Medtronic

WHITE PAPER

Determining efficacy of reduced-energy monophasic shocks

Summary

To support the risk assessment associated with the short circuit protection (SCP) feature resulting in a truncated biphasic waveform being delivered as a reduced-energy monophasic waveform, statistical modeling was used to establish a 1.1% relative decrease in shock efficacy for up to six full-energy shocks delivered for a ventricular fibrillation (VF) episode.

Process to establish relative efficacy

To determine the efficacy of reduced-energy monophasic shocks as compared to full-energy biphasic shocks, the following steps were followed:

1. Using clinical data, the efficacy curve of a biphasic full-energy shock for induced VF was established via statistical modeling.
2. To determine the decrease in efficacy of a monophasic reduced-energy shock relative to the full-energy biphasic shock, monophasic-to-biphasic defibrillation threshold (DFT) ratio was calculated based on literature review.
3. The relative efficacy of a monophasic reduced-energy shock from step 2 was used to establish a monophasic shock efficacy curve.
4. The overall difference in efficacy was used to adjust clinical data of efficacy of up to six biphasic shocks delivered into a spontaneous arrhythmia episode to establish efficacy after multiple monophasic shocks.

Establish efficacy of biphasic shocks

Using data from the GEM™ DR clinical study,[1] statistical modeling was used to estimate the best fit curve of first shock success versus delivered energy for biphasic shocks (Figure 1).

