Relating Capillary Density to Insulin Resistance using a Mathematical Model of Glucose Transport

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Type II diabetes is characterized by decreased sensitivity to insulin resulting in impairment of glucose uptake and high blood glucose concentrations. The cause for this insulin resistance is currently unknown. However, patients with type II diabetes are known to have decreased capillary density in their skeletal muscle, and various studies suggest insulin resistance may be related to capillary density. Therefore, we hypothesize insulin resistance is a result of impaired transport caused by decreased capillary density. This is difficult to test experimentally, as methods for measuring insulin resistance fail to account for the spatial complexity of glucose uptake into the muscle. Therefore, we developed a novel spatial mathematical model for glucose transport in skeletal muscle to assess the effects of capillary density on glucose transport and uptake by skeletal muscle.

We simulated glucose and insulin transport on a 2D geometry using a finite element method; insulin resistance was simulated by decreasing the rate constant describing the kinetics of glucose uptake by a factor related to the severity of the resistance. We found that glucose uptake rate varies approximately linearly with capillary density and varies quadratically with insulin resistance. We were then able to determine a relationship between insulin resistance and glucose uptake. We found that an insulin resistance of 20% corresponds to a typical capillary density for obese Zucker diabetic fatty (ZDF) rats. In summary, we generated a geometric model and explanation for capillary density as a potential mediator of insulin resistance in type II diabetes.