48% of the total collective dose.<sup>6</sup> In children with congenital heart disease, invasive cardiology (with diagnostic and interventional catheterisation) accounts for 6% of all radiological examinations and 84% of the collective dose.<sup>7</sup> Typical effective doses for common cath lab procedures are reported in Table 1.<sup>5,8-12</sup> The high levels of patient exposure imply a significant professional exposure for the interventional cardiologist, who needs to operate near the patient and the radiation source. The single dose per procedure of the operator is on the order of magnitude of one thousandth microSv of the exposure of the patient.<sup>13</sup>

Effective occupational doses per procedure range from 0.02 to 38 microSv for diagnostic catheterisation and may reach even higher values per complex procedure, such as up to 200 microSv per single procedure of endovascular thoracoabdominal aneurysm repair.<sup>13</sup> Each operator performs hundreds or thousands of procedures each year, and therefore the cumulative dose in a professional lifetime is not negligible. The most active and experienced interventional cardiologists in high-volume cath labs have an annual exposure equivalent to around five mSv (below apron) per year, two to three times higher than that of diagnostic radiologists.<sup>14</sup>

Cumulative doses after 30 years of working life are in the range of 50 to 200 mSv, corresponding to a whole body dose equivalent of 2,500 to 10,000 chest X-rays with a projected professional lifetime attributable excess cancer risk of 1 in 100.<sup>15</sup> Of special concern, in interventional cardiologists the head organ dose is 10 to 20-fold higher than the whole-body dose recorded below apron.<sup>16-18</sup>

Although there is a general appreciation that radiation by itself is certainly not a good thing for the patient or the operator, the characterisation of health effects (cancer and non-cancer) of chronic low-dose radiation is still incomplete and difficult.<sup>19-21</sup> Recently, a joint effort of American professional societies led to the formation of the Multi-Specialty Occupational Health Group (MSOHG), dedicated to defining the occupational risks associated with working in a fluoroscopic laboratory in collaboration with experts in occupational health, epidemiology, and radiation effects from the United States Navy and the Radiation Epidemiology Branch of the National Cancer Institute.<sup>20</sup> The main initial goal of MSOHG is to perform epidemiological studies for assessing the incidence of cancer and other serious disease outcomes (including cardiovascular disease and cataracts) by comparing physicians performing fluoroscopically-guided procedures (including interventional cardiologists, radiologists, neuroradiologists and others), with non-interventional radiologists, and physicians who are unlikely to be exposed to occupational radiation (e.g. family physicians or psychiatrists).

Another study has now started in Italy, the Healthy Cath Lab (HCL) study, and is organised by the Italian National Research Council with endorsement from the Italian Society of Invasive Cardiologists.

