IM007 (v1.1.2) interfaced with

the IMPLICITY Remote Monitoring Platform

Instructions for use

Document Reference	Date
IFU2-IM007-INSTRUCTIONS FOR USE	2021-04-29

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1 Objective of this document

This document provides the instructions for use of the medical device IM007 when it is used with the IMPLICITY Remote Monitoring Platform (as "the Platform" in this document).

Device name	**IM007** version 1.1.2
Manufacturer	**IMPLICITY** **USA** 185 Alewife Brook Parkway Suite 210, Cambridge, MA 02138 (USA) **Europe** 5 rue Saint-Fiacre 75002 Paris (FRANCE)
Contact information and technical support	contact@implicity.com phone USA: (+1) 929 350 7056 Europe: +33 (0) 9 61 67 41 14
First CE mark	July 2020

Carefully read all instructions prior to use.

Observe all warnings and precautions noted throughout these instructions.

Failure to do so may result in complications in use of this product.

CE

2 IM007 device information

2.1 Device description

IM007 is a software medical device for the analysis of ECG signals from Insertable Cardiac Monitor (ICM) devices and confirms the presence or absence of arrhythmias.

When it is interfaced with the Implicity Remote Monitoring Platform, IM007 provides additional data to healthcare professionals to support the analysis of abnormal episodes detected by ICM devices.

IM007 receives as input an ECG data signal via the Implicity remote monitoring platform, then processes the signal with a proprietary algorithm designed to detect arrhythmias, and generates as output the result of the analysis to a remote monitoring platform.

IM007 comprises:

- An algorithm (the Algorithm) that analyzes ECG files in order to detect cardiac rhythm abnormalities.
- A communication interface to external applications (the Implicity Remote Monitoring Platform) with the Algorithm and processing of ECG files. The API consists of 2 messaging queues (an input and an output).

IM007 works as follows:

- IM007 receives input data (an ECG file and device parameters) from the Remote Monitoring Platform using the input queue.
- The file is processed by the Algorithm which delineates zones with abnormal waveforms (ECG signals not defined as normal sinus rhythm). The output format is a sequence of waveform labels/start time/end time.
- IM007 sends a response to the Remote Monitoring Platform using the output queue.

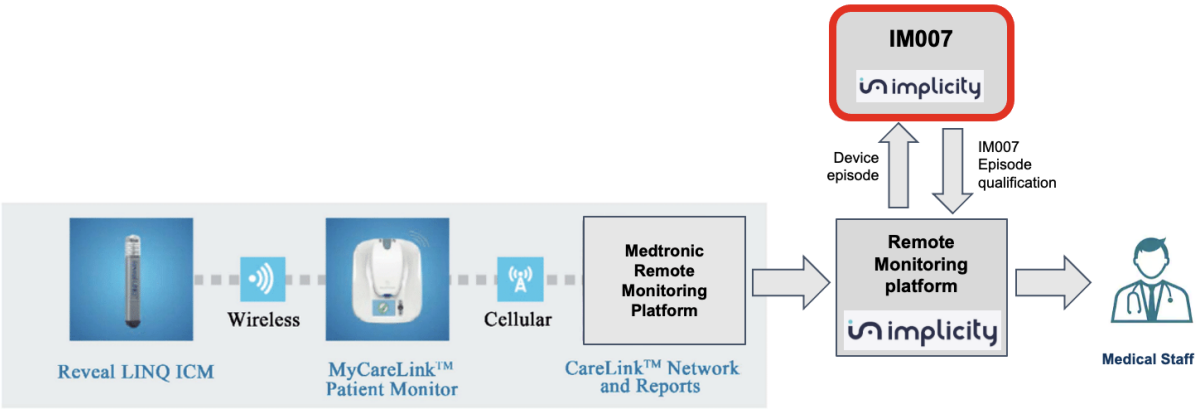


Figure 1: Diagram flow of ICM data with IM007 interface. ECG data from a Reveal LINQ ICM is processed by IM007 via the Implicity remote monitoring platform.

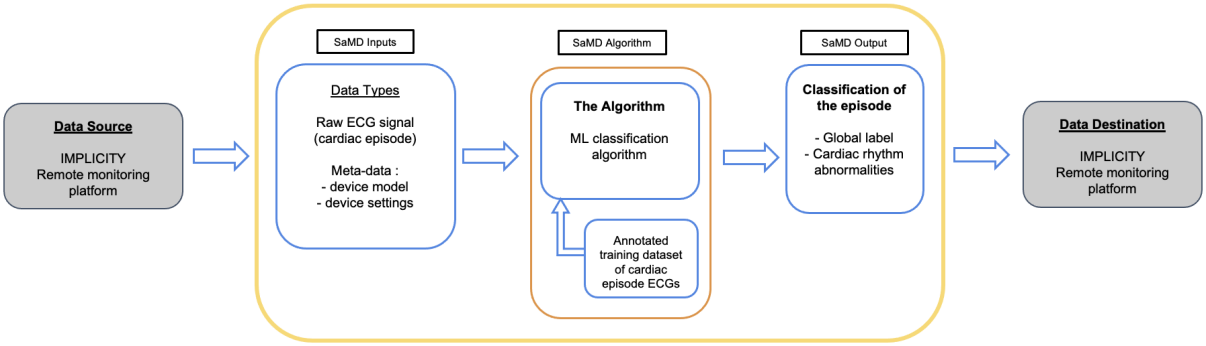


Figure 2: Schematic diagram of the IM007 device, showing the inputs and outputs.

IM007 is interfaced with the Implicity remote monitoring platform from which it receives ICM data file input and to which it transmits the output.

IM007 is designed to be interfaced with a remote monitoring platform, to enable algorithmic analysis of ECGs to identify abnormalities and provide categorization of arrhythmias.

IM007 operates as an adjunct to the ICM and its own user interface. As ICM data is stored on the Medtronic Carelink platform, the ICM output data is always directly viewable from the Medtronic Carelink platform.

2.2 Indication for use

IM007 is intended for use by qualified healthcare professionals for the assessment of arrhythmias in Insertable Cardiac Monitor (ICM) ECG data.

