Background: This analysis presents an update of our institution’s experience using loss of heterozygosity (LOH) mutation pattern comparisons to establish the clonality of ipsilateral breast tumor recurrences after breast-conserving therapy (BCT).

Materials/Methods: The clonality of IBTRs relative to the initial invasive carcinomas were analyzed using a polymerase chain reaction LOH molecular comparison assay in 57 patients treated with BCT. Forty-eight patients were treated with whole breast irradiation (WBI) and 9 were treated with accelerated partial breast irradiation (APBI).

Results: Thirty-four IBTRs (60%) were clonally related to the initial carcinoma and 23 (40%) were clonally different. Clonally related IBTRs were more frequently higher grade (70% versus 32%, p=0.019) and developed sooner after initial treatment (mean time interval to IBTR was 5.1 years in clonally related versus 9.3 years in clonally different cases (p=.002)). Age at diagnosis, positive or close margins, radiation type delivered (WBI vs. APBI), and administration of systemic therapy at diagnosis were not associated with the type of IBTR that developed. Twelve patients subsequently developed distant metastases, of which 9 (75%) had clonally related IBTRs. A trend towards improved cause-specific survival at 5 years after IBTR was identified amongst the clonally distinct population, 86% versus 70% (p=0.15). Clinical IBTR classification and molecular clonality assay results differed in 44% of all cases. The proportion of IBTRs that were clonally related versus recurrences that were clonally distinct changed significantly over time (see table).

Conclusions: Clinical classifications of IBTRs are unreliable methods of determining clonality. Molecular clonality assays can accurately establish the clonality of most IBTRs. Clonally related IBTRs occur sooner than clonally different IBTRs, are more frequently associated with the development of distant metastases and have a worse prognosis. Molecular clonality assays can provide a reliable means of identifying patients who may benefit from aggressive systemic therapy at the time of IBTR and provide an accurate assessment of the efficacy of various forms of local therapy.

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