The Mechanism of Low Dose Radiation Risk Associated with Diagnostic X-rays, PET, and Gamma-rays.

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The goal of this project was to investigate low dose ionizing radiation effects associated with exposure to diagnostic computed tomography (CT) or positron emission tomography (PET) scans. Biological effects were evaluated in wild type and Trp53+/- heterozygous females, following *in vivo* exposure to diagnostic CT (75kVp, 200μA) or PET (^{18}F-FDG) scans. The short term biological effects following CT or PET scans were evaluated in order to understand biological modification of mechanisms, such as DNA repair processes and apoptosis, that might alter long term cancer risk. Corresponding life-time cancer risk studies are in progress. Short-term effects of CT and PET scans on bone marrow were investigated in 7-9 week old female wild-type trp53+/+ mice using three flow cytometry-based endpoints: micronucleated reticulocyte (MN-RET) formation, histone H2AX phosphorylation (γH2AX), and apoptosis.

A dose response was observed for MN-RET formation following *in vivo* whole body CT X-rays of 10 mGy to 100 mGy. It was determined that a 10 mGy CT scan could either reduce or increase MN-RET formation caused by a large 1 Gy challenge dose, depending upon the time interval between the CT and the challenge dose. There was no significant elevation of γH2AX foci in mice receiving 10 mGy, 20 mGy, and 50 mGy CT scans. However, a single 10 mGy CT scan protected against a larger challenge dose. However, this was dependent on the magnitude of the challenge dose. Apoptosis levels were significantly higher in mice receiving 50 mGy and 100 mGy CT scans but no adaptive response was observed.

For the PET studies, mice were injected with 0, 20, 100 or 400 μCi of ^{18}F- FDG corresponding to whole body doses of 0 mGy, 11.7 mGy, 58.3mGy, and 233.2mGy, respectively. There was a dose response for MN-RET formation only at doses ≥ 100 μCi ^{18}F-FDG. A second group of mice were injected with 0, 20, 100 or 400 μCi of ^{18}F- FDG and then challenged *in vivo* with a 1 Gy exposure 24 hours after the PET scan. There was no modifying effect of the PET scan on MN-RET formation in bone marrow when a challenge dose was delivered 24 hours later. This was also true for γH2AX foci formation for all injection doses except 400uCi PET when there was a significant reduction below that of non-injected mice challenged at 24 hours. Levels of apoptosis were not assessed.

Overall, there are measureable biological effects caused by low dose CT and PET scans, although the two modalities seem to produce different responses at similar doses. These diagnostic exposures can also induce an adaptive response that modifies the effects of larger radiation exposures, but the timing between the two exposures is important. These studies will be useful to help interpret the meaning of short-term biological endpoints with actual long-term cancer risk.