

## INTRODUCTION

Skin tissue dielectric constant (TDC) values measured at a frequency of 300 MHz depend on the tissue content of free and bound water (1-5) and have been used to characterize skin tissue water and its change in a variety of settings (6-9). A particularly relevant potential application is the characterization of localized edema or lymphedema in patients who are either at risk for developing these conditions or have lymphedema and are being treated for the condition (10-13). Affected legs in patients with lower extremity lymphedema have been shown to have significantly greater TDC values (14). In breast cancer treatment-related lymphedema (BCRL), tissue dielectric constant (TDC) values, reflecting local skin water, have also been shown to be significantly greater in affected as compared to contralateral forearms (15). However, the magnitude of at-risk side TDC values to contralateral side values prior to surgery has only been preliminarily examined for arms (16) and other anatomical sites (17). Further, changes in pre-surgery TDC values that occur after a patient has had breast cancer surgery have not yet been reported. For the patient that is at-risk for developing lymphedema, pre-surgical evaluations with subsequent follow-ups are clearly the best approach for early BCRL detection. However, in many situations such pre-surgery values may not be able to be taken. So, if TDC values are to be potentially useful as a way to assess or detect early post-surgical lymphedema in the absence of pre-surgery measurements, it is useful to know if breast cancer per se or natural variations between affected (at-risk) and contralateral body sides are associated with significant TDC differences even prior to surgery. Thus the goal of this study was to determine body side differences in TDC values before surgery and secondarily to evaluate the same parameters one year after breast cancer surgery.

## METHODS

With University Institutional Review Board approval, 80 newly diagnosed breast cancer patients were evaluated within two weeks of their pending surgery and 40 of these patients were reevaluated 12 months post-surgery. Bilateral TDC values were obtained using the MoistureMeter-D (Delfin Ltd. Kupio Finland). These were measured to an effective depth of 2.5 mm at anterior forearm (6 cm distal to the antecubital fossa), anterior biceps (8 cm proximal to the antecubital fossa), axilla and lateral thorax (10 cm inferior to the axilla) as shown in figure 1. All measurements were done in triplicate and averaged with the subject in a supine position on a padded examination table. Each TDC measurement takes about 10 seconds and is triggered when the probe makes contact with the skin. The measuring device has a display that reads from 1 to 80. For reference, the dielectric constant of distilled water is about 78. Arm volumes were also determined by measuring arm girth at 4 cm intervals with a spring tension tape measure and calculating volume based on the summation of segmental volumes (18, 19) using the validated frustum model (20-24). In addition to absolute TDC values the ratios of TDC values of at-risk to contralateral sides and the ratios of dominant side to non-dominant sides were also

determined. Pre-surgical parameter values are based on all 80 patients. Comparisons between one-year post surgery and pre-surgery values are based on the 40 patients who were seen both prior to their surgery and also one year post surgery.

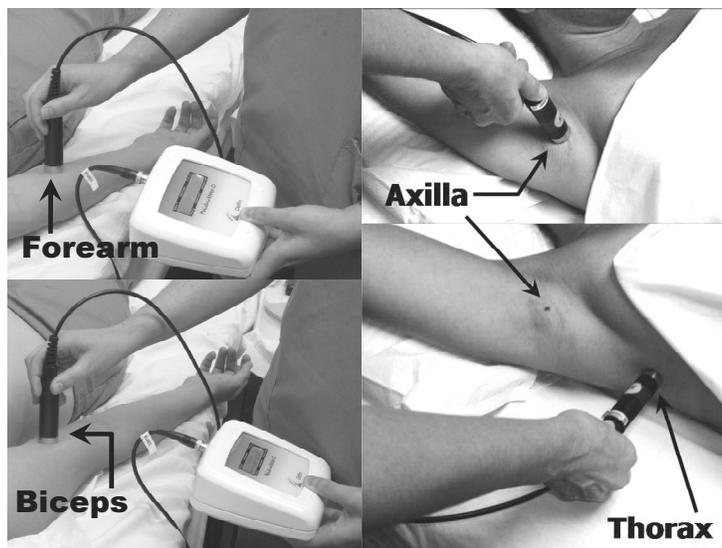


Figure 1. TDC measurement sites

## RESULTS

**Patient Characteristics:** Patient ages (N=80, all data reported as mean  $\pm$  SD) were  $59.7 \pm 13.2$  years with a range from 28 to 82 years. The reported dominant arm was the right arm in 73 of the patients (91.3%) with the remainder reporting their dominant arm as the left (8.7%).

