CRYPTOGENIC STROKE

THERAPY
AWARENESS
PRESENTATION

Medtronic
Further, Together
Epidemiology
Diagnosis
Guidelines and Evidence to Support Reveal LINQ ICM in Cryptogenic Stroke Patients
Cryptogenic Stroke Care Pathway
WHY TALK ABOUT CRYPTOGENIC STROKE?

- 678,000 ischemic strokes every year in the US\(^1\)
  - Leading cause of disability in the US and worldwide
- ~200,000 cryptogenic strokes yearly\(^1\)
- Most cryptogenic stroke patients receive anti-platelet for secondary prevention\(^2\)
- Long-term monitoring reveals AF in ~30% of cryptogenic stroke patients\(^3-9\)
  - These patients benefit from anticoagulant therapy

RISK FOR STROKE IN PATIENTS WITH AF

5-FOLD
increase in ischemic stroke risk for AF patients.¹

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

67%
decrease in AF patient stroke risk with oral anticoagulants.³

<table>
<thead>
<tr>
<th>~800,000</th>
<th>87%</th>
<th>5th</th>
<th>LEADING CAUSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>new or recurrent strokes yearly</td>
<td>ischemic; 13% hemorrhagic</td>
<td>leading cause of death</td>
<td>of serious long-term disability in the US</td>
</tr>
</tbody>
</table>

DISABILITY ASSOCIATED WITH STROKE\textsuperscript{1}

IMPORTANCE OF SECONDARY ISCHEMIC STROKE PREVENTION

Recurrent Stroke Rate among Patients Discharged with a Primary Diagnosis of Stroke, South Carolina, 2002

(N = 10,399)

# Definitions of Cryptogenic Stroke

<table>
<thead>
<tr>
<th>Classification Scheme</th>
<th>Required Work-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>TOAST(^1)</td>
<td>Not specified</td>
</tr>
<tr>
<td>Causative Classification of Stroke (CCS)(^2)</td>
<td>Brain CT/MR, 12-lead ECG, precordial echocardiogram, extra/intravascular imaging</td>
</tr>
<tr>
<td>Embolic strokes of undetermined source(^3)</td>
<td>Brain CT/MR, 12-lead ECG, precordial echocardiogram, extra/intravascular imaging, cardiac monitoring for $\geq$ 24 hours</td>
</tr>
<tr>
<td>ASCO(D) phenotyping(^4)</td>
<td>Does not include a cryptogenic stroke category</td>
</tr>
</tbody>
</table>

---

CRYPTOGENIC STROKE IS A DIAGNOSIS OF EXCLUSION\(^1\)

<table>
<thead>
<tr>
<th>Atherosclerotic</th>
<th>Atherosclerotic*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small arterial occlusion</td>
<td>Arteroembolic*</td>
</tr>
<tr>
<td>Cardioembolic</td>
<td>Aortoembolic</td>
</tr>
<tr>
<td>Other causes</td>
<td>Branch occlusive disease †</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Small arterial occlusion</th>
<th>Small arterial occlusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardioembolic</td>
<td>Cardioembolic</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Paroxysmal atrial fibrillation</th>
<th>Other causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paradoxical embolism</td>
<td>Cancer-related coagulopathy</td>
</tr>
<tr>
<td>Cryptogenic</td>
<td>Cryptogenic</td>
</tr>
</tbody>
</table>

## CONVENTIONAL MONITORING STRATEGIES

<table>
<thead>
<tr>
<th>Monitoring Strategy</th>
<th>Duration</th>
<th>Compliance (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Holter Monitor</td>
<td>24-48 hours of monitoring</td>
<td>62% patient compliance¹</td>
</tr>
<tr>
<td>Event Recorder</td>
<td>Up to 30 days of monitoring</td>
<td>53-90% patient compliance²-⁵</td>
</tr>
<tr>
<td>Mobile Cardiac Telemetry</td>
<td>Up to 30 days of monitoring</td>
<td></td>
</tr>
</tbody>
</table>

* Dependent on type of MCT.

