Diminishment of Photodynamic Therapy by Tumor Incisions is not Due to Differences in Acute Cell Death.

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The implementation of photodynamic therapy (PDT) as a treatment for tumors leads to tumor death in a number of ways: direct acute cell death, vascular damage, and death from following immune response. Through the way of acute cell death, PDT may cause tumor cells to become necrotic or initiate the apoptotic program. Although the debulking of tumors is beneficial for the patient, tumor injury (TI) sustained during the surgery may alter the outcome of PDT treatment, as it affects the tumor microenvironment. Based on previous evidence, we posit that differences in outcome due to tumor injury occur during the immune response following treatment; no differences are expected in the way of acute cell death. Within, we outline two methods for studying the differences in the tumor microenvironment through means of non-invasive imaging and flow cytometry. The first utilizes a chemiluminescent agent to study the activity of neutrophils through the release of a cell-killing peroxidase, myeloperoxidase, and was confirmed through the use of an inhibitor of reactive oxygen species, dimethyl sulfoxide. Second, we analyzed a marker for cell vitality - flow cytometry is used alongside staining for necrotic and apoptotic cell populations to understand differences in acute cell kill. Using these techniques, we demonstrate that neutrophil activity increases early after either PDT or TI/PDT and represents a previously under-characterized mechanism of tumoral killing. Further, it is shown that there are no significant differences in acute cell kill between PDT and TI/PDT treated groups; TI does not alter the ability of PDT to directly kill cells. Taken together, these results demonstrate the significance of the alteration of the immune response when tumor injury is added to PDT and that the diminishment of the effects of PDT by TI is not due to differences in acute cell death.