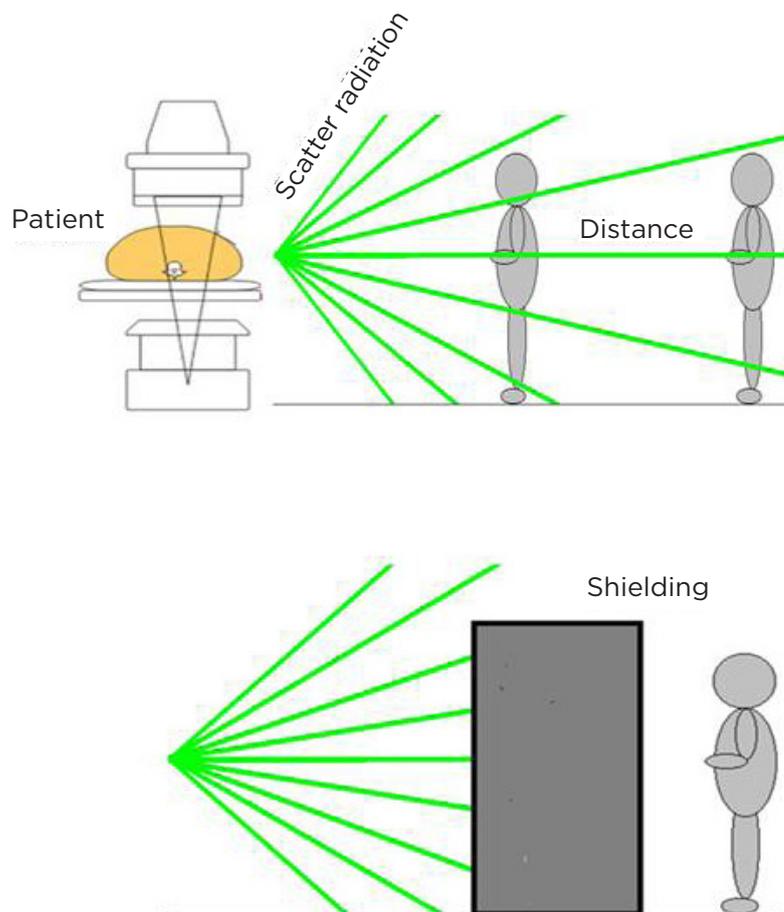
This paper describes the rationale of the ongoing Italian project designed by interventional cardiologists for interventional cardiologists.

## CURRENT STATUS OF KNOWLEDGE

### Radiation Exposure of Interventional Cardiologists

Ionising radiation from the fluoroscopy tube is scattered by the patient while the cardiac intervention is underway (Figure 1). The operator's distance from the patient's skin entrance site is crucial because the level of scatter radiation is inversely proportional to the distance squared.<sup>22</sup> In addition, the operator's position and body height have a major impact on the amount of scatter radiation to different parts of the operator's body.<sup>23-25</sup>

Several investigations clearly showed that the left side of the operator is more exposed than the right side in most cases due to the usual layout of an interventional room, where the cardiologist operates from the right side of the patient so that the scatter radiation comes predominantly from



**Figure 1. Radiation exposure distribution in the interventional cardiologist.**

Radiation exposure on the left is almost double that on the right side.<sup>14,22</sup> Key factors in protection of cardiologists are distance and shielding. Increasing the distance from the radiation beam decreases the risk of exposure. Protective shielding includes structural shielding, mobile shielding and personal shielding. Eye, thyroid and brain that should be carefully protected by glasses, collars and cap.

the patient on his/her left.<sup>23-25</sup> Of special concern, in interventional cardiologists the head organ dose (if left unprotected) is 10 to 20-fold higher than the dose recorded beneath the apron.<sup>26,27</sup>

Annual exposure to the cardiologist's head is in the range of 20–30 mSv per year<sup>27</sup> or much higher if a ceiling-suspended screen is not used.<sup>16,28</sup> This implies that the lifetime estimated organ head dose for a busy interventional cardiologist after 25 years of work in the catheterisation laboratory is in the order of magnitude of 1 to 3 Sv (21). Unfortunately, the practice of interventional cardiology is sometimes accompanied a suboptimal perception of radiation risk and by negligent use of radiation protection tools.<sup>29-31</sup> Radioprotection awareness by operators is dramatically effective in reducing professional exposure by 90%.<sup>16</sup> Today, in most cardiology imaging laboratories and in interventional radiology fluoroscopy rooms, overhead radiation shields, thyroid shields, and leaded aprons are employed to reduce the radiation doses to the head and neck of

operators. It is rare that unprotected radiologists or cardiologist would do an angiography procedure. Unfortunately, this was not the most common situation in the past, and even today it is not the rule in each and every laboratory.<sup>29-31</sup>

### Cancer Risk

The radiation exposure in cath labs is associated with a small but definite stochastic risk of inducing a malignant disease, in the range of 1 in 100 for many operators who cumulate around 100 mSv professional exposure, corresponding to operators who carry out up to 400-800 PCI procedures per year for more than 20 years.<sup>15</sup> To date, however, clinical evidence of an increased cancer risk for interventional cardiologists is only suggestive,<sup>21,32</sup> with anecdotal reports of haematologic malignancies and other cancers being common conversation at societal meetings.<sup>20</sup>

