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Biological and physical methods for risk estimation in interventional radiology: a detrimental effect approach

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Abstract— **Interventional radiologists and staff members are frequently exposed to the effects of direct and scattered radiation, which undergo in deterministic effects (radiodermitis, aged skin, cataracts, telangiectasia in nasal region, vasocellular epitelioms, hands depilation) and/or stochastic ones (cancer incidence). A methodology has been proposed for estimating the radiation risk or detriment from a group of six exposed interventional radiologists of the Hospital Universitario La Fe (Valencia, Spain), which had developed general exposition symptoms attributable to deterministic effects of ionizing radiation. Equivalent doses have been periodically registered using termoluminiscence dosimeters (TLD's) and wrist dosimeters, $H_p(10)$ and $H_p(0.07)$, respectively, and estimated through the observation of translocations in lymphocytes of peripheral blood (biological methods), by extrapolating the yield of translocations to their respective dose-effect curves. The software RADRISK has been applied for estimating radiation risks in these occupational radiation exposures. The minimum and maximum average excess ratio for skin cancer has been, using wrist physical doses, of [1.03 x 10^{-3},5.06 x 10^{-2}], concluding that there is not an increased risk of skin cancer incidence. The minimum and maximum average excess ratio for leukemia has been, using TLD physical doses, of [7.84 x 10^{-2},3.36 x 10^{-1}], and using biological doses, of [1.40 x 10^{-1},1.51], which is considerably higher than incidence rates, showing an excess radio-induced risk of leukemia in the group under study. Finally, the maximum radiological detriment in the group, evaluated as the total number of radio-induced cancers using physical dosimetry, has been of 2.18 per 1000 person-year (skin and leukemia), and using biological dosimetry of 9.20 per 1000 PY (leukemia). As a conclusion, this study has provided an assessment of the non-deterministic effects (rate of radio-induced cancer incidence) attributable to the group under study due to their professional activity. Keywords: Interventional radiology, radiation risk, biological dosimetry, radiation protection**

I. Introduction

Interventional procedures have been rapidly developed during last decade, concerning the type and complexity of examinations and their frequency. Interventional radiologist and staff members applying these procedures are frequently exposed to protracted and fractionated low doses of low-linear energy transfer (LET) ionizing radiation, which extend over all their professional activities (ICRP 85).

Up to now, factors affecting received dose to staff have been analysed, such as fluoroscopy time, number of frames, field size, technical characteristics of radiation equipment, patient size, examination type and operation mode, complication of examination, radiation protection measures and staff experience (Padovani et Rodella 2001, Paulson et al. 2001, Kemerink et al. 2002). Received doses can be considerably increased if inappropriate x-ray equipment or inadequate radiation protection practices are used (Kottou et al. 2005).

Interventional exposures can derive, due to the effects of direct and scattered radiation, in deterministic effects (radiodermitis, aged skin, cataracts, telangiectasia in nasal region, vasocellular epitelioms, hands depilation) and/or stochastic ones (cancer incidence) (Vano et al. 1998a, 1998b). Improved understanding of both the qualitative and quantitative aspects of cancer incidence after exposure is important for developing models about biological mechanisms of induced-radiation carcinogenesis and ensuring guidelines to radiation protection and detriment estimation (ICRP 1991, UNSCEAR 2006)

Since the early 1960s, cytogenetic dose estimation based on analysis of dicentric chromosomes in solid stained metaphases has been used as the most reliable biological dosimetry method. It has been recently observed that there is a relation between the increased level of chromosome aberrations in peripheral blood lymphocytes and the risk of cancer, although it has not been well quantified (Bonassi et al. 2002). Biological dosimetry methods have been applied not only to assess acute doses but also to evaluate protracted doses like those received occupationally in professional activities (IAEA 2001)

In case of past or chronic exposures, an alternative to the conventional use of dicentrics is the analysis of translocations. After an exposure to ionizing radiation, translocations are induced at a frequency similar to dicentrics (Barquinero et al. 1999), but translocations are stable aberrations which remain relatively constant over time (Lloyd et al. 1998, Lindholm et al. 2002). Translocations can be detected easily by fluorescence in situ hybridization (FISH), and their analysis is a valuable tool in cases of past or longterm exposures (Edwards et al.

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2005).

