Overcoming Limitations of Current Insulin Pump Infusion Failure Detection: A Novel Fluid Pressure-Based Machine Learning Solution

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BACKGROUND

- Insulin Pump Infusion Set Failure (IPISF) is a misdelivery of insulin from a continuous subcutaneous insulin infusion pump (CSII) that may cause hyperglycemia, diabetes-induced ketoacidosis (DKA), hospitalization, or even death.[1,2]
- Current CSII IPISF detection is limited to occlusion alarms that can be delayed up to days based on infusion rates and do not alert of other forms of IPISF (i.e., leakage from the infusion site, detachment of infusion set from the body, etc.)[3,4]
- Previous work demonstrates the use of machine learning algorithms to predict and detect IPISF via continuous glucose monitors and historical insulin delivery data.[5-7]
- Monitoring infusion fluid pressure during CSII use has been suggested as a novel method for detecting IPISF, specifically leakages and malplacement of infusion set cannulas.[8]

STUDY AIMS

1. Obtain and analyze a preclinical dataset of CSII infusions during IPISF and normal conditions to examine measurable differences in fluid dynamics.
2. Develop and train a novel IPISF detection model for CSII using infusion fluid pressure by utilizing supervised learning techniques for binary classification of IPISF from normal infusions.
3. Test a novel IPISF detection model for CSII using infusion fluid pressure on data from ambulatory insulin-dependent swine.

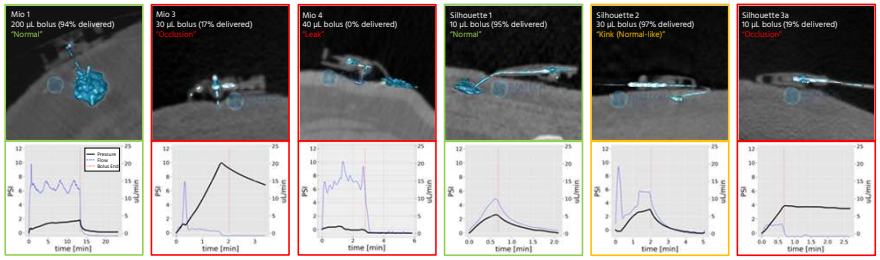
PHASE 1: TRANING DATA & MODEL DEVELOPMENT

- 3 separate preclinical studies (November 2020 – November 2021) were performed using 6 non-insulin dependent anesthetized female swine (mean weight = 75.1 kg).
- 503 boluses (ranging 1 – 250 µL) of a 50/50 mixture of saline and Conray® contrast agent were infused into 142 sites across 8 body regions using Medtronic Minimed® 530G, Minimed® 770G, and Harvard Apparatus Pump 11 Elite infusion pumps affixed to Medtronic Minimed® Mio™ and Minimed® Silhouette™ infusion sets.
- Infusion pressure and flow rate data were collected via in-line sensors retrofitted to the infusion sets. 2D and 3D images of every bolus was captured with a Siemens ARTIS pheno fluoroscopy unit (Figure 1). Sites were excised and stained (Hematoxylin and Eosin) at the end of each study.
- Multi-bolus infusion sites were separated for individual bolus analysis. Normal versus IPISF infusions were labelled based on total volume of infusion delivered, pressure and flow rate dynamics, and imaging data (rendered using 3D Slicer) showcasing fluid deposits from the distal tip of the infusion set cannula. All infusion sites were hand labelled and analyzed using Python.

PHASE 2: AMBULATORY STUDY & MODEL TESTING

- 3 insulin-dependent swine (mean arrival weight = 32.5 kg) in a 16-day ambulatory study.
- Swine fitted with commercial insulin pumps within 3 days; started on Lispro insulin. Pumps housed in specialty jackets with pressure and flow sensors, connected to a proprietary data acquisition device with real-time monitoring via app and online data viewing dashboard.
- Blood glucose monitored via Dexcom G6 CGM and AlphaTRAK 2 meter. Swine fed 2-3 times daily with pre-meal BG checks and as needed. Additional blood draws from subcutaneous vascular access ports during 2 isolated observational periods with and without sedation.
- Collected 189 boluses (0.5 – 17.4 µL) across 6 different 90° infusion sets. All boluses were hand-labeled and analyzed post-study using Python. If a pump's occlusion alarm was triggered, the bolus was labeled as an occlusion, however, further analysis is needed to distinguish between true and false positive alarms.

PHASE 1 RESULTS



Images 1-6. Fluoroscopy images of Normal versus IPISF boluses into subcutaneous tissue with pressure and flow data using Minimed™ Mio and Silhouette infusion sets.

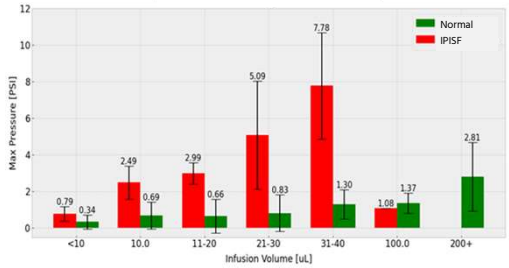


Figure 1. Max Pressure per Target Infusion Volume for Normal versus IPISF shows pressure range of failed boluses and why a dynamic algorithm is preferred over a set max threshold.

Model Development

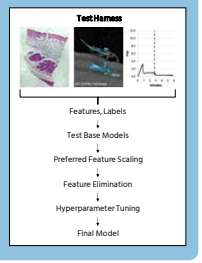


Figure 2. Test Harness begins with features and label creation, followed by testing base models, identified the preferred feature scaling, feature elimination, and hyper-parameter tuning with oversampling as needed (not shown). Stratified k-fold Cross Validation was used with an F2 scoring function that penalizes false negatives.

