## Supplementary File

**Table S1**. Disease and treatment details of patients who experienced a recurrence (n = 9)

| Pt. no. | Post-lumpectomy tumor characteristics | Adjuvant therapy | Time to recurrence [yr] | Therapy completed for recurrence | Current disease status |
|---|---|---|---|---|---|
| 1 | ER+Her2– pT1N0 Grade 2 IDC; close margins, LVSI (–) | AI x 0.3 yr (Oncotype RS 30, declined chemotherapy) | 0.9 | Bilateral mastectomy | NED |
| 2 | ER+Her2– pT1N0 Grade 1 ILC; close margins; LVSI (–) | None | 5.8 | Mastectomy then AI | NED |
| 3 | ER+ pTisN0 Grade 2 DCIS; negative margins; LVSI (–) | None | 1.4 | Partial mastectomy | NED |
| 4 | ER+Her2– pT1N0 Grade 1 IDC; negative margins; LVSI (+) | AI x 5 yr | 8.1 | Fulvestrant/palbociclib due to simultaneous regional and distance metastatic disease | Alive with disease |
| 5 | ER+Her2– pT1N0 Grade 2 IDC; negative margins; LVSI (–) | AI x 5 yr | 6.8 | rmpT1N1a after MRM then Tam (Oncotype 5) | NED |
| 6 | ER+Her2– pT1N0 Grade 2 IDC; close margins; LVSI (–) | None | 2.5 | pT1NX at breast scar after excisional biopsy | NED |
| 7 | ER+Her2+ pT1N0 Grade 2 IDC; negative margins; LVSI (–) | AI x 5 yr | 6.7 | Mastectomy | NED |
| 8 | ER+Her2– pT1N0 Grade 2 IDC; negative margins; LVSI (–) | Tam x 2.5 yr | 2.9 | pT1N0 after partial mastectomy with SLNB | NED |

| Pt. no. | Post-lumpectomy tumor characteristics | Adjuvant therapy | Time to recurrence [yr] | Therapy completed for recurrence | Current disease status |
|---|---|---|---|---|---|
| 9 | ER+Her2– pT1N0 Grade 1 IDC; negative margins; LVSI (–) | None | 1.1 | pT1N0 in different quadrant of ipsilateral breast after partial mastectomy with SLNB and INTRABEAM | NED |

AI — aromatase inhibitor; ER — estrogen receptor; Her2 — human epidermal growth factor receptor; IDC — invasive ductal carcinoma; invasive lobular carcinoma; IDC — invasive ductal carcinoma; invasive lobular carcinoma; LVSI — lymphovascular space invasion; Tam — tamoxifen; MRM — modified radical mastectomy; SLNB — sentinel lymph node biopsy; NED — no evidence of disease; no. — number; yr — year; RS — recurrent score

**Table S2.** Summary of the literature on photon-based intraoperative radiotherapy

| Author/Trial, Year Published | Center and/or Country | Time Period of Inclusion | Multi- or Single Institutional | Number of Patients | Technique Used | Median Follow-up (yr) | Five-year IBTR rate |
|---|---|---|---|---|---|---|---|
| Silverstein et al, 2018 [22] | Hoag Memorial Hospital Presbyterian, US | 2010–2017 | Single | 984 | Photon (50 kV) | 3 | 3.9%* |
| Tejera Hernández et al, 2020 [23] | Hospital Universitario Insular de Gran Canaria, Spain | 2015–2017 | Single | 102 | Photon (50 kV) | 2.2 | No rate reported. Local relapse in 1 patient |
| Vaidya/ TARGIT-A, 2020 [18] | UK, Europe, US, Australia, Canada | 2000–2012 | Multi | 1140 | Photon (50 kV) | 8.6 | 2.11% |
| Obi et al, 2020 [21] | Cleveland Clinic, US | 2011–2019 | Single | 201 | Photon (50 kV) | 1.9 | 2.0%† |
| Nguyen et al, 2020 [24] | University of Oklahoma, US | 2013–2017 | Single | 77 | Photon (50 kV) | 4.6 | 3.9%‡ |
| Tallet et al, 2020 [25] | France | 2011–2015 | Multi | 676 | Photon (50 kV) | 4.5 | 1.7% |
| Valente/TARGIT-R, 2021 [20] | US, Canada | 2007–2013 | Multi | 667 | Photon (50 kV) | 5.1 | 6.6% |

| **Author/Trial, Year Published** | **Center and/or Country** | **Time Period of Inclusion** | **Multi- or Single Institutional** | **Number of Patients** | **Technique Used** | **Median Follow-up (yr)** | **Five-year IBTR rate** |
|---|---|---|---|---|---|---|---|
| Giap et al. (present series) | University of Florida, US | 2010–2017 | Single | 201 | Photon (50 kV) | 5.1 | 2.7% |

*4-year rate; [ł]1.9-year rate; [ǂ]4.6-year rate; Yr — year; IBTR — ipsilateral breast tumor recurrence