R-Wave Sensing in an Implantable Cardiac Monitor without ECG-Based Preimplant Mapping: Results from a Multicenter Clinical Trial

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Introduction: Reducing the form factor of an implantable cardiac monitor (ICM) may simplify device implant. This study evaluated R-wave sensing at a range of electrode distances and a preferred device implant location without mapping.

Methods: Patients scheduled for a Medtronic Reveal® ICM implant (Medtronic Inc., Minneapolis, MN, USA) underwent a preimplant pocket recording using a diagnostic recording catheter. The ICM implant location was left to the discretion of the implanting physician, but a “recommended” position spanned the V2–V3 electrocardiogram electrode location in an oblique 45° angle. R-wave amplitudes were analyzed from ICM follow-up.

Results: Seventeen of 41 subjects (15 male, age 57 ± 16 years) had the maximum surface-filtered R-wave at the recommended location. Fourteen patients underwent diagnostic recording across the range of electrode spacing. There was a strong correlation between the R-wave amplitude and electrode distance ($r^2 = 0.97, P < 0.001$) with an increase of 29 µV per 2.5 mm. Comparing normalized R-wave distributions between the recommended ICM implant group (Group 1, n = 19) and the remaining patients (Group 2, n = 7), the proportion of ICM R-wave counts of amplitude 0.25–1.2 mV was higher (79% vs 46%, $P < 0.05$). Of 17 patients in Group 1 who had ≥1-month ICM follow-up (79 ± 45 days), no sensing-related false arrhythmia detection was found in 16 (93%) patients.

Conclusions: The subcutaneous R-wave amplitude correlates with electrode spacing in the implant zone of ICM patients. Implant locations at the V2–V3 position at a 45° angle offer an adequate R wave for sensing. Preimplant mapping to achieve acceptable R-wave amplitude may not be necessary. (PACE 2014; 37:505–511)

im implant, mapping, implantable cardiac monitor, ECG, R-wave sensing, subcutaneous
As a minimum, the manufacturer recommends achieving a filtered R-wave amplitude $\geq 200 \, \mu V$ when viewed on the programmer screen (or $\geq 300 \, \mu V$ when viewed on the programmer strip chart) while the patient is in a supine position.8 However, posture variations during various daily activities mean that ECG mapping does not guarantee reliable R-wave sensing.

Previous studies have indicated that an anatomical approach may be possible for implantation.7 However, R-wave sensing with smaller bipolar electrode spacing at a specific anatomical location and orientation has not been adequately examined. This study investigated an optimal implant site to achieve acceptable R-wave sensing for ICM without preimplant mapping, and determine the relationship between R-wave amplitude and bipolar electrode spacing.

Methods

The study was a prospective, observational, nonrandomized, multicenter clinical trial involving four centers (Canada and USA) from March 2011 to March 2012. The primary objective of this study was to collect surface ECG mapping data, subcutaneous (SubQ) ECG data with various electrode spacing, and ambulatory ICM “save-to-disk” data for patients who received an implanted device.

All subjects were over the age of 18; a potential candidate for an ICM based on clinical referral for unexplained syncope, infrequent palpitations, or atrial fibrillation (AF); and provided written informed consent. All subjects were able to wear a 24-hour ambulatory Holter monitor. Subjects who received an ICM were implanted with either a Medtronic Reveal DX or Reveal XT ICM (Medtronic Inc., Minneapolis, MN, USA). The study was approved by all local ethics review boards.

R-Wave Amplitude at Various ECG Vectors

Custom surface ECG electrodes (Lead-Lok Inc., Sandpoint, ID, USA) were placed on all patients at electrode locations similar to the ICM-recommended implant locations (Fig. 1). Multivector surface ECG signals were collected using a DR180+ Holter (NorthEast Monitoring, Maynard, MA, USA) with the patient in the supine position for $\geq 1$ minute. To evaluate a potential smaller form factor ICM, center-to-center electrode spacing was set to 30 mm (Reveal XT and DX interelectrode spacing: 43 mm). The high-fidelity bipolar ECG signals at various vectors were first down sampled from 700 Hz to 256 Hz in order to simulate the current ICM R-wave sensing accurately. The filtered R-wave amplitudes (range: 10–32 Hz) were further analyzed.

