Ultrasound for correction of secretory deficiencies as a potential novel treatment for type 2 diabetes

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THE COST OF DIABETES

Type 2 diabetes mellitus is a complex metabolic disease that has reached epidemic proportions in the United States and around the world. Controlling type 2 diabetes is often difficult. Many patients are poorly compliant with lifestyle change recommendations, and pharmaceutical management routinely requires complex therapy with multiple medications, and loses its effectiveness over time. Thus, new modes of therapy are needed that will target directly the underlying causes of abnormal glucose metabolism. The objective of this study is to explore a novel, non-pharmacological approach that utilizes the application of ultrasound energy to augment insulin release from pancreatic β-cells.

THE POTENTIAL PRODUCT

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METHODS AND MATERIALS

• A planar ultrasound transducer was used to sonicate the cells using a wide range of ultrasound parameters.
  • Frequencies: 400 kHz, 600 kHz, 800 kHz, 1 MHz
  • Intensities: 0.5, 1 W/cm²
  • Duty cycle: 100% (continuous) for a duration of 5 minutes
  • β-cells were placed and suspended in an exposure chamber made of polyactic acid (PLA) with acoustic transparent windows made of Mylar (Fig. 3).
  • Cell samples (100 μL) were collected before ultrasound treatment (t = 0 min), 5 min after the start of the treatment and 30 min after the end of treatment.
  • In a separate set of experiments, we used amperometry detection to test controllability of ultrasound-stimulated secretory release from β-cells (Fig. 4).

PRESSURE MAPS & THERMAL MEASUREMENTS

• The experimental setup was modeled with PZFlex and pressure maps were generated for all ultrasound exposures to determine the range of pressures to which the cells are exposed to during treatment (Fig. 5).
• Material properties, parameters and dimensions were compiled from measurements and manufacturers’ data.
• Temperature variations inside the exposure chamber were monitored throughout the ultrasonic treatment by inserting a thermocouple in the chamber.
• In all cases, temperature inside the chamber increased by a maximum of 2°C on average (Fig. 6).

RESULTS

• Our data indicated that application of therapeutic ultrasound can lead to safe increase of insulin secretion from β-cells at a frequency of 800 kHz and intensity of 1 W/cm².
• Amperometry results suggest that ultrasound-stimulated secretory events can be tightly controlled in a Ca²⁺-dependent manner.

CONCLUSIONS AND FUTURE WORK

If proven successful our method may find a clinical application due to the non-invasive nature of therapeutic ultrasound treatment of human pancreas (through an appropriate acoustic window). Our future studies will focus on finding an optimal set ultrasound parameters for applications to the pancreas in an in vivo animal model, to determine whether it would be possible to stimulate β-cells without stimulating other endocrine and exocrine cells of the pancreas.

Acknowledgment: Funded by NIH Award-1R03EB019065-01