Literature Summary for HeartStart AEDs

The following pages list references for numerous studies completed to demonstrate the validity and effectiveness of the HeartStart AED technology. A brief conclusion is listed next to the reference. There is also a citation of the actual source or abstract for additional details.

The Philips HeartStart SMART Biphasic waveform is set apart from other waveforms by the sheer volume of research data available to support it. There are currently over a dozen peer reviewed manuscripts that have been published to support the SMART Biphasic waveform and at this time is the only biphasic waveform to have published data from out-of-hospital cardiac arrests to demonstrate its safety and effectiveness.

When reviewing studies on biphasic waveforms, it is important to understand which biphasic waveform or waveforms are being studied and in what environment. For example, the SMART Biphasic waveform uses a 100 µF capacitor in its design to store the energy that will be delivered to the patient whereas other manufacturers may use 200 µF capacitors. The value of the capacitor makes a significant difference in the amount of energy and the shape that the waveform must take in order to be effective. In addition, defibrillation models developed for animal studies must be proven in out-of-hospital cardiac arrest studies in order to validate the model. If the results of a defibrillation model with animals contradict the results of defibrillation studies with real people in sudden cardiac arrest, then the model is questionable and should be viewed with skepticism.

References

Animal Studies (peer-reviewed manuscripts)	Conclusions
Gliner BE, Lyster TE, Dillion SM, Bardy GH. Transthoracic defibrillation of swine with monophasic and biphasic waveforms. *Circulation* 1995; 92:1634-1643.	"This study demonstrates the superiority of truncated biphasic waveforms over truncated monophasic waveforms for transthoracic defibrillation of swine."
Xie J, Weil MH, Sun S, Tang W, Sato Y, Jin X, Bisera J. High-energy defibrillation increases the severity of postresuscitation myocardial dysfunction. *Circulation* 1997 Jul 15; 96(2):683-8.	"…we observed global myocardial dysfunction after cardiac resuscitation from VF, reminiscent of that observed after regional ischemia. The severity of postresuscitation myocardial dysfunction and the duration of survival corresponded to the magnitude of electrical energy that was delivered for the purposes of defibrillation."
Tang W, Weil MH, Sun S, Yamaguchi H, Povoas HP, Pernat AM, Bisera J. The effects of biphasic and monophasic waveform defibrillation on postresuscitation myocardial function. *JACC* 1999;34:815-822.	"Lower-energy biphasic waveform shocks were as effective as conventional higher energy monophasic waveform shocks for restoration of spontaneous circulation after 4 and 7 min. of untreated VF. Significantly better postresuscitation myocardial function was observed after biphasic waveform defibrillation."

Electrophysiology Laboratory and other studies (peer-reviewed manuscripts)	Conclusions
Bardy GH, Gliner BE, Kudenchuk PJ, Poole JE, Dolack GL, Jones GK, Anderson J, Troutman C, Johnson G. Truncated biphasic pulses for transthoracic defibrillation. *Circulation* 1995; 91: 1768-74.	"The results of this study suggest that biphasic truncated transthoracic shocks of low energy (115 and 130J) are as effective as 200-J damped sine wave shocks used in standard transthoracic defibrillators."
Bardy GH, Marchlinski FE, Sharma AD, Worley SJ, Luceri RM, Yee R, Halperin BD, Fellows CL, Ahern TS, Chilson DA, Packer DL, Wilber DJ, Mattioni TA, Reddy R, Kronmal RA, Lazzara R. Multicenter Comparison of Truncated Biphasic Shocks and Standard Dampled Sine Wave Monophasic Shocks for Transthoracic Ventricular Defibrillation. *Circulation* 1996; 94:2507-14.	"We found that 130-J biphasic truncated transthoracic shocks defibrillate as well as the 200-J monophasic damped sine wave shocks that are traditionally used in standard transthoracic defibrillators and result in fewer ECG abnormalities after the shock."
Ricard P, Lévy S, Boccara G, Lakhal E, Bardy G External cardioversion of atrial fibrillation: comparison of biphasic vs monophasic waveform shocks. *Europace* 2001; 3: 96-99.	"This study suggests that at the same energy level of 150J, biphasic impedance compensating waveform shocks are superior to monophasic damped sine waveform shocks cardioversion of atrial fibrillation."
Reddy, RK, Gleva MJ, Gliner BE, Dolack GL, Kudenchuk PJ, Poole JE, Bardy GH. Biphasic transthoracic defibrillation causes fewer ECG ST-Segment changes after shock *Ann. Emerg. Med.* 1997; 30:127-34.	"Transthoracic defibrillation with biphasic waveforms results in less postshock ECG evidence of myocardial dysfunction (injury or ischemia) than standard monophasic damped sine waveforms without compromise of defibrillation efficacy."
Gundry JW, Comess KA, DeRook FA, Jorgenson D, Bardy GH. Comparison of Naïve Sixth-grade Children with Trained Professionals in the Use of an Automated Eexternal Defibrillator. *Circulation* 1999; 100:1703-1707.	"During mock cardiac arrest, the speed of AED use by untrained children is only modestly slower than that of professionals. The difference between the groups is surprisingly small, considering the naivete of the children as untutored first-time users."

