Performance Qualification of a Novel Subcutaneous Insulin Infusion Set using Medical Imaging

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Background

Subcutaneous (SC) insulin infusion sets have been characterized as the Achilles heel of insulin pump therapy and are associated with hyperglycemia, insulin leakage, pump occlusion alarms, and "silence" occurrences when insulin flow is impeded but no alarm occurs. An investigational continuous subcutaneous insulin infusion (CSI) set (BD FlowSmart™, BD, Franklin Lakes, NJ) with a novel side-ported 28G, 3mm polymer catheter designed to potentially reduce flow interruptions and stabilize insulin delivery is under development.1,2

Evaluating CSI set functional performance is challenging due to the slow response time and intrinsic variability of blood glucose (BG) responses, inability to quantitively delivered insulin in real-time, and impracticability of site observation with sets in place. Various medical imaging techniques allow visualization of sets and delivery in situ to examine device placement, depot patterns, incomplete insertion or leakage; however imaging of CSI sets has not been previously performed.

In the current study, preclinical fluoroscopic imaging and clinical magnetic resonance (MR) imaging were used to assess system performance of the investigational set and other commercial CSI sets in animal and human studies.

Preclinical Swine Fluoroscopic Imaging

Fluoroscopy Material and Methods:

A: A Glenbrook Technologies Labscope™ fluoroscopy unit was used to image CSI sets (FS= BD FlowSmart™; BS= Quick-set™ 6mm; Medtronic, Northridge, CA) in anesthetized Yorkshire swine (~25-45 kg weight range) (Figure 1).

Animals were positioned with the skin surface and CSI set perpendicular to the radiation source for imaging. Skin surface at the set insertion site was highlighted with radiopaque metallic paint to enhance tissue/device contrast.

B: Implants were captured pre and post-inflation, with continuous dynamic video capture during the injection process. Image analysis included tissue characteristics (dermal layer thickness, deformation at infusion site), device function (ability to insert, performance, occlusion, leakage), and infusate deposition characteristics (tissue location, size, depth).

C: Injection and (C) 10U depot delivery for BD FlowSmart™ (FS) investigational catheter showing diffuse multi-depot pattern (D) injection and (E) 10U depot delivery for Quick-set™ (QS) 6mm catheter showing singular depot. Note some QS devices also demonstrate diffuse patterns owing to diffusion through tissue strata. (F) Histogram showing increased tendency for multi-depot patterns in the FS investigational set.

D: Deposition layers

E: Deposition layers

Figure 3. Representative transverse images of standard infusion locations, including (A) upper arm, (B) abdomen, and posterior upper gluteal region, and (C) thigh. Registration marks are visible as circles on the skin surface (arrows), and relevant anatomical landmarks are labeled.

E: Deposition layers

F: Deposition layers

MR Materials and Methods:

A: An observational IRB-approved imaging study of SC placebo infusion across various CSII sets and dosing conditions was performed in N=8 healthy adult subjects (age 34.5±13.1 YO; n=3 MaDe® Female; BMS 2.9±4.0).

B: Imaging was conducted using a Siemens Magnetom Trio 3 Tesla MRI unit (Figure 2), using T1 weighted Gradient Echo, T1 Flash w/ & w/o Fat Suppression sequences in the transverse plane. Anatomical sites for device insertion included the abdomen, thigh, posterior upper arm and gluteal regions (Figure 3). Fish oil caplets were used to mark areas lateral to device placement for the imaging field. External surface imaging coils were used to capture images of the upper arm.

C: Placement infusion solutions included 1:10 galarium contrast agent in saline (1:300 v/v Multihance®, Bracco) and 0.9% saline. Saline alone showed no degradation of image quality and was used for the majority of infusions.

D: CSII sets were placed both manually and with an inserter device (Quick-set®, Medtronic). Some manual placements also included intentionally poor technique (dose and/or angular insertion) to force cannula faults. Side ports of BD FlowSmart™ devices were oriented parallel to the image slice in order to see diffusion across the tissue planes. Both 6mm and 9mm commercial polymer sets (Medtronic Quick-set®) were used as comparators. (Figure 4-7)

E: Catheter set was serially connected with microtube extension sets to keep pumps outside the MR magnetic field. Images were sequentially acquired before and after cannula fill, and at incremental stepwise volume increases up to 30U bolus.

Results and Conclusions

A: An investigational flow-stabilizing ported set for reducing infusion pressure and other marketed SC infusion sets were evaluated using multiple medical imaging modalities.

B: Catheter porting creates an auxiliary tissue flow pathway that may reduce occlusion and stable flow.

C: In vivo fluoroscopy of contrast media infusion provided high resolution visualization of device placement, bolus depot patterning, and delivery faults as incomplete insertion and leakage. Contrast filled polymer catheters were visible in situ.

D: Diffuse SC depot patterns characterized by more depot layers were observed for the novel 28G, 6mm, ported polymer catheter set, potentially owing to side-port delivery.

E: A human MRI study of the investigational set in 8 non-diabetic adults demonstrated effective SC placement and placebo delivery across multiple bolus infusion and various routine insulin infusion sites (arm, thigh, abdomen, and gluteus).

F: Clinical depots were similar to preclinical observations with increased diffusivity in contrast to denser depots observed from marketed CSII sets (Figure 4). Flow from both terminal outlet and side port appeared to be visible at lower velocity and reduced side port visualization was obscured at larger bolus volumes (Figure 5).

G: Variations in delivery depth owing to catheter length were readily detected (Figure 7), as was catheter bending owing to intentional poor insertion technique (Figure 6); however this did not adversely impact delivery.

H: Both fluoroscopic and MR imaging techniques provide effective CSI set characterization for anatomical sites and may enable better comparative device performance assessment.

References


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