Technical University of Denmark

# Modelling the glucose-insulin-glucagon dynamics after subcutaneous administration of native glucagon and a novel glucagon analogue in dogs

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"I confirm that I am aware of conflicts of interest in my presentation. I agree to declare this conflict of interest at the beginning of my presentation during the meeting."

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**MODELLING THE GLUCOSE-INSULIN-GLUCAGON DYNAMICS AFTER SUBCUTANEOUS ADMINISTRATION OF NATIVE GLUCAGON AND A NOVEL GLUCAGON ANALOGUE IN DOGS**


**Background and aims:**
Simulation and prediction based verification are required for glucagon bolus strategies for treatment of severe hypoglycemia in diabetes patients and for glucagon administration strategies by a dual-hormone closed-loop system. We aim to develop an improved simulation model of the complex glucose-insulin-glucagon dynamics.

**Method:**
We adopted a physiological model of endogenous glucose production with multiplicative effects of insulin and glucagon and combined it with the Hovorka model of glucose and insulin. We estimated model parameters using data from 10 experiments in 5 dogs who received two subcutaneous bolus injections of a novel Zealand Pharma glucagon analogue (ZP-GA-1) with increased stability in liquid formulation (20 and 120 nmol/kg). Model parameters were also estimated using data from 20 experiments in 10 dogs who received two subcutaneous bolus injections of native glucagon (20 and 120 nmol/kg or 10 and 50 nmol/kg). We used the Bayesian approach to estimate model parameters by Maximum a Posteriori (MAP) estimation given priors reported in the literature.

**Results:**
We report posterior probability distributions for each of the model parameters. Based on visual inspection, the model fitted data satisfactorily for both glucagons. Paired t-tests confirmed that the estimated parameters were similar after SC administration of native glucagon and ZP-GA-1.

**Conclusion:**
The new model enables more realistic simulations of the glucose-insulin-glucagon dynamics. In a future study, we will estimate human model parameters so the model can be used for comparative simulations of native glucagon and the glucagon analogue in humans, which will benefit the development of dual-hormone closed-loop systems for treatment of diabetes.

Final submission:

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