The aim of the present study is to estimate and compare radiological detriments attributable to a group of interventional radiologists from the radiology department of the Hospital Universitario La Fe (Valencia) using physical and biological dosimetry methods due to their professional activities. This group has been selected from approximately 700 workers exposed to ionizing radiation sources because of the general symptoms observed in routine monitoring medical exposures (i.e. radiodermitis, hands depilation, telangiectasia in nasal region, aged skin, vasocellular epithelioms) In section II the group of radiologists, the dosimetry methods and the methodology for estimating radiation risks are described, the results of the analyses are presented and discussed in section III, and finally the general conclusions of the analyses are presented in section IV.

II. Materials and Methods

A. Study population

There are approximately six thousand workers in the Hospital Universitario La Fe (Valencia, Spain), from which about 700 are exposed (directly or indirectly) to ionizing radiation sources, and among them 193 interventional radiologists. Periodic medical examinations have shown only in a group of six interventional radiologists general symptoms probably attributable to deterministic effects of exposures to ionizing radiation, such as aged skin, telangiectasia in nasal region, hands depilation, brittle nails, radiodermitis or vasocellular epithelioms. This group was exposed to direct and scattered X-rays sources over a variable period between 8 and 28 years, being routinely monitored each month with personal dosimeters: termoluminiscence dosimeters (TLD's) and film badges for wrists. Medical procedures used by the group of radiologists consisted of endoscopic retrograde cholangiopancreatography (ERCP), vascular interventionist, angiography, and insertion of nasoenteric tubes or prosthesis in the gastrointestinal tract.

B. Physically recorded and biologically estimated dosimetry

Physically recorded doses have been obtained from personal dosimeters placed on the wrist, $H_p(0.07)$, and thermoluminescence dosimeters (TLD's) placed near the chest, $H_p(10)$ (ICRP 1991). Biologically estimated absorbed doses have been estimated by extrapolating the yield of observed translocations to their respective dose-effect curves. Chromosome aberrations were detected by fluorescence plus Giemsa staining and fluorescence in situ hybridization (FISH). Biological doses from extrapolating the yield of traslocations have been extended homogeneusly among the years of professional activity, equivalent to the years of wearing TLD dosimeters.

Table I and II show a description of the group of six radiologists and presents physically recorded and biologically estimated doses. As observed, physical recorded doses have been under limits of overexposure. Although a maximum effective dose of 48.7 mSv in a year has been recorded for case 4, average limit of 20 mSv in five years, defined in spanish legislation, has not been overpassed. Wrist dosimeters are not obligatory for interventional radiologists and equivalent doses at the extremities have been in all cases lower than 500 mSv limit. However, wrist equivalent doses could be lower than those delivered to the hands and this limit could be overexposed, as discussed in section III.

TABLE I

Physically recorded doses (mSv)

Case	Sex	Age	Physical doses		
			TLD - $H_p(10)$(mSv)		
			Years (t_j)	$\sum_j d_j$	$[d_{min}, d_{max}]^{(a)}$
1	m	56	22	75.2	[0,14.8]
2	m	43	8	21.3	[0,7.1]
3	f	45	13	60.2	[0.3,26]
4	f	58	25	228.1	[0,48.7]
5	f	57	27	115.2	[0,21]
6	m	54	28	105.8	[0.8,13.8]
			Wrist - $H_p(0.07)$ (mSv)		
			Years (t_j)	$\sum_j d_j$	$[d_{min}, d_{max}]$
1			13	988.9	[0,238.1]
2			5	450.6	[60.7,122.1]
3			12	776.0	[7.8,169.9]
4			3	201.9	[49.8,152.1]
5			1	25.9	[-,-]
6			24	216.6	[0,167.4]

$^{(a)}$ Minimum and maximum registered values during the years wearing TLD/wrist dosimeters

TABLE II

Biologically estimated absorbed doses (mGy) (Montoro et al. 2005)

Case	Biological doses (mGy) with 95 % CL	
	$f_i^{(a)}$	$D^{(b)}$
1	0.0142	546 [236-940]
2	0.0036	46 [0-289]
3	0.0047	99 [0-376]
4	0.0150	596 [73-1710]
5	0.0061	166 [8-440]
6	0.0120	441 [179-773]

$^{(a)}$ Frequency of simple translocations per analyzed cell with FISH stained preparations
$^{(b)}$ Estimated doses for translocations using the dose-effect curve:
$Y = (0.86 \pm 0.13)x10^{-2} + (6.57 \pm 1.06)x10^{-2}D + (4.15 \pm 0.55)x10 - 2D^2$

