Health Policy Advisory Committee on Technology

Technology Brief

ZIO® XT Patch for diagnosis of cardiac arrhythmia

March 2015

HealthPACT emerging health technology
Technology, Company and Licensing

Register ID WP197
Technology name ZIO® XT Patch
Patient indication Patients with suspected cardiac arrhythmia

Description of the technology

The ZIO® XT Patch (iRhythm Technologies, Inc., California, USA) is a discreet, non-invasive, water-resistant, lead- and wire-free ambulatory electrocardiogram (ECG) device that adheres to a patient's chest (Figure 1). The ZIO XT Patch is worn for up to 14 days for continuous cardiac monitoring, and also features a button which allows the wearer to capture symptomatic events. It can remain in place during all daily activities including sleeping, showering and moderate exercise.¹

Figure 1 ZIO XT Patch²

The ZIO XT Patch is a component of the ZIO® Service, which incorporates a patented algorithm for recording and analysing the heartbeat, as well as the provision of a report to the treating physician (the ZIO® Report).¹ A patient wears the ZIO XT Patch over a period of 7 to 14 days. On completion of the monitoring period, the ZIO XT Patch is sent by the patient to the manufacturer. The data is processed and analysed by a certified cardiographic technician, who prepares a ZIO Report. The report contains information regarding arrhythmia events, wear and analysis time and patient-captured events. This document is sent to the prescribing physician for final analysis and interpretation.¹

Company or developer

iRhythm Technologies, Inc., California, USA.

Reason for assessment

This technology has the potential to provide inexpensive continuous cardiac monitoring for the identification of cardiac arrhythmia. The compact and discreet design of the ZIO XT Patch means that the technology has the potential to increase the diagnostic yield of
ambulatory ECG monitoring through increased patient compliance, as well as the provision of considerably longer monitoring periods. This may reduce the morbidity, mortality and costs associated with the adverse outcomes of undiagnosed cardiac arrhythmia.

**Stage of development in Australia**

- ❌ Yet to emerge
- ✗ Experimental
- ● Investigational
- □ Nearly established
- ○ Established
- ○ Established *but* changed indication or modification of technique
- ○ Should be taken out of use

**Licensing, reimbursement and other approval**

The ZIO XT Patch was approved for marketing and sale in the United States in May 2009, (Food and Drug Administration [FDA] 510(k) # K090363).³ The indications for its use, published by the FDA in July 2012, are as follows: “The ZIO® Patch is a prescription-only, single-patient-use, continuously recording ECG monitor that can be worn up to 14 days. It is indicated for use on patients who may be asymptomatic or who may suffer from transient symptoms such as palpitations, shortness of breath, dizziness, light-headedness, pre-syncope, syncope, fatigue or anxiety.”⁴

The ZIO XT Patch does not appear on the Australian Register of Therapeutic Goods (ARTG). While the device is not currently approved for sale in Europe, the manufacturer anticipates that clearance will be granted in December 2014 (personal communication, iRhythm Technologies, Inc.).

**Australian Therapeutic Goods Administration approval**

- ❌ Yes
- ○ No
- □ Not applicable

**Technology type**

- Device

**Technology use**

- Diagnostic

**Patient Indication and Setting**

**Disease description and associated mortality and morbidity**

Cardiac arrhythmia is caused by a problem with the heart’s electrical system which controls the rate and rhythm of a heartbeat.⁵ Some cardiac arrhythmias are harmless, but others are associated with serious adverse outcomes including embolic stroke and death.²⁵ The identification and treatment of cardiac arrhythmias can be difficult, as patients may be
asymptomatic or experience only transient symptoms. When symptoms are present, they usually include palpitations, a slow heartbeat, an irregular heartbeat and/or pauses between heartbeats. Signs of serious cardiac arrhythmia include anxiety, weakness, dizziness, light-headedness, fainting or nearly fainting, sweating, shortness of breath and chest pain. Cardiac arrhythmias may also affect quality of life. Some arrhythmias are highly symptomatic and may reduce an individual’s physical independence and ability to enjoy a normal lifestyle.

