Title: Skin-to-Fat Water in Diabetes Mellitus Assessed by Tissue Dielectric Constant (TDC): Variations with Respect to Depth, Anatomical Site and HbA1C

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Background: Worldwide, there are about 285 million people who have been diagnosed with Diabetes Mellitus and about 1/3 of them manifest with skin changes. Research using ultrasound indicates that patients with DM have thinner skin and less subcutaneous fat than age-matched controls. This finding is consistent with the idea that such biophysical changes may alter the skin-to-fat tissue water content that then alters skin functions. Literature is consistent with the theory that hyperglycemia-induced non-enzymatic glycation of structural and regulatory proteins play a major role in the pathogenesis of diabetic complications. In this scenario, excess supply of glucose in the blood plasma leads to a non-enzymatic chemical reaction between the carbonyl group of glucose and the amino acid of proteins. This glycation of structural and regulatory proteins plays a key role in the pathogenesis of diabetic skin complications such as diabetic ulcer or diabetic foot syndrome; however, it is not clear how changes in tissue water content affect this process.

Objective: We hypothesize that in persons with DM dermal collagen glycation displaces bound water and thereby decreases free water space and that this leads to a reduction in skin tissue water. The purpose of this study is to test this hypothesis.

Methods: Skin-to-fat tissue water was determined by measurements of TDC at 300 MHz at the anterior forearm, lateral calf and foot dorsum in persons with previously diagnosed DM who were presenting for a routine clinic visit. TDC measurements are made by touching the target skin site with a sensor for about 10 seconds. The TDC value largely depends on the amount of free and bound water within the interrogation region. In this study 4 different sensors were used that allowed for measurements to 0.5, 1.5, 2.5 and 5.0 mm below the epidermis. In addition to TDC measurements, body composition parameters of each subject were determined using a bioimpedance scale on which the subject stood for about 15 seconds during the measurement. The parameters measured included percentages of total body water and fat and also limb segmental fat percentages.

Results: Comparisons among depths showed that TDC values monotonically decreased from the most shallow at 0.5 mm to the deepest at 5.0 mm ($p<0.001$). TDC values at each depth were significantly ($p<0.001$) different from each of the others. The one exception is the finding of no difference between 2.5 mm and 5.0 mm depths at the foot. TDC values tended to be highest at the foot, middle at the leg and least at the forearm. However statistical significance of these differences depended on the measurement depth being highly significant at 5.0 mm ($p<0.001$) and not significant at 0.5 mm. There is only a weak correlation between TDC values and HbA1C, and there was no significant correlation at any site or depth.

Conclusions: The trend for a negative correlation between TDC values and HbA1c is not statistically significant at any measured depth. Therefore, with respect to tissue water it is unlikely that HbA1c is of significant clinical importance. However, the depth and site data provide baseline information on patients with diabetes for subsequent use.