A Power Tracking Algorithm for Early Detection of Centrifugal Flow Pump Thrombosis

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Logfiles from the HeartWare HVAD System provide operational pump trend data to aid in patient management. Pump thrombosis is commonly associated with increases in the logfile power that may precede the clinical presentation. A Power Tracking algorithm was developed to detect significant deviations in pump power that may be associated with pump thrombus (PT). The Power Tracking algorithm was applied retrospectively to logfiles captured in the ENDURANCE, ENDURANCE Supplemental, and LATERAL clinical trials. From a combined dataset of 896 patients, available logfiles with suspected PT (n = 70 events in 60 patients) and available logfiles from patients without adverse events (AEs) (n = 106 patients, consisting of 27.4 patient-years of monitoring) were organized into two cohorts. The Power Tracking algorithm detected PT cases on or before the recorded AE date with a sensitivity of 85.7%, with detection occurring an average of 3.9 days before clinical presentation. The algorithm averaged one false alarm for every 6.85 patient-years of monitoring from logfiles without AEs. The favorable performance of the Power Tracking algorithm may enable earlier detection of pump thrombosis and allow early medical management *versus* surgical intervention. *ASAIO Journal* 2021; 67;1018–1025

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The HeartWare HVAD System (Medtronic, Minneapolis, MN) is an intrapericardial continuous-flow left-ventricular assist device (LVAD) with a centrifugal pump design capable of providing full cardiac support in patients with end-stage systolic heart failure. The pump uses magnetic and hydrodynamic forces to elevate and rotate the only moving part of the pump, the impeller, which rotates at a fixed speed determined by the clinician. LVAD survival has improved overall as demonstrated by the 87% 2-year survival with the HVAD System in the most recent bridge to transplant (BTT) clinical trial and its 69% 2-year survival in the most recent destination therapy (DT) trial.[1–3] However, serious adverse events (AEs) such as stroke and pump thrombus (PT) may be limiting wider adoption of LVAD technology. In the most recent HVAD DT trial, device exchange for PT occurred at a rate of 0.04 events-per-patient-year over 24 months of support.[3]

Pump thrombosis is the formation of a blood clot within the LVAD that impedes blood flow.[4–8] The diagnosis and management of PT have been previously described. Patients whose PT cannot be attributed to inflow or outflow abnormalities, which may be surgically or interventionally corrected, should be transferred to an intensive care unit for monitoring and initiation of anticoagulation or thrombolytics.[6,9–12] It has also been shown that earlier detection of PT may facilitate successful treatment with medical therapy, thereby avoiding surgery to replace the pump.[4,5,12–14]

The HVAD controller stores operational device data in the form of logfiles, which include pump parameters such as speed, average power, and average estimated flow. These parameters are recorded every 15 minutes for up to 31 days, on a first in-first-out basis throughout duration of support. Logfiles can be used for the assessment and trending of device parameters.[15–18] Depending on where the PT exists within the pump, derangements of pump parameters often precede clinical symptoms. For example, if the thrombus resides on the spinning impeller, the efficiency of the pump decreases as the power consumption increases[16] resulting in a significant rise in pump power and a falsely elevated pump flow estimate. Figure 1 shows the trended increase in pump power associated with impeller thrombus.

The current standard-of-care for detecting impeller thrombus is to manually set the "High Watt" alarm to a threshold 2 Watts above the patient's average baseline power consumption.[19] More sensitive settings for the High Watt alarm may provide earlier detection of PT, allowing earlier clinical intervention with the potential to avoid pump exchanges.[4,5] A Power Tracking algorithm, designed to detect abnormal changes in pump power that may be associated with a thrombus, was previously developed using retrospective logfile data.[20] Here, through retrospective application to a large clinical database