Sudden Cardiac Arrest (peer-reviewed manuscripts)	Conclusions
White RD. Early out-of-hospital experience with an impedance-compensating low-energy biphasic waveform automatic external defibrillator. *J Interventional Cardiac Electrophysiology.* 1997; 1:203-208.	"Impedance-compensating low-energy BTE waveforms incorporated into an AED terminated VF in OHCA (out-of-hospital cardiac arrest) patients with a conversion rate exceeding that reported with traditional higher energy monophasic waveforms. VF was terminated in all patients, including those with high impedance."

Sudden Cardiac Arrest (peer-reviewed manuscripts)	Conclusions
Poole JE, White RD, Kanz K-G, Hengstenberg F, Jarrard GT, Robinson JC, Santana V, McKenas DK, Rich N, Rosas S, Merritt S, Magnotto L, Gallagher JV, Gliner BE, Jorgenson DB, Morgan CB, Dillon SM, Kronmal RA, Bardy GH. Low-energy impedance-compensating biphasic waveforms terminate ventricular fibrillation at high rates in victims of out-of-hospital cardiac arrest. *J Cardiovasc Electrophysiol.* 1997; 8:1373-1385.	"The low-energy impedance-compensating BTE waveform used in this study's AED consistently terminated long-duration VF as encountered in OHCA. The observed defibrillation rate exceeds that of published studies on higher energy monophasic waveforms. Higher energy is not clinically warranted with this BTE waveform. The efficient user interface and high defibrillation efficacy of this low-energy biphasic waveform allows the AED to have device characteristics consistent with widespread deployment and early defibrillation."
Gliner BE, Jorgenson DB, Poole JE, White RD, Kanz K-G, Lyster TD, Leyde KW, Powers DJ, Morgan CB, Kronmal RA, Bardy GH. Treatment of out-of-hospital cardiac arrest with a low-energy impedance-compensating biphasic waveform automatic external defibrillator. *Biomedical Instrumentation & Technology.* 1998; 32:631-644.	"It is concluded that low-energy impedance-compensating biphasic waveforms terminate long-duration VF at high rates in out-of-hospital cardiac arrest and provide defibrillation rates exceeding those previously achieved with high-energy shocks."
Gliner BE, White RD. Electrocardiographic evaluation of defibrillation shocks delivered to out-of-hospital sudden cardiac arrest patients. *Resuscitation* 1999 Jul;41(2):133-44.	"At each analysis time, there were more patients in VF following high-energy monophasic shocks than following low-energy biphasic shocks. ….we recommend that defibrillation should uniformly be defined as termination of VF for a minimum of 5-s after shock delivery. Rhythms should be reported at 5-s after shock delivery to assess early effects of the defibrillation shock and at 60-s after shock delivery to assess the interaction of the defibrillation therapy and factors, such as post-shock myocardial dysfunction and the patient's underlying cardiac disease."
Schneider T, Martens PR, Paschen H, Kuisma M, Wolcke B, Gliner BE, Russell JK, Weaver WD, Bossaert L, Chamberlain D Multicenter, randomized, controlled trial of 150-J biphasic shocks compared with 200- to 360-J monophasic shocks in the resuscitation of out-of-hospital cardiac arrest victims. *Circulation* 2000 Oct 10; 102(15): 1780-7.	"In summary, the results of the present study show that an appropriately dosed low-energy impedance-compensating biphasic-waveform strategy results in superior defibrillation performance in comparison with escalating, high-energy monophasic shocks in out-of hospital cardiac arrest. Moreover, the 150-J biphasic waveform AED resulted in a higher rate of ROSC and better neurological status at the time of hospital discharge."

