UC UNIVERSITY OF CANTERBURY
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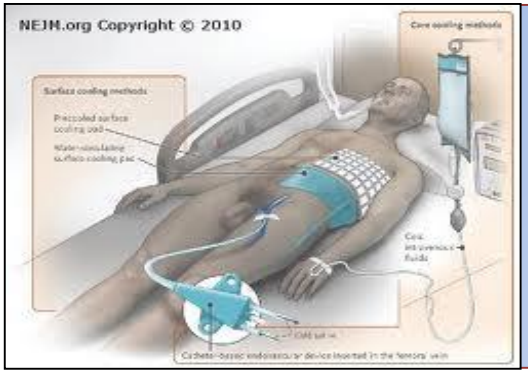
CHRISTCHURCH NEW ZEALAND

UC BIOMEDICAL ENGINEERING

Insulin Sensitivity Variability During Hypothermia

Presented by:.....



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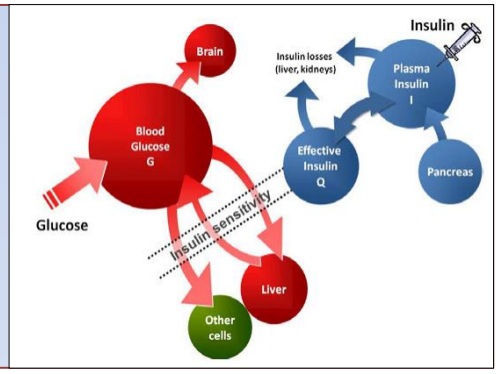
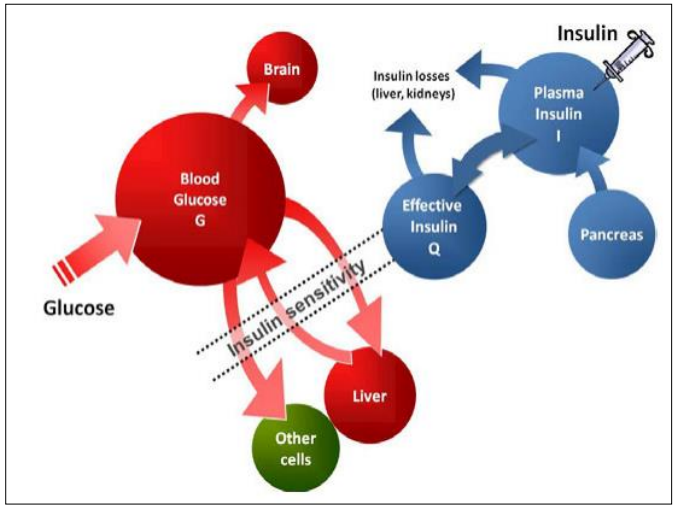


BACKGROUND

1. Tight glycemic control (TGC) has benefited Out-of-Hospital Cardiac Arrest (OHCA) patients, who have low survival rates and often experience hyperglycemia [Neumar et al. 2008].

2. Hypothermia is often used to treat OHCA patients, but its impact on metabolism and insulin resistance in critical illness is unknown.

Objective of the study:
To analyze metabolic dynamics of OHCA patients treated with **hypothermia** using **ICING** model-based insulin sensitivity (SI) for safe and effective TGC.



PATIENTS AND METHODS

Patients Background:

Total: 240 OHCA patient (9988 hrs)

From : Christchurch, Erasme & Lausanne ICU Hospital.

BG & temperature readings were taken 1-2 hourly.

Data were divided into 3 periods:

1. Cool , max: 24 h
2. Warm, max:24 h
3. Idle, max: 2h

Create Virtual 20 OHCA Patients from Clinical Data

START

1) Raw Clinical Data:

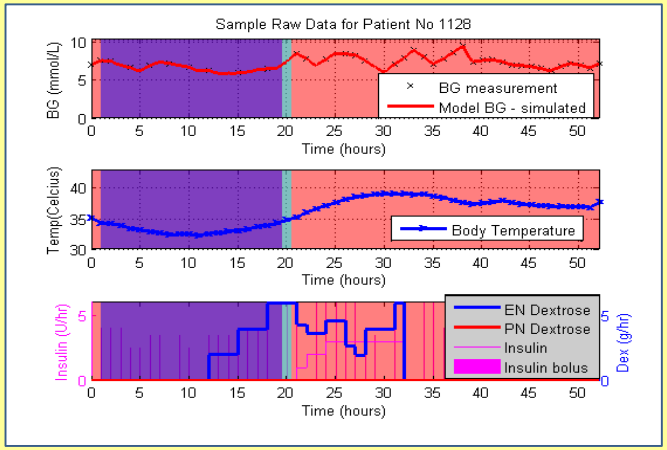
- **BG and Temperature**
- **Insulin time/rates**
- **Enteral and parenteral dextrose time/rates**

