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January 13, 2006

Pam Douglas, MD, FACC
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c/o Rebecca Kelly, Director of Regulatory Affairs
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RE: The CMS proposed decision to deny expansion of coverage for external counterpulsation therapy to include patients with CCS Class II angina and stable NYHA Class II/III heart failure with an EF≤35%.

Dear Dr. Douglas:

As clinicians participating in the International EECP Patient Registry (IEPR), we are writing to request your support of the application to the Centers for Medicare and Medicaid Services (CMS) for expansion of reimbursement coverage of external counterpulsation therapy. This low-cost, noninvasive, safe and effective therapy has amply demonstrated the ability to provide benefit in patients with ischemic heart disease diagnosed with angina or heart failure; especially those not benefiting from more commonly used therapies.

The IEPR is a patient registry sponsored by Vasomedical, Inc. that enrolls consecutive patients undergoing enhanced external counterpulsation (EECP) therapy for chronic angina. The Epidemiology Data Center at the University of Pittsburgh acts as Coordinating Center for the IEPR and performs data management, analysis and reporting tasks. We, a group of practicing cardiologists/investigators whose institutions participate in the registry, manage its scientific affairs. We give direction to the scientific endeavors of the registry and decide on matters of patient protection and confidentiality, data elements appropriate for collection, and topics for reporting of the information contained in the registry database. Each of us has been responsible for a clinical EECP program at our institutions and we have authored the majority of peer-reviewed, published reports based upon IEPR data.

The IEPR began in January 1998, and more than 7,500 patients have been enrolled from >100 centers in the United States and other countries. The IEPR aims to collect data on as broad a range of consecutive patients as possible and the criteria for entry are only that the patient give informed consent and have undergone at least 1 hour of EECP treatment for chronic angina. An initial phase (IEPR-1) collected data on >5,000 patients enrolled between 1998 and 2001 who were followed for 3 years. An additional 2,500 patients were enrolled in a second phase (IEPR-2) between 2002 and 2004 and follow-up on these patients is ongoing.

Briefly, methods in IEPR-1 involved collecting patient demographics, medical history, coronary disease status, and quality-of-life assessments before EECP treatment. After 35 hours of standard EECP treatment (the IEPR only collects data on patients treated with Vasomedical equipment), data were collected on Canadian Cardiovascular Society Classification (CCSC) of anginal status, anti-anginal medication use, and adverse clinical events. Quality-of-life assessment was performed using 5-point scales for health status, quality-of-life, and satisfaction with quality-of-life. Patients were interviewed by telephone 6 months after their last EECP treatment session, and yearly thereafter to record anginal status, quality-of-life, and cardiac events.

Data elements captured by the IEPR changed during the transition from IEPR-1 to IEPR-2, principally to give greater focus to clinical outcomes data and to capture symptom and quality-of-life status specific to patients with a coexisting diagnosis of heart failure. Quality-of-life assessments are performed using validated instruments (Duke Activity Status Index and Kansas City Cardiomyopathy Questionnaire). Site participation is limited to those sites that maintain at least 90% compliance with data submission and, to date, overall compliance in IEPR-2 is greater than 90% at all time points.

More information about the IEPR is available at http://www.edc.gsph.pitt.edu/iepr, including a complete bibliography of published reports and abstracts. To date, seventeen peer-reviewed publications of IEPR data have appeared in the medical literature and several more are in the development phase. Many abstracts and posters have been presented at major cardiology scientific meetings in an effort to disseminate information about external counterpulsation therapy as widely as possible.

Barsness *et al* authored the first report on behalf of the IEPR investigators, published in 2001.[1] The study was undertaken to determine whether EECP is a safe and effective treatment for patients with angina pectoris regardless of their suitability for revascularization by more conventional techniques. Forty-three clinical centers contributed cases, representing over half of all EECP provider sites at that time. The data reported on 978 patients demonstrated that EECP could be administered to patients ineligible for either coronary artery bypass graft (CABG) surgery or percutaneous coronary intervention (PCI), as well as for those who prefer noninvasive treatment to avoid or delay revascularization. Patients enrolled were of all CCS angina classes at baseline (Class I, 5.5%; Class II, 24.8%; Class III, 48.1%, Class IV 21.6%; unstable, 2.8%), and 62% used nitroglycerin. A very high percentage (81%) had been previously revascularized, and most (69%) were considered unsuitable for either PCI or CABG at the time of starting EECP. Eighty-six percent of the patients completed a full treatment course, of which 81% reported improvement of at least one angina class immediately after the last treatment.

More recently, Michaels *et al* reported the long-term (2-year) results obtained in patients enrolled in IEPR-1.[2] A reduction in CCS angina class of ≥1 class was achieved in approximately three-quarters of patients studied (73% of 1,097 patients) and quality-of-life improvements were seen in more than half. These results were sustained at 2-year follow-up, with nearly half having no (29.7%) or class I (18.4%) angina and 74.9% having a lower angina class compared to baseline. Medication usage was similar at all time points, except for a decreased usage of short-acting nitrates. Additional therapies were performed after EECP at relatively low rates (PCI=11%, CABG=5.2%, repeat EECP=16.1%).

The reduction in angina symptoms is not restricted to those with Class III or IV angina. A study by Lawson *et al* to be published shortly in Clinical Cardiology, evaluated the immediate response, durability and clinical events over a two-year period after treatment with EECP in 112 patients with Class II angina.[3] Reduced angina was observed in 68% of patients immediately post-treatment and the effect was maintained up to 2 years in 70% of patients. There were concomitant reduced rates of nitroglycerin use, and quality-of-life was improved. The rate of major cardiovascular events was low. These results suggest that EECP is an attractive consideration for treating patients with milder refractory angina.