IM007 supports downloading and analyzing data recorded in compatible formats from ICMs. This version of the IM007 only supports ECG data from Medtronic ICMs.

IM007 is intended to be electronically interfaced with other computer systems (remote monitoring platforms) that supply the ECG data to IM007 and receive the output of IM007 (analysis) for viewing by healthcare professionals.

IM007 provides ECG signal processing and analysis, to detect asystole, bradycardia, atrial tachycardia or atrial fibrillation, ventricular tachycardia, normal rhythm and artifacts.

IM007 is not for use in life supporting or sustaining systems or ECG monitor and Alarm devices.

IM007 interpretation results are not intended to be the sole means of diagnosis. It is offered to physicians and clinicians on an advisory basis only in conjunction with the physician's knowledge of ECG patterns, patient background, clinical history, symptoms, and other diagnostic information.

2.3 List of compatible devices for use with IM007

This version of IM007 is compatible with the following devices:

- Medtronic LNQ22
- Medtronic LNQ11
- Medtronic REVEAL XT 9529
- Medtronic REVEAL DX 9528

2.4 Device output labels

The output of IM007 is an electronic report containing the classification labels detected by the Algorithm in the ICM ECG episode (the input data). This report is made up of a list of defined labels, as described in the table below.

IM007 output classification label	**Definition**
Asystole	Ventricular pause. Absence of ventricular contraction for a duration equal to or greater than the asystole programmable duration.
Bradycardia	Slow ventricular rate. Lower than the programmable brady rate.
AT/AF	Atrial Tachycardia / Atrial Fibrillation At least one of the following: - Atrial tachycardia (ectopic) - Atrial flutter - Atrial fibrillation
VT	Ventricular Tachycardia (VT) At least one of the following: -Tachycardia that originates in a ventricle. Sometimes life-threatening. - Non-sustained ventricular tachycardia (NSVT)
Unspecified abnormality	Unspecified abnormality. This output prompts the healthcare professional to review the ECG.
Artifact	Uninterpretable signal. Presence of a non-cardiac noise, which distorts the signal and prevents proper medical interpretation of the specified portion.
Normal Rhythm	The ECG does not present any significant abnormality.

Table 1: IM007 output classification labels

All episodes with an output label other than normal (**Asystole, Bradycardia, AT/AF, VT, Unspecified abnormality, Artifact**) need to be reviewed and scrutinized for the presence of an abnormality by a qualified healthcare professional.

3 Directions for use of IM007

3.1 Warnings and precautions

- IM007 is intended to be used:
  - to analyze subcutaneous ECG signals from ICMs:
  - for patients with clinical symptoms or with high risk of cardiac arrhythmia.
  - for patients who have transitory symptom like dizziness, palpitations, syncope and chest pain

  IM007 is intended to be used on signals from patients aged eighteen and over.

- IM007 is not intended to be the sole means of diagnosis. It is offered to physicians and clinicians in an advisory capacity only in conjunction with the physician's knowledge of ECG patterns, patient history, clinical history, symptoms and other diagnostic information.

- This manual contains screen shot examples. These screen shots are provided for reference only and are not intended to convey actual operating techniques.

- IM007 should be used in accordance with the conditions of these instructions for use and the instructions for use of the remote monitoring platform.

- IM007 is intended to be used on episodes:
  - With segments of duration between 9.5 seconds and 5 minutes
  - Which were detected as abnormality by the device, excluding patient activated episodes

- Cybersecurity:
  As IM007 is a software device hosted by a Remote Monitoring Platform, cybersecurity is managed by the Remote Monitoring Platform. User must follow the instructions for use of the Platform.

If you have any questions, please contact Implicity Customer Service at support@implicity.fr.
Any serious incident related to the device should be reported to Implicity at support@implicity.fr and to the competent authority of the Member State in which the user and/or patient is located.

3.2 Activation / deactivation of IM007

Once authenticated to the Platform, the user (the clinician) has to enable a setting page for its Medical Center

The user can find information regarding IM007 (version, description), and can download the instructions for use.

The user can also decide at any time to activate or deactivate IM007 for all the compatible ICM devices associated to his or her medical center in the Platform (by selecting the check box “use the algorithm”):

- Once **“use” is checked**, IM007 is **activated** and every new episode file received from a compatible ICM associated to the medical center will **be processed by IM007** upon receipt in the Platform.
- Once **“use” is not checked**, IM007 is **deactivated** and new episode files received from ICMs associated to the medical center will **not be processed by IM007**.

Figure 3 shows the setting page of IMPLICITY Remote Monitoring Platform used to activate/deactivate IM007.