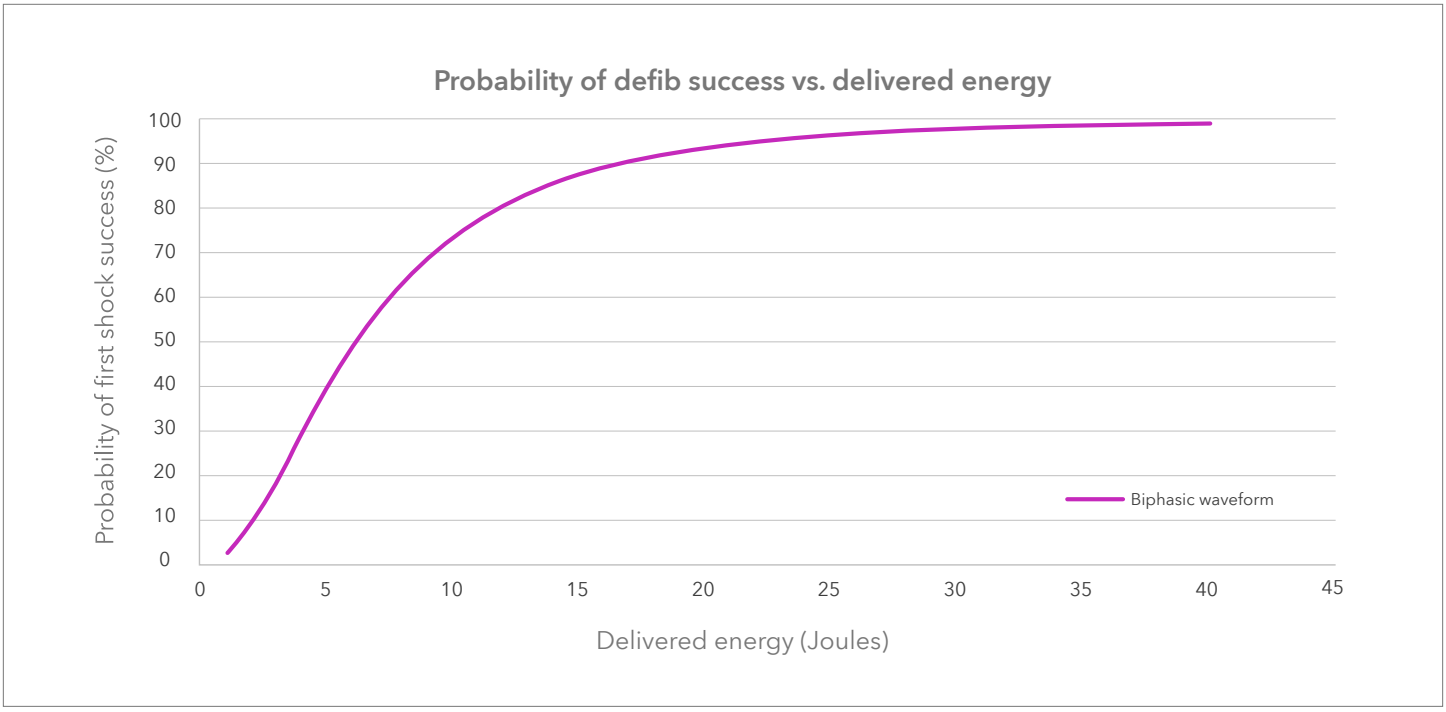

Figure 1: Probability of defib success vs. delivered energy – biphasic (based on GEM DR study data)

Additional data from the PainFREE II clinical study,[2] SCD-HeFT trial,[3] and the OMNI trial,[4] were used to independently validate the fit of the curve (Figure 2).

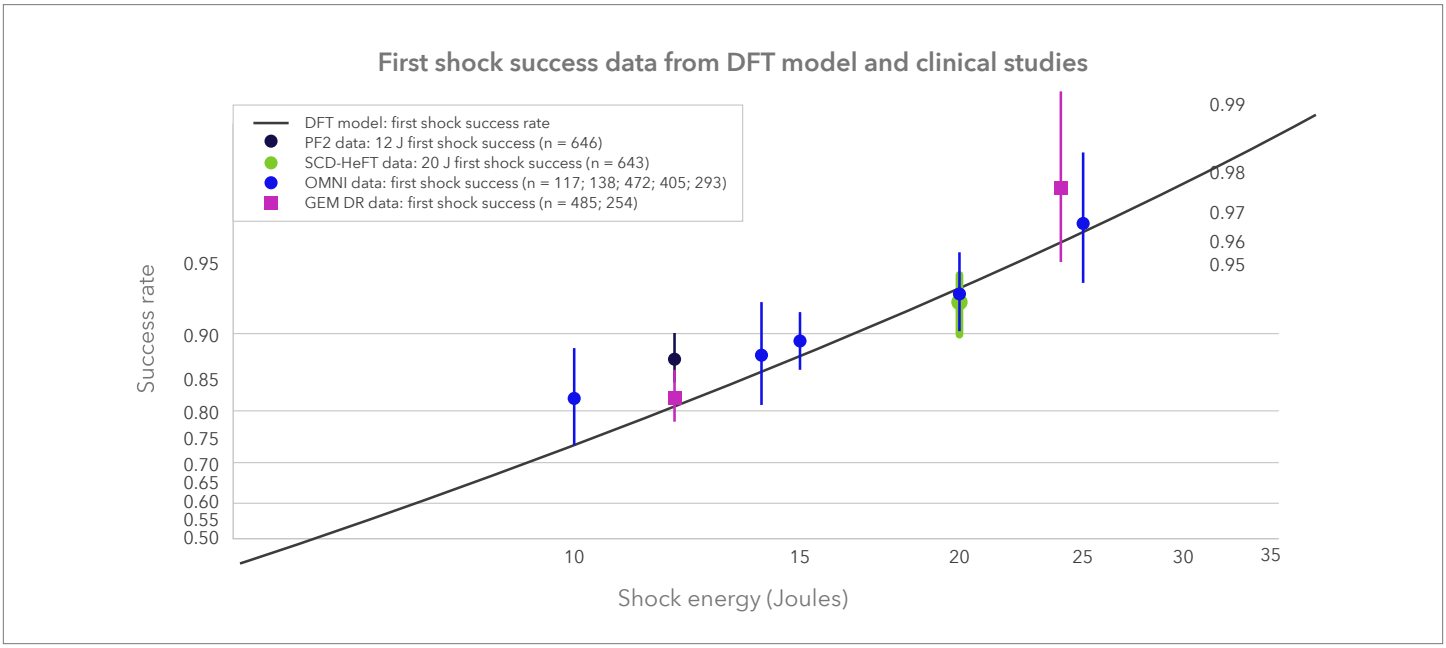

Figure 2: First shock success data from model is shown against data from three independent clinical studies to establish credibility of the model prediction