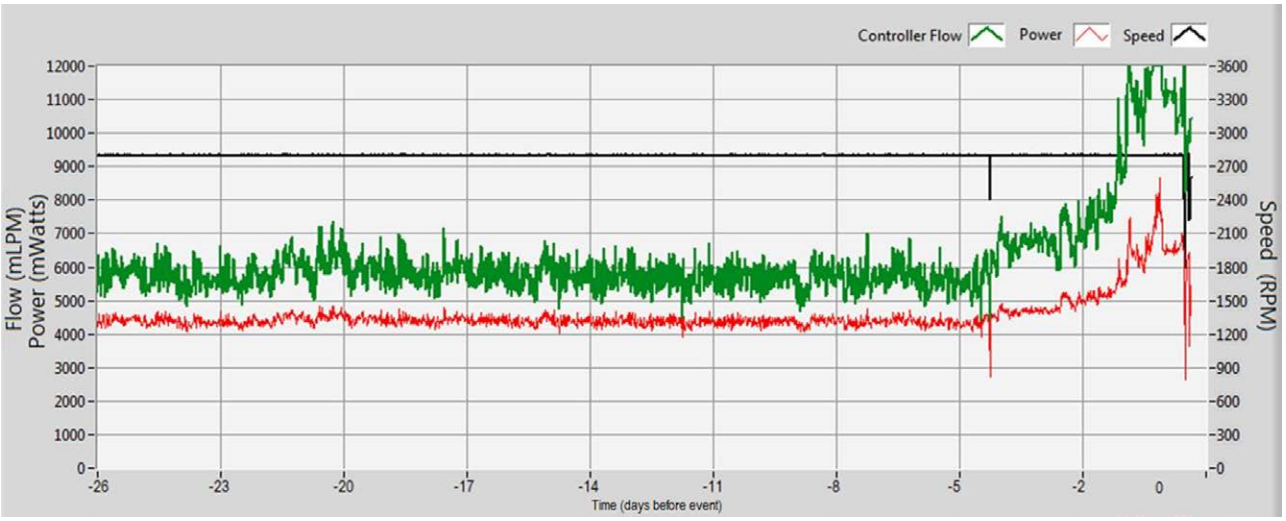

Figure 1. Power and calculated flow increase as a result of pump thrombus observable in logfile data (red = average power, green = average flow, black = pump speed).

with logfiles, we assess the performance of this algorithm in detecting PT earlier while avoiding false detections and unnecessary alarm triggers.

Materials and Methods

Power Tracking Algorithm

The Power-Tracking algorithm is a combination of four independent detectors of abnormal power. The first detector compares a long-term moving average, representative of the patient's historical baseline, to a short-term moving average, representative of the patient's current operating power. The difference between the outputs of the short-term and long-term filters provides a quantitative measure of patient-specific power change that may be associated with evolving thrombus. The power change is divided by the output of the long-term moving average to provide a normalized percentage change. An integrator is used to accumulate the normalized power changes over a moving window of time, and a threshold on the accumulated power changes is used to trigger an alarm condition. The short-term filter operates over a period of hours whereas the long-term filter operates over a period of days. The integration time window is a 24-hour period, and the threshold on the accumulated power changes was tuned to minimize false positives (FPs) while maintaining sensitivity. The first detector is illustrated in Figure 2.

The second detector is designed to provide faster detection for more dramatic power increases that may be associated with thrombus ingestion. This detector continuously monitors the instantaneous HVAD power and an alarm is triggered if the instantaneous power exceeds a predefined percentage of the long-term filter. An illustration of an ingestion power signature is shown in Figure 3.

The third detector is designed to detect abnormal pump power relative to population norms, not patient-specific norms. This detector continuously monitors the instantaneous HVAD power and an alarm is triggered if the instantaneous power exceeds a predefined percentage of the HVAD expected power for the current set speed.[16] This detector is a safety net to detect very slow power growth over a long period of time.

The fourth detector is a temporary detector that operates only during the first 24-hours immediately after initialization (*e.g.*, after pump start or speed change) until the patient-specific power estimates of the first detector have been established. This fourth detector monitors the instantaneous HVAD power and an alarm is triggered if the instantaneous power exceeds a predefined percentage of the HVAD expected power.[16]

Datasets

The performance of the Power Tracking algorithm was assessed using logfile data from 3 clinical trials: ENDURANCE, ENDURANCE Supplemental, and LATERAL. The ENDURANCE trials studied the HVAD System in a DT population; the LATERAL trial studied a BTT population using the thoracotomy approach.[2,3,21] Within each clinical trial, AEs including pump thrombosis were defined and studied. ENDURANCE and ENDURANCE Supplemental trials used Intermacs AE Definitions Versions 2.3 and 3.0 while the LATERAL Trial used Version 4.0, all three of which defined PT similarly as a type of Device Malfunction. Version 4.0 expanded the description of pump thrombosis with the addition of subgroups of confirmed or suspected PT. For the purposes of this analysis, both suspected and confirmed PT events were included.

Available logfile data were separated into two datasets, thrombus and control, using predefined inclusion and exclusion criteria. The thrombus dataset included logfiles from patients with a PT as defined by the clinical trial AE definitions. The event date was defined as the day of clinically reported thrombus onset in the clinical trial. To be included in the thrombus dataset, the following criteria must have been met:

1. Pump thrombus events occurred at postoperative day (POD) 30 or later, to ensure pump parameters were stable before assessing algorithm performance.
2. Logfiles were available on the event date with at least 1 week of available data preceding the event date.

