

the skin covering the ipsilateral breast (i.e., a 5 mm width segment on the breast surface). Treatment plans with EBB were performed and compared to stereotactically guided DCAT. Dose-volume histograms (DVHs) were compared in both treatment techniques. The V90(PTV) (volume of the PTV that received 90% of the prescribed dose), the V50(OARs) (volume of the OARs that received 50% of the prescribed dose), a conformity index (CI), and an inhomogeneity coefficient (IH) were calculated in both techniques. **Results:** Five tumors were located in the left breast, and five in the right one. Three were located superficially (up to 4 cm), and seven were deeply located (>4 cm). The mean CTV and PTV volume were 33.7 cc (range 6.0–79.6), and 109.2 cc (range 48.7–206.0), respectively. The mean coverage of the PTV by the 90% isodose was 94.6% for DCAT, and 92.4% for EBB. The mean minimal and maximal dose to the PTV were 13.5 Gy (range 12.8–13.9), and 17.7 Gy (range 16.0–19.9) for DCAT, and 10.2 Gy (range 8.0–13.8), and 16.8 Gy (range 16.1–17.8), for EBB. The mean V50(OARs) for DCAT and EBB were: ipsilateral breast: 215.1 cc and 239.6 cc; ipsilateral lung: 12.9 cc and 145.32 cc; skin: 23.0 cc and 31.9 cc; and heart: 0 cc and 14 cc respectively. The mean CI value was 1.28 for DCAT and 2.43 for EBB. The mean IH value was 0.30 for DCAT and 0.72 for EBB.

**Conclusions:** Compared with electron beams, stereotactic guided DCAT with 6 MV x-ray beams may be preferred especially for deeply located breast tumors growing close to the chest wall. A marked OARs dose-sparing effect was observed, in addition to potential improvement in cosmesis after treatment.

## 2049

## POSTER

### Adjuvant therapy for early stage breast cancer (EBC): distant disease-free survival (DDFS) as a predictor of overall survival (OS)

H. Rugo. University of San Francisco, Breast Oncology Clinical Trials Programme, San Francisco, USA

**Background:** OS advantages are often difficult to demonstrate in trials evaluating treatment for EBC, as this requires long follow-up (FU) and large trials. Results are also confounded by factors such as further treatment. DFS, the primary end point in many adjuvant trials, is not a consistent predictor of OS, and lack of standard definitions renders its interpretation difficult. A better, quicker end point is needed as a surrogate for OS. Distant metastases (DM), the most common type of recurrence, are responsible for the initial peak of relapse seen at 2 years post surgery and are associated with the highest risk of death compared with locoregional and contralateral events. The sites of distant relapse also affect outcome; patients with bone metastases fare better than patients with visceral disease. As reductions in DM are likely to improve outcomes, DDFS may be a better short-term OS predictor.

**Methods:** The impact of common adjuvant therapies (chemotherapy [CT], tamoxifen [TAM], and aromatase inhibitors [AIs]) on DM risk and OS were examined.

**Results:** CT trials show that improvements in DDFS often precede subsequent improvements in OS. In NSABP B14, TAM significantly improved DDFS at 4 years and OS at 10 years. In ATAC and BIG 1–98, over half of EBC recurrences are DM, but OS differences are limited by short FU. Visceral relapse was the most common site of distant relapse in BIG 1–98. Letrozole therapy significantly reduced DM risk, resulting in fewer soft tissue, bone, and visceral metastases when compared with TAM. ATAC showed no significant reduction in DM risk with anastrozole in hormone receptor-positive patients. The reason for this difference is unclear. The IES initially showed a significant reduction in DM risk, but the number of events at specific sites was not reported. Upon longer FU, a borderline significant benefit in OS in the estrogen receptor-positive/unknown subgroup favoring exemestane was seen.

**Conclusion:** Several adjuvant trials show that improvements in DDFS often precede significant improvements in OS. AIs show superiority over TAM in reducing DM risk (IES, BIG 1–98) in all sites of recurrent disease. DDFS may be a better, more achievable end point than OS for women with EBC and could hasten the development of future adjuvant breast cancer therapies.