Multiple studies have assessed the ability of ICMs to detect AF in patients with cryptogenic stroke:

- Cotter study
- Ritter study
- Etgen study
- Rojo-Martinez study
- SURPRISE
- CRYSTAL AF
<table>
<thead>
<tr>
<th>Study</th>
<th>Duration of monitoring (months)</th>
<th>Definition of AF</th>
<th>Time to Diagnosis (days)</th>
<th>AF detection rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ritter¹</td>
<td>10</td>
<td>&gt;30 seconds</td>
<td>64</td>
<td>17</td>
</tr>
<tr>
<td>Etgen²</td>
<td>12</td>
<td>&gt;6 minutes</td>
<td>152</td>
<td>27</td>
</tr>
<tr>
<td>Cotter³</td>
<td>8</td>
<td>2 minutes</td>
<td>48</td>
<td>25</td>
</tr>
<tr>
<td>SURPRISE⁴</td>
<td>19</td>
<td>&gt;2 minutes</td>
<td>109</td>
<td>16</td>
</tr>
<tr>
<td>Rojo-Martinez⁵</td>
<td>9</td>
<td>2 minutes</td>
<td>102</td>
<td>33</td>
</tr>
<tr>
<td>Ziegler⁶</td>
<td>6</td>
<td>2 minutes</td>
<td>58</td>
<td>12</td>
</tr>
<tr>
<td>Poli⁷</td>
<td>12</td>
<td>&gt;2 minutes</td>
<td>105</td>
<td>33</td>
</tr>
<tr>
<td>Jorfida⁸</td>
<td>14.5</td>
<td>&gt;5 minutes</td>
<td>162</td>
<td>46</td>
</tr>
<tr>
<td>CRYSTAL AF⁹ (ICM arm)</td>
<td>6, 12, 36</td>
<td>&gt;30 seconds</td>
<td>41, 84, 252</td>
<td>9, 12, 30</td>
</tr>
</tbody>
</table>

CRYSTAL AF\textsuperscript{1}: STUDY DESIGN AND END POINTS

- 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

<table>
<thead>
<tr>
<th>End Point</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
<td>Time to first detection of AF at 6 months of follow-up</td>
</tr>
<tr>
<td>Secondary</td>
<td>Time to first detection of AF at 12 months</td>
</tr>
<tr>
<td></td>
<td>Recurrent stroke or TIA</td>
</tr>
<tr>
<td></td>
<td>Change in use of oral anticoagulant drugs</td>
</tr>
</tbody>
</table>

CRYSTAL AF\textsuperscript{1}: STUDY POPULATION

447 patients were enrolled

6 were excluded
- 4 did not meet eligibility criteria
- 2 withdrew consent

441 underwent randomization

221 were assigned to ICM
- 208 had ICM inserted
- 13 did not have ICM inserted

12 crossed over to control
12 exited the study
- 3 died
- 1 was lost to follow-up
- 5 withdrew
- 3 were withdrawn by investigator

220 were assigned to control
- 220 received standard of care

6 crossed over to ICM
13 exited the study
- 2 died
- 1 was lost to follow-up
- 7 withdrew
- 3 were withdrawn by investigator

221 were included in intention-to-treat analysis
220 were included in intention-to-treat analysis

CRYSTAL AF\textsuperscript{1}:
PATIENTS

- Age ≥ 40 years
- Diagnosis of stroke or TIA occurring within previous 90 days
- Stroke was classified as cryptogenic after extensive testing:
  - 12-lead ECG
  - ≥ 24 hours of ECG monitoring
  - TEE
- Screening for thrombophilic states (in patients < 55 years of age)
- Magnetic resonance angiography, computerized tomography angiography, or catheter angiography of head and neck
- Ultrasonography of cervical arteries or transcranial Doppler ultrasonography of intracranial arteries allowed in place of MRA or CTA for patients aged ≥ 55 years

Patients were only categorized with cryptogenic stroke after extensive diagnostic testing.