Cardiac arrhythmias are very common in older people; in particular, the most serious arrhythmia affects adults above 60 years of age. Some reasons for the increased incidence of arrhythmia in this population include their higher chance of having heart disease or other health problems and their sensitivity to medicines that may cause arrhythmia. Particular diseases and conditions which may lead to arrhythmia include: heart attack, heart failure or cardiomyopathy, heart tissue which is too thick or stiff, leaking or narrowed heart valves, congenital heart defects, high blood pressure, diabetes, sleep apnoea and thyroid conditions. Some cardiac arrhythmias are more common in children and young adults, including Paroxysmal Supraventricular Tachycardia (PSVT).

**Number of patients**

The majority of data on the prevalence and incidence of cardiac arrhythmia is related to AF. It is estimated that AF affects 1 to 2 per cent of the Australian population, and is increasing in prevalence. Cardiac arrhythmias were the 20th leading cause of death in Australia in 2010, an increase in ranking from 2001 from when they were the 24th leading cause of death. The total number of hospital separations for ‘arrhythmia, cardiac arrest and conduction disorders without catastrophic or severe complications and/or comorbidities’ in Australia in 2012-13 was 54,729 (39,422 in the public sector and 15,307 in the private sector), and the average length of hospital stay was 2 days.

With respect to the number of patients undergoing continuous cardiac monitoring in Australia, the Medicare Benefits Schedule (MBS) indicates that a total of 234,308 diagnostic investigations were carried out in 2013. This comprised continuous ECG monitoring using the Holter monitor (MBS item 11709).

In New Zealand across 2011-12, a total of 13,536 public patients discharges were recorded for causes classified as: Paroxysmal tachycardia, atrial fibrillation and flutter, other cardiac arrhythmias, and, other conduction disorders.
**Speciality**  
Cardiovascular disease

**Technology setting**  
Ambulatory care

**Impact**

**Alternative and/or complementary technology**

The ZIO XT Patch for continuous cardiac monitoring and identification of cardiac arrhythmia is an alternative to current methods of ambulatory ECG. The device may be an attractive alternative to current approaches as it is less invasive and cumbersome to wear.

**Current technology**

Ambulatory ECG monitoring is the most widely used method of cardiac arrhythmia detection used in an outpatient setting. It is most commonly used in patients for whom the cause of heart palpitations are unclear and in patients where bradycardia or tachycardia is suspected. Current available methods for non-invasive remote cardiac monitoring include continuous monitoring using a Holter monitor for short-term (up to 48 hours, gold standard), patient-triggered cardiac event recorders for moderate-term (2 to 4 weeks) and mobile cardiac outpatient telemetry.

The Holter monitor was introduced to investigate suspected arrhythmia in patients in the late 1940s and remains the most commonly used method of ambulatory ECG monitoring. The device comprises between three and eight electrodes, which adhere to the patient’s chest, attached by wires to a small recording device. The recording device is generally carried in a pouch worn around the patient’s neck or waist. The device is designed to typically be worn for 24 to 48 hours. The short monitoring period combined with the spontaneous and infrequent nature of symptomatic arrhythmia means that the device may fail to detect the presence of arrhythmia. Evidence suggests that the Holter monitor has a diagnostic yield of 15 to 39 per cent. Increasing the length of time that patients that wear the Holter monitor may improve its diagnostic yield; however its cumbersome design, including numerous leads and lead contact points, generally prevents longer-term wear due to patient discomfort and inconvenience.

Cardiac event recorders are also ambulatory monitors. Designed to be worn for longer periods of time, there are two main types of recorders: loop memory monitors and symptom event monitors. Both record abnormal cardiac events when triggered either by the wearer or through the device’s own automatic initiation. This form of recorder represents the largest group of ambulatory cardiac recording devices. The ZIO XT Patch is designed to be worn for a similar period of time as cardiac event recorders and offers the same functional capabilities.
Diffusion of technology in Australia

The ZIO XT Patch is not approved for use in Australia and currently does not appear to be being used in an off-label manner.

