1. Overview

This Report provides an update of the cancer risk from radionuclides deposited in the liver. The liver has been considered an organ with a low risk for cancer induction from ionizing radiation (ICRP, 1991; NCRP, 1993a). This may in part have been because of the long latency period required to detect increases in radiation-induced liver cancer. Other estimates have increased the risk of liver cancer to a value of 300 cancers $10^{-4}$ Gy$^{-1}$ (NAS/NRC, 1988; UNSCEAR, 1994). This Report provides a re-evaluation of the molecular, cellular, experimental animal and human liver cancer data, and an update of the risk of liver cancer from internally-deposited radionuclides.

To determine risk, it is first essential to calculate the radiation dose to the liver. This is dependent on the affinity of the radionuclides for hepatic tissue, the radionuclide’s chemical form, the LET (linear energy transfer) of the emitted radiation, and the radionuclide’s physical and biological half-lives. Risk assessment includes not only an understanding of dose to a tissue, but also an appreciation of biological factors that may impact cancer frequency, such as sensitivity to radiation-induced cell killing and the presence of liver disease such as necrosis, fibrosis and cirrhosis. Other biological factors, such as sex, age at exposure, and exposure to other environmental insults, can also alter the sensitivity for radiation-induced liver cancer. Obviously, variations in any of these relationships will have a significant influence on the risk of radiation-induced liver cancer and the uncertainty associated with such risk. Each of these physical and biological variables are considered in this Report.

For many types of radiation exposures, e.g., chronic exposure to low-LET radiation, there are no statistically significant human data (UNSCEAR, 2000; Volume 2, Table 9). Therefore, animal and cellular data must be used for extrapolation of radiation risk to humans. Liver cancer induced in experimental animals by internally-deposited radioactive materials can be used to estimate human cancer risks. This is done by determining the relative biological effectiveness (RBE) for liver cancer in animals following
exposure to both high- and low-LET radiation. This information can be used to extrapolate to liver cancer risk in humans.

Of principle concern, in relation to the risk of liver cancer from internally-deposited radioactive material, are the radionuclides which concentrate in the liver and emit alpha particles. The major source of information on such human liver cancer risk is from patients injected with a thorium-based contrast media, Thorotrast®. These human data are supplemented with animal and cellular data to solve problems associated with using Thorotrast® data as the basis for human liver cancer risk and for the extrapolation of these risks to other radionuclides. Some of the problems that are addressed in this Report, using animal data, include nonuniform distribution, potential chemical toxicity, disease, and interaction of other biological factors in the cancer induction process. Animal studies support the validity of using the human Thorotrast® cancer data as a model for cancer risk induced by other internally-deposited alpha-emitting radioactive materials (Brooks et al., 1983; Gilbert et al., 1998; Muggenburg et al., 1996; Taylor et al., 1993). This Report updates the risk estimates derived by the Committee on Biological Effects of Ionizing Radiation [BEIR (NAS/NRC, 1988)] and the United Nations Scientific Committee on the Effects of Atomic Radiation [UNSCEAR (1994)]. The liver cancer risk for alpha emitters in this Report is calculated to be $560 \pm 95$ cases $10^{-4}$ Gy$^{-1}$. Extrapolation from animal data makes it possible to estimate the risk for human liver cancer from protracted exposures to beta/gamma emitters as 15 to 40 liver cancers per $10^4$ people per gray. The uncertainty associated with these risk estimates is high because of the need to extrapolate between different types of radionuclides, different species and from very high to low levels of exposure. In all these extrapolations, we have used a linear no-threshold model. Even with these uncertainties, this Report concludes that the liver is not a radio-resistant organ.

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1Thorotrast® (van Heyden Company, Dresden-Radebeul, Germany) is a radiographic contrast medium comprised of a 25 percent colloidal solution of yellow dextrin and thorium dioxide. It has a mean particle diameter of 9.3 ± 4.3 microns (Riedel et al., 1983) containing $^{228}\text{Th}/^{232}\text{Th}$ in a ratio of 0.4 in freshly obtained thorium preparations from natural thorium (van Kaick et al., 1984a). Thorium-228 and its daughter products are responsible for the majority of the radiation dose from Thorotrast®.

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