### CRYSTAL AF<sup>1</sup>: SELECTED BASELINE PATIENT CHARACTERISTICS

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>ICM (n = 221)</th>
<th>Control (n = 220)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>61.6 ± 11.4</td>
<td>61.4 ± 11.3</td>
<td>0.84</td>
</tr>
<tr>
<td>Male</td>
<td>64.3%</td>
<td>62.7%</td>
<td>0.77</td>
</tr>
<tr>
<td>White</td>
<td>87.8%</td>
<td>86.8%</td>
<td>0.60</td>
</tr>
<tr>
<td>Patent foramen ovale</td>
<td>23.5%</td>
<td>20.9%</td>
<td>0.57</td>
</tr>
<tr>
<td>Index event</td>
<td></td>
<td></td>
<td>0.87</td>
</tr>
<tr>
<td>Stroke</td>
<td>90.5%</td>
<td>91.4%</td>
<td></td>
</tr>
<tr>
<td>TIA</td>
<td>9.5%</td>
<td>8.6%</td>
<td></td>
</tr>
</tbody>
</table>

CRYSTAL AF: MONITORING WITH ICM SUPERIOR TO SOC FOR THE DETECTION OF AF¹

Detection of Atrial Fibrillation by 36 months

Hazard ratio, 8.8 (95% CI, 3.5 - 22.2)
P < 0.001 by log-rank test

<table>
<thead>
<tr>
<th>Months since randomization</th>
<th>Control</th>
<th>ICM</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>220</td>
<td>221</td>
</tr>
<tr>
<td>6</td>
<td>194</td>
<td>191</td>
</tr>
<tr>
<td>12</td>
<td>167</td>
<td>173</td>
</tr>
<tr>
<td>18</td>
<td>114</td>
<td>102</td>
</tr>
<tr>
<td>24</td>
<td>72</td>
<td>57</td>
</tr>
<tr>
<td>30</td>
<td>36</td>
<td>29</td>
</tr>
<tr>
<td>36</td>
<td>7</td>
<td>8</td>
</tr>
</tbody>
</table>

CRYSTAL AF\textsuperscript{1}: KEY SECONDARY END POINT

12 months

97% of patients in whom AF was detected received oral anticoagulants

CRYSTAL AF\textsuperscript{1}: MEDIAN TIME TO DETECTION OF AF

84 Days in the ICM group (range 18 to 265 days)

53 Days in control group (range 17 to 212 days)

**EMBRACE VS. CRYSTAL AF\textsuperscript{1,2}: DIFFERENT STUDIES, DIFFERENT RESULTS**

<table>
<thead>
<tr>
<th></th>
<th>CRYSTAL AF\textsuperscript{1}</th>
<th>EMBRACE\textsuperscript{2}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inclusion Criteria</td>
<td>- Age ≥ 40 years</td>
<td>- Age ≥ 55 years</td>
</tr>
<tr>
<td></td>
<td>- Ischemic stroke or TIA within previous 90 days</td>
<td>- Ischemic stroke or TIA within previous 6 months</td>
</tr>
<tr>
<td></td>
<td>- Stroke classified as cryptogenic after extensive work-up</td>
<td>- Stroke classified as cryptogenic after standard work-up</td>
</tr>
<tr>
<td>Primary end point</td>
<td>- Time to first detection of AF at 6 months follow-up</td>
<td>- Detection of ≥ 1 episode of ECG-documented AF within 90 days</td>
</tr>
<tr>
<td>Definition of AF episode</td>
<td>- AF lasting &gt; 30 seconds*</td>
<td>- AF lasting &gt; 30 seconds</td>
</tr>
</tbody>
</table>

* For ICM group, episodes must have been > 2 minutes to be detected.

REAL WORLD VALIDATION OF CRYSTAL AF RESULTS
Rogers, AAN, 2016

- 1247 real-world cryptogenic stroke patients monitored by Reveal LINQ™
- Cryptogenic stroke diagnosis: physician’s discretion
- Follow-up: 12 months
- Diagnostic yield at 12 months: 16.3% (n=147)
- Median time to detection: 86 days
  - Analysis supports results of CRYSTAL AF
  - Continuous monitoring for periods longer 30 days may be warranted in CS patients

