

## Putative Delays in Interstitial Fluid (ISF) Glucose Kinetics Can Be Attributed to the Glucose Sensing Systems Used to Measure Them Rather Than the Delay in ISF Glucose Itself

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### Abstract

#### Background:

Since the advent of subcutaneous glucose sensors, there has been intense focus on characterizing the delay in the interstitial fluid (ISF) glucose response and the effect of insulin to alter the plasma-to-ISF glucose gradient. The Medtronic MiniMed continuous glucose monitoring system (CGMS) has often been used for this purpose; however, many of the studies have used experimental conditions that fall outside its intended use, for example, studies that have assessed the delay during rapid glucose excursions brought about by intravenous infusion of glucose or insulin. Under these conditions, it is possible that the rate of glucose change may exceed that allowed by CGMS filtering routines. If so, the estimated delay may be because of the filter rather than the ISF. Also, sensor characteristics, such as nonspecific offset current or stability, may have been inadvertently attributed to changes in the plasma-to-ISF gradient. The potential for these issues to have confounded the understanding of ISF glucose delay and gradient is investigated.

#### Methods:

An *in vitro* preparation in which no delay or gradient exists between sensor and measurement solution was used to recreate a rapidly changing glucose profile from a previously published *in vivo* study. The CGMS system (N = 6 sensors) was then used to estimate any artifactual delay and gradient introduced by the system per se.

#### Results:

One-point calibration resulted in an apparent change in gradient as glucose was lowered from ~100 to 50 mg/dl. After a two-point calibration, sensor glucose followed the glucose profile as it was decreased slowly from ~100 to ~60 mg/dl; however, when the glucose level was subsequently increased rapidly to ~150 mg/dl, CGMS filtering routines limited the rate of change of sensor glucose and introduced a delay similar to that previously attributed to ISF glucose equilibration delay.

#### Conclusions:

Studies that have previously used the Medtronic MiniMed CGMS system to assess changes in the plasma-to-ISF glucose gradient may need to be reassessed to ensure that the offset current was estimated accurately. Studies that have used the system to assess ISF glucose delay during rapid, unphysiologic changes in glucose and did not remove the CGMS smoothing filters may have attributed CGMS filter delay to ISF glucose equilibration.

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**Abbreviations:** (CF) calibration factor, (CGMS) continuous glucose monitoring system, (ISF) interstitial fluid, (IV) intravenous, (OS) offset, (SG) sensor glucose, (YSI) Yellow Spring Instrument

**Keywords:** CGMS, delay, glucose gradient, glucose sensor, interstitial fluid glucose, one-point calibration, two-point calibration

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