Recently, two reports described the disproportionate number of tumours on the left side of the

brain, the region of the head known to be more exposed to radiation and least protected by traditional shielding.<sup>33,34</sup>

Clearly, the observational nature of these findings do not allow the establishment of a causal connection between occupational radiation exposure and the development of brain cancer, and substantially limits firm conclusions.<sup>34</sup>

On the other hand, there is a growing body of biological data showing cellular changes induced by professional low-dose X-ray radiation exposure in interventional cardiologists to low-dose radiation prompts cellular changes.<sup>35-37</sup>

Indeed, our recent biological data showed that occupational exposure to low-dose radiation is associated with an increased activity of antioxidant enzymes, as protection against the increased production of ROS as well as an increased susceptibility to apoptotic induction which might efficiently remove genetically damaged cells.<sup>35</sup>

Furthermore, interventional cardiologists have a two-fold increase in circulating lymphocytes of chromosome aberrations and/or micronuclei, which represent surrogate biomarkers of cancer risk and intermediate end points of carcinogenesis.<sup>36,37</sup> Importantly, the increase in chromosomal DNA damage is further enhanced in the presence of genetic polymorphisms of genes involved in DNA repair, suggesting that an individual predisposition may play an important role in the cellular response to radiation exposure and health risk.<sup>38</sup>

### **Radiation-Induced Cataracts in Interventional Cardiologists**

Among eye tissues, the lens is the most radiosensitive and thus cataract formation may be the primary ocular complication associated with ionising radiation exposure.<sup>19</sup>

Until recently, the dose threshold for radiation-induced lens opacities was considered two Gy for a single dose or five Gy for fractionated dose. Currently, radiation-induced cataract, previously thought to be deterministic (tissue reactions), is recognised as possibly stochastic in nature, and occurring at much lower radiation exposure level than previously thought.<sup>39</sup>

Indeed, several epidemiological studies showed that an increased incidence of lens opacities at doses below 0.5 Gy.<sup>40</sup> Accordingly, on April 21, 2011 the

International Commission on Radiological Protection (ICRP) slashed the earlier dose limit of 150 mSv in a year for the lens of the eye, to the present 20 mSv in a year, averaged over a defined period of 5 years, with no single year exceeding 50 mSv.<sup>39</sup> Eye cataracts, which can be observed in one-third of staff after 30 years of work<sup>22</sup> and the Occupational Cataracts and Lens Opacities in Interventional Cardiology: the O'CLOC study performed in France indicated a high risk of posterior subcapsular opacities in the population of interventional cardiologists.<sup>41</sup>

