ABSTRACT

Capstone Project

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Invasive lobular carcinoma (ILC) is the most common special histological subtype of breast cancer, accounting for approximately 15% of cases, and presents with unique clinical and molecular characteristics that differentiate it from other breast cancers. Despite its prevalence, ILC is treated similarly to other breast cancers, largely agnostic of tumor histology. We explore challenges and opportunities in treating ILC, with a focus on the underexplored sensitivity of ILC to ionizing radiation therapy (XRT). While ILC presents with forms of resistance to chemotherapy and endocrine therapy, clinical data support that ILC have a distinct vulnerability to XRT, with promising outcomes in reducing recurrence rates, particularly in postmastectomy and postsurgical contexts. Additionally, molecular insights reveal putative defects in DNA damage repair mechanisms in ILC cells that may underpin heightened XRT sensitivity. However, current treatment guidelines inadequately address ILC-specific considerations, limiting the optimization of radiation strategies. The propensity for patients with lobular histology breast cancer to present with subclinical nodal metastases poses challenges for regional nodal management and treatment intensification. Conversely, emerging data suggest that partial breast irradiation (PBI) can be effective in well-selected patients as a means of treatment de-escalation, though historical studies raise concerns regarding recurrence due to the diffuse nature of ILC and current consensus guidelines state it is not recommended for patients with lobular histology. We discuss the critical need for ILC-specific treatment guidelines and highlight gaps in the literature that limit our understanding of XRT efficacy in ILC. Future research should prioritize new analyses of XRT efficacy and mechanistic studies to refine radiation approaches, optimize patient care, and harness the full therapeutic potential of XRT for this unique breast cancer subtype.