72% of AF patients would be missed if monitoring stopped at 30 days

SUMMARY: DAYS TO DETECTION OF AF IN CLINICAL STUDIES OF ICMS¹-⁷

SUMMARY: AF DETECTION YIELD IN CLINICAL STUDIES OF ICMS¹-⁷

<table>
<thead>
<tr>
<th>Study</th>
<th>AF Detection Yield (%)</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cotter¹ (2 min)</td>
<td>25.5</td>
<td>51</td>
</tr>
<tr>
<td>Etgen² (6 min)</td>
<td>27.3</td>
<td>60</td>
</tr>
<tr>
<td>Ritter³ (2 min)</td>
<td>16.7</td>
<td>101</td>
</tr>
<tr>
<td>Rojo-Martinez⁴ (2 min)</td>
<td>33.7</td>
<td>85</td>
</tr>
<tr>
<td>SURPRISE⁵ (2 min)</td>
<td>16.1</td>
<td>441</td>
</tr>
<tr>
<td>CRYSTAL AF*⁶ (2 min)</td>
<td>30.0</td>
<td>1247</td>
</tr>
<tr>
<td>Real-World⁷ (2 min)</td>
<td>16.8</td>
<td></td>
</tr>
</tbody>
</table>

PREDICTORS OF AF OFFER ONLY POOR PREDICTIVE ABILITY

CRYSTAL AF sub-analysis: Thijs, *Neurology*

- Parameters tested:
  - Age, sex, race
  - Body Mass Index,
  - Type and severity of index event
  - CHADS2 score
  - PR-interval
  - Diabetes, hypertension
  - Congestive heart failure
  - Patent foramen ovale
  - Premature atrial contractions

Increasing age and a prolonged PR-interval were independently associated with AF, but the predictive ability of these parameters was only moderate.

Simulated intermittent monitoring was compared to continuous rhythm monitoring in 168 ICM patients.

<table>
<thead>
<tr>
<th>Short-term Monitoring</th>
<th>Periodic Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>24-hour</td>
<td>Quarterly 24-hour Holters</td>
</tr>
<tr>
<td>48-hour</td>
<td>Quarterly 48-hour Holters</td>
</tr>
<tr>
<td>7-day Holter</td>
<td>Quarterly 7-day Holters</td>
</tr>
<tr>
<td>21-day Event Recorder</td>
<td>Monthly 24-hour Holters</td>
</tr>
<tr>
<td>30-day Event Recorders</td>
<td>Monthly 24-hour Holters</td>
</tr>
</tbody>
</table>

Sensitivity was low: 1.3-22.8%
Negative predictive value: 82.3-85.6%

“Intermittent rhythm monitoring would have failed to identify previously undiagnosed AF in the vast majority of CS patients”

In stroke patients, additional ECG monitoring by long-term non-invasive ECG monitors or implanted loop recorders should be considered to document silent atrial fibrillation.

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>In stroke patients, additional ECG monitoring by long-term non-invasive ECG monitors or implanted loop recorders should be considered to document silent atrial fibrillation.</td>
<td>Ila</td>
<td>B</td>
</tr>
</tbody>
</table>

AF = atrial fibrillation; AHRE = atrial high rate episodes; ECG = electrocardiogram; ICD = implantable cardioverter defibrillator; TIA = transient ischaemic attack.

aClass of recommendation.
bLevel of evidence.

REVEAL LINQ™ IS A COST-EFFECTIVE DIAGNOSTIC TOOL

Diamantopoulos, *Int J Stroke*

- Monitoring with and ICM was associated with fewer recurrent strokes and increased QALYs (quality-adjusted life years) compared to standard of care.
- A lifetime Markov model was created to estimate the cost-effectiveness of ICMs in the context of the UK.
- Stroke-related costs were reduced in ICM patients, but overall costs were higher.
- The ICER (incremental cost-effectiveness ratio) was below the £20,000-30,000 willingness-to-pay threshold (£17,175 per QALY gained).