The following assumptions were made in determining the efficacy of biphasic shocks:

- The statistical model assumes defibrillation efficacy asymptotically reaches 100% at some energy, equating to the assumption that every patient can be defibrillated at some energy. (Note that assumption could fail if the patient or defibrillation system is not typical of those represented in prior clinical studies [e.g., electrode position].)
- Data from the trials shock at ≤ 25 J. The model assumes extrapolated estimates remain valid at greater than 25 J.
- The GEM DR data used to develop the predicted defibrillation efficacy curve included a variety of electrode systems. The model assumes similar efficacy is obtained with systems used in the Cobalt™/Crome™ population.

Compare efficacy of monophasic shocks relative to biphasic

A literature review was conducted to find human studies that included a comparison of biphasic and monophasic waveform success during implant defibrillation testing. Four (4) studies were identified and used, as shown in Table 1. The nonweighted average for ratios between monophasic to biphasic defibrillation thresholds (DFTs) was found to be 1.5, which was used as an input for creating the monophasic defibrillation curve.

Reference	Patients	Subgroup	Monophasic DFT	Biphasic DFT	Ratio (StE/StE or V^2/V^2)
Bardy[5]	22	n/a	8.5 J	6.3 J	1.35
Bardy[6]	12	n/a	502 v	504 v	0.99
Wyse[7]	9 12	ICD patients CABG patients	21.1 J 24.2 J	12.3 J 14.6 J	1.72 1.66
Block[8]	36 24 19	SVC - RV SVC + SQ - RV SVC + array - RV	432 v 468 v 387 v	365 v 365 v 295 v	1.41 1.64 1.72

Table 1: Historical paired comparison of DFTs in humans for monophasic vs. biphasic pulses in transvenous systems

The following assumptions were made in determining the efficacy of monophasic shocks relative to biphasic:

- The 50% increase is a nonweighted average and could be as high as 72% or as low as 0% according to studies in the reference list.
- Differences in lead systems, capacitances, and waveform tilt/durations used in the studies are assumed to be insignificant as compared to Cobalt/Crome systems.
- The table reports mean DFTs. While nearly all studies in the literature demonstrate a relative mean improvement of biphasic defibrillation waveforms relative to monophasic defibrillation waveforms for the respective study sample, not every patient shows improved performance with a biphasic waveform. In fact, some patients show better outcomes for monophasic waveforms (Block, et al. – "In six patients, the monophasic waveform showed slightly better results: 5 J in five patients and 10 J in one patient").

Establish monophasic waveform defibrillation efficacy

Using the ratio of 1.5 identified in the previous section, the biphasic defibrillation efficacy curve was adjusted to reflect the expected decrease with a monophasic waveform, as shown in Figure 3.

The comparison of a 40 J biphasic waveform to a 32 J† monophasic shock indicates a relative decrease of 4.5% in single-shock efficacy for induced VF, as shown in green in Figure 3.