C. Hazard functions and radiation risk estimators

The hazard function $\lambda_b(t_k)$ is defined as the natural probability of dying from a cancer type b at age t_k in absence of exposure, that is, the mortality rate of cancer type b, whereas the hazard function $\Lambda_b(t_k|\vec{z})$ is defined as the probability of mortality from cancer b at an age t_k due to an exposure at age t_e. The vector $\vec{z}$ is a set of covariates which takes into account influence of the effects of ionizing radiation in the individual, such as sex, age-of-exposure (t_e), absorbed or equivalent doses (d) or latency period (L). The risk of exposure-induced death (REID) is defined as the probability that an individual died from a radiation induced cancer over all of his or her life (ICRP 1990, 2007). The REID is estimated as

$$REID(t_e|\vec{z}) = \sum_{t_j=t_e+L}^{t_M} s_1(t_j|\vec{z}) EAR_b(t_j|\vec{z}) \qquad (1)$$

where t_e is the age-at-exposure, EAR is the excess absolute risk of the population under study, $\vec{z}$ is the vector of covariates, L is the latency period and $s_1(t_j|\vec{z})$ is the survival function, affected from increased radiation-induced mortality.

The parameter s_1 is dependent on mortality induced by ionizing radiation, through the transport model used for the risk estimation. The lifetime attributable risk (LAR) is an approximation of the $REID$, differing in that the survival function does not take into account of people dying from radiation-induced cancers, simplifying calculations. These estimators are slightly different at low doses, due to difference in the order of magnitude of the EAR and λ_b (Kellerer et al. 2001, Ramos et al. 2005a). The LAR is estimated from an age t_j in which cancer is observed clinically to an age t_M in which death occurs, being calculated as

$$LAR(t_e|\vec{z}) = \sum_{t_j=t_e+L}^{t_M} \hat{s}_1(t_j) EAR_b(t_j|\vec{z}) \quad (2)$$

where the estimator of the survival function is obtained as

$$\hat{s}_1(t_j) = \prod_{t_i=t_e}^{t_j} [1 - \lambda_{all}(t_i)] \quad (3)$$

being λ_{all} the baseline mortality function for all causes of the population under study.

D. RADRISK software

The RADRISK is a software which has been developed by the authors for the estimation of radiological detriments in population exposed to ionizing radiation. This software is based on transport models from epidemiological studies of population exposed to external sources of ionizing radiation, such as Hiroshima and Nagasaki atomic bomb survivors (UNSCEAR 2006). It loads from external files the dosimetric data (received/estimated doses), the incidence/mortality cancer historial and the mortality distribution of the population under study. The epidemiological models are implemented in the software for calculating the lifetime attributable risk (LAR) in the studied population. This software has been developed on Matlab 7.0, based on a previous software which is used for estimating the breast cancer incidence and mortality in screening programmes (Ramos et al. 2005b, Ferrer 2005).

III. Results and discussion

As observed, there is a low increment in predicted cancer incidence in some cases due to exposed radiation, especially for leukemia, using physical doses, and a high important incidence using biological doses. The estimated LAR for induced non-Hodgkin lymphomas is negligible for females, derived from the lack of EAR trend from the UNSCEAR 2006 report (Table III)

In the case of non-solid cancers, analysing cancer incidence derived from physically recorded doses (TLD), the probability that individuals 4 and 6 suffer from leukemia is almost 3 times greater than for individuals 2 and 3. Furthermore, there is a slight increased risk for other non-solid cancer evaluated (Hodgkin's, no-Hodgkin's and multiple myeloma) from estimated LAR in all individuals studied. As observed, higher differences are among cases when evaluating leukemia incidence from biological recorded doses; for individuals 1, 4 and 6 the probability of suffering from this disease is approximately 8 times greater than for cases 2 and 3. For the other non-solid cancer evaluated there is not an increased risk, although cases 1 and 6 has a greater probability of suffering from non-Hodgkin's lymphoma and multiple myeloma. These differences could be caused by the higher accumulated biological doses and the homogeneusly division of biological doses over the exposed period.

