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Conclusions: At 10 years, the risk of local recurrence among individuals treated with HF radiation therapy after BCS for pure DCIS was similar to individuals treated with conventional radiation therapy.

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Preoperative Partial Breast Radiation Therapy: One Year Outcomes and Radiation-Induced Changes in Gene Expression

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Purpose/Objective(s): Women with biologically favorable early stage breast cancer are increasingly treated with accelerated partial breast radiation (PBI). However, many PBI techniques require equipment or skills not readily available. Furthermore, suboptimal cosmetic outcomes have been noted with external beam techniques, likely related to large post-operative treatment volumes. To address these issues, we designed a phase I protocol utilizing widely available radiation techniques to 1) evaluate patients' tolerance of a single radiation treatment delivered preoperatively to a small-volume, intact breast tumor and 2) identify biomarkers of radiation response.

Materials/Methods: Women aged 55 or older with clinically node negative, ER+ and/or PR+, HER2-, T1 invasive carcinomas or low-intermediate grade in situ disease < 2 cm were enrolled (n = 32). Intensity-modulated radiation therapy was used to deliver 15, 18, or 21 Gy to the tumor plus a 1.5 cm margin. Lumpectomy was performed within 10 days. Patients with high-risk pathologic features received conventional radiation (n = 3) post-operatively. Formalin-fixed, paraffin-embedded, pre- and post-radiation patient samples were used for gene expression profiling. Gene expression in paired samples was evaluated with the RMA algorithm and the Bioconductor limma package with correction for multiple comparisons.

Results: No locoregional or distant recurrences have been reported (median follow-up 12.6 months). Cosmetic outcomes are good/ excellent in all patients receiving only preoperative radiation. Chronic toxicities were primarily grade 1-2 and expected (fibrosis, breast pain, skin induration). One grade 3 toxicity (breast atrophy) occurred in a patient receiving post-operative radiation. Genes significantly induced with radiation are listed in Table 1. Specifically, genes involved in apoptosis and cell cycle control were differentially expressed in tumors after radiation.

Conclusions: Preoperative single-dose radiation therapy to the intact breast tumor is efficacious and well-tolerated at one year. Genes governing radiation response, including those involved in cell cycle control and programmed cell death, may play a role in the increased radiation sensitivity observed clinically in ER+ cancers. Our groundbreaking study describes specific pathways modulated by radiation in human breast tumors. We expect this to aid in identification of therapeutic targets for biologically based radiation therapy.

Oral Scientific Abstract 295: Table

Gene	Probe Set (#)	FDR adjusted p value	Protein Family	Function
NR4A1	6	0.0230	Nuclear hormone receptor	Apoptosis
MDM2	4	0.0239	Regulatory enzyme	Cell cycle checkpoint/p53
DUSP1	4	0.0218	Phosphatase	MAPK signal transduction
CDKN1A	2	0.0020	Cyclin-dependent kinase	Cell cycle/p53
EGR1	2	0.0230	Transcription factor	Proliferation
GDF15	2	0.0236	Growth factor	Differentiation/p53
FOS	1	0.0190	Transcription factor	Cell proliferation/apoptosis
FOSB	1	0.0236	Transcription factor	Cell proliferation/anti-apoptosis
SRGN	1	0.0239	Serglycin	Apoptosis

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Intraoperative Radiation Therapy Prior to Lumpectomy for Early-Stage Breast Cancer: A Single Institution Study

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Purpose/Objective(s): To evaluate the safety, cosmesis, and clinical efficacy of intra-operative electron radiation therapy (IOERT) delivered prior to lumpectomy for early-stage breast cancer.

Materials/Methods: From December 2008 to March 2013, 75 breast cancer patients (ages 34 - 66 years) were treated with IOERT during breast conservative surgery. IOERT was delivered using a mobile LINAC. Suitable energy and applicator size were chosen to ensure coverage of the tumor with anterior and posterior margins of 1 cm and lateral margins of 2 cm. Patients with sentinel node metastases or younger than 40 years received 8 Gy as boost followed by a post-operative external beam radiation therapy of 50 Gy in 25 fractions; the others had 15 Gy prescribed to the 90% isodose depth. The dose rate was 10 Gy/min. for all patients. Adjuvant treatment consisted of chemotherapy alone (14 patients), hormonal therapy alone (18 patients), or combined chemotherapy and hormonal therapy (41 patients). Two patients had no adjuvant treatment. The safety, cosmesis, and short-term efficacy were evaluated.

Results: Median follow-up was 49 months (range: 19 - 58 months). Two (2.7%) patients developed post-surgical hematoma. Six (8.0%) patients developed mild breast fibrosis. Eight (10.7%) patients suffered from local pain. One (1.2%) patient experienced a post-operative infection. Sixteen (21.3%) patients developed Grade 1 pulmonary fibrosis. Forty-three (57.3%) patients had an excellent cosmetic result and 23 (30.7%) had a good cosmetic result. Three patients had an ipsilateral breast recurrence, with an actual 3-year local recurrence rate of 4.5%. One patient had an ipsilateral axillary recurrence, resulting in a 3-year regional recurrence rate of 1.4%. No distant metastasis or death was observed. The 3-year disease free survival rate was 94.2%.

Conclusions: IORT delivered prior to lumpectomy is safe and feasible for selected patients with early-stage breast cancer. Early side effects, cosmesis and short-term efficacy are acceptable, but a longer follow-up is needed for evaluation of late side effects and long-term efficacy.

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Outcomes of "Unsuitable" Patients by ASTRO Guidelines Treated with Accelerated Partial Breast Irradiation via Interstitial Multi-catheter Brachytherapy: A Multi-institution Collaborative Study

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