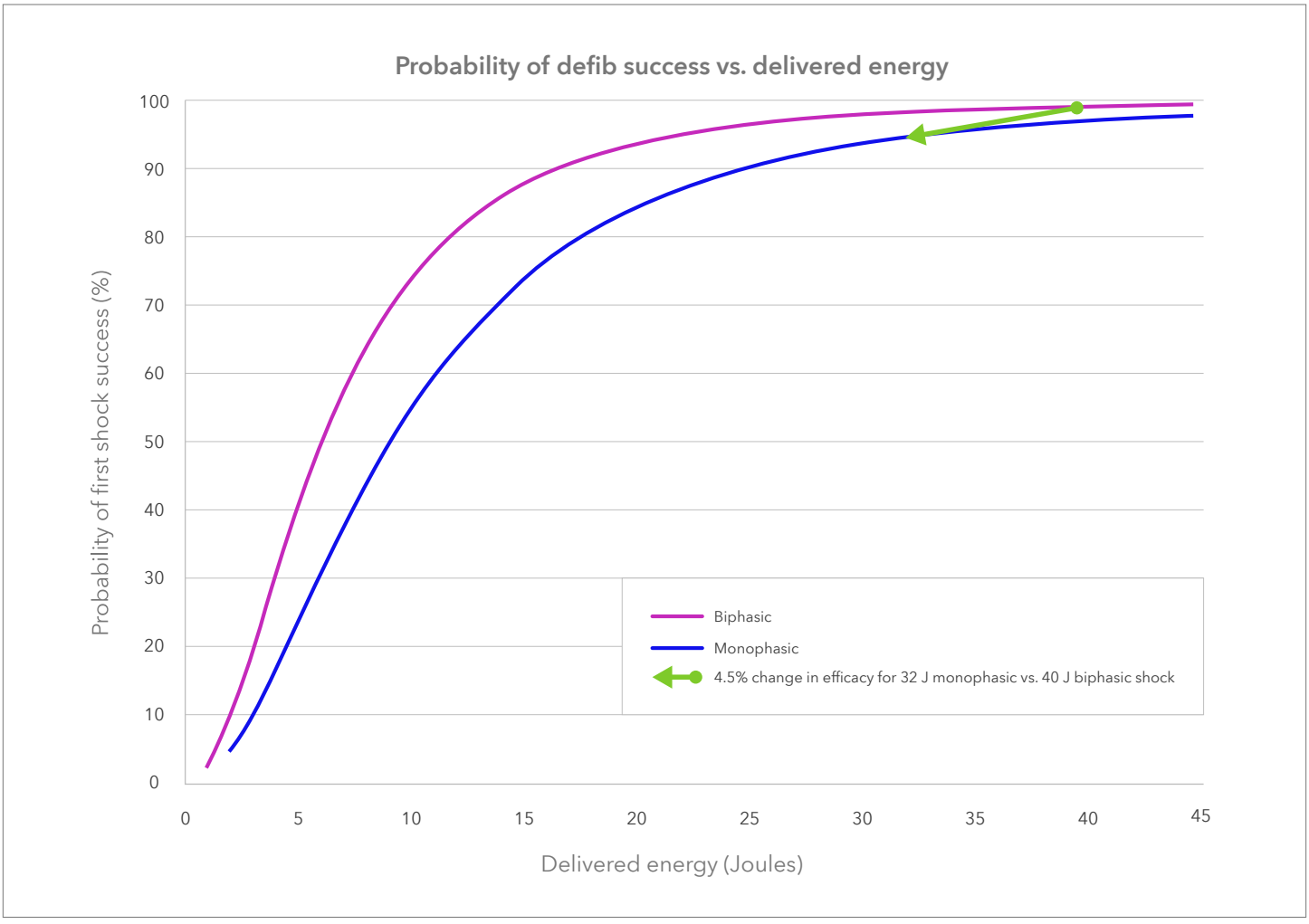

Figure 3: Probability of defib success vs. delivered energy – biphasic and monophasic

†32 J is the theoretical energy delivered in the first phase of the biphasic shock when programmed to 40 J. There could be minor variations (ex: field events ranged from 30.8 J to 34 J with median of 31.6 J).

Impact of up to six available shocks in spontaneous episodes

Three sets of data were used to determine the predicted efficacy for spontaneous episodes for standard biphasic waveforms:

- 439 true VT/VF adjudicated episodes‡ from PainFree-SST[9] (see Table 2)
- 2,842 true VT/VF adjudicated episodes from three clinical studies (PainFree-SST,[9] Shockless,[10] OMNI,[4] see Table 3)
- CareLink™ data during spontaneous VT/VF unadjudicated episodes (~279K from 2010–2018,[11] see Table 4)

Shock number	Number of episodes	Number of successes	Percent successful	Percent failed
1	439	394	90%	10%
2	45	32	71%	29%
3	13	7	54%	46%
4	6	1	17%	83%
5	5	1	20%	80%
6	4	4	100%	0%

Table 2: Incremental shock success rate – PainFREE-SST

Shock number	Number of episodes	Number of successes	Percent successful	Percent failed
1	2,842	2,540	89%	11%
2	275	156	57%	43%
3	114	49	43%	57%
4	58	17	29%	71%
5	29	9	31%	69%
6	12	4	33%	67%

Table 3: Incremental shock success rate – three listed studies

Shock number	Number of episodes	Number of successes	Percent successful	Percent failed
1	279,095	243,865	87%	13%
2	58,447	30,964	53%	47%
3	27,303	9,351	34%	66%
4	14,482	3,638	25%	75%
5	7,359	1,515	21%	79%
6	2,676	431	16%	84%

Table 4: Incremental shock success rate – CareLink

‡This subset excluded shocked episodes with subsequent spontaneous or ATP termination.