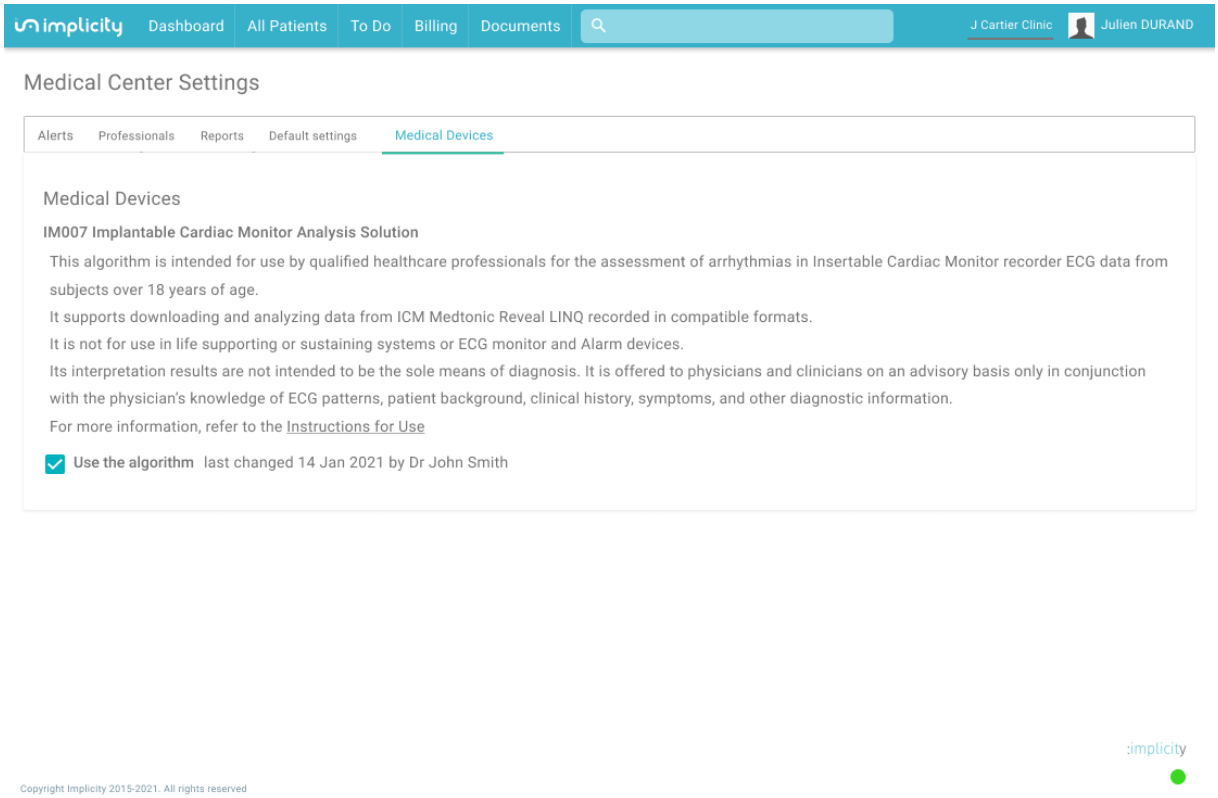


Figure 3. Setting page of IMPLICITY Remote Monitoring Platform

3.3 IM007 output displayed for each episode received

IM007 output results are displayed in the section “Arrhythmias” of the Platform.

The following screenshot is an example of how IM007 results can be displayed in the IMPLICITY Remote Monitoring Platform, next to the classification label provided by the ICM device itself.

In Figure 4, five episodes are listed from an ICM device stored in the platform. For each episode, the physician can see, side-by-side:

- the classification by the ICM device (displayed as “Device classification”)
- the classification by IM007 (displayed as “Implicity suggestion” in column “Classification”)

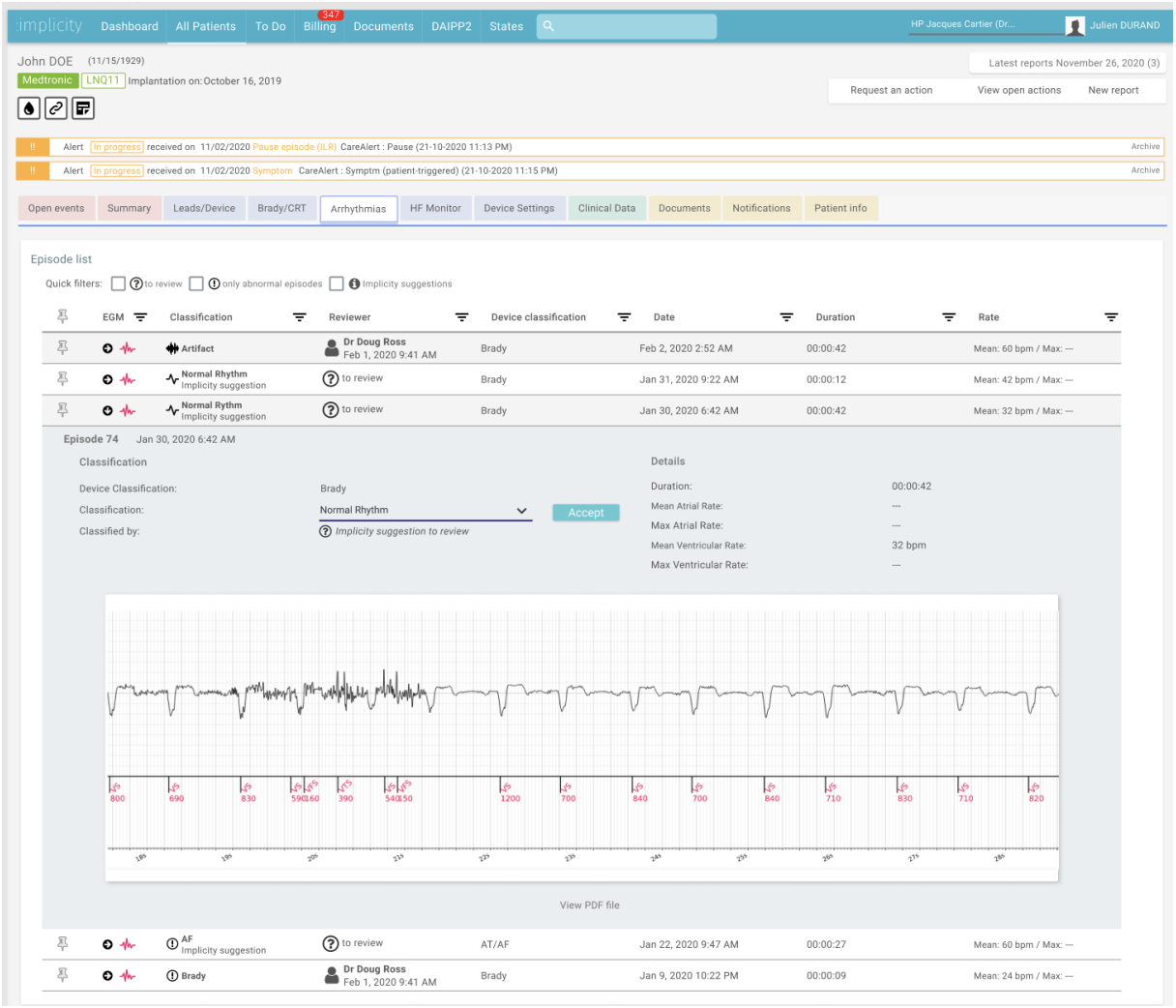


Figure 4: Screenshot example of ICM episodes displayed in the IMPLICITY Remote Monitoring Platform with additional information from IM007 (“Implicity suggestion”)

In the example in Figure 5, we can see 2 false positive “Brady” outputs from the ICM are corrected to “Normal Rhythm” by IM007, demonstrating how false positive arrhythmias can be reduced using IM007.