During the first minute of the DR180+ Holter recording with the patient in the supine position, the proportion of patients with the maximum filtered R-wave among different vectors was summarized to report the optimal location for R-wave amplitude. All R-wave amplitudes were normalized to electrode spacing using linear interpolation prior to analysis.

ICM Implant and Electrophysiology (EP) Catheter Data Collection

Patients with a clinical indication for an ICM were implanted with a Medtronic Reveal IC. Final positioning of the device/pocket was made at the discretion of the implanting physician after patient evaluation and consent. The study protocol recommended that, without preimplant mapping, the ICM would be placed preferentially at or slightly above the standard $V_2-V_3$ ECG electrode location in an oblique 45° angle (implant locations A or B; Fig. 1). These patients constituted Group 1. Group 2 consisted of patients with mapping and implant position other than locations A and B based on investigator’s discretion. While the patient was in the supine position, a 7F decapolar diagnostic EP catheter with a range of bipolar electrode distances (22–41 mm) was placed into a tight straight-tunneled pocket prior to ICM insertion. Filtered SubQ ECGs (1 minute) for R-wave amplitude analysis were obtained using the Reveal sensing software routine written in Matlab (MathWorks, Natick, MA, USA).

Ambulatory SubQ R-Wave Amplitude Distributions and R-Wave Sensing

For each patient with an implanted ICM, distributions of the beat-by-beat device-sensed R-wave amplitude were retrieved from the follow-up
Table I.
Subject Population

| Characteristic† | Males (n = 15) | Females (n = 27) | Total (n = 42) |
|-----------------|---------------|-----------------|---------------|
| Age (years)     | 54 ± 16       | 59 ± 15         | 57 ± 16       |
| Weight (kg)     | 89.5 ± 27.2   | 74.5 ± 18       | 83 ± 22       |
| Height (cm)     | 175.6 ± 8.2   | 160.8 ± 8.3     | 166 ± 11      |
| BMI (kg/m²)     | 30.6 ± 8.3    | 28.9 ± 6.8      | 30 ± 6        |
| Comorbidities‡  |               |                 |               |
| Hypertension    | 7 (47%)       | 14 (52%)        | 21 (50%)      |
| Coronary artery disease | 5 (33%)     | 5 (19%)         | 10 (24%)      |
| Syncope/presyncope | 6 (40%)    | 15 (56%)        | 21 (50%)      |
| Nonischemic cardiomyopathy | 1 (7%)      | 1 (4%)          | 2 (5%)        |
| Myocardial infarction | 1 (7%)      | 1 (4%)          | 2 (5%)        |
| Hyperlipidemia  | 1 (7%)        | 1 (4%)          | 2 (5%)        |
| Aortic stenosis | 0 (0%)        | 1 (4%)          | 1 (2%)        |
| Mitral valve regurgitation | 0 (0%)      | 1 (4%)          | 1 (2%)        |
| Peripheral vascular disease | 1 (7%)      | 0 (0%)          | 1 (2%)        |
| Type 2 diabetes mellitus | 0 (0%)      | 1 (4%)          | 1 (2%)        |
| Supraventricular tachycardia | 1 (7%)      | 3 (11%)         | 4 (%)         |
| Chronic atrial fibrillation (AF) | 1 (7%)      | 0 (%)           | 1 (2%)        |
| Paroxysmal AF   | 0 (0%)        | 1 (4%)          | 1 (2%)        |
| Atrial flutter  | 1 (7%)        | 0 (0%)          | 1 (2%)        |
| Sustained monomorphic VT | 1 (7%)      | 0 (0%)          | 1 (2%)        |
| Sinus node dysfunction | 1 (7%)      | 1 (4%)          | 2 (5%)        |
| AV block        | 1 (7%)        | 1 (4%)          | 2 (5%)        |
| Right bundle branch block | 1 (7%)       | 0 (0%)          | 1 (2%)        |
| Left bundle branch block | 1 (7%)       | 4 (15%)         | 5 (12%)       |
| Sinus bradycardia | 0 (0%)       | 1 (4%)          | 1 (2%)        |
| Left anterior hemi-block | 0 (0%)       | 1 (4%)          | 1 (2%)        |

†Values for characteristics are mean ± standard deviation.
‡Values for comorbidities are prevalence, with percentage in parentheses.
AV = atrioventricular; BMI = body mass index; VT = ventricular tachycardia.

