



The Medtronic Position On Biphasic External Defibrillation: An Update

LINGERING QUESTIONS

Although external defibrillators employing biphasic waveforms have been available for several years, many questions related to their clinical impact remain unanswered. How much, or how little, defibrillation capability is sufficient for the “typical patient”? How much defibrillation capability might be clinically useful in the patient who is difficult to defibrillate or cardiovert? Is there any clinically meaningful downside to offering clinicians a product with incrementally more defibrillation capability than other biphasic defibrillators? Is there any clinically meaningful downside to not offering such incremental improvements? How do the answers to these questions vary for the different clinical applications of external defibrillators?

WHY MEDTRONIC OFFERS BIPHASIC ENERGY CAPABILITY UP TO 360 JOULES (J)

Years of basic research, along with subsequent clinical experience in implantable defibrillators, helped to characterize the advantages of well-designed biphasic waveforms over traditional monophasic waveforms.^{1,2} These advantages created several options for the design of new external defibrillators. In introducing biphasic technology into its external defibrillators, Medtronic recognized that one option was to take advantage of the efficacy of biphasic waveforms to permit a substantial reduction in the maximum energy setting a defibrillator needed to accommodate. Evidence indicated that such a substantial reduction was possible while still producing a device that matched or modestly exceeded the defibrillation capabilities of monophasic defibrillators. Medtronic also recognized that an alternative option was to leverage the efficacy of biphasic waveforms to provide a more substantial improvement in defibrillation capability relative to even the best monophasic defibrillators, by not reducing the maximum energy the defibrillator could accommodate.

Our decision to maintain energy capability up to 360 J while transitioning to the more effective biphasic waveform has been motivated by two well-documented scientific insights. First, the efficacy of the best monophasic defibrillators, while reasonably high, still leaves measurable room for improvement, particularly in more challenging clinical situations. Second, compared to monophasic shocks of the same intensity, well-designed biphasic shocks not only terminate ventricular fibrillation more effectively², but also present

a significantly lower risk of shock-related injury.¹ In light of these observations, Medtronic considered an approach aimed at maximizing efficacy while simultaneously enhancing safety to be the more compelling option. This decision was reinforced by the lack of any clinical evidence indicating how many additional patients might benefit from a biphasic defibrillator designed to maximize defibrillation capability, rather than to meet or modestly exceed conventional monophasic defibrillation capability. Medtronic continues to believe that until such evidence exists, our approach represents a more clinically responsible option.

CHALLENGES TO OUR DECISION

Advocacy of a “low energy” approach and challenges to the Medtronic approach to biphasic external defibrillation has centered on four contentions.

Contention No. 1: The use of 360 J as a maximum energy setting for biphasic defibrillators is arbitrary and clinically unfounded.

In large part because 360 J emerged decades ago without much empirical evidence as a de facto standard for monophasic external defibrillator energy capability, it has been argued that a 360 J biphasic maximum energy setting is a “flawed” choice. It is important to recognize that the introduction of 150 J or 200 J as an alternative maximum biphasic energy setting has been no less arbitrary and no more clinically founded. Prior to market introduction, Medtronic and several other companies performed clinical studies in the electrophysiology laboratory—primarily for the purpose of acquiring FDA clearance—establishing the equivalence^{3,4} or superiority^{5,6} of a submaximal biphasic dose to a conventional monophasic first shock dose of 200 J. *At the time of market introduction, no clinical evidence existed for any biphasic defibrillator addressing the performance of its maximum available dose in more challenging clinical applications.* Moreover, there remains no clinical evidence indicating that any particular biphasic energy setting represents a clinically meaningful threshold—for the maximum defibrillation capability that might be useful in a challenging clinical situation, or for the maximum shock intensity that can safely be made available for use in various clinical applications.

As we considered how much defibrillation capability to design into our biphasic defibrillators, we recognized that 1) a significant track record of performance and expectations had accumulated specific to 360 J monophasic defibrillators, and 2) a wealth of existing scientific evidence indicated use of the maximum energy setting with a well-designed biphasic waveform would provide both better defibrillation efficacy and diminished risk of shock-related injury *with respect to this accumulated experience*. Medtronic thus concluded that despite the origins of the monophasic standard, use of 360 J as a maximum biphasic energy setting was in fact the most reasoned and responsible choice, and that use of any other maximum energy setting would raise additional questions that had yet—and still have yet—to be answered by clinical research.

Contention No. 2: “Low energy” biphasic waveforms are designed to perform better than the Medtronic biphasic waveform, and thus can achieve comparable efficacy with less energy in any clinical setting.

Direct evidence with which to evaluate this contention was lacking for several years, leaving room for both theoretical arguments and speculative extrapolation from the consistently high success rates observed in “ideal” electrophysiology lab studies.³⁻⁶ However, a spate of recently published evidence now solidly contradicts this assertion. To date, three independent randomized clinical studies have compared the efficacy of Medtronic and “low-energy” biphasic defibrillators for cardioversion of atrial fibrillation.⁷⁻⁹ Each study has found that across a wide range of energy settings, Medtronic biphasic shocks provide equivalent cardioversion success rates to shocks of the same energy setting from a “low energy” biphasic defibrillator. In addition, when the few patients failing cardioversion with one defibrillator were given a maximum energy shock from the other defibrillator, a majority of those failing 200 J “low energy” cardioversion could be converted with Medtronic 360 J shocks, but none of those failing Medtronic 360 J cardioversion could be converted with 200 J “low energy” shocks.