The physician can always check the ECG strip to perform his or her own signal analysis, and has the ability to register a review of the classification by selecting a new label from the list. His or her name and date is then added as “Reviewer” of the episode, next to the labels from the device and IM007 (ex: “classified by Dr Doug Ross”).

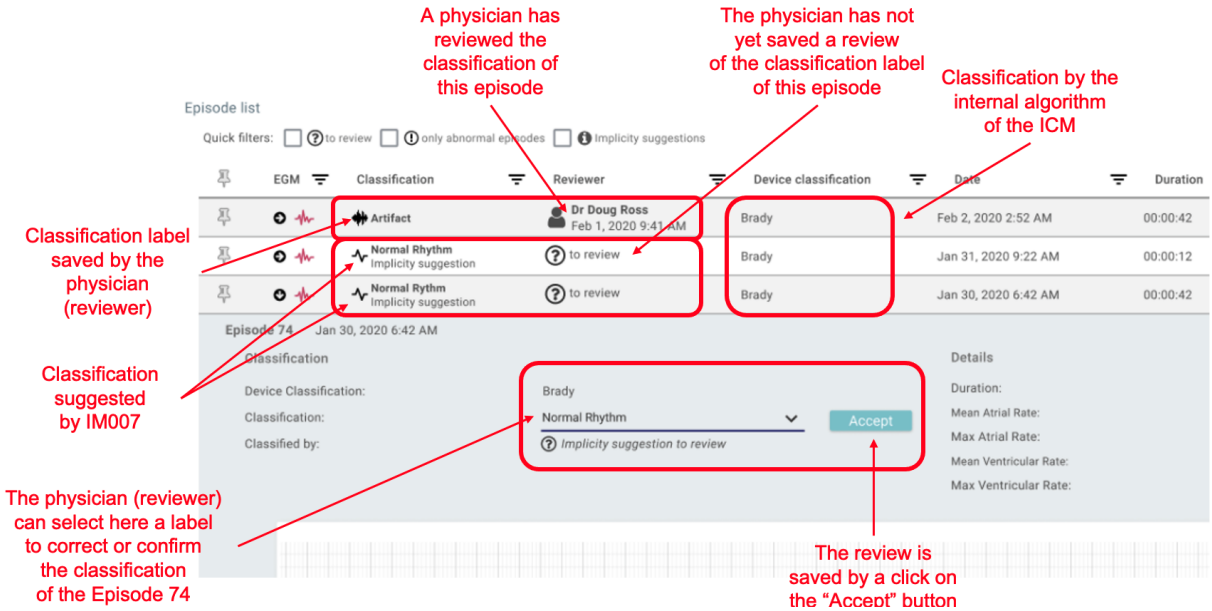
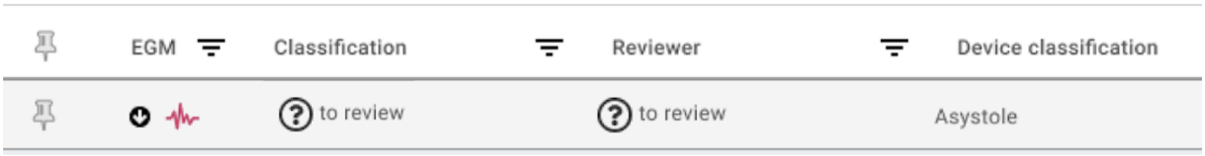


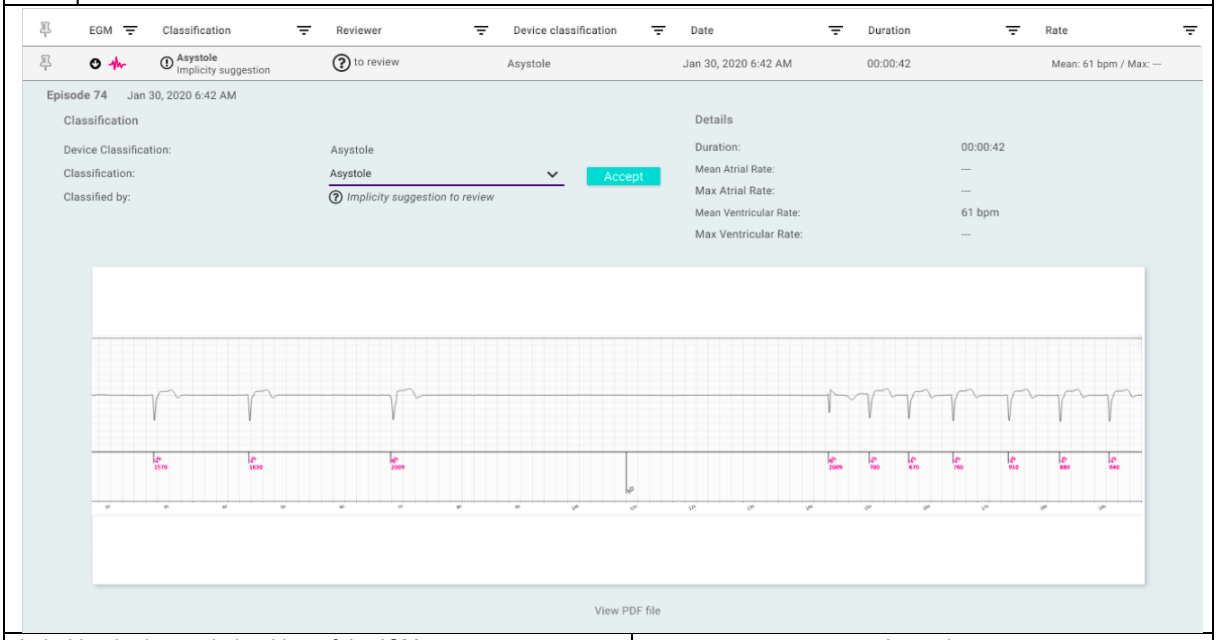
Figure 5: Screenshot example of ICM episodes displayed in the IMPLICITY Remote Monitoring Platform with additional information from IM007 (“Implicity suggestion”)

