INTRODUCTION

OVERVIEW: Tight glucose control (TGC) reduced intensive care unit (ICU) patient mortality up to 45% using a target of 6.1 mmol/L. TGC also reduce organ failure rate, severity and cost.

"Virtual trials" are performed using a clinically validated model of the glucose-insulin system. Insulin sensitivity, $S_g$, is used as the critical marker of a patient’s metabolic state and is assumed independent of the model inputs.

Virtual trials can be used to simulate a TGC protocol using a SI profile identified from clinical data and different insulin and nutrition inputs. Virtual patient trials have been used in design of TGC protocols. The clinical results of SPRINT showed very close agreement to expected results from simulation.

The performance of virtual trials on separate cohorts, independent of the ICU used to generate the virtual patients, has not yet been performed.

GOALS: This study provides a source of independent, matched patient data for two groups treated with different TGC protocols. Patients in the Glucontrol study were randomised into two, matched cohorts with different glycemic protocols and targets.

Only data from one Glucontrol centre (University Hospital of Liege, Belgium) was used.

Virtual trial simulations are used to assess model errors and validate the overall virtual trials approach.

VIRTUAL TRIALS METHODS

CLINICAL DATA

- 211 patients were treated using the Glucontrol protocol at CHU de Liege, Belgium, between March 2004 and April 2005.
- Patients were randomly divided into two groups:
  - Group A – Glucontrol A protocol.
  - Group B – Glucontrol B protocol.

RESULTS & DISCUSSION

SELF & CROSS VALIDATION

SELF VALIDATION:

- Assess the ability of in-silico virtual trials to reproduce the clinical data.
- Differences of simulation results to clinical results are due to model errors and/or lack of perfect compliance.

CROSS VALIDATION:

- Test the assumption that the SI profiles accurately capture patient dynamics, independent of the insulin and nutrition inputs used to create them.
- The patients in simulation will receive very different amounts of insulin compared to what was given clinically.
- Both cohorts are matched clinically, differences can be ascribed to the independence assumption behind this virtual trials method.

CONCLUSIONS

- Self Validation indicates a clinically insignificant error in these virtual patient methods due to model and/or clinical compliance.
- Cross Validation clearly shows the virtual patients enabled by the identified patient-specific SI(t) profiles are independent of the clinical inputs used to generate these profiles.
- These outcomes validate the ability of the virtual patients and in silico virtual trial methods presented to accurately simulate, in advance, the clinical results of an independent TGC protocol, directly enabling rapid design and optimisation of safe and effective TGC protocols with high confidence of clinical success.

REFERENCES