Capture Collective MiRAD™ high-throughput radiation biodosimetry assay

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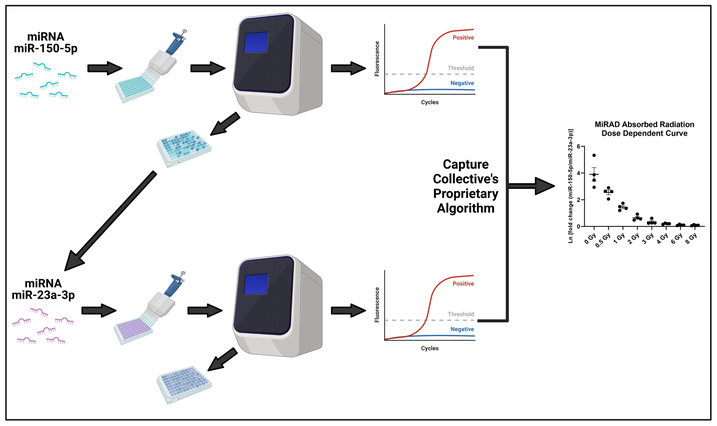
ABSTRACT

A radiological or nuclear incident could expose large populations to highly variable doses of ionizing radiation, resulting in dozens to thousands of individual cases of Acute Radiation Syndrome (ARS) and Delayed Effects of Acute Radiation Exposure (DEARE). Capture Collective is developing MiRAD, a blood-based, high-throughput biodosimetry assay for radiation dose reconstruction to assist clinicians and first responders in making informed triage and treatment decisions. Research on microRNA (miRNA) screening 600 candidate biomarkers found blood-based miR-150-5p to decrease expression in a dose and time-dependent manner in direct correlation with increased radiation exposure while lung-based miR-23a-3p was found to remain stable, making it an ideal biological normalization probe. This technology has demonstrated favorable kinetics and broad analytical range for absorbed dose estimation from samples collected immediately or even weeks post-exposure. Assay efficacy was evaluated in a heterogenous mouse population exposed to various sources of ionizing radiation including improvised nuclear device (IND) spectrum neutron and gamma rays. Feasibility for dose reconstruction in humans was assessed via comparison of mice exposed to fractionated versus single dose treatment to data from humans exposed to fractionated radiation prior to bone marrow transplant. These results indicate the dose dependent decrease of miR-150-5p showing preliminary feasibility in human patients. The MiRAD assay measures levels of miR-150-5p, normalized by miR-23a-3p, to quantitatively detect radiation dose with ± 0.5 Gy sensitivity at critical dose range within 4 to 5 hours. Results are reported using delta-delta Ct, which reduces variability caused by laboratory and equipment drift as well as individual variation of baseline expression. ARS symptoms follow a deterministic path in which dose effects have distinct clinical outcomes, therefore this quantitative detection of the absorbed dose is crucial for timely administration of countermeasures and proper allocation of resources. With rapid delivery of accurate dose estimation, this minimally invasive microRNA-based diagnostic assay demonstrates the potential to guide and improve the clinical response to mass casualty radiological or nuclear events.

Our Product and How It Works



MiRAD is superior to most existing Biodosimetry assays in terms of:

- **Minimally Invasive**
- **Sample Volume**: 1-2 drops of blood (normalization is not volume/quantity dependent)
- **Broad Analytical Range**: Analyte stable from hours to days
- **Robustness**: Response in males and females, young to elderly
- **Rapidity**: Short processing time (~5 hours)
- **Ease of Performance**: Can be done in in a reasonably equipped molecular biology laboratory

Capture's MiRAD assay is unique and advanced in the field of biodosimetry as it assesses for one radiation dose dependent miRNA and one biological normalization miRNA in one collective assay from a single sample. These two miRNAs consist of miR-150-5p, which has been determinedto decrease in expression in direct correlation with absorbed radiation dose, while miR-23a-3p has shown to maintain consistent expression levels despite absorbed dose changes. The dual use of these miRNAs enables the unique ability to biologically normalize the radiation dose dependent miR-150-5p using miR-23a-3p to predict a highly accurate absorbed dose on an individual basis.