These clinical results are consistent with the findings of a recently published randomized experimental study.¹⁰ This study found that when defibrillation was difficult, the recommended first shock energy settings (120 J and 150 J) of “low energy” biphasic defibrillators did not match the efficacy of Medtronic 200 J first shocks, but rather provided significantly lower defibrillation efficacy. Thus while there is growing clinical evidence that lower energy shocks from any biphasic defibrillator are sufficient to treat a majority of patients, there is simultaneously growing evidence that in challenging defibrillation or cardioversion situations, lower energy shocks from “low energy” biphasic defibrillators can not always match the performance of higher energy Medtronic biphasic shocks.

Contention No. 3: “Low energy” biphasic maximum energy settings of 150 J to 200 J provide enough defibrillation capability to optimally treat all patients in all situations.

It is evident that “low energy” biphasic defibrillators can terminate atrial and ventricular fibrillation at rates equivalent to or modestly higher than the best monophasic defibrillators, and that in a large majority of patients, these efficacy rates are quite high. However, it is also evident that in more challenging clinical situations where the efficacy of lower energy biphasic shocks is less impressive, progressively higher defibrillation efficacy can be attained from biphasic shocks greater than 200 J. For example, a recent study in patients with refractory atrial fibrillation documented a 60% relative increase in cardioversion success (from 43% to 69%) when biphasic shock energy was increased from 200 J to 360 J.¹¹ Since the Medtronic biphasic shocks used in this study have independently been shown to provide equivalent success to shocks at equal energy settings from a “low energy” biphasic defibrillator,⁷⁻⁹ these data suggest that the defibrillation capability of “low energy” defibrillators would be far from optimal in these refractory atrial fibrillation patients. To date, the performance of “low energy” defibrillators in this challenging patient cohort has not been evaluated in any randomized clinical trial.

Preliminary data describing “low energy” biphasic defibrillator use by paramedics during advanced life support care of out-of-hospital cardiac arrest patients indicates that the rate of VF termination with a first shock (67%) leaves ample room for improvement.¹² These preliminary data point to another clinical setting where defibrillation may be more difficult than in the electrophysiology lab, and where it may be desirable to evaluate the capability of a defibrillator before it is pronounced “optimal”.

Contention No. 4: “Higher energy” biphasic shocks can cause more injury and result in more myocardial dysfunction than “lower energy” biphasic shocks.

The term “higher energy” has typically been arbitrarily defined as biphasic energy settings above 200 J, and it is important to recognize that this implied “injury threshold” is solely an artifact of clever marketing. There is no clinical evidence suggesting that 200 J, or for that matter any other biphasic energy setting, has any physiologic significance with respect to the risk of shock-induced injury and dysfunction. On the other hand, there is much scientific evidence that peak current intensity, rather than selected or delivered energy, is the pertinent characteristic of a defibrillation shock most correlated to any risk of shock-induced injury or dysfunction. In this respect, it is noteworthy that even though biphasic shocks were already known to be “safer” than monophasic shocks of the same intensity, Medtronic carefully designed its biphasic

waveform to use approximately 40% less peak current than a monophasic damped sine shock of the same energy. The result is a 360 J biphasic shock having roughly the same intensity as a 100 J monophasic damped sine shock, but providing substantially higher efficacy than even a 360 J monophasic damped sine shock.¹¹ In a recent experimental study, measurements of the peak intensity produced by external shocks were made directly inside the heart, confirming that at impedances typical of humans, the maximum intensity of 360 J Medtronic biphasic shocks is no different than the maximum intensity of 200 J shocks from "low energy" biphasic defibrillators.¹³

THE MEDTRONIC POSITION

As clinical experience with biphasic external defibrillation evolves, Medtronic is committed to being at the forefront of emerging clinical insights, and is dedicated to leading the industry in robust research directed at understanding and optimizing defibrillation performance for the benefit of clinicians as well as patients. No company has studied and documented the performance of its biphasic defibrillators in as wide a range of clinical and experimental settings as Medtronic. We are proud that our defibrillators offer the maximum range of energy settings, and the most flexibility in energy protocol configurations, so that existing devices can adapt to take best advantage of the ever-evolving insights from clinical research.

Emerging clinical data indicate the extended defibrillation capability of Medtronic's biphasic defibrillators may be useful and beneficial in some subsets of patients, while there remain no clinical data indicating there might be any harm in offering this enhanced biphasic defibrillation capability. Consequently, Medtronic will continue to provide users with defibrillators featuring the broadest available range of energy settings and the maximum available defibrillation capability. We intend to let clinical evidence, not speculation or marketing trends, shape our product offerings and device usage recommendations.

For further information please call Medtronic Physio-Control at 1.800.442.1142 or consult its Web site at medtronicphysiocontrol.com.

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Medtronic Physio-Control
11811 Willows Road NE
P.O. Box 97006
Redmond, WA 98073-9706 USA
Tel: 425.867.4000
Toll Free (USA Only): 800.442.1142
Fax: 425.867.4146
www.physiocontrol.com
www.medtronic.com

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