

Abstract

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Presentation Title: Understanding Radiation Therapy Sensitivity in Invasive Lobular Carcinoma of the Breast

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Invasive lobular carcinoma of the breast (ILC) affects ~40,000 US women annually and is a top-ten most common cancer affecting women. Despite most ILC having biomarkers of “low risk” disease (e.g. ~95% are estrogen receptor α /ER-positive), ILC is associated with poorer long-term outcomes and anti estrogen resistance. ILC are also notoriously non-responsive to chemotherapy, critically limiting treatment options for advanced or metastatic ILC. However, ILC are highly responsive to radiation therapy (XRT), which suppresses ILC recurrence and improves survival. We hypothesize that this sensitivity may be due to a dysfunction in DNA damage repair unique to ILC cells. We examined formation and resolution of DNA damage repair foci (namely RAD51, γ H2AX and 53BP1 foci) by immunofluorescence with ILC and IDC cell lines treated with ionizing radiation +/- anti-estrogen therapy as surrogates for the initiation and resolution of DNA repair. We also assessed cell growth via 7-day growth assays with ILC and IDC cell lines treated with ionizing radiation. Imaging with immunofluorescence suggested a deficiency in γ H2AX foci formation in ILC cells compared to IDC cells following treatment with XRT, despite robust formation of 53BP1 foci. This suggests that a deficiency in performing DNA damage repair in response to XRT is likely present in ILC cells. Additionally, our growth assays demonstrated an inability in ILC cells to recover from ionizing radiation compared to IDC cells. Taken together, the potential dysfunction in γ H2AX foci formation in ILC cells suggests that ILC cells may not form the appropriate DNA repair structures to initiate the DNA damage response, suggesting that a form of DNA repair deficiency underlies radiation sensitivity in ILC cells.