2) Fit Data:

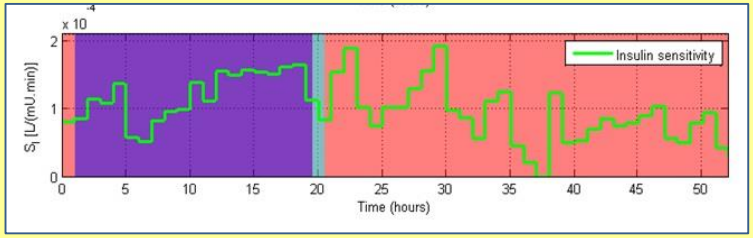
The Insulin Sensitivity (SI (t))profiles is identified hourly using the ICING model.

Virtual Patients with SI Profile

Raw Clinical Data



Insulin Sensitivity (SI(t)) Profile



Legend: Cool period (T<35°) Warm period (T>35°) Idle period (2 hours)

ANALYSIS AND METRICS

The impact of insulin sensitivity (SI) level and variability during cool and warm is analyzed per-cohort and per-patient using 6-hour blocks defined below:

Day	Period	Analysis	Block	Hour Range
1	Cool	6-hour block	1	0 – 6 hours
			2	6 – 12 hours
			3	12 – 18 hours
			4	18 – 24 hours
Idle 2 hour period in between cool and warm				
2	Warm	6-hour block	5	24 – 30 hours
			6	30 – 36 hours
			7	36 – 42 hours
			8	42 – 48 hours

SI LEVEL	
Cohort	Measure SI median per cohort
Per-Patient	Measure SI median for each patient

SI VARIABILITY ($\%\Delta S_I$)	
Cohort	Measure $\%\Delta S_I$ median per cohort
Per-Patient	Measure $\%\Delta S_I$ median for each patient

Where;

$$\%\Delta S_I = \frac{(SI_{n+1} - SI_n)}{SI_n} \text{ x } 100$$

Data is distributed using CDFs and compared using Wilcoxon rank-sum test (all cohort) and signed rank test (patient specific cool-warm pairs). In all cases, $p < 0.05$ is statistically significant.

SI LEVEL ANALYSIS

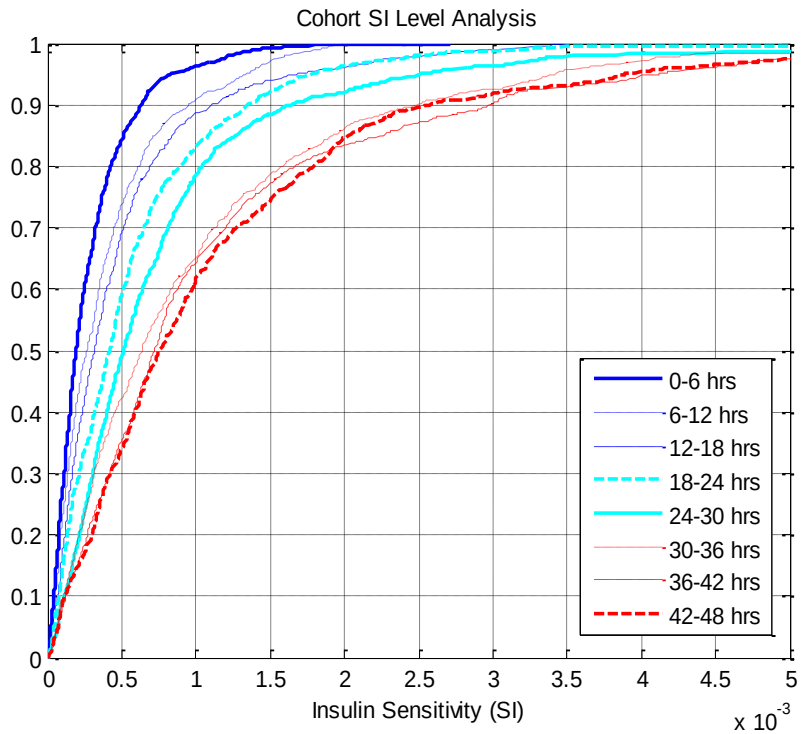


Figure 1: Insulin sensitivity (S_I) level distribution per-cohort for OHCA patients, treated with hypothermia using 6-hour blocks for both cool and warm periods.