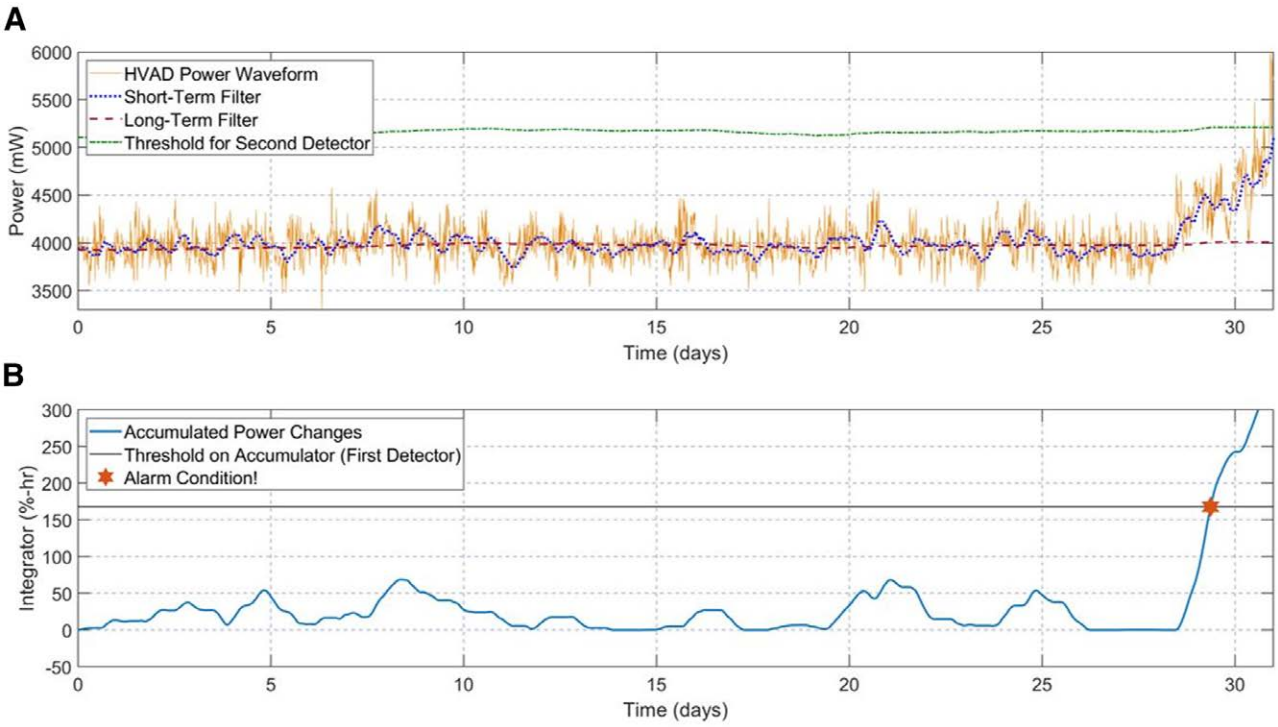

Figure 2. Schematic of the power tracking algorithm. **A**: Short-term and long-term filters for the first detector and threshold for the second detector. **B**: Accumulated power changes and threshold for the first detector.