TABLE III

Average excess ratio of radio-induced cancers (η) and total radiological detriment of radio-induced cancers per 1000 PY - Skin and non-solid cancers

Physical dosimetry			
Case	Skin cancer[(a)] (η)	Leukemia (η)	Total (A)
1	5.06 x 10^{-2}	2.06 x 10^{-1}	2.18
2	3.09 x 10^{-2}	7.84 x 10^{-2}	1.04
3	4.75 x 10^{-2}	1.07 x 10^{-1}	1.45
4	1.31 x 10^{-2}	3.36 x 10^{-1}	2.05
5	1.03 x 10^{-3}	2.10 x 10^{-1}	1.15
6	1.26 x 10^{-2}	3.22 x 10^{-1}	2.19
Biological dosimetry			
Case	Leukemia (η)	Total (B)	
1	1.42	8.68	
2	1.40 x 10^{-1}	0.85	
3	1.78 x 10^{-1}	0.96	
4	1.04	5.62	
5	3.05 x 10^{-1}	1.64	
6	1.51	9.20	

[(a)] Non-melanoma skin cancer baseline incidence

The minimum and maximum average excess ratio for skin cancer has been, using wrist physical doses, of [1.03 x 10^{-3},5.06 x 10^{-2}]. Light pigmented skin races have high and frequent incidence cases of non-melanoma skin cancers, which are not continuosly followed-up in cancer registries, and consequently, this excess ratio is still lower, concluding that there is not an increased risk of skin cancer. However, eventual carcinomas on hands or extremities are expected to be analysed in the future. The minimum and maximum average excess ratio for leukemia has been, using TLD physical doses, of [7.84 x 10^{-2},3.36 x 10^{-1}], and using biological doses, of [1.40 x 10^{-1},1.51], which is considerably higher than incidence rates, showing an excess radio-induced risk of leukemia in the group under study. For other non-solid cancers, the excess ratio has been in the order of or lower than baseline rates, in the case of physical doses, whereas in the case of biological doses, are slightly higher than natural ones, derived from higher values of biological doses. Finally, the maximum radiological detriment in the group, evaluated as the total number of radio-induced cancers has been of 2.18 per 1000 person-years (skin and leukemia) using physical dosimetry, and using biological dosimetry of 9.20 per 1000 PY (only leukemia).

Differences in these results are due to the fact that physical doses are lower than biological doses, although radio-induced skin cancer incidence has been included in the former.

There are a great source of uncertainties in the registration and estimation of physically recorded doses and the biologically estimated ones. Biological estimated doses were clearly higher than the accumulated equivalent doses from TLD's reading. These differences could be explained considering that radiologists did not always wear their dosimeters (hypothesis 1), or that dosimeters were not always in the radiation field with a possible partial body exposures (hypothesis 2), or due to the uncertainties derived from the use of a dose-effect curve (hypothesis 3), but it is remarked that the 95% inferior confidence limit of the biological doses is higher than the physical accumulated received doses for radiologists 1 and 6, pointing that the reason of discrepancy could be due to hypothesis 1 and 2. The low discrepancies between physical and biological doses for radiologists 2, 3 and 5 can be explained by hypothesis 3, while for radiologists 4, this discrepancy could be explained by all of three hypothesis. Hypotheses 1 and 2 are validated due to the fact that the numer of years wearing wrist and TLD dosimeters are not the same and that the minimum registered dose (d_{min}) in a year is in some cases zero. A lack of registration in the use of wrist dosimeters, compared with the high values of TLD's equivalent doses, reveals the necessity of increase the follow-up and control in radioprotection practices.

IV. Conclusions

Despite all uncertainties transporting risks, the average radiological detriment, expressed as the Lifetime Attributable Risk (LAR) and the excess ratio of radio-induced cancers, is appreciable for some cases and some cancer incidence, such as skin cancer and leukemia. Other non-solid cancer radio-induced rate is negligible or slighly higher than baseline incidence ones, but they are estimated from an hypothesis of constant excess-absolute risk (EAR) over the whole life of the radiologists. Furthermore, new cohorts are still needed to increase knowledge and provide new information on some specific cancer risks in medical exposures, such as skin cancer and non-solid cancer radio-induced mortality, anc comparing with other models.

Because the observed appreciable risk of leukemia and cancer incidence in the group of radiologists, it is necessary for suitable theoretical and practical education and training for the involved medical staff in radiology/cardiology and nuclear medicine departments. Training in radiological protection for patients and staff should be an integral part of the education for those using interventional techniques. Risks and benefits, including detrimental effects, should be taken into account when new interventional techniques are introduced (ICRP 85).

Professionals in intervetional practices are highly dependent on radiation protection measures taken, such as the use of protective screens and shields or the wearing of lead aprons. Dosimeters are not used unfortunately every day for the majority of interventional procedures (DIMOND 2003). Presented results are in accordance with DIMOND report. Cytogenetic studies, including FISH techniques, should be extended to more radiologists and technicians to assess the risk derived from their occupational exposure.

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