Millimeter-Wave Non-Invasive Monitoring of Glucose in Anesthetized Rats

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***Abstract*—The realization of a non-invasive monitor for determining blood glucose concentrations in human subjects is a prescient driver for many new techniques spanning optical, chemical, electronic and radio sensors. Microwaves offer the possibility of simple, compact, non-invasive, and continuous measurement of glucose level in superficial tissue layers without significant heating, enzymatic reactions, or any short or long term deleterious effects on the tissue. This paper demonstrates the first real-time direct correlative measurements of the blood glucose concentration (using commercial blood test strips) and millimeter-wave (MMW) absorption during intraperitoneal injections of glucose, insulin, and saline in a live anesthetized animal. MMW transmission and reflection in the Ka band (27-40 GHz) was measured with a commercial vector network analyzer and non-invasive waveguides positioned on the ear. The data shows strong correlation between the blood glucose levels and MMW absorption during the experimentally induced hyper- and hypoglycemia.**

I. INTRODUCTION

COMPACT transportable and continuous monitoring of blood glucose levels without the need for invasive sampling of the blood is considered to be a "Holy Grail" for multiple clinical applications, and particularly for use in diabetic and hospital-bound patients during sleep [1]. MMW absorption in human blood samples has been shown to correlate with the glucose concentration through the complex refractive index [2]-[5]. In this study, we aim to evaluate the correlation of MMW absorption and reflection in vivo through the ear of anesthetized rats, with the absolute blood glucose levels as measured by a commercial glucometer. The results provide a strong incentive for the development of a portable non-invasive instrument for continuous monitoring of glucose in humans, based on simple and inexpensive microwave absorption techniques.

II. EXPERIMENTS

We have developed and tested a simple waveguide-to-waveguide active transmission probe (Fig. 1) that can clamp on the ear, finger webbing, or any loose skin fold for continuously monitoring of MMW transmission or reflection using a vector analyzer or simple microwave source and detector. Using power levels below the safe exposure limit of 1 mW/cm^2, we have been able to detect significant changes in the absorption and reflection coefficient (magnitude and phase) of MMW signals in Ka band (27-40 GHz) measured through the ear (including the skin and underlying perichondrium) during 0.5-ml intraperitoneal injections of glucose and insulin in anesthetized rats. The injected amounts of glucose (1g per kg of body weight) and insulin (2 Units per kg of body weight) produced considerable hyper- and hypoglycemia that are characteristic of changes observed in diabetic patients [6]. As a negative control, the animal was also injected with 0.5 g/kg of saline.

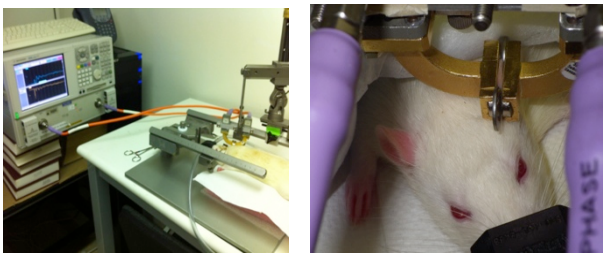

Fig. 1. Left: Microwave vector network analyzer with coax-waveguide transitions. Available sweep frequency is 27-40 GHz. Transmission and reflection data is collected at all frequencies as a function of time. Right: Photo showing two waveguide ports gently clamped around the ear of an anesthetized rat.

In our first set of measurements we injected MMW power between 0.1 and 2 mW onto the waveguide delivery system around the ear. We continuously monitored the transmitted and reflected power (magnitude and phase) as the frequency was repeatedly stepped through the range of frequencies (27-40 GHz) every 2 seconds, and the cycle repeated every 30 seconds. The total power absorption varied between 17 and 20 dB and the reflected power was approximately 3 dB. The vector network analyzer had more than sufficient dynamic range to record both transmitted and reflected power with high signal-to-noise ratio (>30 dB). Changes observed in both transmitted and reflected power magnitude and phase, correlated with the time-course of blood glucose changes and were independent of the body temperature (data not shown).

In a second series of measurements, we replaced the vector network analyzer with a simple MMW source and square law detector, and measured only the transmission magnitude. In these measurements we injected a power between 0.04 and 0.3 mW (0.3-2.2 mW/cm^2) over the same Ka band frequencies (27-40 GHz) with the same frequency step and cycle duration. The blood glucose concentration was measured using a commercial test kit (Alpha TRAK 2 Blood Glucose Test Strips, Abbott Diabetes Care) and sub-microliter blood samples taken from animal's leg or tail at regular intervals (every 10-15 minutes). The MMW transmission magnitude vs. time and frequency was continuously recorded for more than 4 hours during the intraperitoneal (i.p.) injections of glucose, insulin, and saline. Body temperature and respiration were also continuously monitored.

The changes observed (Figs. 2 and 3) – an increase in MMW transmission after glucose injection, and a decrease in transmission after insulin injection - are consistent with the reported decrease in MMW conductivity and index of refraction of in vitro blood samples with increasing glucose concentration [7] and follow a Cole-Cole model for dielectric change

with frequency [8]. A relatively slow time constant for the observed changes (10-15 minutes for glucose and 20-40 minutes for insulin) correlates well with the expected speed of glucose and insulin metabolism. The lack of significant changes in MMW transmission upon injection of saline (Fig. 4) indicates the selectivity of MMW absorption to the tissue concentration of glucose.

