Proceedings of BIO2006
2006 Summer Bioengineering Conference
June 21-25, Amelia Island Plantation, Amelia Island, Florida, USA

BIO2006-151744

A METHOD TO MEASURE LOCAL TISSUE WATER AND ITS APPLICATION TO EVALUATE BREAST CANCER TREATMENT-RELATED LYMPHEDEMA

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INTRODUCTION

Although several methods are available to assess overall limb edema from segmental volume measurements [1] such methods are generally not applicable to determine local edema or edema in body parts other than the limbs. Quantitative assessment of local tissue edema, such as on the periphery of skin wounds or in focal areas of edema, such as present in several clinical conditions, could provide useful information not previously available. Recently, a device, potentially useful for this purpose, became available [2]. Its working principle is based on the fact that tissue electrical properties depend on water content which in turn affects the value of the tissue dielectric constant (TDC). Measurement of the TDC thus provides an index of the skin-to-fat relative tissue water (RTW) on a scale of 1 to 80. Our goal was to determine the suitability of this approach to detect edema in patients with unilateral arm lymphedema secondary to breast cancer treatment. We hypothesized that the TDC of affected arms would be significantly elevated compared to contralateral non-affected arms.

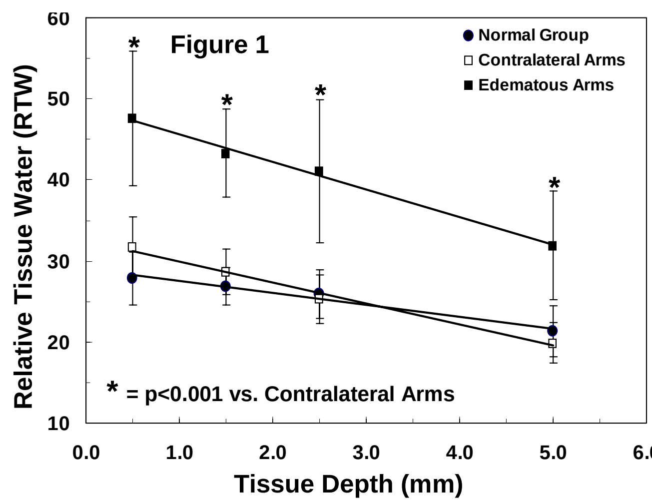
MATERIALS AND METHODS

The device used measures local TDC using an open-ended coaxial probe placed in contact with the skin [3-5]. A 300 MHz wave that is injected into the skin is partly absorbed, mostly by water, and the remainder reflected. Analysis of the reflected wave allows for the determination of the RTW. The depth of penetration of the incident energy depends on the probe dimensions, with larger diameter probes allowing for greater penetration depths [6]. In this study four different size probes were used with effective penetration depths of 0.5, 1.5, 2.5 and 5 mm (MoistureMeterD, Delfin Technologies Ltd, Finland).

RTW was determined from measured TDC in edematous (E) and contralateral normal (N) forearms of 10 women who had unilateral arm lymphedema subsequent to mastectomy and other treatments for breast cancer. Measurements were done in triplicate at a standardized volar forearm site located 7 cm distal to the antecubital crease prior to the start of lymphedema therapy. Similar measurements were also done in a control group of 15 healthy women. In 10 of these controls, measurements were repeated during three sequential visits separated by 14 days. These sequential measurements were done to characterize normal values and temporal variability. In addition to the RTW measures, volume (V) of a four-cm segment encompassing the RTW measurement site was determined by arm circumferences and calculations using an elliptical frustum model [7]. For the patient group, edema percentage was calculated as $100(V_E - V_N)/V_N$. All data in graphs and elsewhere are given as mean values ± sd.

RESULTS

RTW values obtained at the initial visit for the control group (N=15) and patient group (N=10) as a function of depth are shown in Figure 1.

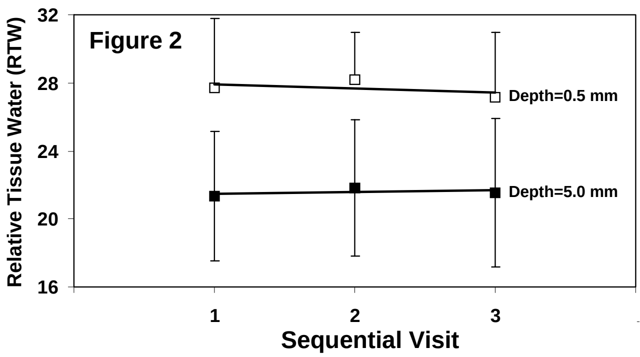


In Figure 1 the solid lines are determined by linear regression and are all highly significant ($p<0.001$) with R^2 values being 0.994, 0.989 and 0.975 for the affected arms, contralateral arms and normal arms respectively. The mean value of RTW for affected arms is greater than for contralateral arms at all tissue depths measured ($p<0.001$). Contrastingly, RTW of non-affected contralateral arms of the patient group does not differ from the normal control group RTW values.

