BIOPHYSICAL PARAMETERS AS POTENTIAL INDICATORS OF PRE-CLINICAL LYMPHEDEMA

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BACKGROUND and GOALS

Several methods can be used to assess limb edema such as limb volumes or electrical impedance measures. However, these are not suitable to determine local edema or edema in body parts other than limbs. Quantitative assessment of local edema could provide information not previously available to help initially detect, assess and track edema or lymphedema progression. Reports have shown that local tissue water (LTW) can be assessed by a tissue dielectric constant (TDC) method in patients who have breast cancer treatment-related lymphedema[1-3]. Our main goal was to determine if TDC might be useful as a quantitative measure with the potential for detecting sub-clinical or latent lymphedema.

SUBJECTS and METHOD OVERVIEW

A total of 67 women with ages (mean ± SD) of 60.1±13.5 years (range 28 to 82) and BMI of 28.3 Kg/m^2 (range 17.8-48.0), were evaluated after signing an IRB approved informed consent. All had recently (within one month) been diagnosed with breast cancer and were awaiting breast surgery. All were evaluated prior to their surgery (Visit 0, V0) and then up to five additional times with the 1st follow-up scheduled for 3 months post-surgery. Measurements included arm volumes determined by girths at 4 cm intervals; Arm bioimpedances and TDC based on a probe with a measuring depth of ~2.5 mm. Measurements were done bilaterally and the ratio of affected/control (A/C) side values determined for each measure. Three standard deviations (SD) above the mean pre-surgery A/C was used as an exploratory tentative lymphedema threshold.

BIOIMPEDANCE MEASUREMENTS

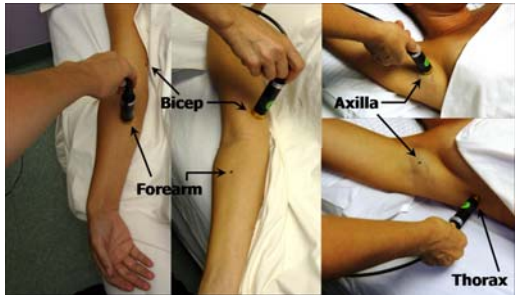
Arm bioimpedances were determined with a single frequency (50KHz) device (www.impedimed.com). Electrical conductance of the arm (reciprocal of resistance) is proportional to the tissue's free water.

Details of this and related methods are available in the literature[4].

1. Mayrovitz HN. Assessing local tissue edema in postmastectomy lymphedema. *Lymphology* 2007; 40: 87-94.
2. Mayrovitz HN, Weingrad D, Davey S. Local tissue water in at-risk and contralateral forearms of women with and without breast cancer treatment-related lymphedema. Lymphedema Research and Biology 2009;7:153-158
3. Mayrovitz HN. Local tissue water assessed by measuring forearm skin dielectric donstant: Dependence on measurement depth, age and body mass index. Skin Research and Technology 2010;16:16-22
4. Ward LC, Czerniec S, Kilbreath SL. Quantitative bioimpedance spectroscopy for the assessment of lymphoedema. Breast Cancer Res Treat. 2009;117:541-547
5. Alanen E, et al. Measurement of dielectric properties of subcutaneous fat with open-ended coaxial sensors. *Phys Med Biol* (1998); 43: 475-485.
6. Nuutinen J et al. Validation of a new dielectric device to assess changes of tissue water in skin and subcutaneous fat. *Physiol Meas* (2004); 25: 447-454.

TDC MEASUREMENTS

Tissue Dielectric Constant (TDC) was measured with the MoistureMeter-D, (Delfin Technologies Ltd, www.delfintech.com). It consists of a cylindrical probe connected to a control unit that displays the TDC value when the probe contacts the skin. The physics and principle of operation has been well described[5-6]. In brief, a 300 MHz signal is generated within the control unit and is transmitted to the tissue via the probe that is contact with the skin. The portion of the incident electromagnetic wave that is reflected depends on the dielectric constant of the tissue, which itself depends on the amount of free and bound water in the tissue volume through which the wave passes. For reference, pure water has a value of about 78.5. The effective penetration depth depends on probe dimensions; larger spacing between inner and outer conductors corresponding to greater penetration depths. In this study a probe with an effective depth of ~2.5 mm was used at the forearm, biceps, axilla and thorax as shown below.