### **Reproductive Health**

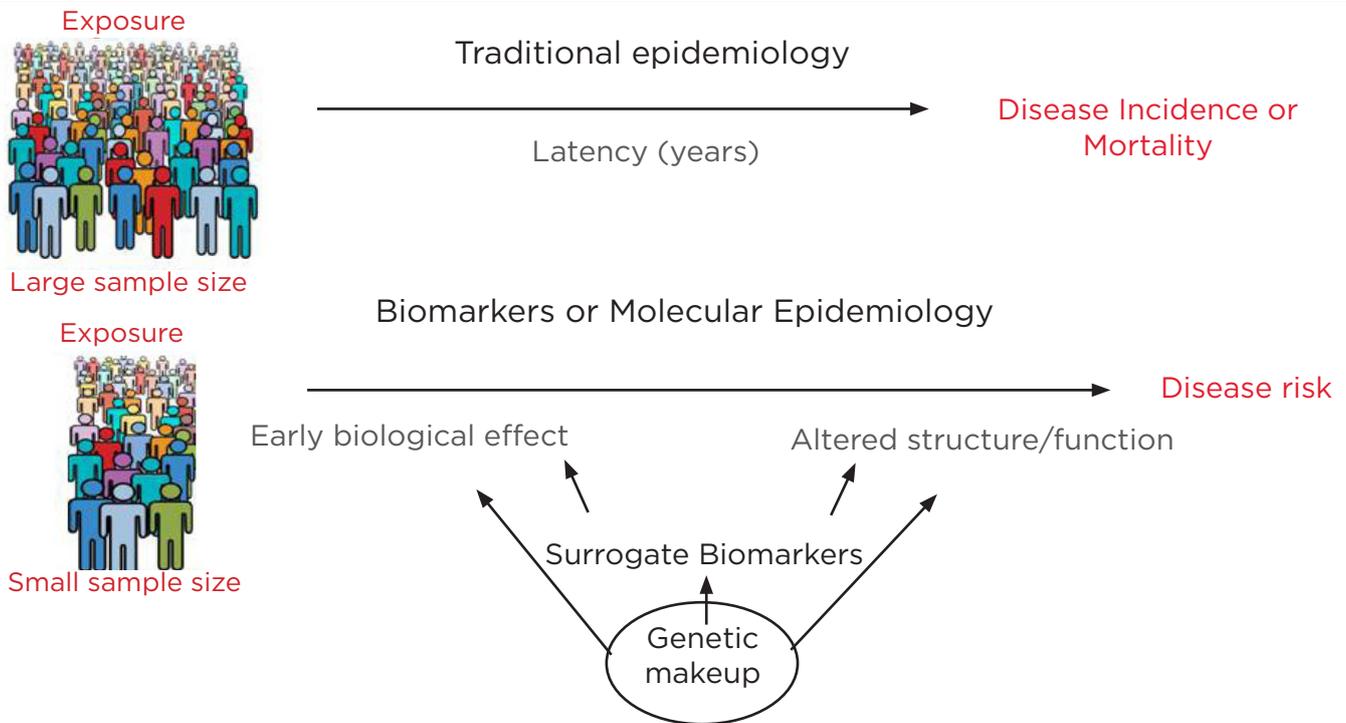
Ionising radiation exposure can affect the reproductive health of exposed fathers and exposed mothers.<sup>42,43</sup> For interventional cardiologists, the gonad dose (below lead apron) is in the same order of magnitude of the shielded thyroid dose, with a median of 10-100 microSv per cine-angiography procedure. The dose can be ten-fold higher for a complex interventional procedure. This leads to a cumulative exposure in the 0.5-1 Sv range over a professional lifetime of 30 years.<sup>44</sup>

A borderline increase with respect to chromosomal abnormalities (excluding Down's Syndrome) in children of female radiographers has been reported in the literature.<sup>45</sup> Furthermore, a small study on 90 exposed male radiographers (and 90 unexposed controls) reported a worrisome increase in the risk (with relative risks ranging from 2 to 10) of reproductive health problems, including miscarriages, still births, and major congenital abnormalities at birth.<sup>46</sup> Furthermore, exposed fathers might be mostly fathers of daughters, as suggested by preliminary data obtained in male radiographers.<sup>47</sup>

However, the human data on adverse hereditary effects that could be attributed to radiation remain contradictory, and exact quantification remains a scientific and social challenge.<sup>44,48</sup>

### **Non-Malignant Thyroid Diseases**

Thyroid disease is another important target for deleterious effects of ionising radiation. Several studies have reported that the risk for malignant and benign thyroid nodules increased with external irradiation and internal radiation exposure as well as an association between autoimmune thyroid diseases and radiation exposure.<sup>49</sup> However, the effects of low dose radiation on functional thyroid diseases remains largely unknown.<sup>49</sup>



**Figure 2. Conceptual model for using biomarkers and surrogate endpoints to assess exposure risk.**

Traditional epidemiology aims at identifying the relationship between the exposure and disease incidence or mortality. Along the continuum between exposure and disease development, selected biomarker sets may provide information on the extent of biological effects and early changes in the disease process as well as identify individuals with a particularly high risk of disease development, allowing to implement disease prevention programs.

