REVEAL AF IN YOUR CRYPTOGENIC STROKE PATIENTS

Are You Looking Long Enough?

Medtronic
Each year, at least 200,000 cryptogenic strokes occur in the United States. Cryptogenic stroke accounts for approximately one-third of ischemic strokes in the majority of modern stroke registries and databases. Cryptogenic stroke is as prevalent as large vessel stroke.

5-FOLD increase in ischemic stroke risk for AF patients.

2X more likely for AF-related ischemic stroke to be fatal as non-AF stroke.

67% decrease in AF patient stroke risk with oral anticoagulants.

AF detection and monitoring modality selection matters for cryptogenic stroke patients:
- The ability to identify AF in patients with cryptogenic stroke has profound implications for long-term medical management.
- Recurrence was more frequent and functional deficits were more likely to be severe among survivors of AF-related ischemic stroke.
- Guidelines also recommend anticoagulant therapy for stroke prevention in most patients with AF.

2016 ESC Guidelines for the management of atrial fibrillation:
- Guidelines developed by the Task Force for the management of atrial fibrillation of the European Society of Cardiology (ESC).
- Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC.
- Endorsed by the European Stroke Organisation (ESO).

Guidelines Recommendation:
In stroke patients, additional ECG monitoring by long-term noninvasive ECG monitors or implanted loop recorders should be considered to document silent atrial fibrillation.
ARE YOU MONITORING CRYPTOGENIC STROKE PATIENTS LONG ENOUGH?

Short- and intermediate-term cardiac monitoring may miss many patients with paroxysmal AF.

AF episode
Repeated short-term monitoring

**Long-term, continuous monitoring (up to 3 years)**

Median time to detect AF following cryptogenic stroke:

<table>
<thead>
<tr>
<th>Time Period</th>
<th>Median Time to Detect AF</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 days</td>
<td>84 days</td>
</tr>
<tr>
<td>12 months</td>
<td></td>
</tr>
<tr>
<td>24 months</td>
<td></td>
</tr>
<tr>
<td>36 months</td>
<td></td>
</tr>
</tbody>
</table>

**84 DAYS**

is the median time to AF detection in cryptogenic stroke patients.

**79%**

of first AF episodes were asymptomatic at 12 months.

**88%**

of patients who had AF would have been missed if only monitored for 30 days.

*Based on Kaplan-Meier estimates.

INFORM YOUR CLINICAL DECISIONS WITH THE REVEAL LINQ™ ICM SYSTEM

Up to **3 YEARS** of continuous cardiac monitoring

The revolutionary Reveal LINQ Insertable Cardiac Monitoring System transforms your ability to diagnose atrial fibrillation with its proven AF detection algorithm.

**Simple, minimally invasive insertion procedure**

- The Reveal LINQ ICM is placed just under the skin of the patient’s chest in a simple procedure
- The ultra-discreet heart monitor is not visible in most patients
- Patients prefer the Reveal LINQ ICM over external wearable monitors

Safe for use in MRI setting same day at 1.5 and 3.0 Tesla*

*Reveal LINQ ICM has been demonstrated to pose no known hazards in a specified MRI environment with specified conditions of use. Please see the Reveal LINQ ICM clinician manual or MRI technical manual for more details.

The world’s smallest insertable cardiac monitor

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**The Reveal LINQ ICM**

continuously records heart rhythm data and sends them wirelessly to the MyCareLink™ Patient Monitor.

**The MyCareLink Patient Monitor**

transmits data from the Reveal LINQ ICM to the clinic via a global cellular connection.

**The clinic**

receives easy-to-use and clinically actionable Reveal LINQ reports via the CareLink™ Network.
The CRYSTAL-AF Study demonstrates the superiority of ICM for AF detection in patients with cryptogenic stroke.