International utilisation

<table>
<thead>
<tr>
<th>Country</th>
<th>Trials underway or completed</th>
<th>Limited use</th>
<th>Widely diffused</th>
</tr>
</thead>
<tbody>
<tr>
<td>India</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Netherlands</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>United States</td>
<td>✓</td>
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</table>

Cost infrastructure and economic consequences

The cost of the single-use ZIO XT Patch and its mandatory diagnostic service is USD 400. (personal communication, iRhythm Technologies, Inc.). There would be minimal infrastructure and training costs associated with the adoption of the ZIO XT Patch into mainstream healthcare.

MBS item 11709 describes the continuous ECG recording of ambulatory patients for 12 or more hours using the Holter monitor. The fee for this item is $167.45 (75% benefit $125.60; 85% benefit $142.35). The ZIO XT Patch monitor is a single use device, whereas Holter monitors and External event recorders are reusable. Holter monitors range in cost from $295 to $860, External event recorders range in cost from $80 to $200. These costs do not include interpretation of recorded data.

The ZIO XT Patch may provide indirect cost savings through increasing the detection rates for cardiac arrhythmia. Increased detection rates leading to appropriate treatment may reduce the number of emergency complications arising from cardiac arrhythmias, and the costs associated with treating those complications. AF, the most common form of cardiac arrhythmia, is associated with a higher stroke risk and increased likelihood of death following stroke, as well as a higher risk of heart failure. In 2008-09 the estimated annual cost of AF to the Australian economy was approximately $1.25 billion, and a large proportion of these costs were attributable to hospitalisations, stroke and heart failure.

Ethical, cultural, access or religious considerations

No cultural, religious or access considerations for the ZIO XT Patch were identified.
Evidence and Policy

Safety and effectiveness

A total of three studies were selected for inclusion in this technology brief. An overview of the studies is provided in Table 1. Two were non-randomised comparative studies\(^2,^{13}\) and the third was a large case series study\(^{18}\). Both comparative studies compared the diagnostic utility of 14-day cardiac monitoring using the ZIO XT Patch with 24-hour cardiac monitoring using the Holter device.

Discussion of the three studies in this technology brief centres on the effectiveness of the ZIO XT Patch. The studies did not focus on adverse events, and while it is possible that either device could have resulted in an adverse event, such as skin irritation or an allergic reaction, no such events were reported in the studies.

Table 1  Characteristics of included studies

<table>
<thead>
<tr>
<th>Study/ Design</th>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
<th>Number of patients</th>
<th>Conflicts of interest</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barrett et al 2014(^2)</td>
<td>Patients aged 18 years or older under evaluation for cardiac arrhythmia and capable of providing informed consent and complying with continuous ECG monitoring for up to 14 days.</td>
<td>Patients with any known skin allergies, conditions or sensitivities to any components of the adhesive patch. Patients receiving or anticipating receiving pacing or external direct current cardioversion during the monitoring period. Patients anticipating exposure to high-frequency surgical equipment during the monitoring period</td>
<td>146</td>
<td>Industry sponsorship</td>
</tr>
<tr>
<td>Rosenberg et al 2013(^{13})</td>
<td>Not reported</td>
<td>Not reported</td>
<td>74</td>
<td>Industry sponsorship</td>
</tr>
<tr>
<td>Turakhia et al 2013(^{18})</td>
<td>All consecutive patients receiving first time ZIO XT Patches at a single enrolling site over a 12-month period.</td>
<td>Patients undergoing repeated or subsequent ZIO XT Patch monitoring</td>
<td>26,751</td>
<td>Industry sponsorship</td>
</tr>
</tbody>
</table>

ECG, electrocardiogram
Barrett et al 2014²

Patients referred for ambulatory ECG monitoring from a single cardiac investigation laboratory were eligible for inclusion in this non-randomised within-patient comparative study (level III-2 diagnostic evidence). Patients were simultaneously fitted with a ZIO XT Patch (over their left pectoral region) and Holter monitor. Patients were instructed to wear the ZIO device for as long as possible, ideally for the targeted 14-day period. Upon removing the ZIO XT Patch the patient was instructed to return the device to the manufacturer by prepaid mail. The Holter monitor was worn for 24 hours and returned to the referring laboratory. Data was collected for 146 patients (median age 64 years, range = 22-94).