Success rate during an arrhythmia episode with up to six shocks

The median shock failure rate from the three clinical data sets was used as an input to the final reduced efficacy estimate. The median shock failure rate to account for monophasic reduced-energy delivery was also calculated, as shown in Table 5.

Shock number	Median shock failure rate from 3 data sets (biphasic)	Cumulative median % episodes not terminated by biphasic shocks	Failure rate increased by 4.5% for reduced-energy monophasic	Cumulative % episodes not terminated by monophasic shocks	Reduced efficacy from biphasic to monophasic
1	**11%**	11%	**15.5%**	15.5%	4.5%
2	43%	4.7%	47.5%	7.4%	2.6%
3	57%	2.7%	61.5%	4.5%	1.8%
4	75%	2.0%	79.4%	3.6%	1.6%
5	79%	1.6%	83.9%	3.0%	1.4%
6	67%	**1.1%**	71.5%	**2.2%**	**1.1%**

Table 5: Shock failure rate per number of shocks – biphasic and monophasic

Table 6 shows the first shock cumulative success rate of a biphasic full-energy shock as compared to the monophasic reduced-energy shock. The relative difference in shock efficacy over a maximum of six shocks is 1.1%.

	40 J biphasic delivery	32 J monophasic delivery
Estimated first shock success	**89%**	**85%**
Estimated cumulative shock success (up to 6)	**99%**	**98%**

Table 6: First shock and cumulative shock success rates – biphasic and monophasic

Conclusion

Based on a comparison of biphasic waveform shock efficacy by energy and adjusting for decreased efficacy with a monophasic reduced-energy waveform, the relative decrease in first shock success is 4.5% when maximum output is programmed, reducing the biphasic success rate of 89% to about 85%. When adjusting the efficacy of a series of up to six shocks, the overall cumulative shock efficacy decreases by about 1.1%, reducing the 99% success rate to about 98% should a reduced-energy monophasic waveform occur repeatedly in the episode.

References

[1] GEM DR clinical study, Medtronic data on file.
[2] PainFREE II clinical study, Medtronic data on file.
[3] SCD-HeFT clinical trial, Medtronic data on file.
[4] OMNI trial, Medtronic data on file.
[5] Bardy GH, Ivey TD, Allen MD, Johnson G, Mehra R, Greene HL. A prospective randomized evaluation of biphasic versus monophasic waveform pulses on defibrillation efficacy in humans. *J Am Coll Cardiol*. September 1989;14(3):728-733.
[6] Bardy GH, Allen MD, Mehra R, Johnson G. An effective and adaptable transvenous defibrillation system using the coronary sinus in humans. *J Am Coll Cardiol*. October 1990;16(4):887-895.
[7] Wyse DG, Kavanagh KM, Gillis AM, et al. Comparison of biphasic and monophasic shocks for defibrillation using a nonthoracotomy system. *Am J Cardiol*. January 15, 1993;71(2):197-202.
[8] Block M, Hammel D, Böcker D, et al. A prospective randomized cross-over comparison of mono- and biphasic defibrillation using nonthoracotomy lead configurations in humans. *J Cardiovasc Electrophysiol*. July 1994;5(7):581-590.
[9] PainFREE SST clinical study, Medtronic data on file.
[10] Shock-Less clinical study, Medtronic data on file.
[11] De-identified Medtronic CareLink data on file.