## Cardiovascular Disease

At the present time, there is good evidence that at moderate doses (>500 mSv) ionising radiation is a risk factor for cardiovascular disease, but it is unclear whether risks still persist in low doses.<sup>21</sup>

According to International Commission on Radiological Protection (ICRP) 2012, a dose of 500 mSv may lead to approximately 1% of exposed individuals developing cardiovascular or cerebrovascular disease, more than 10 years after the exposure, in addition to the 30-50% suffering of disease independently of the exposure.<sup>50</sup>

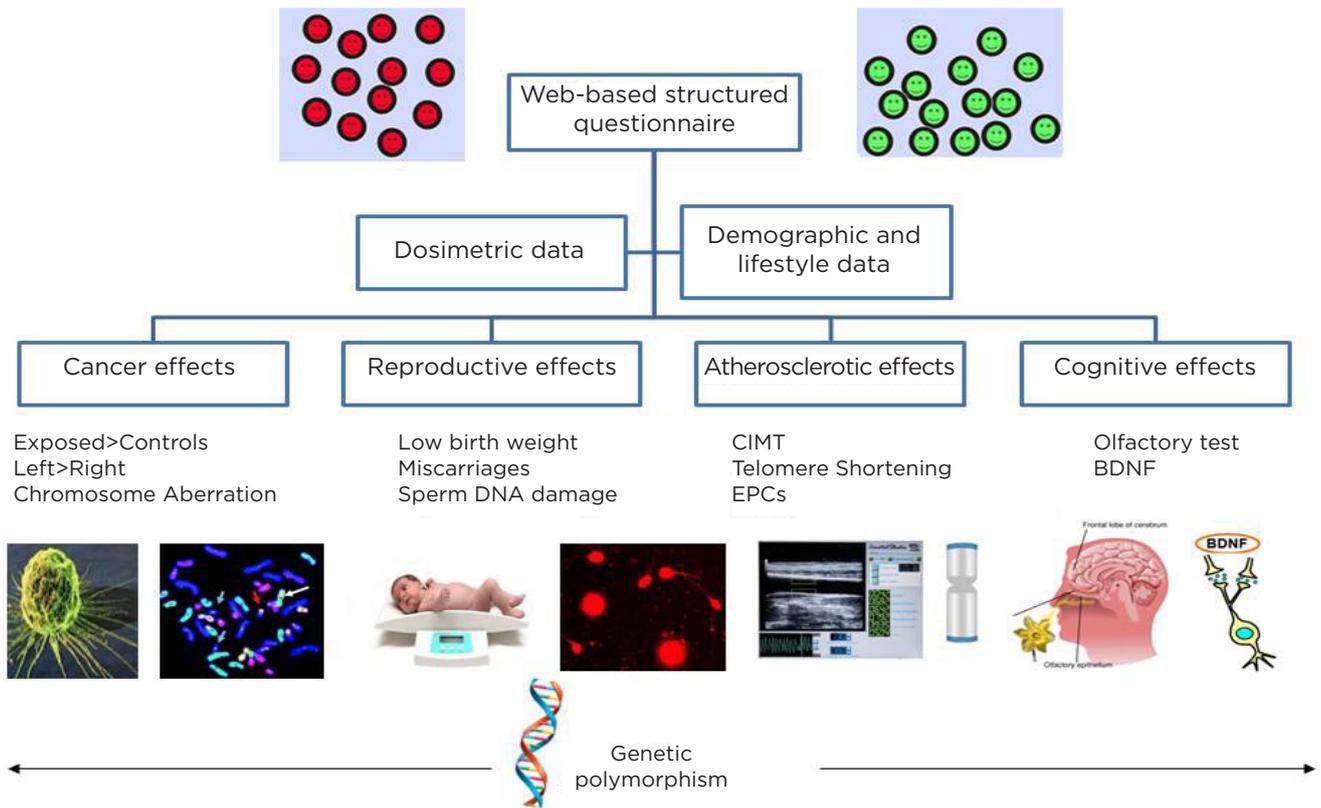
It is unclear whether or not the threshold is the same for acute, fractionated, and chronic exposures, and in the absence of evidence, it is assumed that the threshold dose is the same in all cases (50). A recent meta-analysis showed excess population risks for all circulatory disease from low-dose (cumulative mean <500 mSv) whole-body exposure or exposures at a low dose rate (i.e. <10 mSv/day) ranging from 2.5% to 8.5%/mSv, indicating that population-based excess mortality risks for circulatory disease are similar to those for radiation-induced cancer.<sup>51</sup> However, most of the epidemiologic evidence on low dose radiation