save-to-disk or Carelink data transfer. Normalized R-wave amplitudes were compared between patients (Group 1, recommended ICM implant location vs Group 2, other location). Among a subgroup of ICM patients, 24-hour ICM data were also collected using the DR220+ Holter (NorthEast Monitoring), a monitor that provides simultaneous recording of ICM sense markers, SubQ ECGs, as well as the usual surface ECGs. For each patient with at least a single 1-month follow-up visit, automatically recorded episodes were reviewed for false automatic arrhythmia detections due to R-wave over- or undersensing. For each patient, overall sensing and detection were classified as appropriate when the following were not encountered: (1) small R waves leading to over- or undersensing, (2) P-wave/T-wave oversensing or other false automatic detections due to noise/artifact after implant, and (3) >1 episode per month of false automatic detections due to inappropriate sensing.

Statistical Analysis
The relationship between the filtered R-wave amplitude and electrode spacing was assessed using a balanced analysis of variance model. The proportion of normalized ICM R-wave counts in the 0.25–1.25-mV range was compared between the recommended ICM implant group and the other group using Student’s t-test. Statistical analysis was performed using Minitab® statistical software v16 (Minitab Inc., State College, PA, USA). P values <0.05 were considered significant. All results are expressed as mean ± standard deviation.

Results
Forty-two subjects were enrolled (15 male, age 57 ± 16 years, Table I). All subjects completed
Device location and orientation to achieve maximum R-wave amplitude with the same electrode spacing (n = 41) using the DR180+ Holter data. Data presented are normalized to the electrode space difference. (Inset) Vectors analyzed using customized DR180+ Holter electrodes.

Figure 2.}

the DR180+ Holter monitoring period (up to 24 hours). Twenty-seven subjects received an ICM implant. Complete EP catheter data were obtained from 22 subjects. There was no incidence of device explant due to patient’s discomfort of ICM implant. Two subjects exited the study prior to completing follow-up and two subjects were lost to follow-up, with 23 subjects completing the 1-month follow-up visit. Fourteen patients had complete DR220 data.

R-Wave Amplitude in Surface ECGs

All 42 subjects completed the DR180+ Holter monitoring period (average duration: 18.5 ± 8.0 hours), and 41 subjects had useful surface ECG data at all vectors (1 minute at the supine position). Comparing four different ECG vector orientations (0°, 45°, 90°, 135°) in the supine position, 41% (17/41) of patients had the maximum filtered R wave at V2–V3 at the 45° angle (Fig. 2).

SubQ R-Wave Amplitude at Various Electrode Spacing

Among the 27 patients who underwent ICM implant, 19 (10 female, nine male) were implanted at the recommended location and orientation and constituted Group 1 (14 in location A, and five in location B, Fig. 1). The other eight (seven female, one male) patients had the ICM placed in other locations and constituted Group 2. For the combined Group 1 and Group 2 patients, there was a correlation between the filtered R-wave amplitude and electrode distance with valid SubQ ECG recordings (R² = 0.927, P < 0.001, n = 22, Fig. 3A). No over- or undersensing occurred at various electrode distances. Likewise, there was significant correlation between the R-wave amplitude and electrode distance at the recommended ICM implant location (R² = 0.922, P < 0.001, n = 14, Fig. 3B). At the preferred location (Group 1), every 2.5-mm reduction in electrode spacing resulted in a 5% reduction in R-wave amplitude (28 µV). An example of the SubQ ECG waveform at different electrode spacing is shown in Figure 4.

ICM R-Wave Distributions

We analyzed filtered amplitude for each sensed beat at different amplitude ranges since implant in 26 patients, from the latest device data with a median of 4 million sensed beats (range 5,000–26,000,000 sensed-beats, Fig. 5). Comparing normalized R-wave distributions between Group 1 (n = 19, Fig. 4A) and Group 2 (n = 7, Fig. 4B), the proportion of R-wave counts in the 0.25–1.2 mV range was significantly higher (79% vs 46%, P = 0.03).