### Results: CRYSTAL AF—NOAC

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Ischemic Stroke</th>
<th>QALYs</th>
<th>Costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>SoC</td>
<td>0.447</td>
<td>7.216</td>
<td>£17,045</td>
</tr>
<tr>
<td>ICM</td>
<td>0.404</td>
<td>7.367</td>
<td>£19,631</td>
</tr>
<tr>
<td>Incremental</td>
<td>-0.044</td>
<td>0.151</td>
<td>£2,587</td>
</tr>
<tr>
<td><strong>ICER GBP</strong></td>
<td><strong>UK Threshold = £30,000</strong></td>
<td></td>
<td><strong>£17,175</strong></td>
</tr>
<tr>
<td><strong>ICER USD</strong></td>
<td><strong>US Threshold = $50,000</strong></td>
<td></td>
<td><strong>$28,308</strong></td>
</tr>
</tbody>
</table>

**NNI* to avoid stroke** 20

---

WHY EXTENDED MONITORING?
SHORT- AND INTERMEDIATE-TERM MONITORING MAY MISS MANY PATIENTS WITH PAROXYSMAL AF

79% of first AF episodes were asymptomatic at 12 months \(^1\)

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

Median time to detect AF following cryptogenic stroke: \(^{13}\)

84 DAYS

Short-term monitoring (up to 1 week)
Intermediate-term monitoring (up to 30 days)

Note: For illustrative purposes only.
REVEAL LINQ™ SYSTEM ADVANTAGES
REVOLUTIONIZING CARDIAC MONITORING

The smallest, most powerful insertable cardiac monitor

- One-third the size of a AAA battery (1.2 cc)
- Up to a 3-year longevity for long-term monitoring\(^1\)
- MR Conditional at 1.5 and 3.0 Tesla
- Minimally invasive, simplified insertion procedure\(^2\)
- 96.7% of patients very satisfied or satisfied with Reveal LINQ ICM after insertion\(^3\)

---

\(^1\) Reference the Reveal LINQ ICM Clinician Manual for usage parameters.
REVEAL LINQ™ SYSTEM ADVANTAGES
SIMPLE INSERTION PROCEDURE

Best location:
45 degrees to sternum over 4th intercostal space,
2 cm from left edge of sternum

97% of physicians found the insertion tool simple and intuitive.¹

Requires minimal procedure time and clinical resources

Reveal™ XT

With FullView™ Software

NEW Pause algorithm with diminishing R-wave analysis

NEW AF algorithm and improved noise discrimination

NEW simplified insertion and tight pocket for better signal

NEW AF algorithm with increased accuracy

TruRhythm™ Detection

Streamlined episode review for clinic efficiency

NEW algorithms with:
- Smart filtering
- Self-learning intelligence

AF

PAUSE

BRADY

PAUSE

AF

2009

2011

2014

2017

SMART FILTERING

NEW second sensing filter analyzes rhythms for possible undersensing in Brady and Pause

SELF-LEARNING

Exclusive fifth-generation atrial fibrillation algorithm learns and adapts to patient’s rhythm over time

BRADY & PAUSE

AF
REVEAL LINQ™ ICM SYSTEM
PROVEN ARRYTHMIA DETECTION.
INFORMED CLINICAL DECISIONS.

99.7%  
Reveal LINQ™ ICM is proven to find AF
Highest published AF detection accuracy on the market, at 99.7%¹

50+  
As the most clinically-validated ICM, with 50+ detection performance papers, Reveal LINQ™ ICM is the reliable choice for arrhythmia management²

TRURHYTHM™ PROVEN DETECTION CONFIDENCE ACROSS INDICATIONS

Cryptogenic stroke

Why Reveal LINQ™ ICM? 88% percent of AF patients would be missed if monitoring stopped at 30 days*1

Why TruRhythm™ Detection? Don’t miss an AF episode† with high sensitivity and streamlined data review2

Syncope

Why Reveal LINQ™ ICM? 78% of patients with recurrent syncope are diagnosed with an ICM3

Why TruRhythm™ Detection? Spend half the time reviewing false detect data, with significant improvement in Brady and Pause detections**2,4

Atrial fibrillation

Why Reveal LINQ™ ICM? Short and intermittent monitoring will likely miss many patients with paroxysmal AF1

Why TruRhythm™ Detection? Manage AF patients over time with more actionable and accurate reports2

The Reveal LINQ ICM is guideline-recommended for Cryptogenic Stroke and Syncope5,6

---


* Based on Kaplan Meier estimates
† Episodes detected are ≥ 2 minutes
** Compared with the Reveal LINQ™ ICM without TruRhythm™ Detection
CLINICAL RIGOR
EVIDENCE SUPERIORITY.
REAL-WORLD IMPACT.