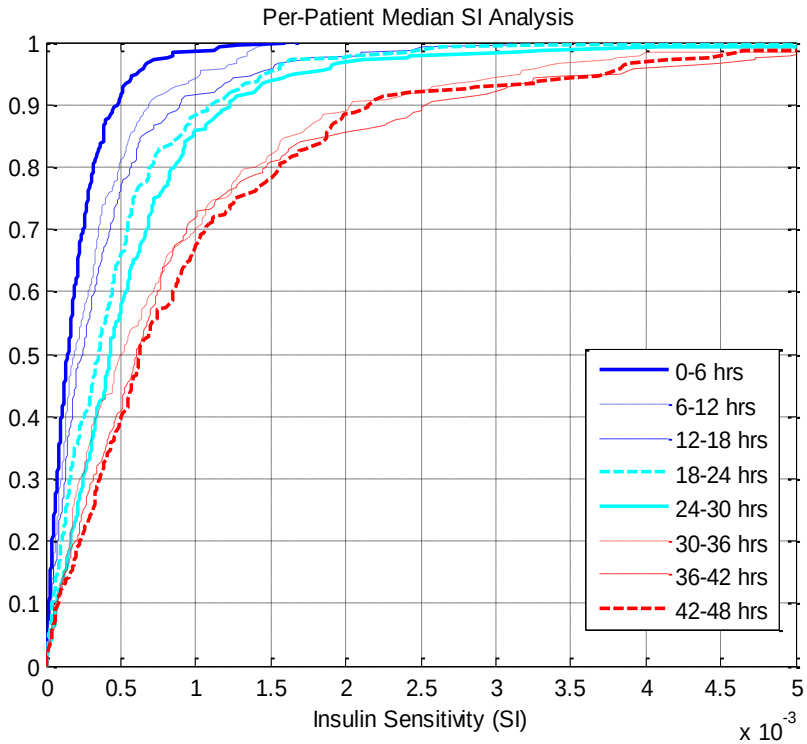


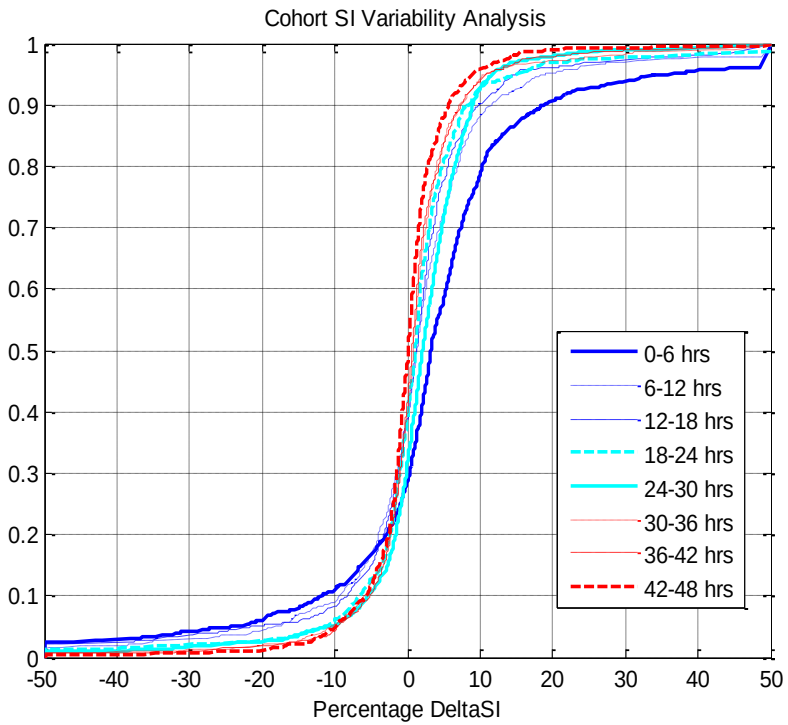
Figure 2: Insulin sensitivity (S_I) level distribution per-patient for OHCA patients, treated with hypothermia using 6-hour blocks for both cool and warm periods.