The cancer was present in the breast of the dominant side in 40 patients (50%) and on the non-dominant side in 50% of the patients. Body mass index (BMI) for the group was  $28.5 \pm 7.5$  Kg/m<sup>2</sup> with a range from 17.8 to 48.1 Kg/m<sup>2</sup>. With respect to BMI classification, the percentage of patients considered to be obese (BMI  $\geq 30$  Kg/m<sup>2</sup>) was 31%, considered to be overweight (BMI  $\geq 25$  Kg/m<sup>2</sup> and  $< 30$  Kg/m<sup>2</sup>) was 32.5%, considered to be normal weight (BMI  $\geq 18.5$  Kg/m<sup>2</sup> and  $< 25$  Kg/m<sup>2</sup>) was 35.1% and considered to be underweight (BMI  $< 18.5$  Kg/m<sup>2</sup>) was 1.4%. Patient ages for those evaluated pre-surgery and also followed one year post-surgery (N = 40) were  $57.8 \pm 12.5$  years with a BMI of  $28.5 \pm 6.9$  Kg/m<sup>2</sup>; both parameters were insignificantly different from the pre-surgery group of 80.

**Pre-surgery Parameters:** For the pre-surgery group, absolute values of TDC  $\pm$  SD were determined for each site for cancer vs. healthy sides (figure 2) and for dominant vs. non-dominant sides (figure 3). Comparisons between sides showed no significant difference between sides at any site for either cancer vs. healthy side or for dominant vs. non-dominant side. However based on a general linear model analysis with site as the repeated measure, an overall significant difference ( $p < 0.001$ ) among sites was demonstrated with TDC values at each site significantly different ( $p < 0.001$ ) from each other site. As shown in figures 2 and 3 the TDC value order from greatest to least was axilla  $>$  thorax  $>$  forearm  $>$  biceps.

**Pre-surgery TDC Ratios:** Because of variability in absolute TDC values among patients it is useful to determine the ratio of side-to-side TDC values. Table 1 summarizes these values for [at-risk/contralateral] side ratios and [dominant/non-dominant] side ratios for 80 pre-surgery patients. These ratios indicate near symmetry of TDC values between paired sides with ratios insignificantly different than unity.

Table 1.	Pre-Surgery TDC Ratios				
Ratios Between Sides	Arm Volumes	Forearm	Biceps	Axilla	Thorax
(At-Risk/Contralateral)	$0.993 \pm 0.052$	$0.999 \pm 0.094$	$1.014 \pm 0.158$	$1.029 \pm 0.194$	$0.995 \pm 0.119$
(Dominant/Non-Dominant)	$1.002 \pm 0.053$	$0.991 \pm 0.092$	$1.015 \pm 0.150$	$1.052 \pm 0.212$	$1.006 \pm 0.120$

It is notable that there were no significant differences in any of these ratios among anatomical sites.

**Pre- to One Year Post Surgery Changes:** Figure 4 below shows pre and post surgery TDC and arm volume ratios for 40 patients who were seen both prior to surgery and also at one year post surgery.