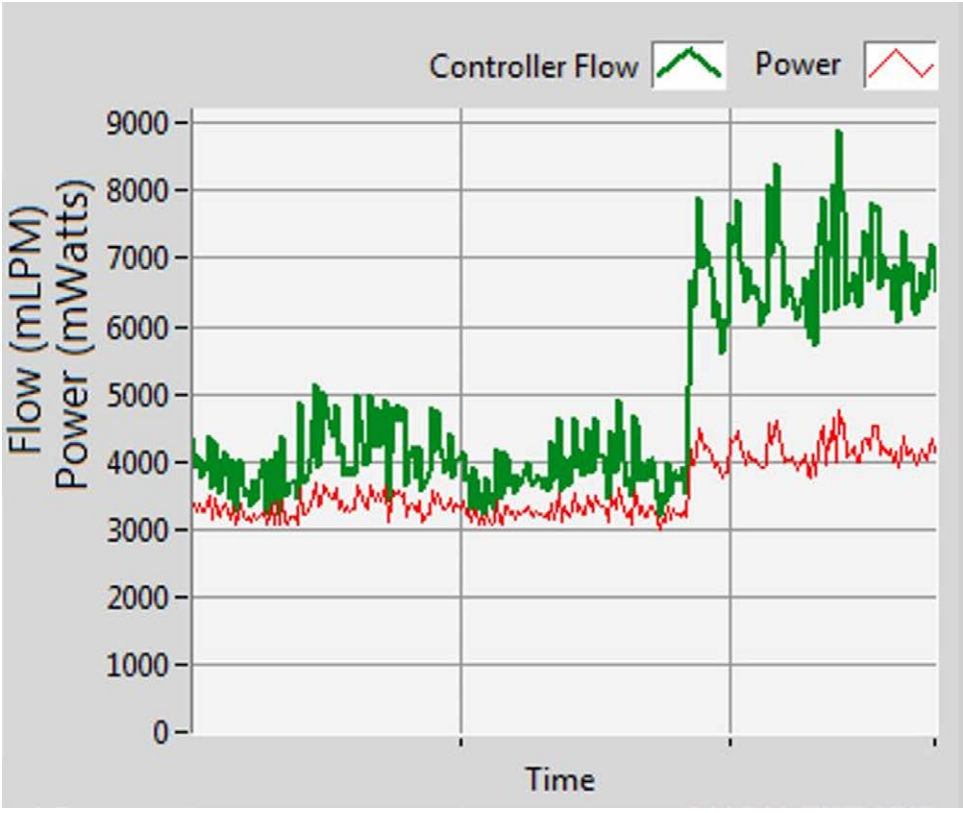

Figure 3. Thrombus ingestion power signature as demonstrated by sudden elevated pump power and calculated flow.

3. Only intra-pump thrombosis events were considered; events with suspected or confirmed thrombus in the inflow cannula or outflow graft were excluded from the analysis.
4. A maximum of 30 days of preceding data were included for each thrombus event.
5. A maximum of three thrombus events per patient were allowed if: (i) therapy was administered for the thrombus, returning the power to the baseline level and (ii) there were at least 30 days between clinical resolution of the prior thrombus event and the clinical observation of the new event.

The final resulting thrombus dataset included 70 events in 60 patients.

The control dataset consisted only of patients with no AEs recorded throughout support in the clinical trial. At least 30 consecutive days of available logfile data with logfile date POD 30 or greater were required for inclusion in the control dataset. A maximum of 120 days of data were allowed for each control patient. The final resulting control dataset included 106 patients, consisting of 27.4 patient-years of monitoring.

Performance Metric Definitions

The Power Tracking algorithm was applied to all data strips in both the thrombus and control datasets. The Power Tracking algorithm provided a binary trigger output (alarm = yes if any of the four independent detectors were triggered, or no alarm otherwise) for each point within the associated data logfile. The following definitions converted the binary trigger outputs into overall algorithm performance:

True-positive (TP): True positives were only determined from the database containing thrombus events. A TP was counted if the Power Tracking algorithm triggered on or before the recorded event date in the data strip containing a thrombus event.

False-negative (FN): False-negatives were only determined from the database containing thrombus events. An FN was counted if the Power Tracking algorithm did not trigger in the data strip containing a thrombus event, or if the trigger occurred after the recorded event date.

Sensitivity: Sensitivity was determined using the following calculation:

$$\text{Sensitivity} = \frac{TP}{TP+FN}.$$

Early warning: For each TP, the early warning was the duration between the first occurrence of the Power Tracking alarm and the thrombus event date (when the thrombus was clinically identified). The resolution of this calculation for each event was 1 day.

False-positive (FP): FPs were only determined from the control database. An FP was counted if the Power Tracking algorithm triggered during a control data strip. Power Tracking alarms separated by 14 days or less were combined into a single alarm.

Total patient-years: Total patient-years were only determined from the control database, defined as the sum of logfile durations in years. This metric was used to calculate the FP rate.

False-positive rate: False-positive rate was defined as the number of false-positives per patient-years (FP-PPY). The FP rate was determined using the following calculation:

$$\text{FP rate} = \frac{FP}{\text{Total patient-years}}.$$

Results

Thrombus Dataset

In the thrombus dataset, the Power Tracking algorithm was triggered on or before the event date in 60 of the 70 total cases. In six cases, the algorithm triggered on the day after the event date and in four cases, the algorithm did not trigger. The resulting sensitivity was 85.7%.

In the four cases where the algorithm failed to trigger, a slow rise in power was observed over time which was just beneath the detection thresholds. A representative case is shown in Figure 4.