Arrhythmia events were classified by type: supraventricular tachycardia (SVT); atrial fibrillation/flutter (>4 beats); pause greater than 3 seconds; atrioventricular block (Mobitz type II or third-degree atrioventricular block); ventricular tachycardia (>4 beats); or polymorphic ventricular tachycardia/ventricular fibrillation.

Analysis of the event-detection rates of the ZIO XT Patch and Holter monitor was undertaken based on two groupings of arrhythmia types. The first group comprised all six arrhythmia types (arrhythmia event group 1) and the second group contained the five most clinically significant arrhythmia types (SVT was excluded; arrhythmia event group 2).

Effectiveness

Median wear time was 11.1 days (range, 0.9 to 14.0 days) for the ZIO XT Patch and 1 day (range, 0.9 to 1.0 days) for the Holter monitor. Complete survey data was available for 143 of the 146 patients (98%); of these, 93.7 per cent (n=134) found the ZIO XT Patch comfortable to wear compared with 51.7 per cent (n=74) who found the Holter monitor comfortable. The ZIO XT Patch affected the daily activities of 10.5 per cent of patients (n=15) and the Holter monitor affected the daily activities of 76.2 per cent of patients (n=109). Of respondent patients (n=137), 81 per cent (n=111) said they would prefer to wear the ZIO XT Patch.

One hundred and two physicians were surveyed and 90 per cent (n=92) thought that the ZIO XT Patch provided a definitive diagnosis, compared with 64 per cent (n=65) for the Holter monitor.

Overall device performance over the total wear time and 24-hour wear time was calculated for the two arrhythmia event groups. The ZIO XT Patch, over total wear time, detected significantly more arrhythmia events than the Holter monitor for both groups. For group 1, the ZIO XT Patch detected 96 events compared with 61 by the Holter monitor (p<0.001). For group 2 the ZIO XT Patch detected 41 events, compared with 27 for the Holter monitor (p<0.001).

When device performance was compared over a 24-hour period the ZIO XT Patch detected fewer group 1 and group 2 arrhythmia events than the Holter monitor. The difference in the
number of events detected was significant for group 1 events, with the ZIO XT Patch detecting 52 events compared with 61 events detected by the Holter monitor ($p<0.013$). For group 2, the ZIO XT Patch identified 24 events, compared with 27 events detected by the Holter monitor ($p<0.083$).

Rosenberg et al 2013

This non-randomised within-patient comparative study (level III-2 diagnostic evidence) involved consecutive patients receiving care for AF at a single centre. Data on 74 patients (mean age 64.5 years) were available for analysis. Each patient received the ZIO XT Patch and Holter monitor simultaneously to determine their pattern of AF, document their response to therapy, and potentially diagnose further arrhythmia. Patients were instructed to wear the ZIO XT Patch for as long as possible, ideally for the targeted 14-day period, and the Holter monitor for a 24-hour period. Following completion of the monitoring period the ZIO XT Patch was returned to the manufacturer by mail. Holter monitor data was examined by independent cardiologists and technical staff.

Significant arrhythmia was defined as AF or atrial flutter (these arrhythmias were grouped); other SVT for more than 4 beats; sustained ventricular tachycardia (>4 beats); junctional rhythm; sinus bradycardia (<50 beats/minute); and complete or high-grade heart block.

Effectiveness

The mean wear time for patients ($n=74$) was 10.8 days (standard deviation [SD] 2.8) for the ZIO XT Patch and 22.5 hours (SD 1.8) for the Holter monitor. Reasons for discontinuing use of the ZIO Patch include; study completion ($n=49$), device falling off ($n=16$), patient decision ($n=6$), battery malfunction ($n=1$), need for other cardiac intervention ($n=1$), and unknown ($n=1$).

