

## The Pseudo Pelger-Huët Cell as a Retrospective Dosimeter: Analysis of a Radium Dial Painter Cohort

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Recently the pseudo-Pelger Huët anomaly (PHA) in peripheral blood neutrophils was described as a new radiation-induced, stable biomarker. In this study, we have examined PHA in peripheral blood slides from a cohort of 166 former radium dial painters, 35 of whom had zero marrow dose. The slides were made available in collaboration with the U.S. Transuranium and Uranium Registry (USTUR). Members of the radium dial painter cohort had ingestion of <sup>226</sup>Ra and <sup>228</sup>Ra at an early age (average age 20.6 ± 5.4 y; range 13-40 y) during the years 1914-1955. Exposure duration ranged from 1-1,820 weeks with marrow dose 3-13,500 mGy-Eq. The peripheral blood slides were prepared in 1960-1965 during medical follow-up and were quite suitable for light microscope evaluation after 50+ y. PHA in neutrophils is characterized by oval, symmetric bilobed nuclei, which are joined by a thin mitotic bridge. PHA is known to be caused by a decreased amount of the lamin B receptor (LBR). The B-type lamins are the building blocks of the cell's nuclear lamina, and the LBR gene is known to be located on the long arm of chromosome 1, 1q42.12. PHA expressed as a percentage of total neutrophils in this cohort rises in a nonlinear fashion over five decades of red marrow dose. Six subjects in this cohort eventually developed malignancies: five osteosarcomas and one mastoid cell neoplasm. The PHA percentage in these cases rises linearly with RBE-weighted red marrow dose ( $r^2 = 0.71$ ). No sarcomas are seen for RBE-weighted red marrow dose under 10,000 mGy-Eq (500 mGy). In the context of these experiments, Receiver Operating Curve (ROC) methodology may be used to evaluate the PHA% as a binary laboratory test to determine whether there is alpha dose to bone marrow. A cutpoint of 5.74% PHA is found for identification of the dose category (AUC 0.961, sensitivity 97.8%, specificity 74.2%, PPV 94.3% for this dataset). PHA from peripheral blood is therefore a reasonable dose surrogate to evaluate alpha dose to bone marrow. Acknowledgements: this work was supported by the U.S. Department of Energy under contract number DE-AC05-06OR23100 with Oak Ridge Associated Universities and award number DE-HS0000073 to Washington State University.

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