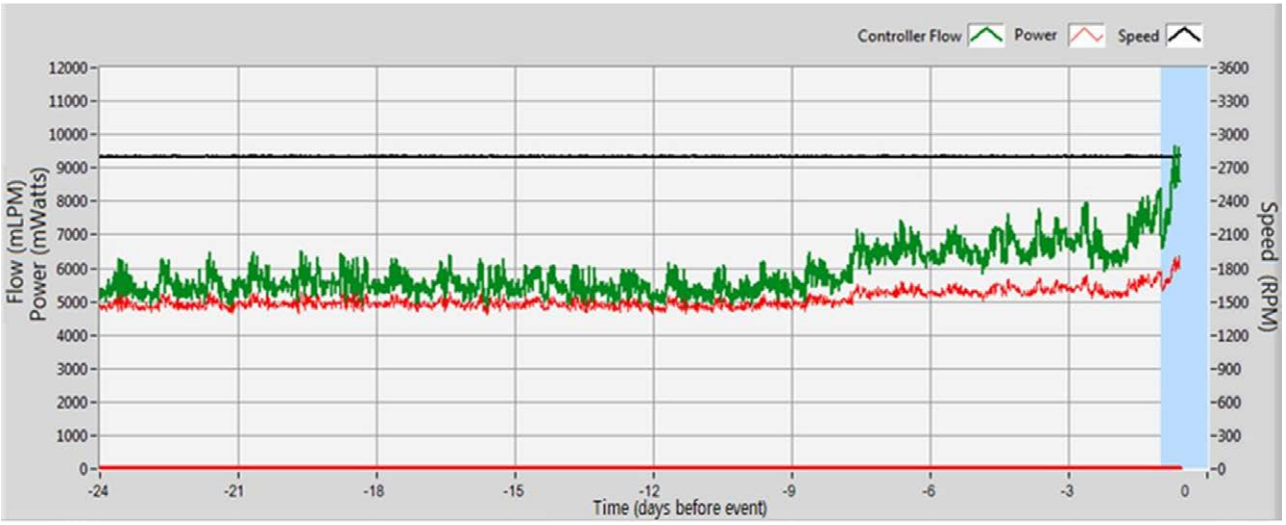

Figure 4. Representative case of a false-negative algorithm response.