Brief Statements

Cobalt™/Crome™ MRI SureScan™ ICD and CRT-D Systems

Indications: The Cobalt™ XT, Cobalt™, and Crome™ HF CRT-D MRI SureScan™ systems are indicated for use in patients who are at significant risk of developing atrial and/or life-threatening ventricular arrhythmias and who have heart failure with ventricular arrhythmias. Heart failure patients must have experienced one or more of the following conditions:

- NYHA Functional Class III or IV patients who remain symptomatic despite stable, optimal medical therapy and have LVEF ≤ 35% and a prolonged QRS duration
- NYHA Functional Class II patients who have left bundle-branch block (LBBB) with a QRS duration ≥ 130 ms and a left ventricular ejection fraction ≤ 30%
- NYHA Functional Class I, II, or III who are on stable, optimal medical therapy (if indicated), and have LVEF ≤ 50%,atrioventricular block (AV block), and are expected to require a high percentage of ventricular pacing that cannot be managed with algorithms to minimize right ventricular pacing

The Cobalt XT, Cobalt, and Crome VR and DR ICD MRI SureScan systems are indicated for the automated treatment of patients who have experienced, or are at significant risk of developing, atrial and/or life-threatening ventricular arrhythmias through the delivery of antitachycardia pacing, cardioversion, and defibrillation therapies.

MRI Conditions for Use: Medtronic SureScan ICD and CRT-D systems are MR Conditional, and as such are designed to allow patients to undergo MRI under the specified conditions for use. ICD and CRT-D SureScan system patients may be scanned using a horizontal field, cylindrical bore, clinical 1.5T or 3T MRI system for hydrogen proton imaging. When programmed to On, the MRI SureScan feature allows the patient to be safely scanned while the device continues to provide appropriate pacing. A complete SureScan defibrillation system, which is a SureScan device with appropriate SureScan lead(s), is required for use in the MR environment. To verify that components are part of a SureScan system, visit http://www.mrisurescan.com/. Any other combination may result in a hazard to the patient during an MRI scan.

Contraindications: The Cobalt XT, Cobalt, and Crome VR and DR ICD and CRT-D MRI SureScan systems are contraindicated for use in the following situations:

- If implanted with a unipolar pacemaker
- If incessant VT or VF exists
- If the primary disorder is chronic atrial tachyarrhythmia with no concomitant VT or VF
- If tachyarrhythmias with transient or reversible causes exist, including the following known issues: acute myocardial infarction, drug intoxication, drowning, electric shock, electrolyte imbalance, hypoxia, and sepsis.

Warnings and Precautions: Changes in a patient's disease and/or medications may alter the efficacy of the device's programmed parameters. Patients should avoid sources of magnetic and electromagnetic radiation to avoid possible underdetection, inappropriate sensing and/or therapy delivery, tissue damage, induction of an arrhythmia, device electrical reset, or device damage. Do not place transthoracic defibrillation paddles directly over the device. Patients and their implanted systems must be screened to meet the following requirements for MRI: no lead extenders, lead adaptors, or abandoned leads present; no broken leads or leads with intermittent electrical contact as confirmed by lead impedance history. The device must be operating within the projected service life, and the system must be implanted in the left or right pectoral region.

Potential Adverse Events: Potential adverse events include, but are not limited to, the following events: allergic reactions, atrial fibrillation, bradyarrhythmia, cardiac arrest, device migration, discomfort, dizziness, dyspnea, erosion, excessive fibrotic tissue growth, heart failure or loss of CRT (for CRT-D patients), hematoma, hemorrhage, inability to deliver therapy, inappropriate shock, infection, lead migration/dislodgement, lethargy, loss of pacing, mental anguish, necrosis, nerve damage, oversensing, palpitations, seroma, syncope, tachyarrhythmia, tissue damage due to heating of the device, undersensing, and wound dehiscence. Potential MRI complications include, but are not limited to, lead electrode heating and tissue damage resulting in loss of sensing or capture or both, spontaneous tachyarrhythmia, potential for VT/VF induction, device heating that results in tissue damage, stimulation of the leads that results in continuous capture, VT/VF, hemodynamic collapse, damage to the device or the leads, causing the system to fail or treat the patient's condition incorrectly, and movement or vibration of the device or the leads, resulting in dislodgement.

See the device manuals for detailed information regarding the implant procedure, indications, contraindications, warnings, precautions, and adverse events. See the MRI SureScan Technical Manual before performing an MRI Scan. For further information, call Medtronic at 1-800-328-2518 and/or consult the Medtronic website at medtronic.com *or* mrisurescan.com.

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

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