

## BIOMARKERS FOR PARTIAL-BODY IRRADIATION AND ORGAN SPECIFIC INJURIES

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In the event of a mass-casualty radiological or nuclear event, biodosimetry will be important for both triage and clinical care decisions. Although most research efforts on biomarkers focus on whole-body irradiation, partial-body exposures are actually more likely in real cases. Non-homogeneous exposures can have a major impact on clinical outcomes. Treatment will depend on knowledge of an individual's injury due to the absorbed dose and dose distribution. Treatment based on whole-body dose assessments may not be appropriate for partial-body exposures, especially when local doses are high. Rapid diagnosis will be essential to protect organ systems that are seriously impacted by radiation including bone marrow, the gastrointestinal tract and skin.

The Armed Forces Radiobiology Research Institute held a workshop in May 2008, to explore the current state of knowledge, identify biomarkers and approaches for partial-body dose assessment, assess utility and impact on treatment, develop consensus on research gaps and overall integration, and future directions. Approximately 90 scientists from the United States, France, United Kingdom, Germany, the Netherlands, Canada and Sweden participated. This presentation will review some of the concepts raised at this meeting.

Cytogenetic analysis of circulating blood lymphocytes is a mature approach that can be used to assess acute partial-body radiation exposure. This approach requires that the exposure is prompt; an exposure extended over several hours diminishes the value of this diagnostic approach. The number of dicentrics per cell exhibits a Poisson distribution for acute homogeneous exposure. With partial-body exposures, the number of cells without any dicentrics is relatively high and the chromosome aberration frequency is over-dispersed.

Markers in skin, teeth and nails can localize exposures to specific areas of the body. Radiation elicits a stable EPR signal in teeth and nails that is independent of other intrinsic biological factors. Changes in skin may reflect local surface injury rather than whole-body damage since low penetrating radiation can cause significant damage to superficial layers without affecting deeper organs.

Organ-specific clinical signs and symptoms are currently used to indicate the severity of radiation injury to organ systems at risk. Biomarkers are in development for specific organ systems, including gut, kidney, lung, skin, as well as bone marrow. These markers can provide information on the distribution of dose as well as score the severity of specific organs at risk. Organ-specific biomarkers might also be able to predict delayed effects, which would allow the use of mitigators when available and the preparation of patients for upcoming health consequences.

Many gaps remain for partial body biodosimetry. Inter-individual variability, the quality of radiation, dose rate, confounding treatments, stressors, and other factors can affect the appearance of biomarkers and dose assessment. The time course of appearance and disappearance of biomarkers can present challenges. Understanding the functional implications of the biomarkers will help with their interpretation. Follow-up studies in the event of a radiological or nuclear event will help to define the validity of these assessments for both acute and delayed effects of radiation.