

**2057 THE IMPACT OF RADIATION THERAPY TREATMENT VOLUME ON CHEMOTHERAPY ADMINISTRATION AND THE 5 AND 10 YEAR DISEASE OUTCOMES FOR STAGE I/II BREAST CANCER PATIENTS TREATED WITH CONSERVATION THERAPY**

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**Purpose:** The purpose of this retrospective study was to: 1) evaluate how radiation treatment volume affected chemotherapy doses (10% or more dose reduction) as stratified by CT and RT sequence; 2) how CT/RT sequence affected elapsed time for completion of RT (COT) and 3) establish the impact of CT dose reduction by CT/RT sequence for IBTR, DFS and OS.

**Materials and Methods:** Between 1969 and 1992, 839 patients with AJC Stage I/II breast cancer were treated with conservation therapy at MIR, Department of Radiation Oncology and affiliated institutions. This analysis included all patients. Radiation doses to the breast and regional lymphatics were 45.0-50.4 Gy with breast boost doses to a total of 55.0-66.0 Gy. Patients were stratified by RT volume (2 breast tangential fields vs. 3-5 fields with lymphatic irradiation) and by type and sequence of systemic therapies (none or hormone only, CT-RT, RT-CT and CT+RT concurrent-including sandwich). Median follow-up was 66.4 months. Chemotherapy was CMF (71%) or Adriamycin (29%) based regimens. Statistical analysis was completed with BMDP Statistical Program utilizing Generalized Salvage (Mantel-Cox) analysis. A *p*-value of 0.05 or less was considered statistically significant.

**Results:** (See Table) Chemotherapy dose reduction was frequently seen in patients receiving 3-5 field RT, regardless of CT/RT sequence, and with the CT+RT concurrent sequence, regardless of RT volume. For RT-CT sequence, the influence of volume was more apparent compared to the affect of RT-CT sequence alone (RR 5.8 vs. 1.6). Concurrent CT + RT had frequent dose reductions, regardless of radiation volume (RR 4.0 - 2 fields vs. 3.9 - 3-5 fields). RT volume appeared as the predominant factor influencing elapsed time for COT (mean difference 5 days). Affect of treatment sequence on elapsed time for COT was minimal. Improved 10 yr IBTR was seen in the 3-5 field groups for RT-CT (0%) compared to the CT+RT (14%) group. Only 5 year data is available for the CT-RT group. These indicated comparable outcomes to the CT+RT group except for higher IBTR (17% vs. 4%) in the 3-5 field group. No disease outcome measures (IBTR, DFS and OS) were significantly affected by RT volume, CT dose or by treatment sequence.

**Conclusion:** These data confirm that both RT volume and sequence of systemic CT and radiation are important predictors of CT dose reduction. Lower IBTR was seen in RT(CT patients without an obvious trend toward impaired OS.

TABLE: Elapsed Time for Cot and Proportion of Patients With CT Dose Reduction by RT Volume and CT/RT Sequence

Sequence	2-Fields				3-5 Fields			
	Elapsed Time (days)	n	%	Relative Rate	Elapsed Time (days)	n	%	Relative Rate
None or Hormone Only	45	490	....	....	50	122	....	....
CT + RT	48	30/77	39	(3.9)	51	18/63	28	(4.0)
RT→CT	43	5/31	16	(1.6)	48	9/22	41	(5.8)
CT→RT	44	2/21	10	(1.0)	47	1/14	7	(1.0)

**2058 SEVEN YEAR EXPERIENCE WITH HDR BOOST IN CONSERVATIVE TREATMENT OF BREAST CANCER**

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**Purpose:** To analyze the results obtained in a prospective group of patients with stage I or II breast cancer treated by conservative surgery and radiotherapy with boost to the tumor bed with HDR brachytherapy.

**Materials and Methods:** Two hundred and fifty three patients with T1-2 N0-1 breast adenocarcinoma were treated by lumpectomy and axillar lymphadenectomy between December 1991 and March 1998, followed by external radiotherapy and HDR boost to the tumor bed. External beam radiotherapy was given by 6 MeV or Co60 photons. A central dose of 50.40 Gy was given in 28 fractions over 5.5 weeks. Brachytherapy was given between 2 and 3 weeks after completion of external beam radiotherapy. Stainless steel needles or, preferably, plastic tubes were used. The number of catheters implanted ranged between 3 and 11. HDR dose per fraction ranged between 2 and 9 Gy. Total HDR dose was calculated by the Lineal Quadratic model and tried to be equivalent for early effects as it would be an implant of LDR of 20 Gy for tumors without intraductal carcinoma and 1 cm or more clear margins; 25 Gy for tumors of less than 1 cm of diameter but with intraductal component or 0.5-1.0 cm clear margins and 30 Gy for those tumors greater than 1 cm of diameter with less than 0.5 cm margins or extensive intraductal carcinoma component or tumor greater than 1 cm of diameter with less than 1 cm clear margins. Follow-up visits were done monthly for the 6 months after treatment, every 2 months for 2 years, every 3 months during the third year and every 6 months since then. Special attention was done to local recurrences, distant metastases, late effects and cosmetic results.

**Results:** During the seven year follow-up period, with 12 months minimum follow-up, 8 local recurrences, 10 distant metastases and

3 deaths were recorded. Seven year actuarial survival was 98%; disease free survival 90% and local control 96%. Those data were compared with another group of patients of similar characteristics treated at the same institution and at the same period of time with LDR brachytherapy. Local control was higher in the HDR group, meanwhile disease free survival and survival was similar in both groups of patients. Treatment tolerance was excellent in the HDR as well as in the LDR group of patients. No severe, early or late, complications were detected. In 97% of cases cosmetic results were considered to be excellent or good.

