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PROPOSAL FOR A PATIENT DATABASE ON CARDIAC INTERVENTIONAL EXPOSURES FOR EPIDEMIOLOGICAL STUDIES

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Relatively high organ doses absorbed by patients in interventional cardiology suggest the opportunity to define these patients as a cohort to be followed forward in time in an epidemiological study of the cancer risks associated with exposure to low-dose ionising radiation. In this paper, the UNSCEAR 2000 Report risk estimates for the most exposed organs/tissues in cardiac interventional procedures are reviewed, as well as the critical features of such an epidemiological study that is anticipated to have an intrinsically low statistical power because of the low levels of risk and possible confounding factors. To overcome these limitations, data collected in different institutions can be combined provided that a common design and conduct are used for dose assessment. A minimum dataset to be collected on a patient basis is proposed that can be implemented routinely in most facilities. This data should be linked to the local patient information system in order to retrieve all the exposures of a given patient.

INTRODUCTION

Patients submitted to cardiac interventional procedures can receive relatively high organ doses due to long exposure times, as well as repetition of diagnostic and therapeutic procedures[1]. Local skin doses up to some sieverts have been reported. Significant doses up to 100 mSv can also be estimated to lungs; also oesophagus, stomach and bone marrow can be irradiated to significant doses of the order of tens of millisievert, while female breast, though at elevated risk, should receive less doses[2].

These findings suggest the opportunity to define these patients as a cohort to be followed forward in time to examine the occurrence of radiation-induced stochastic effects in an epidemiological study of the cancer risks associated with exposure to low-dose ionising radiation. In view of the highest doses, of particular interest could be to assess risk of skin, lung, oesophagus, stomach cancer and leukaemia.

EPIDEMIOLOGICAL RELEVANT DATA

Direct information on radiation-induced cancer is available from epidemiological studies of a number of human populations. These include the survivors of the atomic bombings in Japan and groups that have been exposed to external radiation or to incorporated radionuclides, either for medical reasons or occupationally. Such studies provide quantitative information on the risk of cancer at intermediate to high doses and are reviewed in the UNSCEAR 2000 Report Annex I, 'Epidemiological evaluation of radiation-induced cancer'[3]. At lower levels of exposure, however, quantitative estimates of risk are not so readily obtained, and inferences need to be made by downward extrapolation from the information available at higher doses. The UNSCEAR 2000 Report Annex G, 'Biological effects at low radiation doses'[4], examines the sources of data that are available for assessing the risks of radiation-induced cancer (and hereditary disease) at low dose for both low-LET and high-LET radiation and their uncertainties. It concludes that direct observations are hampered by statistical limitation in providing clear indications of effects at acute doses much less than about 100 mGy (low-LET).

Relevant studies of the effects of exposures to low-LET radiation are listed in Table 2 of Annex I of the UNSCEAR 2000 Report[3], whereas in Table 3 of the same Annex the strengths and limitations of these studies are summarised.

Although the Life Span Study of the Japanese atomic bomb survivors is the single most informative study on the effects of low-LET exposure of humans, a considerable amount of data is available from many other epidemiological studies. Among these, studies of patients with diagnostic exposures are very scarce: studies of patients who received multiple fluoroscopies in the course of treatment for

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tuberculosis in both Canada[5] and US (Massachusetts)[6]; case–control study of US diagnostic X-ray procedures[7]; case–control study of diagnostic medical and dental X rays (Los Angeles)[8]; case–control of diagnostic X rays in Sweden[9] and mortality study of patients submitted to X-rays for scoliosis disease in USA[10]. In these studies, statistically significant results [excesses in the exposed group (cohort studies) or a higher proportion of the cases were exposed to radiation (case–control studies)] were observed only for breast cancer, oesophagus cancer, parotid gland cancer and chronic myeloid leukaemia. No excess of lung or skin cancer was demonstrated.

Table 1 shows an abstract of the UNSCEAR 2000 Report[3,4] nominal estimates of cancer risk for the most exposed organs/tissues in cardiac interventional procedures. As it can be seen, mean organ doses observed in those studied populations are some hundreds of millisievert, that is one order higher than the doses absorbed in cardiac interventional procedures, with the notable exception of skin.

PREMISES FOR AN EPIDEMIOLOGICAL STUDY

According to UNSCEAR[3], epidemiological studies of people with partial body exposures, such as those from medical examinations, provide valuable information on risks of specific cancers. In addition, there is a need for determining how to transfer radiation-induced risks from one population to another, in view of the differences in baseline rates for cancers between the Japanese atomic bomb survivors and many other countries.

A very important feature of any epidemiological study is its statistical power, i.e. the probability that it will detect a given level of elevated risk with a specific degree of confidence. The statistical power depends on the range of doses received by the study population and the spontaneous cancer rate. Summary measures of the doses received by a population, such as collective doses, are not, by themselves, suitable for determining statistical power. Indeed, it is essential when calculating statistical power to take account of the distribution of dose within the study population. Studies such as those of women given multiple chest fluoroscopies[11], based on the large cohorts that received a wide range of doses and have a long follow-up, are particularly informative about radiation-induced cancer risks.

In cases where the statistical power is inherently low, owing to the low predicted level of risk, combining studies with similar designs can be very helpful in attempting to increase power. One of the main difficulties that can arise in a meta-analysis is a lack of comparability of the studies under consideration, for example, because of differences in the form of data collected on exposures. So, a prospective approach where studies are constructed around a common protocol is more advantageous than a retrospective pooling exercise[3].