SI LEVEL ANALYSIS

Table 1: Increasing cohort and per patient median S_I during cool (Blocks 1-4) and warm (Blocks 5-8) periods

S_I level analysis	**Cohort analysis**		**Per-patient analysis**	
	% S_I Median Increase	*p-value*	% S_I Median Increase	*p-value*
Block 1-2	35.1	< 0.05	26.4	< 0.05
Block 2-3	19.2	< 0.05	31.1	< 0.05
Block 3-4	31.8	< 0.05	42.4	< 0.05
Block 4-5	23.4	< 0.05	18.3	< 0.05
Block 5-6	23.9	< 0.05	23.2	< 0.05
Block 6-7	13.1	0.1	15.8	0.2
Block 7-8	4.4	0.4	3.2	0.5

SI VARIABILITY ANALYSIS



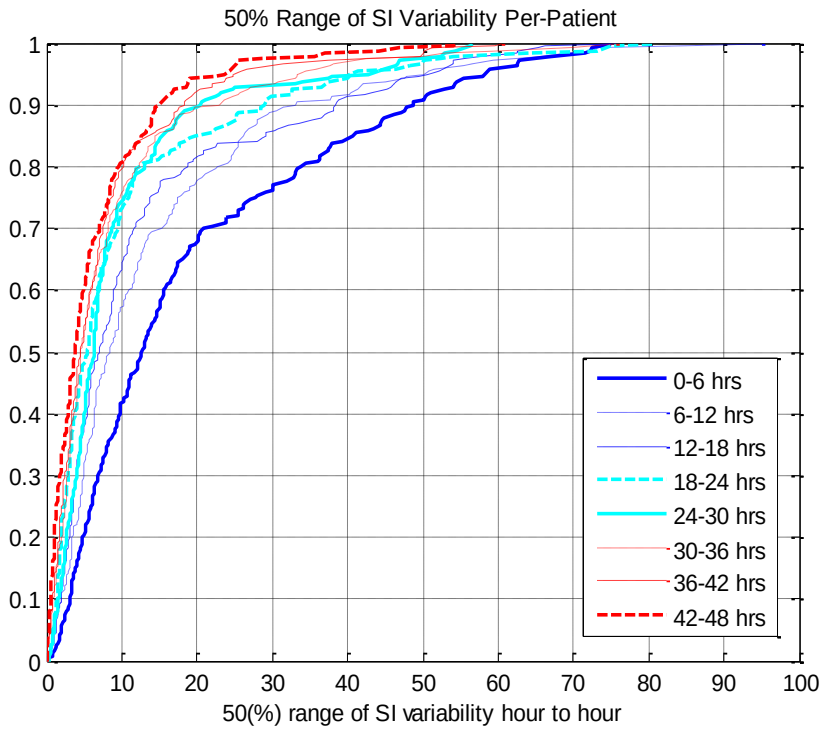


Figure 3: : Insulin sensitivity variability distribution ($\%\Delta S_I$) per-cohort for OHCA patients, treated with hypothermia using 6-hour blocks for both cool and warm periods.

Figure 4: Per-patient 50% range of *SI* variability distribution of OHCA patients, treated with hypothermia using 6-hour blocks for both cool and warm periods.

SI VARIABILITY ANALYSIS

Table 2: Reductions in the interquartile range (IQR) and percentage of median S_I variability decrease per patient during cool (Block 1-4) and warm (Block 5-8)

S_I variability analysis	Cohort analysis		Per-patient analysis	
	% Reduction of IQR	*p-value*	% Median Decrease	*p-value*
Block 1-2	11.1	< 0.05	33.6	< 0.05
Block 2-3	20.7	0.8	15.8	0.1
Block 3-4	14.4	0.4	22.6	0.05
Block 4-5	-19.7	<0.05	-14.9	< 0.05
Block 5-6	23.1	< 0.05	26.4	< 0.05
Block 6-7	4.6	0.8	0.8	0.5
Block 7-8	13.0	0.05	17.1	0.06

CONCLUSION

1. S_I level is much lower during hypothermia and consistently increases over time, transitioning from cool to warm, matching from other studies. [Pretty et al. 2012]

2. Insulin sensitivity is more variable during the cool period and decreases over time. However, it shows <u>contrasting behavior during cool-warm transition period between 18 – 30 hours</u>, which indicates that there are major changes in physiology and metabolic conditions between cool and warm as influenced by human body temperature.

- **These results have significant potential clinical impact on the metabolic treatment of these patients.**
- **Changes in therapy method are required to safely treating patients as they transition in each period**

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ACKNOWLEDGEMENT

This work was supported by EU FP7 IRSES (FP7-PEOPLE-2012-IRSES) program, project title: eTime - Engineering Technology-based Innovation in Medicine, Grant No. 318943.