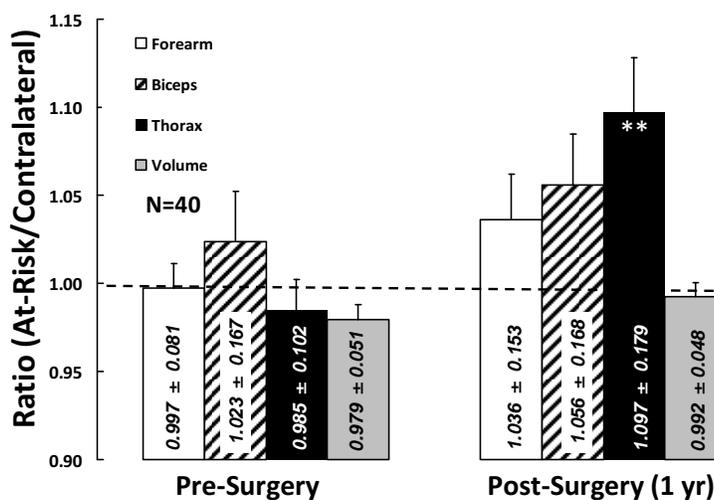


Figure 4. TDC Ratios: Pre and One Year Post Surgery

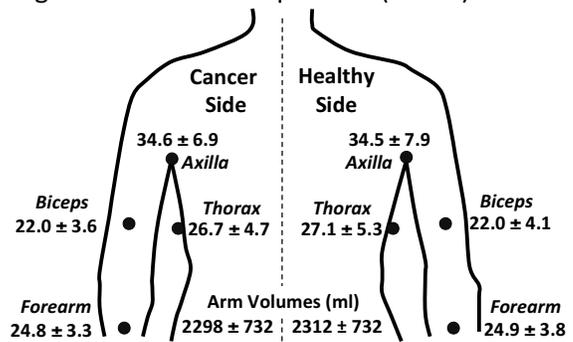


Figure 2. Pre-surgery TDC values: Cancer vs. healthy side

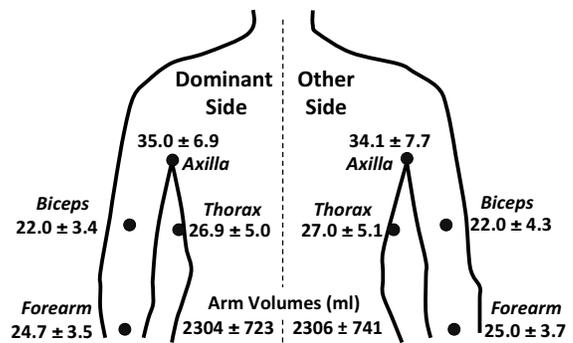


Figure 3. Pre-surgery TDC values: Dominant vs. other side

for 40 patients who were seen both prior to surgery and also at one year post surgery. For the graphic the values in the boxes are mean ratios  $\pm$  SD and bars are sem. Note the trend for an increase in all these parameters at one year but importantly only for the thorax TDC ratio and its absolute change was there a significant increase ( $p < 0.001$ ). The absolute TDC values are summarized below.

N=40	VOLUME (ml)		FOREARM		BICEPS		THORAX	
	PRE	1 YR	PRE	1 YR	PRE	1 YR	PRE	1 YR
mean	2193	2152	25.1	25.7	22.0	22.1	27.0	30.9
sd	615	591	3.6	4.7	3.4	4.5	5.0	7.4

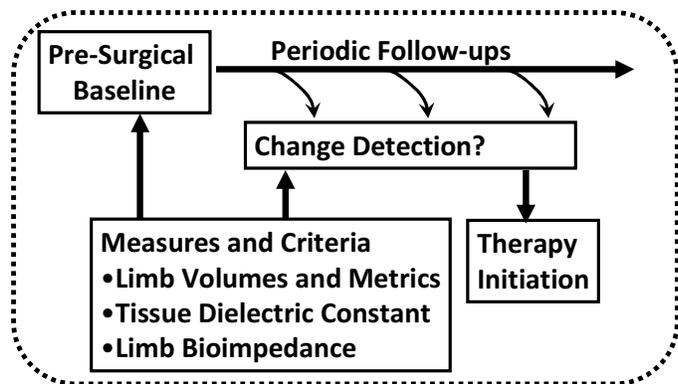
## DISCUSSION and CONCLUSIONS

One of the main goals of the present study was to lay the ground work for the potential use of TDC measurements as a way to provide early detection of incipient lymphedema in at-risk patients. As one step in this process it was important to determine if the presence of the breast cancer itself significantly altered tissue water features of the at-risk side. The results of the present study indicate minimal differences between at-risk and contralateral sides as assessed via absolute TDC values and perhaps more importantly the observation that at-risk to contralateral side ratios are near unity and now have defined inter-patient variances. One aspect of the importance of this finding is its possible use when pre-surgery measurements are not done. Although pre-surgery measurements are clearly the most desirable with respect to detecting possible changes in a manner

schematized in figure 5, there are times and conditions that disallow pre-surgery measurements. However, armed with the knowledge of the pre-surgery “reference” values and their variance it may still be possible to make post surgical measurements that can be used to reasonably assess possible lymphedema emergence. One approach is to consider post-surgical measurements to be indicative of lymphedema when the ratio of at-risk to contralateral side values exceeds the reference groups mean value by a threshold amount equal to a multiple of the standard deviation (SD). Based on the present seminal

findings this might best be applied to the thorax TDC ratio since it was the only ratio that significantly increased at one year post surgery. Choice of threshold at this time is arbitrary but using a threshold of 2.5SD would include more than 99% of cases and yield a detection threshold ratio of 1.29. The threshold ratio if forearms are used is 1.23. The accuracy of these ratios for predictive purposes needs prospective testing. However examination of the present data set indicates that at one year post surgery the thorax threshold was exceeded by 4 patients (10%) and of these patients, 3 showed at least a 10% increase in their arm volume ratio. This would tentatively suggest that the ratio is a good index arm volume increases and possibly more sensitive than either arm volume changes or other whole arm indicators.

In conclusion, the small and statistically insignificant differences between side-to-side parameter values determined prior to surgery suggests that if pre-surgery measurements are unavailable, subsequent differentials between sides that exceed established thresholds may, on average, be diagnostically useful. Based on the isolated elevation of the thorax TDC value at one year post-surgery, it may be that a first indication of incipient lymphedema occurs in thorax tissue. Potential early detection of tissue water changes in this area and other non-limb areas would be possible using the local tissue dielectric constant (TDC) measurement method. Based on a 2.5SD threshold, a thorax side-to-side TDC ratio of 1.29 and/or a forearm ratio of 1.23 may be useful to detect early subclinical lymphedema in persons treated surgically for unilateral breast cancer.



**Figure 5. Approach to Earlier Detection and Intervention**

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