If the episode has not been analyzed by IM007 for some reason (IM007 not activated or error in process), the Classification row is filled with the message “(?) to review” as shown:



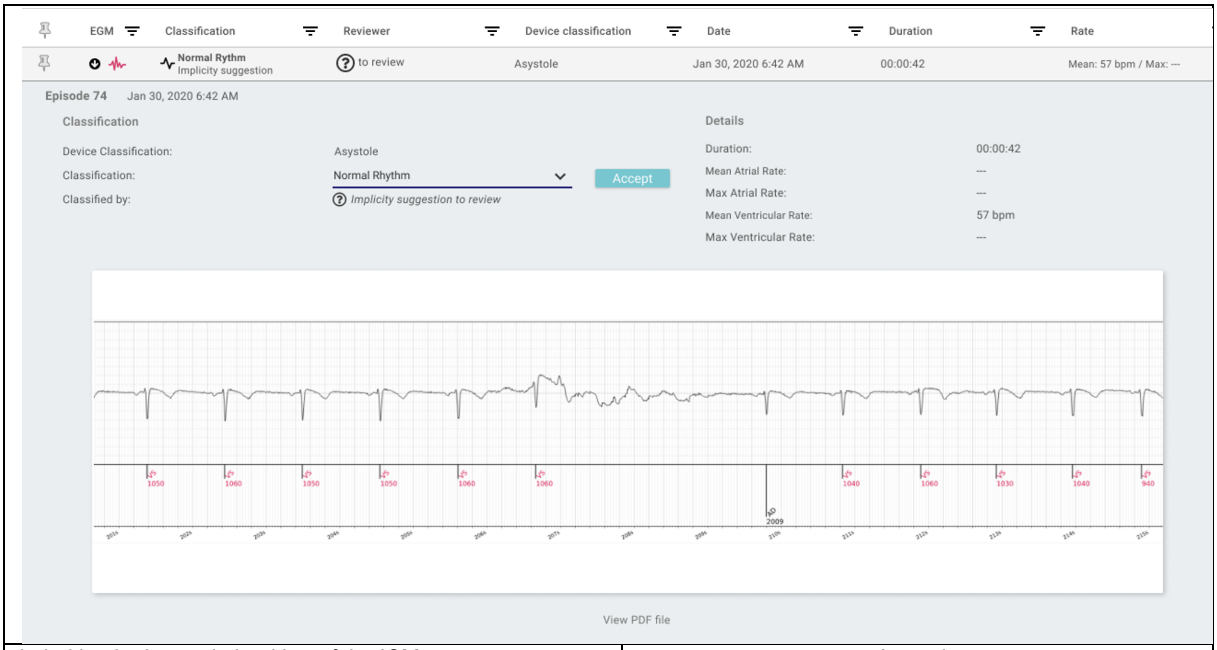
4 Examples of output results from IM007

The following examples show output results from IM007 compared to original labels from the ICM.

Example #1	
	
Label by the internal algorithm of the ICM:	Asystole
Label suggested by IM007:	Asystole

Example #2	
	
Label by the internal algorithm of the ICM:	VT
Label suggested by IM007:	AT/AF

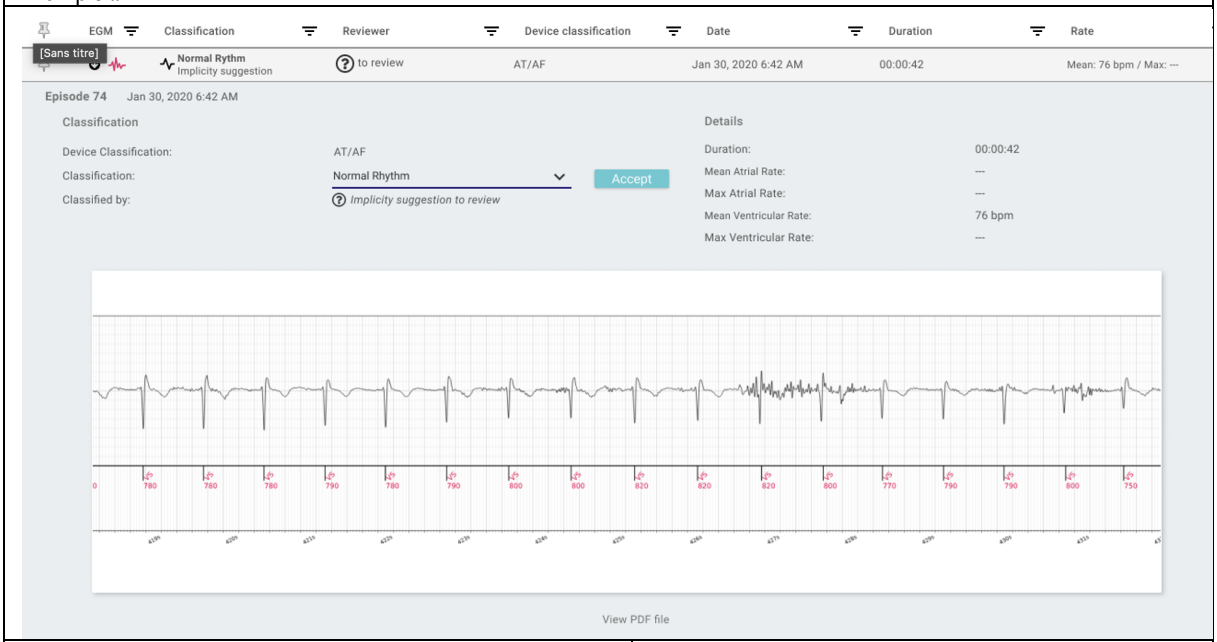
Example #3



Label by the internal algorithm of the ICM:	Asystole
Label suggested by IM007:	Normal Rhythm

Remark: in this case, the Asystole detected by the ICM device is due to undersensing. The Normal Rhythm is still visible, and it is classified as Normal Rhythm by IM007.