**Study Design**
- Randomized, controlled clinical trial with 441 patients
- Compared continuous, long-term monitoring with Reveal™ ICM vs. conventional follow-up
- Assessment at scheduled and unscheduled visits
- ECG monitoring performed at the discretion of the site investigator
- ≥ 40 years of age
- Cryptogenic stroke (or clinical TIA) with infarct seen on MRI or CT within the previous 90 days and no mechanism identified after:
  - 12-lead ECG
  - 24-hour ECG monitoring (e.g., Holter)
  - Transesophageal echocardiography
  - CTA or MRA of head and neck to rule out arterial source
  - Screening for hypercoagulable states in patients < 55 years old

**Patient Inclusion Criteria**
- ≥ 40 years of age
- Cryptogenic stroke (or clinical TIA) with infarct seen on MRI or CT within the previous 90 days and no mechanism identified after:
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**Endpoints**
- **Primary**
  - Time to first detection of AF at 6 months of follow-up
- **Secondary**
  - Time to first detection of AF at 12 months of follow-up
  - Recurrent stroke or TIA
  - Actions taken after patient diagnosed with AF

**Clinical Impact: More Appropriate Care**
Short-term cardiac monitoring is **not** sufficient for AF detection in cryptogenic stroke:
- Extensive external monitoring found few patients with AF
  - In the control group at 6 months, only 3 patients were found to have AF, yet there were 88 conventional ECGs, 20 24-hour Holters, and 1 event recorder used
- Reveal ICM detected 7 times more patients with AF at the 12-month end point

**CRYSTAL-AF Study Results**
- Hazard ratio: 8.8 (95% CI: 3.5 - 22.2)
- P < 0.001 by log-rank test

**Detection of Atrial Fibrillation by 36 months**

<table>
<thead>
<tr>
<th>Months since randomization</th>
<th># at risk</th>
<th>Atrial Fibrillation Detected (% of patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>Control</td>
<td>1.4%</td>
</tr>
<tr>
<td></td>
<td>ICM</td>
<td>8.9%</td>
</tr>
<tr>
<td>12</td>
<td>Control</td>
<td>2%</td>
</tr>
<tr>
<td></td>
<td>ICM</td>
<td>12.4%</td>
</tr>
<tr>
<td>18</td>
<td>Control</td>
<td>8.9%</td>
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<tr>
<td></td>
<td>ICM</td>
<td>12.4%</td>
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<tr>
<td>24</td>
<td>Control</td>
<td>12.4%</td>
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<td>30%</td>
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<td>Control</td>
<td>3%</td>
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*As published in the New England Journal of Medicine*
ISCHEMIC STROKE PATHWAY

Ischemic Stroke/TIA

- Embolic appearing stroke with no history of AF:
  - Multiple foci of infarction
  - Cortical watershed distribution
  - Cerebellar

- History of AF

- Standard stroke work-up

- Antiplatelet agent

- Multiple foci of infarction
- Cortical watershed distribution
- Cerebellar

Lacunar infarction: small vessel disease

- Standard stroke work-up

- CTA of intracranial vessels
- Transesophageal Echocardiogram (TEE)

- Symptomatic carotid stenosis, greater than 50%

- CEA or stent

- Angiogram
- Lumbar puncture
- Vasculitis work-up

- Medical management
- Antiplatelet agents

- Monofocal
- Multifocal

- Glucose control
- Blood pressure management
- Hypercoagulation labs if age < 50

Standard stroke work-up:

- Carotid dopplers
- Telemetry bed
- Fasting lipid panel

CRYPTOGENIC STROKE PATHWAY

Patient Diagnosed with Cryptogenic Stroke/TIA

- Could detection of suspected AF impact patient management?
  - YES
  - Refer to cardiology to insert Reveal LINQ ICM
  - Inpatient/ outpatient insertion
  - Insert Reveal LINQ ICM prior to discharge
  - If unable to insert prior to discharge, potential external monitor bridge and schedule Reveal LINQ ICM
  - Enroll in CareLink Network & perform remote monitoring
  - Schedule clinical follow-up with treating physician and ensure long-term adherence to monitoring

- NO
  - Not a candidate

- AF detected
  - Insert Reveal LINQ ICM

- AF not detected
  - Insert Reveal LINQ ICM

Pathway based on the consensus of the Cryptogenic Stroke Pathway steering committee. February 2016.

