**Title:** Investigation of glycosylation effects on skin-to-fat tissue water content in persons with diabetes mellitus (DM) assessed by skin tissue dielectric constant (TDC)

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**Background:** World wide, about 285 million people live with DM and about 1/3 undergo some form of skin changes. While patients with type I diabetes are more likely to suffer from autoimmune related skin lesions, patients with type II diabetes are more prone to cutaneous infections. Prior research indicates that diabetic patients have thinner skin and less subcutaneous fat compared to age-matched controls. The presence of such skin changes may indicate biophysical changes that alter skin-to-fat tissue water content that may precipitate further changes that depend on the degree of glucose control. It is well established that excess glucose leads to non-enzymatic chemical reactions between the carbonyl group of glucose and amino acids. 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. But, it is not clear how changes in tissue water content affect this process.

**Objective:** We hypothesize that the skin-to-fat tissue water as measured by TDC is inversely related to HbA1c in persons with DM. The study objective 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. The target number of persons scheduled for inclusion is 40 and at this writing we have fully evaluated 15 subjects.

**Results:** Comparisons among depths showed that TDC values monotonically decreased with increasing effective measurement depth at all measured sites (forearm, leg and foot) with TDC values at 0.5, 1.5, 2.5 and 5.0 mm being significantly (p<0.001) different from each other. Comparisons among sites showed that the presence of significant differences among sites depended on the measurement depth. At 0.5 mm depth there was no difference among sites whereas at depths of 2.5 and 5.0 mm all sites differed from each other with TDC values of the foot greater than the leg and the leg greater than the forearm (p<0.001). Analyses further showed that at all measured depths foot TDC values were negatively correlated with HbA1c with r values ranging from -0.421 to -0.582 but that statistical significance was demonstrated as yet only for a depth of 1.5 mm.

**Conclusions:** The tentative inverse correlation between TDC values and HbA1c, if substantiated by inclusion of more subjects, would suggest a previously unknown link between DM status and skin water with several potential clinical implications.