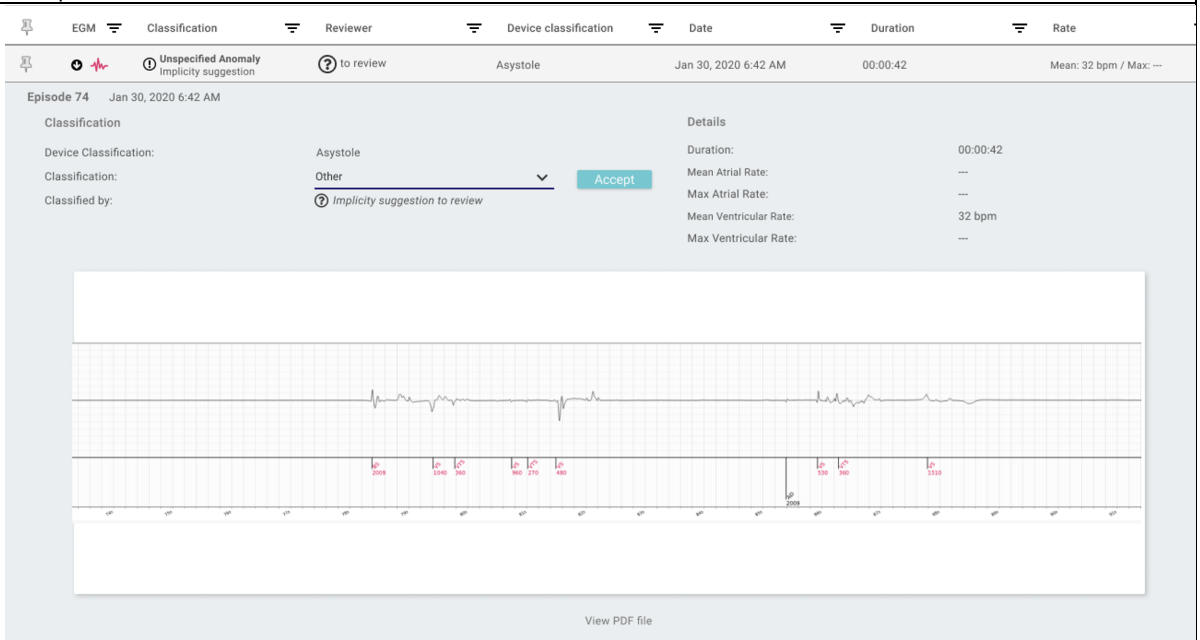
Example #4



Label by the internal algorithm of the ICM:	AT/AF
Label suggested by IM007:	Normal Rhythm

Remark: In this case the signal is noisy but the normal rhythm is still visible, leading IM007 to classify it as “Normal Rhythm”.

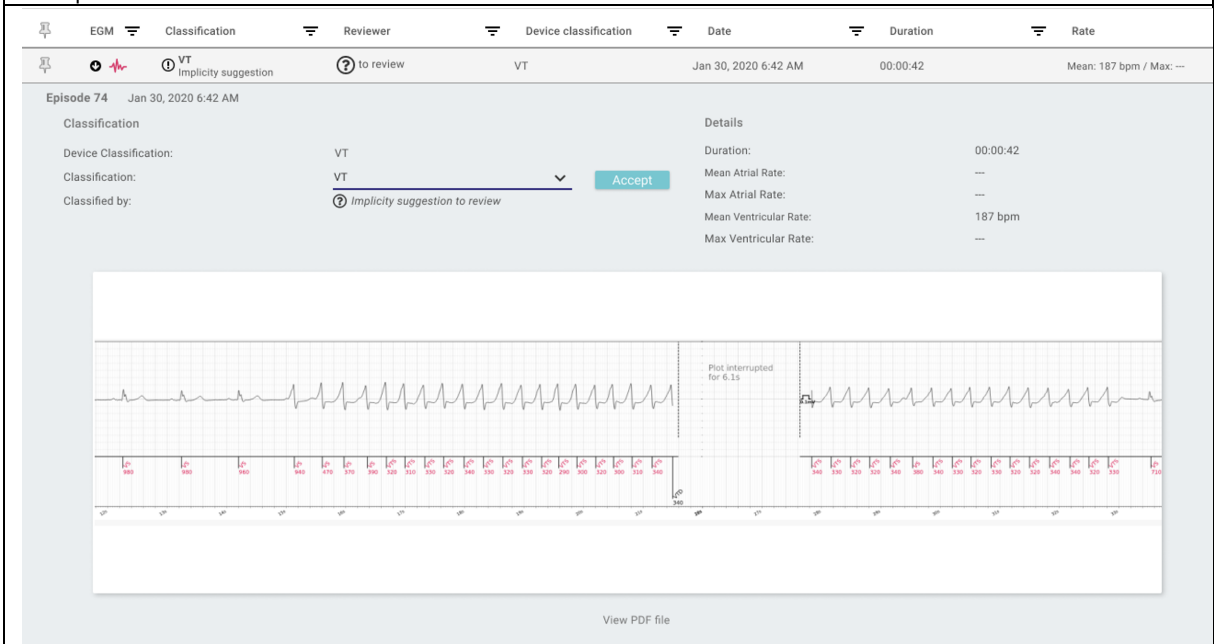
Example #5



Label by the internal algorithm of the ICM:	Asystole
Label suggested by IM007:	Unspecified Anomaly