Medtronic Disclosure Statement: This pathway is provided for educational purposes and should not be considered the exclusive source for this type of information. It is the responsibility of the practitioner to exercise independent clinical judgment. Refer to the brief statement for indications, warnings/precautions, and complications for the Reveal LINQ ICM.
References


Brief Statement

Indications

Reveal LINQ™ LINQ11 Insertable Cardiac Monitor and Patient Assistant

The Reveal LINQ™ Insertable Cardiac Monitor is an implantable patient-activated and automatically-activated monitoring system that records subcutaneous ECG and is indicated in the following cases:

• Patients with clinical syndromes or situations at increased risk of cardiac arrhythmias
• Patients who experience transient symptoms such as dizziness, palpitations, syncope, and chest pain, that may suggest a cardiac arrhythmia

This device has not specifically been tested for pediatric use.

Patient Assistant

The Patient Assistant is intended for unsupervised patient use away from a hospital or clinic. The Patient Assistant activates the data management feature in the Reveal Insertable Cardiac Monitor to initiate recording of cardiac event data in the implanted device memory.

Contraindications

There are known contraindications for the implant of the Reveal LINQ Insertable Cardiac Monitor. However, the patient's particular medical condition may dictate whether or not a subcutaneous, chronically implanted device can be tolerated.

Warnings/Precautions

Reveal LINQ LINQ11 Insertable Cardiac Monitor

Patients with the Reveal LINQ Insertable Cardiac Monitor should avoid sources of diathermy, high sources of radiation, electrosurgical cautery, external defibrillation, lithotripsy, therapeutic ultrasound, and radiofrequency ablation to avoid electrical reset of the device, and/or inappropriate sensing as described in the Medical procedure and EPI precautions manual. MRI scans should be performed only in a specified MRI environment under specified conditions as described in the Reveal LINQ-MRI Technical Manual.

Patient Assistant

Operation of the Patient Assistant near sources of electromagnetic interference, such as cellular phones, computer monitors, etc., may adversely affect the performance of this device.

Potential Complications

Potential complications include, but are not limited to, device rejection phenomena (including local tissue reaction), device migration, infection; and erosion through the skin.

Medtronic MyCareLink™ Patient Monitor, Medtronic CareLink™ Network and CareLink™ Mobile Application

Intended Use

The Medtronic MyCareLink Patient Monitor and CareLink Network are indicated for use in the transfer of patient data from some Medtronic implantable cardiac devices based on physician instructions and as described in the product manual. The CareLink Mobile Application is intended to provide current CareLink Network customers access to CareLink Network data via a mobile device for their convenience. The CareLink Mobile Application is not replacing the full workstation, but can be used to review patient data when a physician does not have access to a workstation. These products are not a substitute for appropriate medical attention in the event of an emergency and should only be used as directed by a physician. CareLink Network availability and mobile device accessibility may be unavailable at times due to maintenance or updates, or due to coverage being unavailable in your area. Mobile device access to the Internet is required and subject to coverage availability. Standard text messaging rates apply.

Contraindications

There are known contraindications.

Warnings and Precautions

The MyCareLink Patient Monitor must only be used for interrogating compatible Medtronic implantable devices.

See the device manual for detailed information regarding the implant procedure, indications, contraindications, warnings, precautions, and potential complications/adverse events. For further information, please call Medtronic at 1-800-328-2518 and/or consult the Medtronic website at www.medtronic.com.

Caution: Federal law (USA) restricts these devices to sale by or on the order of a physician.
The CRYSTAL-AF Study found that continuous monitoring with Reveal ICM is superior to standard medical care for the detection of AF in cryptogenic stroke patients.

2016 ESC AF Guidelines recommend cardiac monitoring with Reveal LINQ ICM for cryptogenic stroke patients.\textsuperscript{11}

*Endorsed by the European Stroke Organisation

Visit CRYSTAL-AF.com for complete study information.

84 Days is the median time to AF detection in cryptogenic stroke patients\textsuperscript{13}

30% AF-Detection Rate at 3 Years\textsuperscript{13}

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