and risk of cardiovascular death have important limitations, mainly due to the heterogeneity among studies (particularly for non-cardiac endpoints), the statistical power and small sample size and the lack of information on potential confounders.<sup>51</sup>

## Brain Function Effects

The brain is a paradigm of a highly differentiated organ with low mitotic activity and is thus considered radio-resistant according to a fundamental law of radiobiology ('law of Bergonié and Tribondeau', 1906). However, cognitive dysfunction has been linked to white matter damage in the brain following radiotherapy.<sup>52</sup>

Furthermore, there is clinical evidence (Chernobyl fall-out) of cognitive impairment and schizophrenia.<sup>53</sup> Experimental studies showed a reduction in adult neurogenesis by prenatal irradiation that may be associated with schizophrenia-like behaviour in rodents<sup>54</sup> and Alzheimer's disease.<sup>55</sup> Additional studies have provided evidence for apoptosis, neuro-inflammation, loss of oligodendrocyte precursors and myelin sheaths with apparent preservation of axons,<sup>56</sup> and irreversible damage to the neural stem cell compartment with long-term impairment



**Figure 3. Overall view of the Health Cath Lab project.**

Within a case-control study design, the project will employ molecular markers and clinical surrogate endpoints to investigate if occupational radiation exposure correlates with the risk of cancer and non-cancer disease.

of adult neurogenesis.<sup>57</sup> For any given cumulative dose, repetitive exposures are more detrimental for neurogenesis than single acute exposures.<sup>58</sup>

### RATIONALE FOR THE ITALIAN HEALTHY CATH LAB STUDY

The overall picture is not completely reassuring and underlines the need to define the occupational cancer and non-cancer risks of accumulated radiation exposure in the cath lab.

The detection of the potentially increased health risks remains difficult through the epidemiological approach. This approach requires one million people followed-up for several decades to detect an extra-incidence of fatal cancer of moderate entity.<sup>59</sup> An alternative strategy to the epidemiological approach, is to detect the potentially increased radiation health risks through ‘early warning’ signs, which evaluate initial damage through surrogate endpoints which are easy to measure, non-invasive, and are capable of identifying long-term health risks (Figure 2).

The HCL study is focused on the use of surrogate but robust biomarkers for cancer and other disease,

according to a recent recommendation of the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR 2008), asking that ‘more attention should be given to other (radiation-induced) non cancer disease entities, and future epidemiological studies should be designed to assess clinical and sub-clinical endpoints as well as biomarkers’.<sup>60</sup>

The HCL research is a case-control study that will include a cohort of 500 highly exposed subjects (interventional cardiologists and nurses and technicians working in the catheterisation lab >3 years) and a ‘best match’ control group of 500 unexposed subjects (matched for age and gender).