ASSESSMENT OF RADIATION DOSES

The assessment of doses received by individuals in an epidemiological study is a key aspect in estimating cancer risk following radiation exposure. Depending on the method of dose assessment, dose estimates could be subject to systematic or random errors or both, which could then affect the dose–response analysis.

To examine the risks of specific types of cancer, it is desirable to use the radiation dose to the organ under study. For doses received from some type of medical exposures, it may be possible to reconstruct organ doses based on the patient records and

Table 1. UNSCEAR 2000 Report[3,4] Epidemiology Data: estimates of cancer risk for the most exposed organs/tissues in cardiac interventional procedures.

Organ/Tissue	Risk	Study	Mean organ dose (Sv)
Skin	ERR = 1.9 at 1 Sv $2.3\ 10^{-2}\ Sv^{-1}$	Life span UK population NRPB	0.33
Lung	ERR = 0.48 at 1 Sv ERR = 0 at 1 Sv	Life span Canada and Massachusetts Tubercolosis patients	0.23 1.02 and 0.84, respectively
Oesophagus	ERR = 0.23 at 1 Sv ERR = 0.37 at 1 Sv	Life span Ankylosing spondilitis	0.23 5.5
Stomach	ERR = 0.30 at 1 Sv	Life span	0.23
Bone marrow	ERR = 4.37 at 1 Sv	Life span	0.25

ERR = Excess relative risk.

exposure measures in combination with computer models.

Errors in the assessment of individual doses affect statistical power. Random errors in individual dose estimates tend to bias the dose response towards the null[3], particularly when the predicted level of risk is low.

Attention should be paid also to exclude the bias due to self-reporting of past exposures, as there is evidence that cases are more likely to report increased exposure to presumed risk factors than controls (differential recall bias). Among the limitations of the studies concerning diagnostic examinations exposure, the UNSCEAR 2000 Report[3] identifies the following factors: uncertainties in dose estimates related to fluoroscopic exposure time, patient orientation, in dosimetry; doses likely to have been underestimated; dose estimates subject to bias as well as random error; analyses based on number and type of X-ray procedures rather than actual doses; no available records of X rays (potential for recall bias).

PROPOSED COLLATION OF DOSE DATA

It is important that the data for assessing doses be collected with epidemiology in mind. Consequently, dosimetric records and practices should be examined, as well as sources and magnitude of errors, in order to evaluate whether doses can be estimated with sufficient accuracy and precision for the purposes of epidemiology.

In interventional cardiology, the type of fluoroscopy-guided procedures is fairly limited; nevertheless, it is necessary to reach a consensus on their classification (nomenclature) or grouping in order to allow a common assessment and comparison of doses.

For sufficient information to provide accurate dose assessment, a minimum dataset to be collected for every procedure could be that suggested by the DIMOND-concerted action dosimetry sub-group (see Table 2 in Ref.[12]) to provide an indication of the potential for deterministic effects and the risk of stochastic effects. However, this would imply special features of radiological equipments (that allow the display and automated transfer of the pertinent dosimetry data) not universally available at the moment. In addition, methods to collect the relevant data from the DICOM header of each image run could be implemented.

A more reduced and feasible dataset would comprise:

- Type of procedure,
- Fluoroscopy time,
- Number of exposures,
- Total dose–area product (DAP) [i.e. the integral of air kerma (absorbed dose to air) across the entire X-ray beam emitted from the X-ray tube].
- Cumulative dose (CD) to interventional reference point (IRP) (i.e. the air kerma accumulated at a specific point in space relative to the fluoroscopic gantry (the interventional reference point) during a procedure).

DAP is a surrogate measurement for the entire amount of energy delivered to the patient by the beam. DAP is measured in Gy cm^2. CD does not include tissue backscatter and is measured in Gy. CD is sometimes referred to as cumulative air kerma. Although CD can be used as a surrogate for maximum skin dose (but it tends to overestimate it), DAP measures can be used for organ dose estimation provided that patient-specific Monte Carlo simulations are available for the various types of procedures. For this, observational studies in every centre are needed to determine the technical factors of a typical procedure.

The proposed minimum dataset should be stored in a computerised database for every procedure and retrieved on a patient basis. It would be desirable to link this data to the hospital (or regional) patient information system in order to retrieve all the X-ray exposures of a given patient.

From a dosimetric point of view only, the open issues to be faced with are the following:

- Measurement uncertainties, arising from systematic and random errors. These include dosemeter calibration and performance, as well as data storage.
- Dose estimate uncertainties, arising from simulations of typical procedures (with typical technical factors) for standard patient size.
- Patient radiation exposures other than fluoroscopy-guided cardiological procedures (e.g. CT exams, nuclear medicine stress test, and so on).
- Input errors when dose values or procedure data are manually entered.

CONCLUSION

This paper explores the premises and feasibility of a prospective epidemiological study to estimate the cancer risk following radiation exposure of patients during cardiac interventional procedures. To enhance the statistical power of such a study, anticipated low due to the low levels of risk associated, it stresses the importance to gather a large number of observations collected and analysed with a common design, as well as to reduce the magnitude of random and systematic errors in dose estimation. A minimum dataset to be collected on a patient basis

is proposed that can be implemented routinely in most facilities.

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