Sudden Cardiac Arrest (peer-reviewed manuscripts)	Conclusions
Page RL, Joglar JA, Kowal RC, Zagrodzky JD, Nelson LL, Ramaswamy K, Barbera SJ, Hamdan MH, McKenas DK. Use of automated external defibrillators by a U.S. airline. *NEJM* 2000; 343:1210-1216.	"The use of the automated external defibrillator aboard commercial aircraft is effective, with an excellent rate of survival to discharge from the hospital after conversion of ventricular fibrillation. There are not likely to be complications when the device is used as a monitor in the absence of ventricular fibrillation."
Martens PR, Russell JK, Wolcke B, Paschen H, Kuisma M, Gliner BE, Weaver WD, Gossaert L, Chamberlain D, Schneider T. Optimal Response to Cardiac Arrest Study: Defibrillation Waveform Effects. *Resuscitation* 2001; 49:233-243.	"A low-energy impedance-compensating biphasic waveform strategy results in superior defibrillation performance, in terms of first shock efficacy and defibrillation in the first set of two or three shocks, when compared to traditional escalating energy monophasic defibrillators of both MTE and MDS design. The biphasic devices were also quicker to first shock and to first successful shock."
White RD, Hankins DE, Atkinson EJ. Patient Outcomes Following Defibrillation With a Low Energy Biphasic Truncated Exponential Waveform in Out-of-Hospital Cardiac Arrest. *Resuscitation* 2001; 49:9-14.	"Low-energy (150J) non-escalating biphasic truncated exponential waveform shocks terminate VF in out-of-hospital cardiac arrest with high efficacy; patient outcome is comparable with that observed with escalating high-energy monophasic shocks."

Animal Studies (abstracts)	Conclusions
Tang W, Weil MH, Sun Shijie, et.al. Defibrillation with low-energy biphasic waveform reduces the severity of post-resuscitation myocardial dysfunction after prolonged cardiac arrest. *J Crit Care Med* 1999;27:A43	"Low-energy biphasic waveform was as effective as monophasic waveform for successful defibrillation after 7 minutes of untreated VF but produced significantly less post-resuscitation myocardial dysfunction."
Tang W, Weil MH, Klouche K, et.al. Effects of low- and higher-energy biphasic waveform defibrillation on success of resuscitation and post-resuscitation myocardial function. *Circulation* (suppl)1999;100(18):I-662(Abstract #3491).	"We conclude that low energy biphasic shocks increase the likelihood of successful defibrillation and minimize post resuscitation myocardial dysfunction after prolonged cardiac arrest."
Tang W, Weil MH, Klouche K, et.al. Low capacitance biphasic waveform shocks improve immediate resuscitation after prolonged cardiac arrest. *Circulation* (suppl)1999;100(18):I-663(Abstract #3493).	"Low-capacitance biphasic defibrillation therefore significantly improved the success of initial resuscitation but not post resuscitation myocardial function after prolonged cardiac arrest."

Out-of-Hospital Study (abstract)	Conclusions
Snyder D, Lyster T. Performance of an Automatic External Defibrillator in the Presence of Implanted Pacemaker Artifact. *Circulation* (suppl)1998; 98(17):I-411 (Abstract #2163)	"A new AED shock advisory algorithm achieves excellent rhythm detection specificity and VF/VT sensitivity in the presence of pacemaker artifact."