ICM R-Wave Sensing and Automatic Detection

Twenty-three ICM patients had a follow-up visit approximately 1 month postimplant (46.9 ± 46.8 days; range 9–117 days). Of the 14 patients with a valid 1-month DR220 Holter, 11 had the ICM implanted in the recommended locations with a correlated filtered SubQ R wave of 512 ± 305 µV. There was no or minimal over- or undersensing in nine patients with appropriate initial filtered R wave (581 ± 294 µV). Two of the 11 patients had minor under- and oversensing attributed to small baseline R waves; however, no false automatic detection was triggered during the 24-hour Holter recordings. Furthermore, there were no sensing issues in 16 of 17 (93%) patients with the recommended ICM implant locations during 79 ± 45 days of follow-up (range 28–163 days). One patient had 89 false pauses due to small R waves and transient loss of signal in the first 4 days postimplant, with resolution after reprogramming.

Discussion

The V2–V3 implant site, or the lower chest V2–V3 area between the fourth and fifth rib, has been reported as a viable ICM implant option that results in improved arrhythmia detection compared to a standard pacemaker pocket site, and is one of the current recommended locations of the Medtronic Reveal® ICM. This study investigated the use of a precise implant location to avoid the reliance upon supine ECG.
ICM R-WAVE SENSING

This study demonstrated that the sensed R-wave amplitude correlates with electrode spacing in the implant zone of ICM patients ($R^2 \geq 0.92$). A small reduction in bipolar electrode spacing had minimal impact on the R-wave amplitude. Implant locations at the upper left chest or near V$_2$–V$_3$ at a 45° angle offers adequate R-wave for clinical use, even at shorter electrode spacing (Fig. 3). Previously, Grubb et al. reported adequate SubQ ECG tracings without the need for preoperative cutaneous mapping in 62 patients using

Figure 3. (A) Correlation of R-wave amplitudes and electrode spacing in the supine position ($n = 22$). (B) Correlation of R-wave amplitudes and electrode spacing in the supine position for subjects with recommended Reveal implant location ($n = 14$, $P < 0.001$, $R^2 = 0.922$).

mapping, and determined the sensing effects of reducing the electrode pacing. Based on this study, the recommended location for the device is either the left parasternal area extending to the midclavicular line between the first intercostal space and the fourth rib, or the V$_2$–V$_3$ implant site mentioned above. To our knowledge, this was the first multicenter clinical study to evaluate the feasibility of ICM implant without preimplant mapping at current available or reduced electrode spacing.
Figure 4. Sample recorded electrograms from a patient illustrating correlation of the interelectrode spacing with signal amplitude. Wider interelectrode spacing (41 mm vs 22 mm) resulted in higher amplitude R-waves. Of note, R-waves remained acceptable (>200 µV) with interelectrode spacing as low as 22 mm.

Figure 5. Distributions of normalized ICM sensed R-wave amplitudes retrieved from implanted ICM. Each bar represents the average normalized R-wave bin counts at defined device-sensed R-wave amplitude range. (A) Group 1 recommended implant locations A or B (n = 19). (B) Group 2, non-A/B implant locations (n = 7).
than the other traditional implant location even with preimplant mapping. From the analysis using device-detected automatic arrhythmia episodes, 93% of patients had no sensing issues during an average of 79 days follow-up, indicating that R-wave amplitudes were consistently large to avoid significant noise oversensing or posture-related R-wave amplitude drop. To our knowledge, there was no reported complaint of patient’s discomfort due to our prespecified implant location and device orientation. Finally, our preferred implant site without the need for surface ECG-based preimplant mapping provides an opportunity to simplify the implant procedure and shorten the implant time.

Limitations

The SubQ ECG mapping results presented were in the supine location, and thus did not capture the effect of posture on signal amplitude, which is known to affect the ECG signal. Although these data are limited by small sample size, the results are in agreement with previous studies indicating an optimal placement of the ICM near the center of the chest, and that the resultant placement of the ICM within our recommended location is not influenced by body position.1,12

Conclusion

The SubQ R-wave amplitude correlates with electrode spacing in the implant zone of ICM patients, and the R-wave amplitude was minimally impacted by a reduction in bipolar electrode distance. Implant locations at the $V_2-V_3$ location at a 45° angle provided adequate R-wave sensing, even at shorter electrode spacing. Thus, ICM placement at the recommended location obviates the need for preimplant ECG mapping.

Acknowledgment: The authors would like to acknowledge Jodi Koehler for statistical analysis support.

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