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ORIGINAL ARTICLE

Insulin Depot Formation in Subcutaneous Tissue

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Abstract

Background:

The size and geometry of an insulin depot that is formed during subcutaneous administration by an insulin pump is evaluated. A novel method is used to visualize accurately the depot formation for small volumes of insulin (of the order of 10–100 μl) at a given point in time. Conventional visualization methods such as magnetic resonance imaging are unable to provide such accurate measurements because of their coarse imaging resolution and long measurement time.

Methods:

The described method consists of subcutaneously infusing dyed insulin into porcine tissue and subsequently shock freezing it with liquid nitrogen. The frozen sample is then sliced into thin layers using a cryomicrotome. A digital image of each layer is taken and then processed with proprietary software, which identifies the dyed areas on each layer and reconstructs a three-dimensional model of the insulin depot with a planar resolution of 30 × 30 μm^2 and a depth resolution of 100 μm. Since this process is not viable for living organisms, porcine tissue was used immediately following slaughter of the animal.

Results:

To date, it is most often assumed that the insulin depot takes the shape of a sphere around the tip of the cannula (e.g., 50 μl insulin equates to a spherical radius of 2.3 mm). However, in practice, such a depot form is never observed. Instead, the insulin depot initially spreads laterally (i.e., parallel) to the skin surface and in the collagen matrix that binds the adipose cells together. The depot outreach increases with larger infused volumes, e.g., maximum outreach measured at 5.0/5.7/7.1 mm (quartiles, n = 17) for 50 μl of infused insulin. Beyond a given infused volume (approximately 100 μl), the insulin also starts to spread perpendicular to the skin surface.

Conclusions:

It is concluded that formation of the insulin depot depends on the opening of channels at the boundaries between adipose cells. Hence the insulin follows a path of least resistance and depot formation is determined by the local structure of the subcutaneous tissue.

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Abbreviations: (3D) three-dimensional, (HSV) hue/saturation/value

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