RESULTS

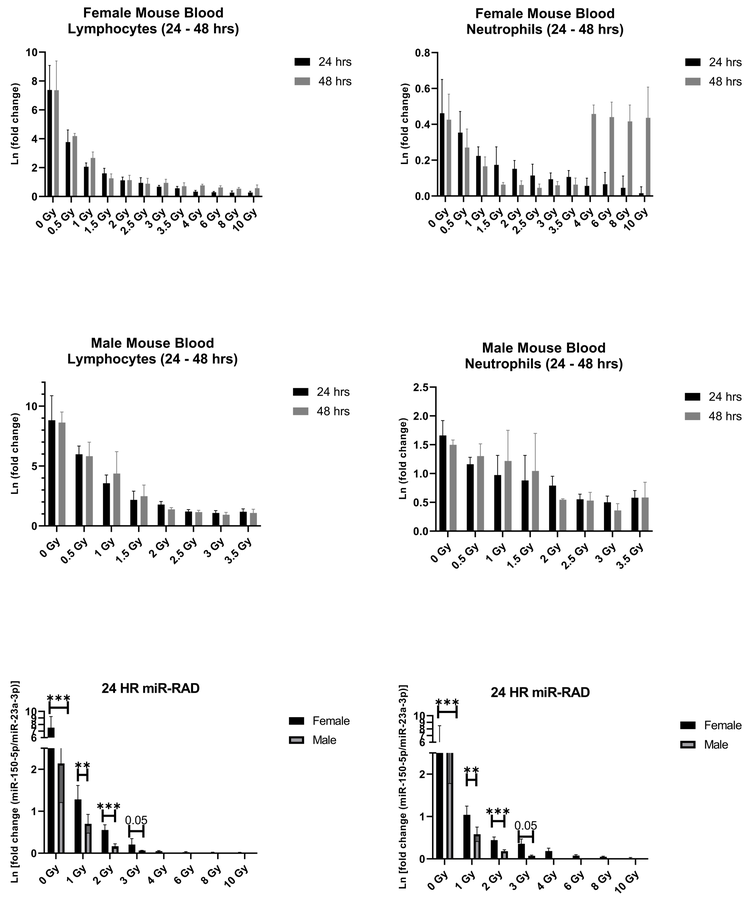


Figure 2: Panel A) B) C) D) E) F)

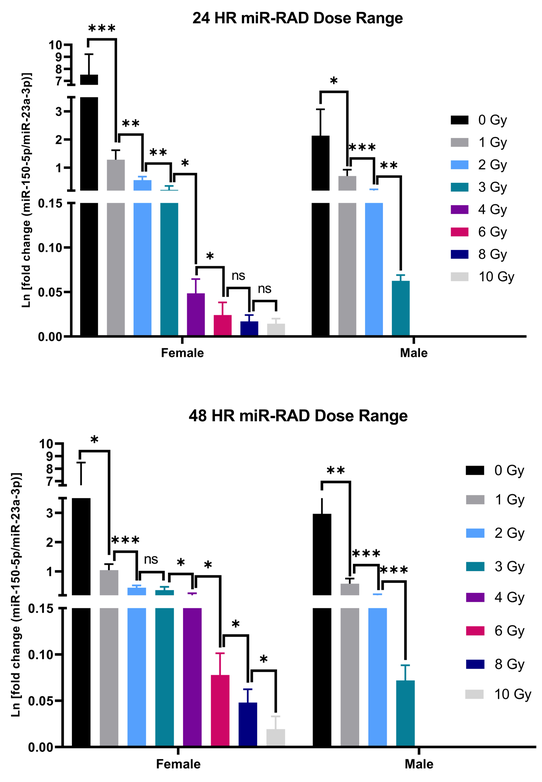


Figure 3: A) B)

CAPTURE

RESULTS

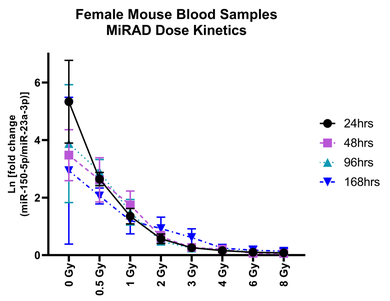


Figure 4:

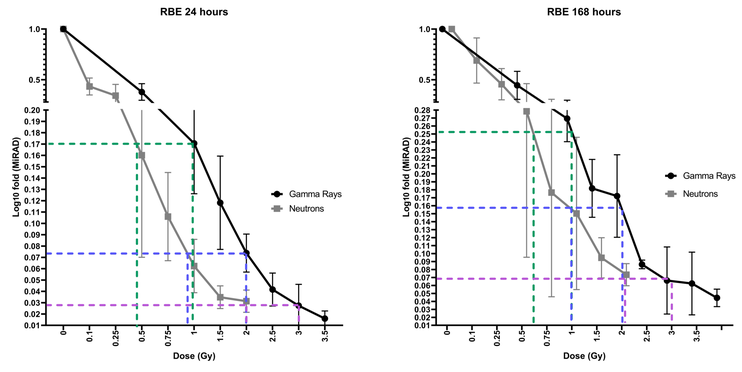


Figure 5: A) B)

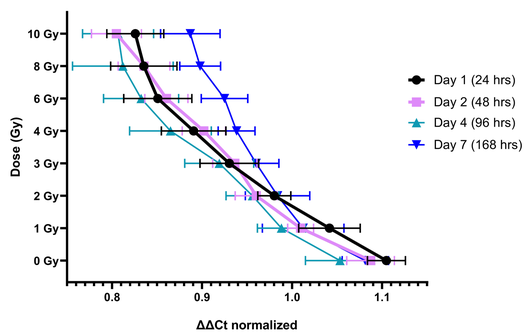


Figure 6:

CONCLUSIONS

This novel tool enables accounting for radiation sensitivity and resistance due to biological confounding variables and pre-existing conditions in a population of varying ages from pediatric to elderly. The sensitive blood assessment allows dose estimation with an accuracy of ± 0.5 Gy at critical dose range only requires one to two drops of blood making it minimally invasive and easy to use at a triage site. When this technique is combined with the efficient analysis protocol, in which results are completed within four to five hours, it enables favorable kinetics and broad analytical range allowing estimation of absorbed dose from hours or weeks post exposure with unprecedented simplicity and accuracy critical for individualized therapeutic guidance.

The HT assay kit has been developed to reflect the current stage of development with opportunities to further optimize the size and assay time. One part of the kit consists of collection devices and transport materials sufficient to obtain a small sample of patient blood at the point of care facility or field-based triage site. Part One is then transported to a central testing facility which has received or maintained storage of the assay reagents and oligonucleotide primers to perform the analysis. This assay specifically uses commonly available reagents to enhance the ease and readiness of use for laboratory facilities capable of completing PCR assessment throughout the United States. Further, results would be reported via standard clinical laboratory operating procedures to the attending physician(s) or emergency personnel to enable patients to receive specific and applicable care as necessary.