Most Studied ICM

With an evidence portfolio of 500+ published clinical articles and abstracts¹

Most Clinically Validated ICM

Across Cryptogenic Stroke, Syncope, and Atrial Fibrillation patient populations²-⁴

Only ICM with Premier Clinical Evidence

Published in multiple premier journals, including Heart Rhythm, The New England Journal of Medicine, and JACC²,³,⁵

CONCLUSIONS

- The more you look, the more you find
  - Short- to intermediate-term cardiac rhythm monitoring may not be enough to detect paroxysmal AF in your cryptogenic stroke patients
  - CRystal AF demonstrates superiority of continuous, long-term monitoring of cryptogenic stroke patients with an ICM
  - 2016 ESC guidelines recommend monitoring with Reveal LINQ in cryptogenic stroke patients

- Reveal LINQ™ ICM
  - Up to 3 years of continuous cardiac monitoring with the world’s smallest and smartest ICM
  - Proven AF detection algorithm with industry leading accuracy
  - 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.
ISCHEMIC STROKE WORK-UP

Used with permission from Matthew C. Holtzman, MD. Neurology Michigan P.C.

This pathway represents Dr. Holtzman’s clinical practice.

Medical judgment should be used to determine if adopting pathway is appropriate.

STROKE

Lacunar infarction: small vessel disease

- Standard stroke work-up

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

- Standard stroke work-up

History of AF?

- Standard stroke work-up

Embolic appearing stroke with no history of AF:

Antiplatelet agent

- Standard stroke work-up

History of AF?

- Anticoagulation

- MRA or CTA of intracranial vessels
- Transesophageal Echocardiogram (TEE)

Symptomatic carotid stenosis greater than 50%

- CEA or stent

- Intracranial stenosis

- Positive TEE

- Anticoagulant

- Monofocal
  - Medical management
  - Antiplatelet agents

- Multifocal
  - Angiogram
  - Lumbar puncture
  - Vasculitis work-up

All testing negative?

Cryptogenic Stroke/TIA
CRYPTOGENIC STROKE PATHWAY

PATIENT DIAGNOSED WITH CRYPTOGENIC STROKE/TIA

Could detection of suspected AF impact patient management?

NO
Not a candidate

YES

Refer to cardiology to insert Reveal LINQ ICM

Inpatient

If unable to insert prior to discharge, potential external monitor bridge and schedule Reveal LINQ ICM

Insert Reveal LINQ ICM prior to discharge

Enroll in CareLink™ Network & perform remote monitoring

Schedule clinical follow-up with treating physician and ensure long-term adherence to monitoring

Inpatient/outpatient insertion

Outpatient

Insert expeditiously

Bridge with external monitor

AF not detected

AF 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.
CONCLUSIONS

- Approximately one-third of ischemic strokes are classified as cryptogenic, and up to 30% many have previously undiagnosed AF
- The more you look, the more you find
  - Short- to intermediate-term cardiac rhythm monitoring may not be enough to detect paroxysmal AF in your cryptogenic stroke patients
  - CRYSTAL AF demonstrates superiority of continuous, long-term monitoring of cryptogenic stroke patients with an ICM
  - 2016 ESC guidelines now recommends monitoring with Reveal LINQ ICM in cryptogenic stroke patients
- Reveal LINQ™ ICM
  - Up to 3 years of continuous cardiac monitoring with the world’s smallest ICM
  - Proven AF detection algorithm with industry leading accuracy
  - 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.
EVIDENCE SUMMARY
ICMS FOR AF DETECTION IN CRYPTOGENIC STROKE

- ICM detects low burden/asymptomatic AF in cryptogenic stroke patients
  Etgen’13, Cotter’13, Rojo-Martinez’13, SURPRISE’14

- ICM offers higher diagnostic yield than 7-day Holter, Ritter’13 standard monitoring
  CRYSTAL-AF’14 and intermittent monitoring Choe’15

- Continuous monitoring with ICM is guideline recommended in cryptogenic stroke patients - 2016 ESC guidelines for AF screening

- ICM is a cost-effective diagnostic tool for the prevention of recurrent stroke in cryptogenic stroke patients Diamantopoulos
CONCLUSIONS

