Women (N=80), newly diagnosed with BC, were initially evaluated within two weeks of their pending surgery to design their treatment. Follow-up visits were planned for 3, 6, 12, 18 and 24 months post-surgery. Of 80 evaluated pre-surgery (month 0), decreasing numbers returned for later visits. This resulted in sub-sets in which 60 pts were evaluated at months 0-3, 53 at months 0-3, 47 at months 0-3, 32 at months 0-6, 24 at months 0-12, 18 and 35 at all months, 0-3, 53 at months 0-3, 53 at months 0-6, 24 at months 0-12, 18 and 35 at all months, 0-3, 53 at months 0-6, 24 at months 0-12, 18 and 35 at all months.

**Methods**

Subsets: Women (N=80), newly diagnosed with BC, were initially evaluated within two weeks of their pending surgery to design their treatment. Follow-up visits were planned for 3, 6, 12, 18 and 24 months post-surgery. Of 80 evaluated pre-surgery (month 0), decreasing numbers returned for later visits. This resulted in sub-sets in which 60 pts were evaluated at months 0-3, 53 at months 0-3, 47 at months 0-3, 32 at months 0-6, 24 at months 0-12, 18 and 35 at all months, 0-3, 53 at months 0-6, 24 at months 0-12, 18 and 35 at all months, 0-3, 53 at months 0-6, 24 at months 0-12, 18 and 35 at all months.

**Procedure Sequence and Order:** At each visit pts. were assisted to a supine position on a padded examining table in a private room. Arms were marked at sites of subsequent girth measurements. Marks were also made for later TDC measurements (forearm, biceps, axilla and lateral thorax) on both body sides (Figure 1). Girths were measured first. Then TDC measurements were begun with a 2.5 mm effective depth probe at the at-risk forearm and then to biceps, axilla and thorax, each in triplicate. Immediately thereafter the same TDC measurement sequence was started on the other body side. TDC measurements were then made to effective depths of 0.5, 1.5, 2.5 and 5.0 mm at the forearm. For each depth the 1st measurement was on the at-risk arm and a paired-measurement on the contralateral arm. These three pairs of arm to arm measured values constitute one measurement set for each depth. At the end of TDC measurements the bioimpedance electrodes were fitted as shown in Figure 2 and measurements made. Prior to any measurements pts. completed a questionnaire aimed at soliciting her perceived symptoms. The questionnaire asked if any of 12 sensations were now or had been experienced since her last visit in her arm, hand, fingers, axilla or chest. The sensations were: pain, weight, heaviness, tightness, fullness, tingling, tenderness, aching, pain, warmth, cold, swelling and stiffness.

**Background and Objectives**

Background: A woman’s risk of getting breast cancer (BC) treatment-related lymphedema (BCRL) depends on surgery extent, radiation use and type, chemotherapy and obesity. Since lymphedema severity grows without treatment the need for early detection is clear. Researchers have tried to predict pts’ occurrence with arm size and arm bioimpedance measures. Metric based criteria, tested to define BCRL presence, include inter-arm girth differences or changes > 2 cm, inter-arm volume differences > 200 ml and volumes > 10% between at-risk and contralateral arms or changes in these amounts measured at at-risk arms compared with at-risk arms pre-surgery values. A new parameter possibly useful to characterize the lymphedematous state is the tissue dielectric constant (TDC); an index of local skin tissue water (LTW). Two features of this technology render it different from whole limb measurements of volume and bioimpedance; 1) it can rapidly and non-invasively measure any tissue depth relying LTW indices not restricted to arms or legs and 2) it can easily interrogate tissue volumes to different depths revealing changes in depth distributions of water from epidermis to hypodermis. Information regarding TDC in several conditions has been published but there has been no description of the pattern of sequential changes in TDC after breast cancer treatment. These patterns may reveal the natural temporal history of the post-surgical process and have utility as a bare bone TDC

**Main Results**

**Figure 1. Tissue Dielectric Constant (TDC) measurements and sites.** Bilateral TDC measurements were to an effective depth of 2.5 mm at anterior forearm (A), lateral thorax (10 cm inferior to the antecubital fossa, anterior biceps (8 cm proximal to the antecubital fossa), wrist (10 cm inferior to the wrist) and lateral thorax (10 cm inferior to the axilla). Each measurement takes about 10 seconds and starts when the probe is placed on the skin. In addition to the TDC measurements at the various pictured sites TDC was also measured on anterior forearm to effective depths of 0.5, 1.5, 2.5 and 5.0 mm. TDC measurements provide an index of both free and bound water. Pure water has a value of about 78.5.

**Figure 2. Bioimpedance Arm bioimpedance values were determined using five electrodes; two pairs on the dorsal surface of the hand separated by five cm and one on the foot dorsum. After cleaning sites with alcohol, measurement electrodes were placed on the wrist at the level of the process of the radial and ulnar bones and the driving electrodes were placed at least five cm distal on the dorsal surface of the third metacarpal bone of the hands. Impedance measurements were taken with subjects supine and arms slightly abducted and palm down. Smaller impedance values reflect greater amounts of total arm extracellular water. Frequency is stated as ≤ 30 KH. Arm volumes were calculated by measuring arm girths at 4 cm intervals with a spring tension tape measure and calculating volume based on the summation of segmental volumes (www.limbvolumes.org) using the validated frustum model. Girths were measured starting at the wrist with measurements continued up the arm until reaching a pre-marked level close to the level of the axilla.

**Figure 3. TDC probes calibrated by exposing to varying ethanol-H2O concentrations. TDC value is linear with %H2O**

**Figure 4. Forearm TDC depth-dependence:**

**Figure 5. Sequential Ratios** Ratios (at-risk / control) are shown for patients followed for 6 months post-surgery and for each of the other sub-sets. Error bars are standard errors and the single and double asterisk signify mean ratios different than pre-surgery at <0.05 or <0.01 levels. Basic sequential patterns found for this group were then compared to the sub-sets groups comprised of pts. who had been consecutively followed for up to 18, 12, 6 or 3 months post-surgery. Since by 24 months P the number of the same patients seen at each visit was reduced by attrition to 35 from the initial 80 pts, additional sub-set analyses were done to determine if the significance of any observed pattern for the 0-24 month data set was consistent with or better clarified if more pts. were included at specific follow visits. TDC values, arm volumes and bioimpedances and their inter-side differences and inter-side ratios were used in the analyses. Normality of values, tested by the Shapiro-Wilk test, indicated a non-normal distribution (p<0.01) only for arm volumes. Significance of differences between sides (at-risk vs. control) was determined using paired t-tests except for arm volumes for which the Mann-Whitney test was used. Tests for statistical significance of pattern changes over time were based on a general linear model with repeated measures and significance of changes at any month compared to pre-surgery assessed via within-contrast tests. Analysis of significance of overall arm volume pattern changes were done using the non-parametric Friedman test.

**Figure 6. Percent of Pts. experiencing increases in A/C Ratios Data are for threshold ratios of 1.10 and 1.20 threshold increases of 10% and 20% compared to pre-surgery ratios.**

**Conclusions**

TDC measurements were a convenient, portable, non-invasive way for us to rapidly characterize local skin tissue water changes at multiple body sites and at various effective depths below the epidermis. Results of using TDC measurements in the present study to track changes over as long as 24 months suggest that TDC side-to-side ratios at the lateral thorax may be the most likely and sensitive parameter for potentially detecting early BCRL. However other sites may also be useful. Further work is warranted and needed to specifically associate threshold values with well documented evidence of BCRL presence.