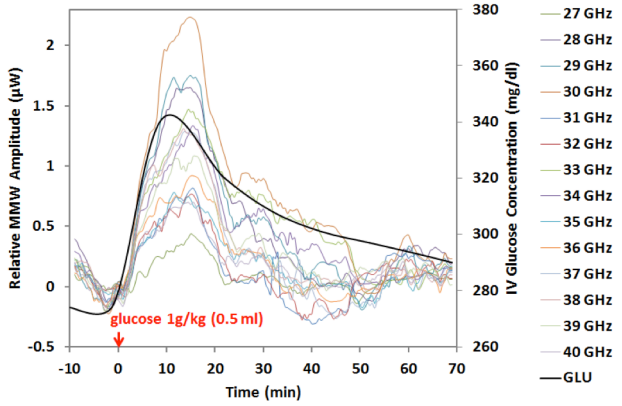

Fig. 2. Time-course of changes in MMW absorption at 27-40 GHz and blood glucose concentration (black line) after i.p. injection of glucose.

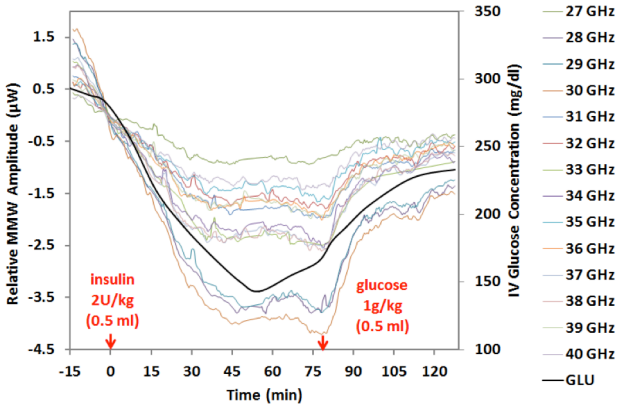

Fig. 3. Time-course of changes in MMW absorption at 27-40 GHz and blood glucose concentration (black line) after i.p. injection of insulin (at 0 min) followed by i.p. injection of glucose (at 78 min).

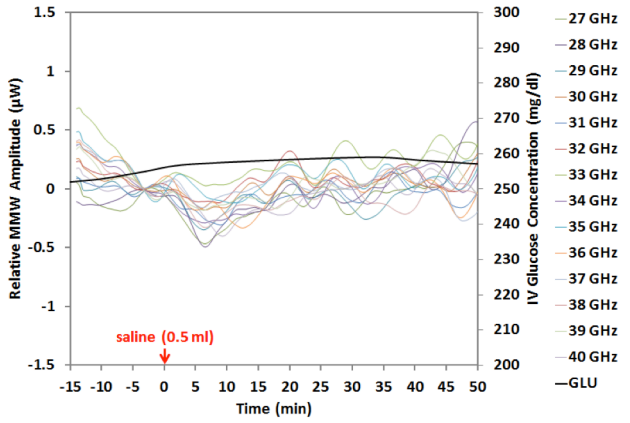

Fig. 4. Time-course of changes in MMW absorption at 27-40 GHz and blood glucose concentration (black line) after i.p. injection of saline.

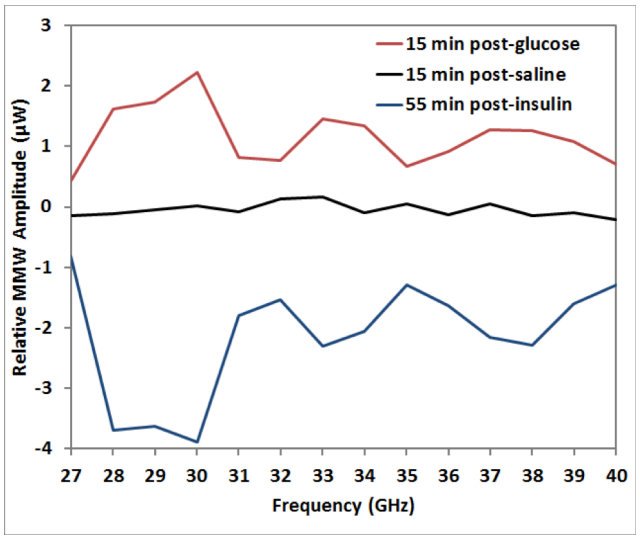

Fig. 5. MMW absorption versus frequency at indicated times after i.p. injections of glucose (red), saline (black), and insulin (blue). Frequency-dependent variations represent the standing wave in the waveguides. The power levels shown here and in Figs. 2-4 are extrapolated from the measured square law detector responsivity (approximately 0.28 mV/uW) and are close to threshold levels of a few tenths of a microvolt.

III. SUMMARY

To the authors' knowledge, these experiments provide the first published demonstrations of real time non-invasive monitoring of glucose concentration in vivo using millimeter-wave signals. Follow-up experiments will utilize a more portable, compact sensor/source arrangement on active (non-anesthetized) animals. MMW transmission data can then be correlated with blood glucose concentration and sorted out from any confounding influence of glucose-coupled biochemical and/or physiological parameters.

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