Related Papers and Publications	Conclusions
Gurnett CA, Atkins DL. Successful use of a biphasic waveform automated external defibrillator in a high-risk child. *Am J Cardiol* 2000 Nov 1;86(9):1051-3.	"This case report suggests that in young children, defibrillation can be accomplished and risk of myocardial damage using currently available truncated biphasic waveform defibrillation may be small."
Cecchin F, et al. Is Arrhythmia Detection by Automatic External Defibrillator Accurate for Children?. *Circulation*. 2001; 103:2483-2488.	"There was excellent AED rhythm analysis sensitivity and specificity in all age groups for ventricular fibrillation and nonshockable rhythms. The high specificity and sensitivity indicate that there is a very low risk of an inappropriate shock and that the AED correctly identifies shockable rhythms, making the algorithm both safe and effective for children."
American Heart Association Task Force on Automatic External Defibrillation, Subcommittee on AED Safety and Efficacy. AHA Scientific Statement. Automatic external defibrillators for public access defibrillation: Recommendations for specifying and reporting arrhythmia analysis algorithm performance, incorporating new waveforms, and enhancing safety. *Circulation* 1997;95:1277-1281.	Summary: "These recommendations are presented to enhance the safety and efficacy of AEDs intended for public access. The task force recommends that manufacturers present developmental and validation data on their own devices, emphasizing high sensitivity for shockable rhythms and high specificity for nonshockable rhythms. Alternate defibrillation waveforms may reduce energy requirements, reducing the size and weight of the device."
Cummins R, et.al. Low-Energy Biphasic Waveform Defibrillation: Evidence-Based Review Applied to Emergency Cardiovascular Care Guidelines: A Statement for Healthcare Professionals from the American Heart Association Committee on Emergency Cardiovascular Care and the Subcommittees on Basic Life Support, Advanced Cardiac Life Support, and Pediatric Resuscitation. *Circulation*, 1998; 97:1654-1667.	"Positive evidence supports a statement that initial low-energy (150J), nonprogressive (150J-150J-150J), impedance-adjusted biphasic waveform shocks for patients in out-of-hospital VF arrest are safe, acceptable, and clinically effective."

Related Papers and Publications	Conclusions
American Heart Association. *Guidelines 2000 for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care*. August, 2000	In reference to SMART Biphasic waveform: "The growing body of evidence is now considered sufficient to support a Class IIa recommendation for this low energy, BTE waveform." (I-63) Class IIa defined as: "Good to very good evidence", a "standard of care", "intervention of choice" (I-5) "At this time no studies have reported experience with other biphasic waveforms in long-duration VF…"(I-63) "When such data becomes available it will need to be assessed by the same evidence-evaluation process..." (I-63) "The safety and efficacy data related to specific biphasic waveforms must be evaluated on an individual basis in both in-hospital (electrophysiology studies, ICD testing) and out-of-hospital settings." (I-63)
ECRI. External Biphasic Defibrillators. Should You Catch the Wave? *Health Devices* 2001;30:219-225.	"It is likely that the optimal energy level for biphasic defibrillators will vary with the units' waveform characteristics. An appropriate energy dose for one biphasic waveform may be inappropriate for another. … So it's necessary to refer to the supplier's recommendations to determine the proper energies to be used for a given waveform."
Jordan D. The fundamentals of automated external defibrillators. *Biomedical Instrumentation and Technology* 2003;37:55-59.	General article about automated external defibrillators and the technology used to design and build them.

Study Summaries

HeartStart Defibrillation Therapy Testing in Adult Victims of Out-of-Hospital Cardiac Arrest

Introduction

The HeartStart FR2 utilizes the patented SMART Biphasic waveform. This waveform has been extensively tested in pre-clinical and both electrophysiology laboratory and out-of-hospital clinical studies. The following information summarizes the results of a large study comparing the use of SMART Biphasic AEDs to conventional monophasic in out-of-hospital emergency resuscitation situations.

Background

Heartstream conducted an international, multicenter, prospective, randomized clinical study to assess the effectiveness of the SMART Biphasic waveform in out-of-hospital sudden cardiac arrests (SCAs) as compared to monophasic waveforms. The primary objective of the study was to compare the percent of patients with ventricular fibrillation (VF) as the initial monitored rhythm that were defibrillated in the first series of three shocks or fewer.

Methods

Victims of out-of-hospital SCA were prospectively enrolled in four emergency medical service (EMS) systems. Responders used either 150 J SMART Biphasic AEDs or 200-360 J monophasic waveform AEDs. A sequence of up to three defibrillation shocks was delivered. For the biphasic AEDs there was a single energy output of 150 J for all shocks. For monophasic AEDs, the shock sequence was 200-200-360 J. Defibrillation was defined as termination of VF for at least five seconds, without regard to hemodynamic factors.