## 2050

## POSTER

### Endocrine effects of adjuvant letrozole plus triptoreline versus tamoxifen plus triptoreline in premenopausal patients with early breast cancer

E. Rossi<sup>1</sup>, F. Perrone<sup>2</sup>, G. Esposito<sup>3</sup>, G. Landi<sup>1</sup>, F. Di Rella<sup>1</sup>, R. Thomas<sup>4</sup>, C. Gallo<sup>5</sup>, K. Monaco<sup>2</sup>, A. Morabito<sup>2</sup>, A. de Matteis<sup>1</sup>. <sup>1</sup>National Cancer Institute of Naples, Medical Oncology C, Naples, Italy; <sup>2</sup>National Cancer Institute of Naples, Clinical Trials Unit, Naples, Italy; <sup>3</sup>National Cancer Institute of Naples, Biochemistry, Naples, Italy; <sup>4</sup>National Cancer Institute of Naples, Senology, Naples, Italy; <sup>5</sup>Second University of Naples, Medical Statistics Unit, Naples, Italy

**Background:** We are conducting a phase 3 trial (Hormonal adjuvant treatment Bone Effects – HOBEO) in patients with early breast cancer, comparing Tamoxifen (Tam), Letrozole (L) and L + Zoledronate (Z) for the effect on bone mineral density at 1 year. Postmenopausal and premenopausal patients are eligible, the latter also receiving monthly triptorelin (Tr). The aim of the present study is to describe endocrine effects of 6 months of adjuvant treatment with L plus Tr in premenopausal early breast cancer patients and to compare such effects with those of 6 months of Tam plus Tr.

**Patients and Methods:** Prospectively collected hormonal data were available for 81 women, of whom 30 have been assigned to receive Tam+Tr and 51 to L+Tr±Z, assuming that Z has no endocrine effects. Serum 17- $\beta$ -estradiol, FSH, LH, D4-androstenedione, testosterone, dehydroepiandrosterone-sulphate, progesterone, ACTH and cortisol are measured at baseline and after 6 months of treatment. We compared, for each hormone, 6-months values between treatment groups, by applying Exact Wilcoxon-Mann-Whitney test. Differences between 6-months and baseline values have not been calculated to avoid dilution due to chemotherapy-induced postmenopausal values.

**Results:** There were no differences in change of plasma levels of testosterone, progesterone, ACTH, androstenedione, and dehydroepiandrosterone between the two groups. Significant differences are reported in the table (p < 0.05).

Hormone	Median value (range)		p value
	Treatment arm		
	Tam+Tr	L+Tr (±Z)	
Estradiol pg/ml	7.95 (<5–43.9)	4.9 (<5–24.5)	0.0008
FSH mU/ml	2.65 (0.9–26.5)	10.8 (2.2–131.1)	<0.0001
LH mU/ml	0.3 (0.1–1.2)	0.2 (0.1–0.8)	0.0005
Cortisol µg/d <sup>a</sup>	18.45 (4.6–30.3)	10.5 (5.3–17.9)	<0.0001

<sup>a</sup>Median cortisol serum levels were within normal range in both groups.

**Conclusions:** These data suggest that letrozole in combination with triptorelin, induces a more intense estrogen suppression also in premenopausal patients, as compared to tamoxifen. Such evidence makes reasonable the hypothesis that the higher efficacy of letrozole versus tamoxifen shown in postmenopausal patients could be confirmed also in premenopausal patients.

## 2051

## POSTER

### Tantalum and titanium surgical clips as fiducial markers for breast radiotherapy in a tissue equivalent phantom

C. Thomas<sup>1</sup>, A. Nichol<sup>1</sup>, J. Park<sup>2</sup>, J. Hui<sup>3</sup>, A. Ross<sup>3</sup>, S. Grahame<sup>3</sup>, K. Otto<sup>4</sup>. <sup>1</sup>BC Cancer Agency, Radiation Oncology, Vancouver, Canada; <sup>2</sup>BC Cancer Agency, Surveillance and outcomes unit, Vancouver, Canada; <sup>3</sup>BC Cancer Agency, Radiation Therapy, Vancouver, Canada; <sup>4</sup>BC Cancer Agency, Medical Physics, Vancouver, Canada

**Background:** Surgical clips are used to facilitate image guided 3D conformal radiotherapy for breast cancer. This study was designed to determine which clip type: medium tantalum (MTa), small tantalum (STa), medium titanium (MTi) or small titanium (STi), can best be visualised in a tissue equivalent phantom, using different imaging modalities.

**Materials and Methods:** The visibility of each clip type in each breast quadrant was graded by three blinded observers for BrainLAB ExacTrac floor mounted kilovoltage (kV), isocentric kV, and isocentric megavoltage (MV) imaging modalities. A three point grading system was used: "clearly visible", "some uncertainty" and "not visible". Binomial logistic regression and pairwise comparisons were used for analysis. For computed tomography (CT), the volume of artifact generated by each clip type in the phantom was determined at different slice and index thickness.

**Results:** MTa clips were best visualised (MTa > STa > MTi > STi, p < 0.0001). The visibility for different clip materials, sizes and locations was