For the patient group, arm segment edema was determined to be 39.0±17.6% with absolute segmental volumes of 268±53 ml for the edematous arm compared with 195±42 ml for the non-affected contralateral arm, $p<0.0001$. In comparing right vs. left arms for the normal control group, neither segmental volumes (181±39 vs.179±38 ml), nor RTW values differed significantly between arms at any depth ($p>0.5$). However, over the range of segmental edema present in the patient group (9-69%) there was no significant correlation between segmental percentage edema and corresponding RTW values.

Long Term Repeatability

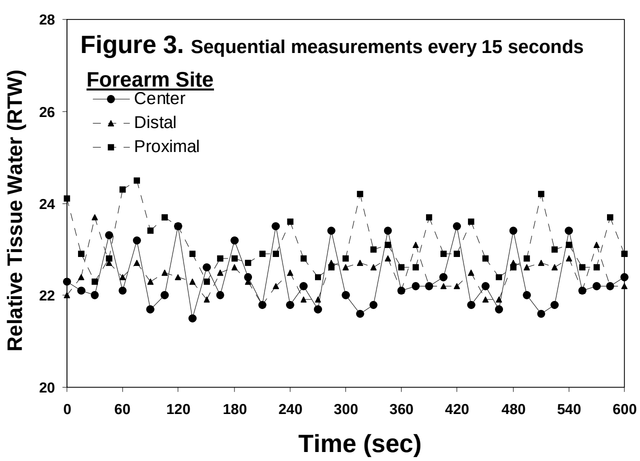
The sequential values of RTW obtained for the 10 normal subjects measured 14 days apart are shown in Figure 2 for the minimum tissue depth (0.5 mm) and maximum tissue depth (5.0 mm).



The constancy of the RTW values obtained for these repeated measures as well as the uniformity of the variances among subjects shown in Figure 2 attests to the long-term repeatability of this measurement method. Results were similar for 1.5 and 2.5 mm depths.

Short Term Repeatability and Spatial Variability

Sequential measurements at the center of a target forearm site and at sites two cm distal and proximal to the center are shown in Figure 3.



The pattern seen in Figure 3 indicates good short term repeatability at the central site (coefficient of variation = 2.8%) with small differences between the center site and the proximal and distal sites.

DISCUSSION

The present study is the first to investigate the possibility of using this method and device to evaluate local tissue edema in patients with lymphedema. The RTW values found for edematous arms exceeded those in the corresponding contralateral arm of all patients. The short term (Figure 3) and longer-term (Figure 2) repeatability results suggest that the method is suitable for tracking changes in RTW over time and that the values obtained are not greatly sensitive to the exact location of the measurement when done in intact skin.

The results (Figure 1) demonstrate a significant dependence of the RTW value on the effective depth of the measurement. This was true in the edematous tissue and in normal tissue in both patients and controls. Such dependence is consistent with the known variation in tissue constituents and their water content with depth below the skin surface. Since effective measurement depth is determined by the depth of field penetration, larger diameter probes will result in an increased effective measurement depth. Thus, the net RTW value that is determined is increasingly influenced by the deeper tissue constituents such as subcutaneous fat and their smaller relative water content.

Despite the significantly greater RTW values obtained in the patient's edematous arm segments compared to their contralateral arms, no significant correlation was found between the relative RTW values and the amount of excess volume of the edematous segments. This finding is consistent with the fact that RTW values reflect water content within the effective measuring depth, which in this study was not greater than 5 mm. In contrast, the effective arm radius included in the volumetric assessment of edema for the patients averaged 45.8±4.8 mm, with a range of 37 to 53 mm. Thus, similar values of RTW could occur despite substantial differences in total arm segment volume. This feature suggests that the RTW value may have a greater sensitivity to the detection of early edema or lymphedema than corresponding volumetric indices.

CONCLUSIONS

Results suggest that this method may serve as a rapid quantitative assessment procedure to document lymphedema and possibly for early detection of incipient lymphedema not yet clinically observable.

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