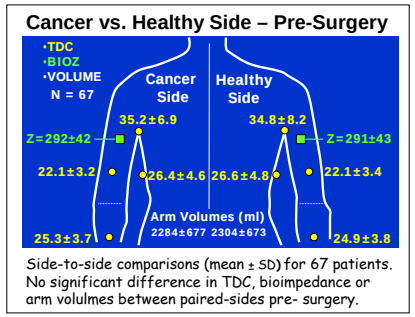
Measurements were done with subjects supine at four paired standardized sites (both sides) as follows: volar forearms, 6 cm distal to the antecubital crease, medial biceps 6 cm proximal to the antecubital crease, axilla and lateral thorax 8 cm below the axilla. Measurements were obtained in triplicate-pairs alternating between body sides. At each site the three measurements were averaged and used to characterize the site average TDC value. The time required to obtain a single measurement, once the probe was placed in contact with the skin, was about 10 seconds.

ARM VOLUME DETERMINATIONS

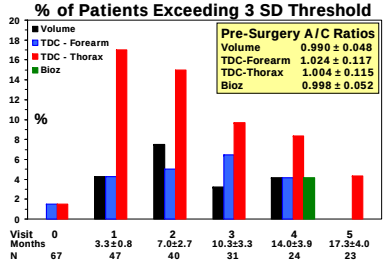
Arm circumferences were measured with a Gulick tape measure at 4 cm intervals starting at the wrist and progressing to the axilla. Volumes were calculated using girth values in a truncated-cone model using a standardized and widely used software package. (Limb Volumes Professional 5.0, www.limbvolumes.org).

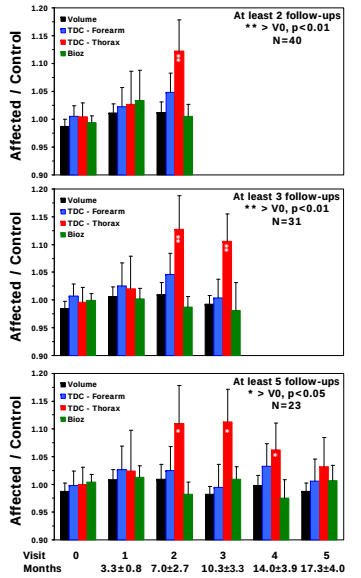
Dr. Mayrovitz invites you to e-mail him at mayovit@nova.edu with any questions or comments or to request an electronic copy of this poster.

MAIN RESULTS



Side-to-side comparisons (mean ± SD) for 67 patients. No significant difference in TDC, bioimpedance or arm volulmes between paired-sides pre- surgery.





SUMMARY AND CONCLUSIONS

1. In 67 newly diagnosed breast cancer patients, biophysical measures to detect incipient lymphedema showed no difference in any parameter between the cancer affected side and the control side prior to the patient's breast cancer surgery.
2. Follow-up post surgical assessments revealed a statistically significant increase in the tissue dielectric constant (TDC) of the affected thorax that reflects an increase in local tissue water.
3. The TDC increase at the thorax was first noted about 7 months post-surgery in patients seen for at least 2, 3 and 5 follow-up visits. In the 5 follow-up visit group, the increase that was noted at month 7, tended to decrease toward pre-surgery levels at 17 months post-surgery.
4. No other biophysical parameter showed a significant increase as compared to pre-surgery values.
5. An exploratory lymphedema threshold was formulated based on the pre-surgery mean (Y) and standard deviation (SD) of affected to control side values (A/C). A value equal to Y + 3 SD at any post-surgical visit was taken as a tentative estimate of sub-clinical incipient lymphedema.
6. Application of this exploratory threshold revealed that the thorax TDC measurement resulted in the greatest theoretical early detection warning parameter.

In conclusion, the present results suggest a possible utility of tracking local tissue water in the thorax as the earliest warning of impending breast cancer treatment-related lymphedema. Other sites and methods may show themselves to be useful as more patients are followed for longer times. Also, since the TDC approach to characterizing lymphedema is not limited to limbs, it should be possible to assess localized lymphedema and its change in the hand, finger, head, neck, genitalia, and so on.