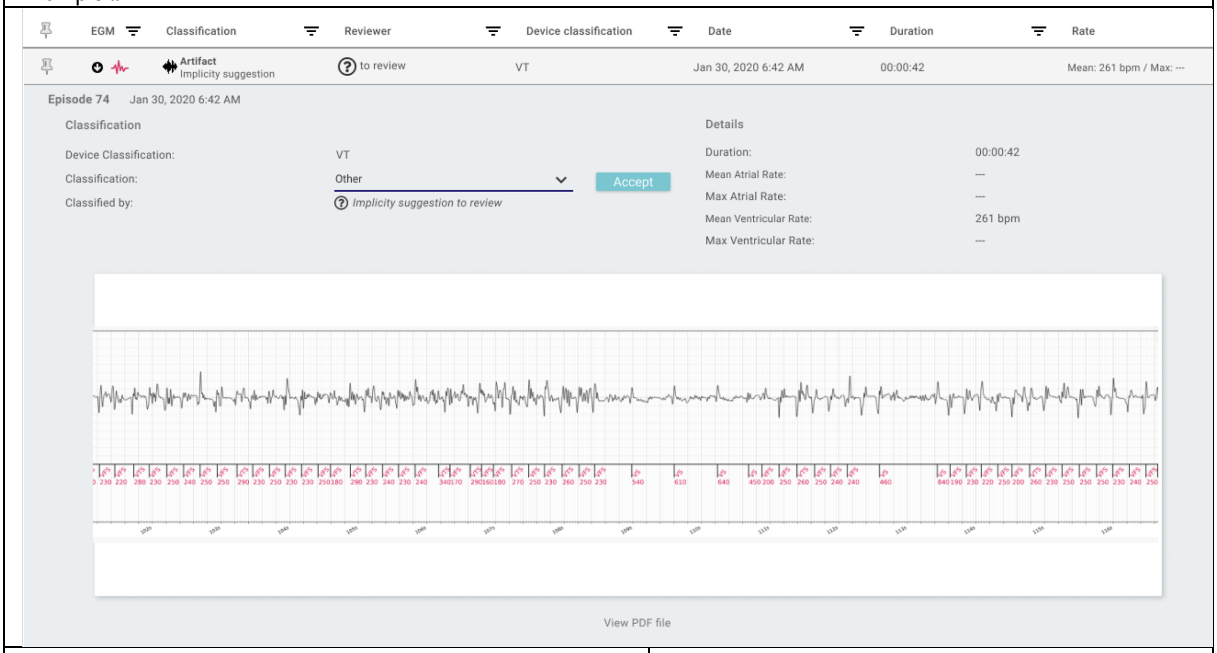
Remark: In this case, a loss of signal is classified as Asystole by the ICM device, and classified as “Unspecified Anomaly” by IM007, as it failed to identify another abnormality in the signal.

Example #6



Label by the internal algorithm of the ICM:	VT
Label suggested by IM007:	VT

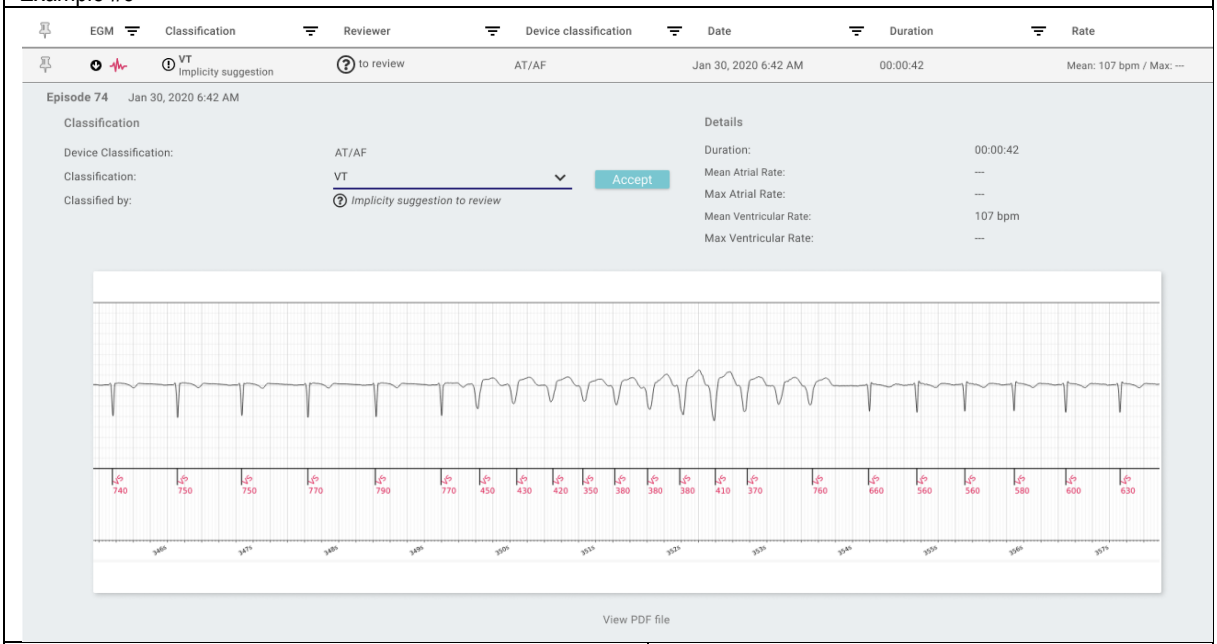
Example #7



Label by the internal algorithm of the ICM:	VT
Label suggested by IM007:	Artifact

Remark: In this case, a noisy signal is detected as VT by the ICM device. However, the artifact prevents proper medical interpretation of the ECG, leading IM007 to classify it as “Artifact”.

Example #8



Label by the internal algorithm of the ICM:	AT/AF
Label suggested by IM007:	VT

5 Clinical need and performance requirements

Remote patient management of cardiovascular conditions has become the standard of care for individuals with known or suspected life-threatening arrhythmias. Thirty years ago, patient's ECGs were commonly monitored with 24hour Holters, or via trans-telephonic monitoring of those with implantable pacemakers. Today millions are monitored and diagnosed via sophisticated, wireless telemetry systems providing long-term measurement of ECG signals emitted from implantable pacemakers, defibrillators, resynchronization devices and subcutaneous insertable cardiac monitors (ICMs). This evolution has provided significant improvements in the clinician's ability to determine the significance of patient arrhythmias and provide timely therapeutic options. For example, the use of ICMs has enabled much longer-term patient monitoring of patients with suspected arrhythmias than is possible with a Holter monitor.