CLINICAL IMPACT: More Appropriate Care

- Reveal™ ICM detected over 7 times more patients with AF compared to standard monitoring at the 12-month end point
- At 12 months, 97% of patients in the ICM arm who had AF detected were prescribed OAC
- Reveal LINQ™ ICM should be included in all pathways and protocols for cryptogenic stroke patients
CRYPTOGENIC STROKE

PATIENT CASE STUDIES
CRYPTOGENIC STROKE PATIENT IMPACT

SCOTT’S STORY

Reveal LINQ™ ICM used to discover AF in 22-year-old stroke patient

On his way to a soccer game, 22-year-old Scott suddenly began wobbling. His head started throbbing. What he thought was dehydration turned out to be much worse. The college student had suffered a stroke. Surgeons removed a blood clot in his brain, but a looming question remained: What caused the stroke in this seemingly healthy young man?

Scott’s doctors suspected it was the result of atrial fibrillation (AF). So Scott’s doctors turned to the Reveal LINQ™ ICM, which, within a few months, confirmed he had AF.

The diagnosis not only gave Scott’s doctors the information they needed to prescribe stroke-preventive blood thinners; it gave Scott the peace of mind to live life fully again.

Actual patient photo. This story reflects one person’s experience. Not every person will receive the same results.
CASE STUDY

- 51-year-old woman
- Episode of unsteady gait and dizziness (< 1 hour)
- On admission:
  - BP 140/86
  - HR 68 BPM
  - No neurologic deficits
- After urgent MRI, admitted to intensive care unit for further assessment
CASE STUDY
CASE STUDY

- Two areas of infarct were identified in the left cerebellum

- MRA of head and neck and chest x-ray returned normal results

- TTE showed normal LV size and function

- Subsequent TEE confirmed these results, also showed that her atrial size was at the upper limits of normal

- TEE showed that there was no thrombus and normal velocities in the LAA, a normal aortic arch, and no evidence of a patent foramen ovale

- 24-hour telemetry monitoring was negative for arrhythmia
CASE STUDY

- Patient discharged on clopidogrel 75 mg/day and was followed for an additional 14 days with MCT
- No arrhythmias identified during this period
Five weeks after her initial stroke presentation, she developed a recurrence of unsteadiness and dizziness

Patient also developed a right-sided headache with nausea and vomiting

Symptoms lasted 2 hours

Patient was admitted to the ICU after an urgent brain MRI
CASE STUDY
CASE STUDY
SUMMARY

- The patient underwent extensive additional evaluation, including a work-up for hypercoagulability, which was negative.
- She was subsequently implanted with an ICM and discharged on clopidogrel and aspirin.
- After 2 months of monitoring, episodes of paroxysmal AF lasting 15 to 90 minutes were detected.
  - Episodes were asymptomatic despite mean ventricular rates in > 120 BPM.
- The patient was subsequently prescribed an oral anticoagulant.
BRIEF STATEMENT

Reveal LINQ™ LNQ11 Insertable Cardiac Monitor and Patient Assistant

Indications

Reveal LINQ™ LNQ11 Insertable Cardiac Monitor
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, palpitation, syncope and chest pain, that may suggest a cardiac arrhythmia.

This device has not been specifically 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 no 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™ LNQ11 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 EMI precautions manual. MRI scans should be performed only in a specified MR 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.

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 Medtronic’s website at www.medtronic.com.

Caution: Federal law (USA) restricts this device to sale by or on the order of a physician.
BRIEF STATEMENT (CONTINUED)

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

The Medtronic MyCareLink Patient Monitor and the Medtronic CareLink Network are indicated for use in the transfer of patient data from Medtronic implantable cardiac devices. These products are not a substitute for appropriate medical attention in the event of an emergency. Data availability and alert notifications are subject to Internet connectivity and access, and service availability. The MyCareLink Patient Monitor must be on and in range of the device. Alert notifications are not intended to be used as the sole basis for making decisions about patient medical care.

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 message rates apply.

Contraindications
There are no 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 Medtronic’s website at www.medtronic.com.

Caution: Federal law (USA) restricts this device to sale by or on the order of a physician.