A national survey has been launched by the Italian Society of Interventional Cardiology SICI-GISE in order to investigate all aspects of in-room personnel radiation exposure, including the presence of equipment, the standard safety precautions, the dosimetry methodologies adopted in all national cath laboratories, and all practice performed in working life (e.g. type and number of procedures, use of protective devices). Information on the health status of each participant will be collected through

a structured questionnaire, including questions on all study endpoints as well as on items concerning smoking habits, alcohol intake, drug consumption, medical history including diagnostic radiation exposures, and all other lifestyle and socioeconomic confounding factors.

Furthermore, the project will directly evaluate potential radiation-health risk damage through the systematic use of surrogate markers for subsequent clinically overt disease.

Examples of surrogate endpoints adopted in the present study include chromosome aberrations analysis in circulating peripheral lymphocytes for cancer risk, increased carotid intima-media thickness and telomere shortening for atherosclerosis, low birth weight in offspring and DNA damage in the male germ cell line for reproductive damage, olfactory dysfunction and circulating plasma brain-derived neurotrophin (BDNF) for neurodegenerative conditions (Figure 3). Finally, the evaluation of genetic polymorphism associated with radiation-response will help to identify subjects more vulnerable to radiation-induced health effects.<sup>38</sup>

## CONCLUSION

Chronic radiation exposure represents major occupational health concern among interventional physicians. Further data will soon be available from both North American and Italian studies.

The Multispecialty Occupational Health Group (MOHG) is undertaking a cohort mortality study comparing cancer and other serious disease outcomes, including cardiovascular disease and cataracts.

However, epidemiological studies on occupational exposures require hundreds of thousands of workers followed-up for decades to detect a small increase in risk. Individual variability and poorly understood adaptive mechanisms may further weaken the link between physical dose and observed damage. HCL study will use surrogate but robust biomarkers for health risk in order to better define the fundamental biochemical, cellular and molecular mechanisms involved at chronic low-dose exposure.

The expected project output will be the development of potential biomarkers for a more effective radioprotection program. Such biomarkers may be useful to identify a subset of individuals more vulnerable to radiation damage, which might represent the target of preventive measurements (by radiation sparing policy or attempts to pharmacologic or dietary radioprotection). Finally, the project is expected to have a more profound impact on the growth of the suboptimal culture of safety among invasive cardiologists, contributing to eradicate the 'radiological machismo' which profoundly contributes to disseminating useless doses (and risks) in the catheterisation lab.<sup>30</sup>

	Diagnostic procedure	Average effective, mSv dose (range)	Equivalent number of chest x-rays
<b>ADULT</b>	Diagnostic invasive coronary angiogram	7 (2-16)	350 (100-800)
	Percutaneous coronary intervention	15 (7-57)	750 (350-2850)
	Dilation chronic coronary occlusion	81 (17-194)	4050 (850-9600)
	Aortic valvuloplasty	39	1950
	Head and/or neck angiography	5 (1-20)	250 (50-1000)
	Thoracic angiography of pulmonary artery or aorta	5 (4-9)	250 (200-450)
	Abdominal angiography or aortography	12 (4-48)	600 (200-2400)
	Endovascular thoraco-abdominal aneurysm repair procedure	76-119	3880-5950
	Pelvic vein embolisation	60 (44-78)	3000 (2200-3900)
	<b>PEDIATRIC*</b>	Diagnostic cardiac cath	6.0 (0.6-23.2)
ASD		2.8 (1.8-7.4)	Age-dependent
Patent ductus arteriovenous occlusion		7.6 (2.1-37)	Age-dependent
Balloon dilation		8.1 (2.9-2.0)	Age-dependent

**Table 1. Typical effective doses from cath procedure exposure.**

mSv = DAP x 0.183 \*In pediatric catheterisation, the conversion factor is higher and very dependent on the patient's age: mSv = DAP x 3.7 for newborns; 1.9 for 1 year; 1.0 for 5 years; 0.6 for 10 years; 0.4 for 15 years.

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