Results

Randomization to the use of monophasic or SMART Biphasic AEDs was done in 338 SCAs from four emergency medical service systems. VF was observed as the first monitored rhythm in 115 patients. The biphasic and monophasic groups for these 115 patients were similar in terms of age, sex, weight, primary structural heart disease, cause and location of arrest, and bystanders witnessing the arrest or performing CPR.

The 150 J SMART Biphasic waveform defibrillated 98% of VF patients in the first series of three shocks or fewer compared with 69% of patients treated with monophasic waveform shocks. Outcomes are summarized as follows:

	SMART biphasic patients number (%)	monophasic patients number (%)	P value (chi square)
defibrillation efficacy			
single shock only	52/54 (96%)	36/61 (59%)	<0.0001
</= 2 shocks	52/54 (96%)	39/61 (64%)	<0.0001
</= 3 shocks	53/54 (98%)	42/61 (69%)	<0.0001
patients defibrillated	54/54 (100%)	49/58 (84%)	0.003
ROSC	41/54 (76%)	33/61 (54%)	0.01
survival to hospital admission	33/54 (61%)	31/61 (51%)	0.27
survival to hospital discharge	15/54 (28%)	19/61 (31%)	0.69
CPC = 1 (good)	13/15 (87%)	10/19 (53%)	0.04

Conclusions

The 150 J SMART Biphasic waveform defibrillated at higher rates than the 200-360 J monophasic waveforms, resulting in more patients achieving return of spontaneous circulation (ROSC) (p=0.01). EMS system outcomes of survival discharge were not significantly different statistically. However, patients resuscitated with the lower-energy SMART Biphasic waveform were more likely to have good cerebral performance (CPC, cerebral performance category) (p=0.04).

HeartStart Patient Analysis System Testing with Pediatric Rhythms

Background

Heartstream sponsored a multicenter study to develop an ECG database of shockable and non-shockable rhythms from a broad range of pediatric patients and then test the accuracy of the HeartStart Patient Analysis System (PAS) for sensitivity and specificity with those rhythms.

Methods

Two sources were used for the database: (1) RECORDED DATA, a clinical study where rhythms were recorded from pediatric patients via a modified ForeRunner AED and (2) DIGITIZED DATA, a collection of infrequently observed shockable pediatric rhythms, solicited from pediatric electrophysiologists worldwide, that had been captured on paper and were subsequently digitized. The study resulted in a database of 697 rhythm segments from 191 patients, collected from four investigational sites. The children were divided into three groups according to age: up to 1 year, greater than 1 year and less than 8 years and 8 years through 12 years. The demographic characteristics for the three groups are displayed in Tables 1 and 2 for the recorded and digitized groups, respectively. Patient enrollment was initiated on October 2, 1998, and patient enrollment concluded on August 28, 1999.

Table 1. Recorded Rhythms

age group (n)	median age (range)	median weight (range)	gender (m/f)
≤1 year (59)	90 days (1 day–1 yr)	4.7 kg (2.1-10.1 kg)	40/19
>1 <8 years (40)	3 yrs (1.1-7 yrs)	15.5 kg (7.6-38.0 kg)	20/20
≥8 ≤12 years (35)	9 yrs (8-12 yrs)	34.2 kg (22.0-70.7 kg)	21/14
Total (134)	1.8 yrs	10.0 kg	81/53

Table 2. Digitized Rhythms

age group (n)	median age (range)	median weight (range)	gender (m/f)
≤1 year (15)	0.5 yr (16 days – 1 yr)	6.8 kg (3.0-9.1 kg)	7/8
>1 <8 years (22)	5.0 yrs (1.2-7.7 yrs)	16.8 kg (10-31 kg)	10/12
≥8 ≤12 years (20)	10.9 yrs (8-12 yrs)	43 kg (24-61.4 kg)	12/8
Total (57)	6.0 yrs	18.0 kg	29/28

Results

The results of this study are provided in Table 3. The "AHA goal" columns refer to the American Heart Association's performance goals for AED algorithms, which were established for adults. Although the scope of these performance goals does not apply to pediatric patients, the values are provided here for reference.