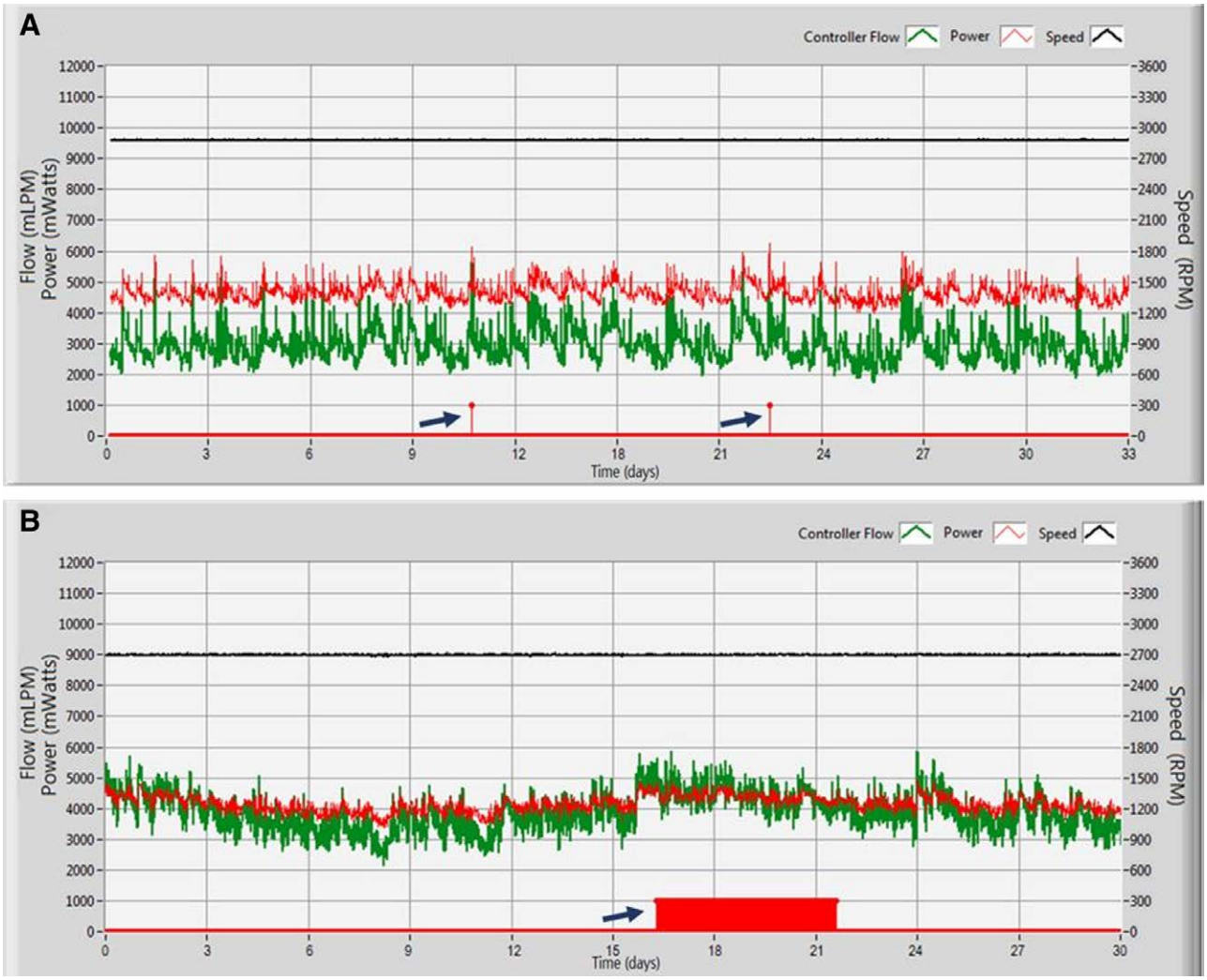

Figure 5. Representative cases of logfiles with false-positive algorithm detection (indicated by arrows). **A**: Second Power Tracking detector triggered for abrupt power increase. **B**: First Power Tracking detector triggered for fluctuating increased power trend.

Control Dataset

In the control dataset, the Power Tracking algorithm incorrectly triggered in 2 of the 106 patients, with four total false-positives (two FPs per patient). A total of 27.4 patient-years were assessed in the control database, yielding an FP rate of 0.15 events PPY.

Logfiles from patients where the Power Tracking algorithm triggered FPs are shown in Figure 5. The control data in the top panel show a circadian cycle with sharp power increases in excess of 1 Watt. The sudden change in power triggered the second Power Tracking detector, designed to detect abrupt increases in power associated with thrombus ingestion. The bottom panel of Figure 5 shows a fluctuating power trend with a power increase that triggered the first Power Tracking detector.

Early Warning

In the thrombus dataset, the first Power Tracking algorithm trigger was compared with the clinical trial event date to determine the early warning time. In 43 cases of 60 Power Tracking

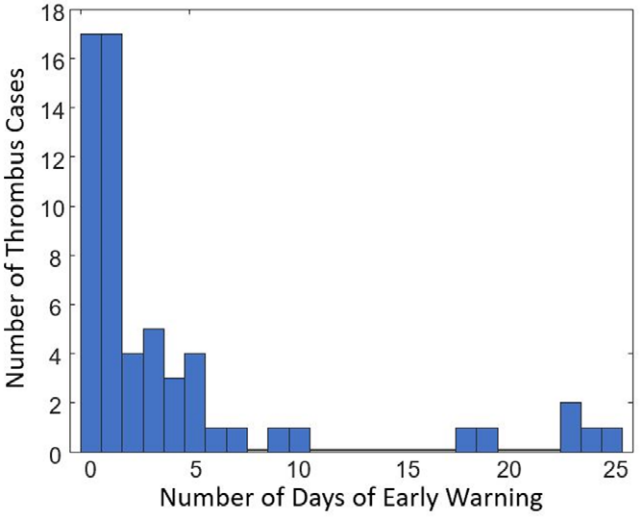

Figure 6. Distribution of early warning detections relative to the date of clinically reported onset of the event (time 0).

detections (72%), the algorithm triggered at least 1 day before the event date, with 17 triggers occurring on the same day. On average, Power Tracking detections occurred 3.9 days before the event date. The distribution of early warning time is plotted in Figure 6.

There were six cases (10%) where the algorithm detected a change in the power signal >15 days before the event date. In the representative case of Figure 7, the shaded blue area is the event date, and the red rectangles indicate several Power Tracking algorithm detections preceding the event date.

Summary Data

To summarize all the cases studied in this analysis, raw power trends are plotted and superimposed in Figure 8. The top panel contains power data from all control patients, trimmed to a maximum of 30 days, normalized, and overlaid. The resulting visual shows a tight clustering of pump power throughout the 30-day period. The bottom panel of Figure 8 contains power data from all thrombus cases, aligned by their respective event dates (day 0 on the x-axis). Power for each case was normalized and overlaid. The resulting visual shows a tight clustering of pump power on the left side of the plot (baseline power data) and diverging increases in power moving towards the right along the x-axis, approaching the event date.

