Optical Prediction of Metastatic Outcome Using Second Harmonic Generation

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Following a diagnosis of invasive breast cancer, the primary tumor is removed and hormonal therapy is begun. At this point a significant decision must be made: should the patient receive additional systemic chemotherapy to attack cells that have escaped the tumor? In the majority of cases the cancer has not yet spread to the adjacent lymph nodes ("N0"), and the choice is unclear. Current data suggests that the majority of N0 patients that are systemically treated would *not* have developed metastases, did *not* need to suffer the toxic effects of systemic therapy, and were "overtreated." Hence there is a pressing need to predict who will (and will not) develop metastases, to minimize overtreatment. Current attempts to meet this need are primarily based upon genomic methods and hence focus on tumor cells, while less attention is paid to the extracellular matrix through which metastasizing cells travel. We and others have studied an optical signal called second harmonic generation (SHG) that is intrinsic to fibrillar collagen. We have demonstrated that tumor collagen structure, as measured with SHG, influences tumor cell motility and that manipulation of tumor SHG signatures alters metastatic outcome. This suggests that SHG may provide prognostic information about metastasis that is complementary, or even superior, to current cell-focused methods. Therefore we explored one SHG measure of collagen structure, the forward- to backwards-scattering ratio (F/B), in 125 ER+ untreated patients with Invasive Ductal Carcinoma. We found that F/B is a significant prognostic indicator of time to metastasis in these patients (based upon 10 year followup data). It is also a prognostic indicator in 60 ER+ IDC patients treated with tamoxifen. Finally, F/B is a significant prognostic indicator in 69 patients with Stage I colon adenocarcinoma. This suggests that F/B may be useful as a rapid and inexpensive way to predict metastatic outcome in several tumor types, to reduce "overtreatment" of cancer patients.