During the first 24 hours all AF events recorded by the Holter device were recorded by the ZIO XT Patch. The estimated AF burden (time spent in AF) of these events was also comparable between the devices, with the mean burden 54.7% for the ZIO XT Patch and 58.4% for the Holter monitor ($p<0.0001$).

A total of 454 patient-days were recorded using the ZIO XT Patch, diagnosing an additional 43 AF episodes (Holter patient-days not reported). The incidence rate of AF in this population was 0.095 events per patient-day, with a median time to detection of one day. There was no difference in AF detection between patients with or without AF symptoms.

Overall, as a result of longer wear time, AF episodes were detected in an additional 18 patients with the ZIO XT Patch, compared with the Holter monitor ($p<0.0001$). The clinical classification of AF (persistent or paroxysmal) was changed in 21 patients (28%) as a result of ZIO XT Patch data. Alterations included changes in anti-arrhythmia medication ($n=13$) and anticoagulation status ($n=4$) and recommendations for pacemaker placement ($n=2$).
atrioventricular junction ablation (n=1), pulmonary vein isolation (n=1) and cardioversion (n=2).

Turakhia et al 2013\textsuperscript{18}

This cross-sectional study (level IV diagnostic evidence) used de-identified data from the manufacturer of the ZIO XT Patch regarding consecutive patients who underwent first-time cardiac monitoring using the device for clinical indications at a single institution. A total of 26,751 patients (mean age 60.2 years) were eligible for inclusion in the study.

The recorded arrhythmia episodes were classified into three groups according to type: first occurrence, first symptomatic occurrence (if occurring 45 seconds before or after the patient registered the event) and longest duration. The arrhythmias were also classified as: AF; pause longer than 3 seconds; second-degree Mobitz II or complete atrioventricular block; SVT; ventricular tachycardia; or symptomatic bradycardia.

**Effectiveness**

Data for ZIO XT Patch wear time and overall arrhythmia detection are summarised in Table 2. There were no significant differences with respect to wear time and patient age.

**Table 2 Wear time and arrhythmia detection**

<table>
<thead>
<tr>
<th>ZIO XT Patch</th>
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</thead>
<tbody>
<tr>
<td>Mean wear time (days)</td>
<td>7.6 (SD 3.6)</td>
</tr>
<tr>
<td>Median wear time (days)</td>
<td>7.0 (interquartile range 5.9 to 9.3)</td>
</tr>
<tr>
<td>Percentage of patients who wore device &gt;48 hours</td>
<td>95.9%</td>
</tr>
<tr>
<td>Percentage of patients who wore device ≥6 days</td>
<td>74.3%</td>
</tr>
<tr>
<td>Percentage of patients who wore device ≥13 days</td>
<td>16.1%</td>
</tr>
<tr>
<td>Median time</td>
<td>99% (interquartile range 94% to 99%)</td>
</tr>
<tr>
<td>Percentage of patients with analysable time equivalent to ≥22 hours/day</td>
<td>87.1%</td>
</tr>
<tr>
<td>No. of arrhythmias detected, excluding chronic AF</td>
<td>16,142</td>
</tr>
<tr>
<td>No. of patients with single arrhythmia</td>
<td>12,298</td>
</tr>
<tr>
<td>No. of patients with multiple arrhythmia</td>
<td>3,083</td>
</tr>
<tr>
<td>No. of patients with single chronic AF</td>
<td>2,003</td>
</tr>
<tr>
<td>No. of patients with single other* arrhythmia, in addition to chronic AF</td>
<td>761</td>
</tr>
</tbody>
</table>

* Other: Single or multiple instances of arrhythmia

Overall, the mean and median time to first arrhythmia was 1.7 days (SD 2.2) and 0.8 days (interquartile range, 0.2 to 2.4 days) respectively. The mean and median time to first
symptom-triggered arrhythmia was 3.0 days (SD 2.9) and 2.1 days (interquartile range, 0.8 to 4.4 days). In general, the diagnostic yield of the ZIO XT Patch improved with extended monitoring. Of those patients who were found to have arrhythmia, regardless of symptoms, 71 per cent were identified during the first two days of monitoring and 90 per cent were identified by the fifth day of monitoring.