Discussion

Early detection of pump thrombosis with high sensitivity (85.7%) and low FP rate (0.15 FP detections PPY) would provide clinically meaningful data for early intervention and potentially successful treatment. On average, the algorithm would provide an average of 3.9 days early warning compared with conventional methods of thrombus detection. As shown by Jorde *et al.*[4], early detection of thrombosis may permit successful medical management, avoiding the need for surgical intervention.

The power increases that precede clinical presentation for thrombus are prominent (Figure 8), suggesting the potential for earlier detection. Grabska *et al.*[13] described a method of manually setting the high-power alarm limit tighter than the recommended 2-Watts based on the circadian variation. In this method, the authors showed the potential to detect changes in the power signal up to 2 days before the readmission date for pump thrombosis. From our analysis, we observed the Power Tracking algorithm to trigger even earlier, providing an average of 3.9 days of warning. Cases such as the one illustrated in Figure 7 showcase the need for alternative methods of detecting thrombus and highlight the possibility for much earlier clinical detection with the Power Tracking algorithm.

In the cases where the Power Tracking algorithm failed to trigger, such as the representative example shown in Figure 4, a slow rise in power was observed over time. These cases fell just beneath the detection threshold set for the algorithm. In developing the algorithm, the threshold was adjusted by design to minimize FP detections and maximize sensitivity. Although the algorithm did not provide early detection in these cases, it is expected that the Power Tracking algorithm would have triggered as the power level continued to rise from either the first or the third detector.

The clinical reasons for the FP detections of Figure 5 are unknown. The sudden spikes in power in the top panel are not representative of signatures observed in routine data. The changing power signal in the bottom panel of Figure 5 may indicate a physiologic change in condition (such as an ingested thrombus) that warrants clinical investigation. In both instances of FP detection, most programs would want to see the patient to ensure that there is not a significant clinical problem. Thus, the rare FP result is still potentially detecting a clinically meaningful event, interrogation of which might be beneficial to the patient and the managing team.

Overall, the performance of the algorithm is very promising and should enable clinically meaningful improvements in thrombus management.

Limitations

This analysis has some limitations which should be considered when interpreting the data. The analysis was a

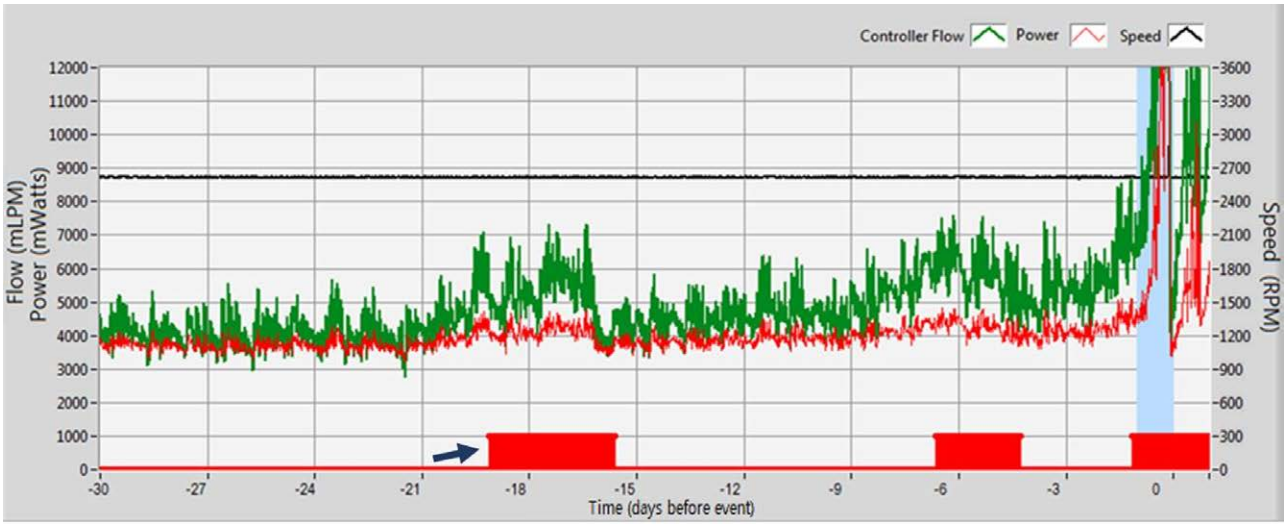

Figure 7. Representative case showing >15 days of early warning detection (indicated by arrow) before the date of clinically reported onset of the event (time 0).