Though revolutionary in terms of patient management, the proliferation of these wireless remote patient management systems has had a significant impact on the workload of healthcare professionals treating patients with underlying cardiovascular conditions. The volume of ECG rhythm strips requiring interpretation by professionals trained in electrogram analysis has grown several orders of magnitude in the past three decades. Accurate interpretation of ECG strips has become increasingly difficult as the origination of these signals has transitioned from the standard 12-lead ECG performed in an office or hospital setting, to remote, long-term recordings from miniature subcutaneous implants with two leads and extremely limited antenna length.

ICM device manufacturers have developed algorithms to interpret and categorize these ECG signals to automatically identify segments of ECG that contain possible arrhythmias and provide these to physicians via a web platform, along with a classification of the arrhythmia event detected. While the success of these systems varies significantly by vendor and algorithm, peer reviewed literature suggests that while these systems have a very high sensitivity to arrhythmias [ref 2] they generate false positive interpretations in 40-80% of their readings [ref 1]. This false positive rate significantly compounds the burden on healthcare professionals to review and cross-check ECG recordings and the identification of arrhythmias.

Given this background, there is a significant unmet clinical need for an improved ECG analysis tool that can provide more accurate categorization of normal sinus rhythm and various arrhythmias, and to reduce the burden of ECG interpretation by health care professionals. By reducing this burden on healthcare professionals, patients will benefit from more timely feedback and clinical decision making about the management of their cardiovascular symptoms.

Implicity has developed a proprietary machine learning algorithm which processes ECG inputs and classifies each electrogram as normal rhythm or one of a number of arrhythmia categories. In particular, the clinical need is for an analysis algorithm that takes the output of ICMs as input and generates an output that substantially reduces the false positive rate without significantly impacting the false negative rate. The performance required to meet this clinical need is a false positive rate of less than 40%.

Utilization of the Implicity algorithm will support clinicians in interpretation of ECG signals from patients with known or suspected cardiovascular conditions. It will reduce the burden on these health care professionals in the reviewing of this diagnostic data, and will benefit patients with faster, more accurate therapeutic solutions based on this ECG analysis tool.

6 Performances of IM007

Performance of IM007 has been evaluated to establish the sensitivity of the algorithm and to determine the clinical benefit. Evaluation has been done on a dataset of 879 episodes from Medtronic ICM devices, including 635 Reveal LINQ (LNQ11) episodes, extracted from the Implicity remote monitoring platform, including about half US patients and half European patients.

A statistically significant clinical evaluation was performed to validate the IM007 algorithm, and the summary results are as follows.

These performance results (Table 3 and 4) demonstrate that IM007 meets the unmet clinical need described above, with a low false positive rate while having a very high sensitivity. None of the 7 false negatives was both a significant and certain diagnosis. All have been considered normal by at least one of the two expert annotators. The abnormalities were mostly uncertain (inferred regular AT) or abnormalities outside ICM scope.

The misclassification proportion (proportion of misclassified, False Positive or False Negatives episode over the 635 LNQ11 episodes included in the study) of LNQ11 alone versus LNQ11 used with IM007 demonstrates a 26.84% absolute reduction (79.45% relative reduction) in the misclassification proportion, in favor of LNQ11 + IM007.

- IM007 sensitivity was evaluated on the 516/879 episodes adjudicated as “Abnormality” (AT/AF, Asystole, Bradycardia, VT, Other) by the adjudication committee
- IM007 False Positive rate was evaluated on the 283/879 episodes adjudicated as “Normal Rhythm” by the adjudication committee
- The misclassification proportion was evaluated over the 635/879 LNQ11 episodes included in the primary study.

	Results	**95% CI**
IM007 Sensitivity	98.64 % (509/516)	[97.22%; 99.45%]
IM007 False Positive rate	24.03 % (68/283)	[19.17%; 29.44%]

Table 3: Performance summary on ICM dataset

Misclassification Proportion (n/N) **LNQ11**	**Misclassification Proportion (n/N)** **LNQ11 + IM007**	**Difference** **95% CI**	**P-value**
34.49% (219/635)	7.56% (48/635)	-26.84% [-30.58%; -23.52%]	P < 0.0001

Table 4: Misclassification summary on Reveal LNQ11 dataset, comparing LNQ11 alone to LNQ11 used with IM007

7 Material Requirements

No material required.

8 Explanation of Symbols used

Symbol	Name	Description
	Manufacturer	This symbol displayed on the label is accompanied by the name, address of the manufacturer (Implicity) and product version release date (date of manufacture).
	Catalogue Number	This symbol displayed on the label is accompanied by the manufacturer's catalogue number.
	Caution	This symbol displayed on the label is a safety symbol, indicating that there are specific warnings or precautions associated with the device which are not found on the label. These precautions/warnings are described in the Instructions for Use.
	Consult Instruction for Use	This symbol displayed on the label indicates that the Instruction for Use for the device should be consulted.
	CE mark	This symbol displayed on the label indicates that medical device has been awarded the CE mark.
RxOnly	Rx Only	This symbol displayed on the label is applicable in the United Stated and means: "CAUTION: Federal law restricts this device to sale by or on the order of a physician."

9 References

[Ref 1] Shen WK, Sheldon RS, Benditt DG, et al. 2017 ACC/AHA/HRS Guideline for the Evaluation and Management of Patients With Syncope: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society [published correction appears in Circulation. 2017 Oct 17;136(16):e269-e270]. Circulation. 2017;136(5):e25-e59. doi:10.1161/CIR.0000000000000498

[Ref 2] Sanders P, Pürerfellner H, Pokushalov E, et al. Performance of a new atrial fibrillation detection algorithm in a miniaturized insertable cardiac monitor: Results from the Reveal LINQ Usability Study. Heart Rhythm. 2016;13(7):1425-1430. doi:10.1016/j.hrthm.2016.03.005