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Biodynamic signatures from ex vivo bone marrow aspirates are associated with chemotherapy-induced neutropenia in cancer-bearing dogs

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Abstract

Background: Neutropenia is the most common dose-limiting side effect of cytotoxic chemotherapy in cancer-bearing dogs. Biodynamic imaging (BDI) is a functional imaging technology that measures dynamic light scattering from living, three-dimensional tissues to characterize intracellular motion within those tissues. Previous studies have associated BDI biomarkers with tumour sensitivity to chemotherapy agents in dogs with naturally occurring cancer. We hypothesized that BDI, performed ex vivo on bone marrow aspirate samples, would identify dynamic biomarkers associated with the occurrence of specific degrees of neutropenia in tumour-bearing dogs receiving doxorubicin chemotherapy.

Materials and Methods: Bone marrow aspirates were collected from 10 dogs with naturally occurring cancers prior to initiation of doxorubicin treatment. BDI was performed on bone marrow samples treated ex vivo with doxorubicin at 0.1, 1, 10 and 100 μM along with 0.1% DMSO as a control. Dogs then were treated with doxorubicin (30 mg/m^2, intravenously). Peripheral blood neutrophil counts were obtained on the day of treatment and again 7 days later. Receiver operating characteristic curves identified provisional breakpoints for BDI biomarkers that correlated with specific changes in neutrophil counts between the two time points.

Results: Provisional breakpoints for several BDI biomarkers were identified, specifying dogs with the largest proportionate change in neutrophils and with neutropenia that was grade 2 or higher following doxorubicin treatment.

Conclusions: Biodynamic imaging of bone marrow aspirates may identify those dogs at greater risk for neutropenia following doxorubicin chemotherapy. This approach may be useful for pre-emptively modifying chemotherapy dosing in dogs to avoid unacceptable side effects.

KEYWORDS

adverse events, cancer chemotherapy, precision medicine, spectroscopy