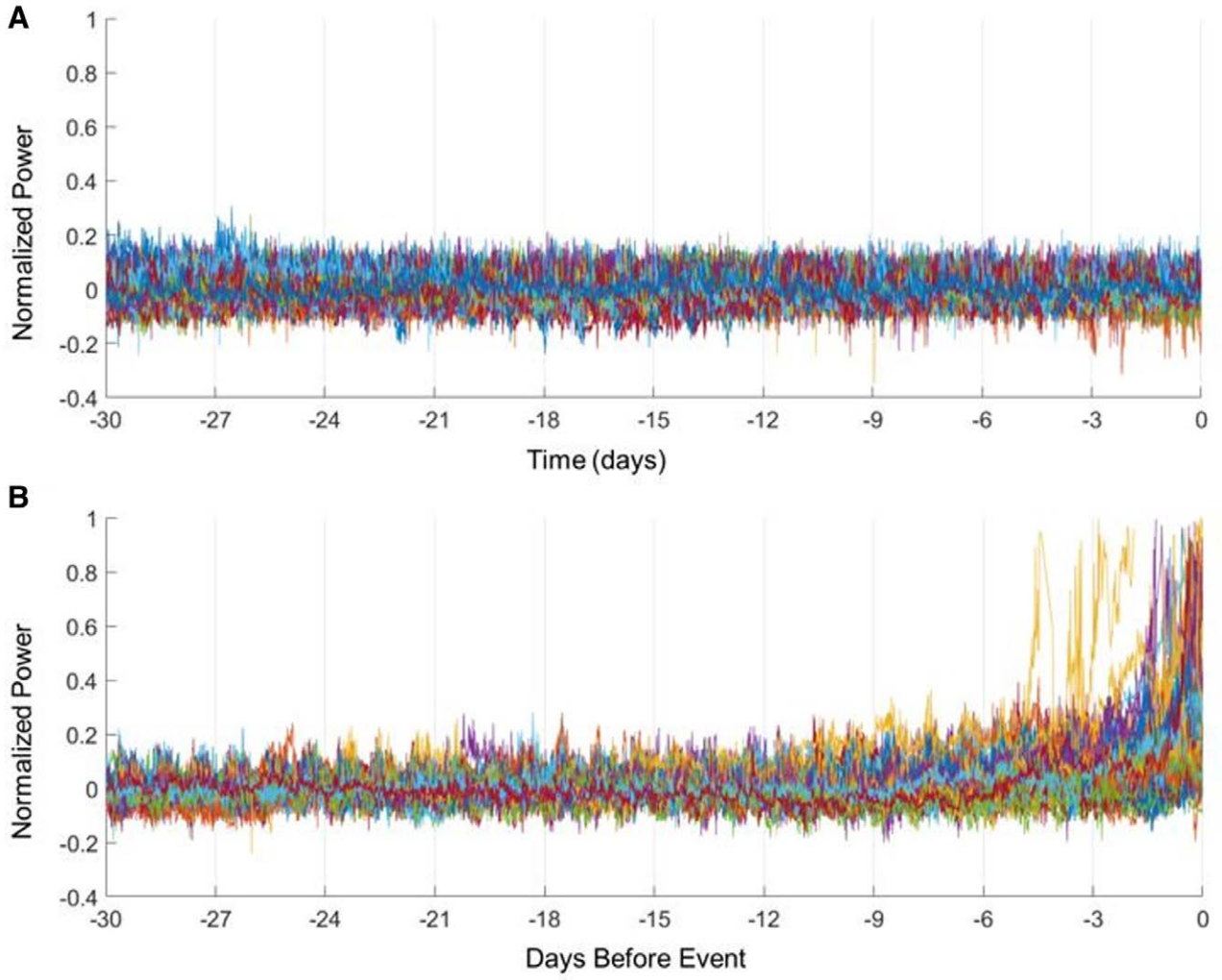

Figure 8. Superimposed normalized power signals for all subjects per study cohort. **A**: Control. **B**: Thrombus.

retrospective assessment but represents real-world data and clinical experiences. Additional data will be needed to confirm these findings and document consistent earlier intervention with potentially improved outcomes as a result. From the clinical trial data, only the event date is available, not the hour and minute of detection. This limits the resolution of calculating early warning to days. Additionally, the limited availability of clinical correlates in the control data means that we cannot explain all changes in pump power. This iteration of the power tracking algorithm is designed to detect increases in power associated with intra-pump thrombosis; a future iteration may be developed to detect power signatures associated with pre-pump (inflow) and post-pump (outflow graft) thrombosis.

Conclusion

In this analysis, the Power Tracking algorithm detected pump thrombosis with high sensitivity (85.7%) and a low FP rate (0.15 FP-PPY), whereas providing an average early warning of 3.9 days. Early detection of pump thrombosis with Power Tracking may permit successful medical management of PT, avoiding the need for surgical intervention and improving clinical outcomes.

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