



“Enhancing survival outcomes through breast-conserving therapy in ipsilateral breast tumor recurrence: insights into metastasis and treatment strategies”

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We were greatly interested in Qu et al.’s recent editorial, which discussed the de-escalation of surgery for Ipsilateral Breast Tumor Recurrence (IBTR) and the potential integration of genomic features with location and pathology to differentiate between true IBTR and second primary tumors [1]. However, the authors did not delve into the potential biological mechanisms behind the clinical observation that repeat breast-conserving surgery does not seem to compromise overall survival compared to total mastectomy. We would like to highlight emerging evidence suggesting that Breast-Conserving Therapy (BCT) may provide an overall survival (OS) advantage over mastectomy in IBTR cases among patients previously treated with BCS and RT. A recent meta-analysis lends strong support to this notion, revealing that undergoing repeat BCS, with or without repeat RT, correlates with improved OS (Risk Ratio = 1.040, 95% CI: 1.003–1.079; $p = 0.032$, $I^2 = 70.8\%$) [2]. Furthermore, Gentile et al. have reported compelling findings, demonstrating significantly improved Distant Disease-Free Survival (DDFS), OS, and Breast Cancer-Specific Survival (BCSS) in patients undergoing BCS for triple-negative or HER2-enriched IBTR when compared to mastectomy ($p = 0.009$, $p = 0.002$, $p = 0.001$, respectively) [3]. These results echo the growing body of evidence supporting the OS benefits of BCT over mastectomy in the initial treatment of early breast cancer [4].

We posit that a true IBTR represents a metastatic event initiated by circulating and disseminated tumor cells that undergo reactivation due to intrinsic and extrinsic factors,

ultimately thriving in the primary site through mechanisms orchestrated by the tumor microenvironment. When the breast is removed via total mastectomy, these activated cells may seek an alternative metastatic niche in distant organs. Our hypothesis provides a potential explanation for the superior OS associated with second primaries compared to true IBTR [5].

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