



Partial-Body Cutaneous Radiation Injury: Liposomal Glutathione Treatment and Monitoring by Optical Reflectance Spectroscopy

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Recent events have highlighted that terrorist actions may be intended to set up a nuclear explosion or disseminate radioactive materials using a radiological dispersal device. Under these conditions, significant whole body radiation exposures are likely to be accompanied by local cutaneous radiation injury. The skin response to high-dose ionizing radiation involves multiple inflammatory and necrotic reactions. Recent information on molecular and cellular mechanisms of skin radiation injury suggests that adhesion molecules defining cell surface structure, cellular signalling processes, and alteration of the redox status play an important role in both injury and healing. The cascade of effects is initiated by the formation of free radicals following exposure to ionizing radiation. These include DNA damage, protein oxidation, and lipid peroxidation leading to apoptotic cell death, confusion of the cell signalling pathways, arrest of the cell cycle, and NF κ B-related inflammation. Inflammation with the concomitant generation of reactive oxygen and reactive nitrogen species (ROS/RNS), and activation of multiple signalling pathways is associated with a reduction in the antioxidant capacity of the irradiated tissue. It has been suggested that the collapse of skin antioxidant status interferes directly with wound healing in the cutaneous radiation injury.

Tissue levels of glutathione, an antioxidant that is found in almost every cell, depend on the ability of the liver to produce and excrete glutathione into the circulation, as well as the ability of tissues to synthesize the peptide intracellularly. Gamma radiation has been shown to deplete the function of glutathione reductase and decrease glutathione. The depletion of glutathione can occur systemically or locally in affected tissues. Oxidative stress, which accompanies low glutathione can result in peroxidation of red blood cell membranes with increased levels of malondialdehyde, as well as increased formation of 3-nitrotyrosine in tissues modulating ROS/RNS and interfering with the healing process. We hypothesized that combined administration of topical and systemic glutathione would reduce the severity of cutaneous radiation injury and accelerate healing. A stable liposomal encapsulation of glutathione that can be orally and topically administered has recently become available. Liposomal glutathione has been demonstrated to exhibit the antioxidant and antiatherogenic properties relevant to the cutaneous radiation injury. In this report we will describe the effect of topical and oral treatment with liposomal glutathione on skin injury induced by gamma radiation exposure in Fisher F344 rats. As part of this study, we evaluated the potential of using optical spectroscopy for non-invasive evaluation of the severity, progression, and effect of glutathione treatment on cutaneous radiation injury. This approach has the potential for conducting non-invasive *in vivo* biodosimetry in partial body radiation exposures. For this, an ultra-violet/visible (UV-vis) spectrometer coupled fiber-optically with a reflectance/backscattering probe was used to analyze the functional characteristics of radiation-exposed leg tissue from day 1 to day 40 post-exposure. A principal component analysis (PCA) of the data was successful in differentiating between levels of exposure (0, 20, and 40 Gy) as well as between treated and control animals.