#### Conclusions:

- HDR is a highly effective treatment as a boost to the tumor bed in patients with breast carcinoma treated conservatively. It is very well tolerated and no significant side effects were noted.
- Uniform dose distributions with a sharp dose gradient in the limits of the implant permits to increase the dose to the tumor bed. This allows a high local control rate with no significant brachytherapy related sequelae or complication.

## 2059 E-CADHERIN: THE MOST SIGNIFICANT PROGNOSTIC MARKER IN BREAST CANCER PATIENTS WITH LONG FOLLOW-UP

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**Purpose:** The purpose of the study is to determine whether the expression of E-cadherin a homophilic epithelial adhesion molecule correlates with the metastatic proclivity of human breast cancer and determine its significance for prognosis in relation to other markers of metastatic progression in small node-negative breast cancer.

**Patients and Methods:** We used archival material from node-negative patients who underwent mastectomy and received no adjuvant systemic therapy. The median age is 57 y (29-82). The median follow-up is 164 months. The median tumor size is 2 cm. In 89% of patients the tumors are  $\leq 3$  cm. Expression of E-cadherin, nm23H1, and estrogen receptor were determined using immunohistochemistry. Angiogenesis was determined by microvessel count (MVC). Multivariate analysis was performed to identify the significant prognostic variables.

**Results:** There is a trend for decreased E-cadherin expression in tumors  $> 2$  cm. 14% of  $\leq 2$  cm tumors have low E-cadherin compared to 25% of  $> 2$  cm tumors. Women  $< 50$  had a higher proportion of low E-cadherin tumors (29%), compared to women  $\geq 50$  (15%). There is a direct correlation between E-cadherin and nm23H1 ( $p=0.006$ ), inverse correlation with tumor grade ( $p=0.001$ ) and MVC (0.1). The 14 y disease-free survival (DFS) is 84%, 80%, and 56% respectively for high, intermediate and low E-cadherin ( $P < 0.001$ ). The 14 y DFS as function of nm23H1 is 93% vs 69% ( $P < 0.001$ ). If both nm23H1 and E-cadherin are high the prognosis is excellent. In patients in whom nm23H1 is low if angiogenesis is also low the 14y DFS is 89%, compared to 62% if angiogenesis is high. In the low nm23H1/low angiogenesis group most patient have intermediate or high E-cadherin expression, thus E-cadherin does not offer additional prognostic value. If nm23H1 expression is lost and angiogenesis is high the 14y DFS as a function of high, intermediate and low E-cadherin expression is 76%, 61%, 44% respectively ( $P=0.01$ ), thus identifying an extremely poor prognosis group ( $< 50\%$  DFS) in node-negative breast cancer. In multivariate analysis E-cadherin, nm23H1 and MVC are the most important variables. Size, grade, or age are not significant.

**Conclusion:** E-cadherin has the potential for being a significant prognostic marker in node-negative breast cancer. Low E-cadherin alone results in only 56% 14y DFS but the outcome is worse if nm23H1 expression is also lost and angiogenesis is high, 44% 14y DFS. E-cadherin is a stronger prognostic marker than angiogenesis and nm23H1. But nm23H1 and angiogenesis still contribute prognostic information. Combining the three markers of metastatic proclivity E-cadherin, nm23H1, and angiogenesis we are able to identify patients with very good prognosis who may not need adjuvant therapy, those with high nm23H1 and high E-cadherin or low angiogenesis. The patients with the worst prognosis group are those who have loss of nm23H1, E-cadherin, and have high angiogenesis. They may benefit from intensive systemic therapy. The intermediate prognosis groups need additional prognostic markers. Combining markers of metastatic proclivity allows for better prognostic information and may permit the tailoring of the adjuvant therapies based on the tumor phenotype.

## 2060 BILATERAL BREAST CANCER-DOUBLE JEOPARDY, DOUBLE TROUBLE? AN EVALUATION OF RISK FACTORS AND OUTCOMES

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**Purpose:** To compare the outcome of bilateral breast cancer (BBC) patients to that of patients with unilateral disease.

**Materials and Methods:** From 1960-1995, 1461 stage 0-III patients with primary breast cancer were treated by either mastectomy or breast conservation therapy at the Kimmel Cancer Center of Jefferson Medical College and Thomas Jefferson University Hospital. There were 1313 (89.9%) unilateral, 102 (7.0%) metachronous and 46 (3.1%) synchronous breast cancer patients. Synchronous breast cancers were defined as having a contralateral cancer diagnosed within one year of initial diagnosis. Overall and NED survival, local control and distant metastatic disease rates from the time of the second diagnosis were calculated for synchronous and metachronous patients. These were then compared to the unilateral breast cancer patients and to each other.

**Results:** There were 49.4% of bilateral breast cancer patients with stage 0/I at initial diagnosis and 67.6% were stage 0/I at subsequent diagnosis. For metachronous breast cancers, the median interval between first and second diagnosis was 44 months (range 13-287 months). Median follow-up time was 58 months for the synchronous cancers (range 12-229 months) and 87 months (range 0.25-414 months) for metachronous cancers. The 5- and 10-year overall survival was 81.8% and 76.3% for synchronous breast cancer patients compared to 96.7% and 90.2% for metachronous patients. The 5- and 10-year survival was 91.3% and 82.4% for unilateral breast cancer patients. These differences were not statistically significant. The interval to 2nd breast cancer of  $\leq 4$  years portend a worse 5- and 10-year survival compared to the interval