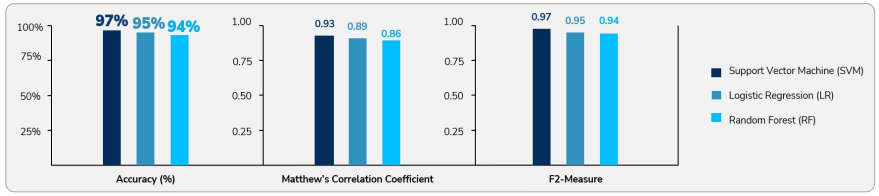
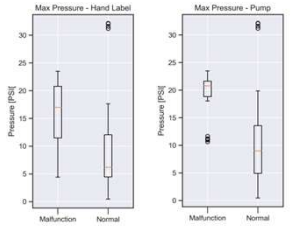


Figure 3. The best classification performance was obtained with SVM showing 96.9% accuracy on the test set, Matthew's Correlation Coefficient (MCC) of 0.927 and weighted F2-measure of 0.97. This was followed by LR (95.3%, 0.893, 0.952) and RF (93.7%, 0.857, 0.94).

PHASE 2 RESULTS

Images 7-8. (Left) Swine is shown with custom jacket that houses the insulin pump, infusion set, sensors, and data acquisition device. (Right) Picture of infusion set and CGM placed on the upper neck.



Figures 4-5. Max pressures for Malfunctions (IPISF) versus Normal infusions, comparing hand labeling (Left) and pump-reported data (Right). Graphs reveal distinct groupings detected by Diatech pressure sensor, suggesting pump occlusion thresholds. Hand-labeled data highlights the dynamic nature of IPISF due to diverse max pressures.

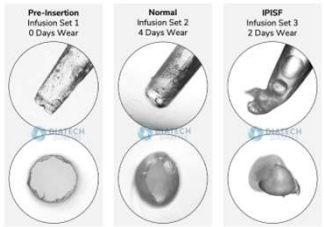
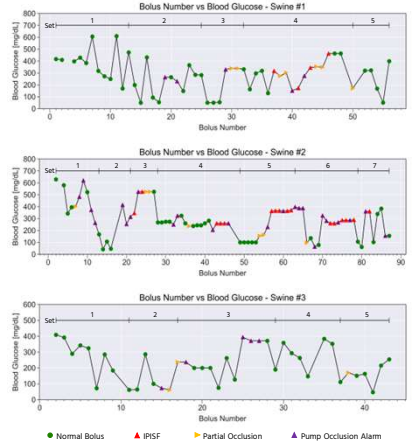


Figure 6. 10X images of infusion set cannula side and tip at pre-insertion and post-removal (Normal versus IPISF).



Figures 7-9. Boluses numbered and graphed using logged CGM values at delivery time (blood glucose meter values used if CGM was not recorded or registered "HIGH" or "LOW"). All pump detected occlusions were treated as true positive IPISFs. Further analysis will identify false-positive pump occlusion alarms. 5 infusion sets were used by Swine #1 (mean wear time 2.37 ± 0.76 days), 7 infusion sets by Swine #2 (mean wear time 1.66 ± 0.85 days), and 5 infusion sets by Swine #3 (mean wear time 2.18 ± 0.84 days).

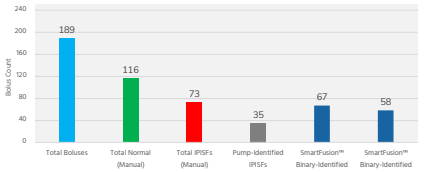


Figure 10. Of 73 labeled IPISFs, pumps detected 35 (48%); SmartFusion SVM Binary Model identified 67 (91%) and SmartFusion RF Model 58 (79%).

PHASE 1 RESULTS

- Analysis of collected data identified 299 normal infusions and 126 IPISFs. 78 infusions were removed due to sensor/delivery errors. A total of 425 infusions (Mean ± SD 20.7 µL ± 31.1 µL) were used for final model development.
- Ranges in IPISF max pressures highlights how "silent occlusions" may go undetected if they do not cross a pump's occlusion detection pressure threshold.
- Overall, SVM showed the best performance, but it is evident that all models are capable of highly accurate classifications.

PHASE 2 RESULTS

- 43 patient days were recorded across 3 insulin-dependent ambulatory swine. 6 infusion sets were tested with an average set wear period of 2.02 ± 0.84 days across 3 different tubed insulin pumps.
- Post-infusion BG response times varied from 20-45 mins. Normal infusions had a -30.2 ± 63.3 mg/dL response at 30 mins and -48.8 ± 93.7 mg/dL at 60 mins, while malfunctions showed -9.7 ± 49.4 mg/dL and -22.7 ± 88.5 mg/dL responses at the same intervals.
- Of the 73 Malfunctions, only 35 (48%) were correctly identified by the pumps compared to Diatech's machine-learning based algorithm with 91% of all malfunctions detected.

CONCLUSION

- Diatech's machine learning-based classifiers using fluid pressure only were shown to be more accurate than existing insulin pump infusion failure detection systems, even with environmental noise during an insulin study.
- Utilized framework may be extended to multi-class classification for more advanced decision making.
- Supervised learning approach allows for failed bolus classification regardless of volume size, max pressure, and is pump agnostic.

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