Table 3. Pooled Rhythms Sensitivity and Specificity
n (%) and Lower Confidence Limits

rhythm	sensitivity	specificity	AHA goal	90% one-sided LCL[1]	AHA LCL goal
VF	73 (95.9%)	NA	>90%	91.1%	87%
VT, rapid	58 (70.7%)	NA	>75%	61.7%	67%
SR	NA	173 (100%)	>99%	98.7%	97%
SVA	NA	116 (100%)	>95%	98.0%	88%
VEB	NA	95 (100%)	>95%	97.6%	88%
idio	NA	40 (100%)	>95%	94.4%	88%
asystole	NA	39 (100%)	>95%	94.3%	92%

1 Armitage P and Berry G, *Statistical Methods in Medical Research*, Blackwell Scientific Publications, 2nd edition, 1987.

This study demonstrated that the HeartStart PAS has excellent sensitivity to pediatric VF rhythms (95.9%), and excellent specificity for all non-shockable rhythms (100%). The AHA sensitivity and specificity performance goals as stated for adult patients were met in all pediatric rhythm categories except for rapid VT, where sensitivity is slightly lower (70.7% vs. 75%). Although the adult performance goal was missed for this group, a conservative approach in this rhythm category for pediatric patients is appropriate due to both the higher uncertainty of association of pediatric tachycardias with cardiac arrest, and the low rate of presenting VT occurrence in the out-of-hospital setting. Further, non-perfusing tachycardias are likely to rapidly degenerate into VF. With regard to the intermediate rhythm group in which the benefits of defibrillation are limited or uncertain, the PAS was appropriately conservative, tending not to advise shocks. Importantly, these data show that the PAS is highly unlikely to inappropriately shock a pediatric rhythm. This is important in light of safety concerns for the use of an automated external defibrillator with children. This study indicates that the HeartStart Patient Analysis System can be used safely and effectively for both adults and children.

HeartStart Defibrillation Therapy Testing in a Pediatric Animal Model

Background

The FR2 AED with attenuated defibrillation pads delivers at least a 2 J/kg dose in the intended patient population, based on United States Center for Disease Control growth charts. Two animal studies were conducted to demonstrate the safety and effectiveness of the Heartstream biphasic waveform at 50 J in a pediatric animal model across the weight range of the intended patient population.

Methods

The first study utilized a research AED capable of delivering the Heartstream impedance-compensating biphasic waveform at a 50 J energy setting in 20 pigs in four weight categories ranging from 3.5 to 25 kg and corresponding to weights of human newborn, six month, three year and eight year old patients. The pigs in the smallest group were just over two weeks old. The second study utilized prototype attenuated electrodes with an FR2 AED in nine additional animals in three of the weight categories, including 3.5 and 25 kg weight groups. In both studies, VF was induced in the pigs, and allowed to be sustained for seven minutes prior to delivery of up to three shocks using a fixed 50 J Heartstream biphasic waveform.

A porcine model was used for these studies, because the chest configuration, anatomy and physiology of the porcine cardiovascular and pulmonary systems are similar to humans. In addition, prior studies have shown that pigs require higher energy dose per kilogram than humans and therefore they present a good “worst case” model for defibrillation effectiveness.

Results

In both studies, all animals across all weight categories were successfully resuscitated with fixed, 50 J Heartstream biphasic shocks, and all survived for the duration of the follow-up period (up to 72 hours). The results showed that the delivered peak currents were close to those expected for human pediatric patients. These studies showed no difference in hemoglobin and oxyhemoglobin, blood gas measurements, arterial lactate, end-tidal CO_2, pulmonary artery pressure, right atrium pressure, calculated coronary perfusion pressure and neurological alertness among the groups prior to arrest and after successful resuscitation. There was no difference in post-resuscitation myocardial function as measured by echocardiographic ejection fraction and fractional area change among the groups. Stroke volume, cardiac output and left ventricular volumes returned to baseline values within 120 minutes after successful resuscitation in all groups.

These studies demonstrated that fixed 50 J Heartstream biphasic waveform shocks successfully resuscitated pigs ranging from 3.5 to 25 kg regardless of weight. All animals survived and there was no evidence of compromised post-resuscitation systolic or diastolic myocardial function.