**Economic evaluation**

No economic evaluation studies for the ZIO XT Patch were identified. As the MBS item 11709 does not differentiate between the types of ambulatory monitors, and due to questions relating to the appropriateness of the comparisons in the included studies, no economic evaluation was attempted.

**Ongoing research**

**NCT02031484**: Ongoing prospective case study comparing the Carnation™ Ambulatory Monitoring (CAM) System (Bardy Diagnostics, Inc., Washington, USA) with the ZIO XT Patch. The trial is sponsored by Bardy Diagnostics, Inc., the manufacturer of the CAM system. Patients eligible for inclusion are those with pre-syncope, syncope or palpitations of uncertain aetiology, and patients requiring management of known AF or supraventricular arrhythmias. Outcomes of interest include ECG signal quality and device comfort. Despite an expected completion date of July 2014 the trial is listed as not yet open for participant recruitment.

**Other issues**

All of the included studies received funding from iRhythm Technologies. It is unclear how or if this may have influenced the reported results. Clinician feedback for this Technology Brief has identified that the use of the Holter monitor as a comparator may not be appropriate. A Holter monitor is designed to be worn for a few days but an event recorder is designed to be worn for weeks. It was identified that a comparison assessing the diagnostic yield of the ZIO XT Patch with a Holter monitor over the same period would be preferable. Wearing a Holter monitor for an equivalent period of time, however, may be contrary to the standard use of this device. The diagnostic yield of the ZIO XT Patch with an event recorder over the same period may provide a more accurate assessment of the devices efficacy.

**Summary of findings**

Two studies of level III-2 diagnostic evidence suggested that the ZIO XT Patch performed significantly better than the Holter monitor in terms of detecting suspected cardiac arrhythmia when measured for overall wear time (i.e. up to 14 days for ZIO XT Patch and 24 hours for the Holter monitor). Although one study reported improved detection rates using the Holter monitor over a 24- to 48-hour period, the use of the ZIO XT Patch allowed for longer periods of cardiac monitoring, which improved the diagnostic yield. Importantly, this
enabled reclassification of arrhythmias in one study. This device therefore may have the potential to increase the correct alignment of services and to improve patient outcomes.

Patient willingness to wear non-invasive, longer term cardiac monitors, such as the ZIO XT Patch, supports a move towards such devices provided that further evidence continues to prove their efficacy.

**HealthPACT assessment**

The Zio Patch could potentially change the diagnostic/detection yield of arrhythmia over 24 hour monitoring and the way arrhythmias are investigated. It offers patients greater comfort and ease of use compared to the conventional Holter monitor, however issues were raised regarding data safety. In addition, the economics of the device are questionable as, although the Zio Patch may result in reduced hospital visits, the technology is significantly more expensive than the comparator. HealthPACT recommends that no further research on its behalf is necessary at this time, however, should normal horizon scanning activity detect TGA approval for the device or use in the jurisdictions, further research may be warranted.

**Number of studies included**

All evidence included for assessment in this Technology Brief has been assessed according to the revised NHMRC levels of evidence. A document summarising these levels may be accessed via the HealthPACT web site.

<table>
<thead>
<tr>
<th>Total number of studies</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of Level III studies</td>
<td>2</td>
</tr>
<tr>
<td>Total number of Level IV studies</td>
<td>1</td>
</tr>
</tbody>
</table>

**Search criteria to be used (MeSH terms)**

- Zio Patch
- Zio XT Patch
- ECG patch
- Electrocardiographic patch AND cardiac arrhythmia
- Electrocardiographic monitoring AND adhesive patch

**References**