Investigators noted early on that patients enrolled in the IEPR had long-standing, advanced coronary artery disease with multiple risk factors and most had undergone prior interventions in attempts to revascularize their coronary vessels. Many of the patients suffered from significant co-morbid disease, such as diabetes, hypertension, non-cardiac vascular disease and heart failure. Several publications from the IEPR have focused on the results obtained in these patient sub-groups (a copy of the IEPR bibliography is attached). The level of diastolic augmentation achieved and its relationship to changes in patient outcomes has been reported on two occasions, and investigators reported on other predictors of patient outcomes on two occasions as well.

Linnemeier *et al* reported on the outcomes seen in the elderly population treated with EECP therapy and found that octogenarians could be safely and effectively treated with this technique.[4] Of 3,037 patients analyzed, 249 (8%) were ≥80 years old. As a group, they were more likely to be female and have a history of congestive heart failure (41% vs. 29%; $p<0.001$) and were less likely to have had previous revascularization. Fewer of the elderly (76% vs. 84%; $p<0.01$) completed a full course of treatment, but of those who completed treatment, 76% reported a reduction in angina and their quality-of-life improved significantly. Treatment-related adverse events were infrequent and 81% reported maintenance of angina improvement at 6-month follow-up. The authors concluded that enhanced external counterpulsation is a low-risk intervention offering elderly patients the ability to return to more normal activity and a better quality-of-life.

Early on, investigators became interested in the effects of EECP therapy in patients with coexisting heart failure[5] or left ventricular dysfunction,[6] since substantial portions of the overall IEPR population suffered from those conditions and there was uncertainty as to the safety of external counterpulsation therapy in such patients.

A report by Soran *et al,* just now appearing in print, examines the results obtained with EECP therapy at 2-year follow-up in a cohort of 363 patients with refractory angina who

had severe left ventricular dysfunction (EF≤35%).[7] Average duration of coronary artery disease was nearly 13 years and 84% had multi-vessel disease. Ninety-three percent were not candidates for further revascularization due to the extent and severity of disease, LV dysfunction, co-morbid conditions, prior interventions, or risk/benefit ratio. Cardiac risk factors were prevalent in most and 93% presented with severe angina (Class III/IV), with over 50% reporting poor quality-of-life. After completion of treatment there was a significant reduction in severity of angina ($p< 0.001$). Seventy-seven percent of patients decreased by ≥1 angina class, 18% had no angina, and only 2% had an increase in angina class. The mean number of weekly angina episodes decreased by 8.2 ($p<0.001$) and of those taking as needed nitroglycerin, 52% discontinued its use after EECP. Quality-of-life also showed a significant increase ($p<0.001$).

At two-years, 83% survived and the event-free survival rate was 70%. Forty-three percent had no cardiac hospitalization and 81% had no CHF event. Comparing the patients who showed no angina improvement to those who did show reduction in angina there was no difference in major adverse cardiovascular events at 2 years however, those who showed no initial response did report significantly more unstable angina in the 2-year period (28% vs. 16%, $p=0.02$). Survival at 2-year follow-up was less likely in those failing to complete treatment compared to those who completed the treatment (71% vs. 85%, $p<0.001$). Reduction in angina class was sustained in 55% of survivors compared to post-EECP status and the improvement in quality-of-life was maintained as well.

A very recent analysis of data from the IEPR indicates that EECP therapy has the potential to reduce health care resource utilization in refractory angina patients with severe left ventricular dysfunction. Soran *et al* presented an abstract at the European Society of Cardiology – Heart Failure meeting held in Lisbon, Portugal, in June of 2005 entitled "Does Enhanced External Counterpulsation Treatment Reduce Emergency Room Visits and Hospitalizations in Refractory Angina Patients With Left Ventricular Dysfunction? A Six Month Follow up Study." This report was designed to assess whether improvements observed in symptoms in such patients correlate with a reduction in emergency room (ER) visits and hospitalizations. One hundred fifty-four patients undergoing EECP therapy and enrolled in the IEPR were studied. Clinical outcomes, number of ER visits and hospitalizations within the six months prior to EECP were compared with those at 6-month follow-up. Consistent with other reports, symptomatic and quality-of-life improvements were seen immediately after and again at 6 months after completion of therapy in this cohort of patients with very advanced CAD, multiple cardiac risk factors, and high prevalence of prior MI and prior PCI or CABG.

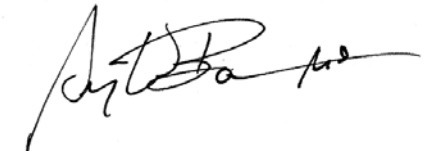
Forty-seven percent of patients had at least 1 ER visit and 63% had at least 1 hospitalization in the 6 months prior to EECP. Importantly, following treatment, the mean number of ER visits was reduced from 0.7±1.0 pre-EECP to 0.1±0.3 at six months ($p<0.001$) and hospitalizations were reduced from 1.2±1.7 to 0.2±0.5 ($p<0.001$). This represents an 86% and 83% relative reduction in the rate of ER visits and hospitalizations. A manuscript reporting updated results in detail is nearing completion.

We believe that the results observed in large numbers of patients enrolled in IEPR confirm the beneficial results seen in the two randomized, controlled trials of EECP therapy, namely the MUST-EECP trial in patients with chronic, stable angina, and the PEECH trial

in chronic, stable systolic heart failure patients with mild-to-moderate symptoms. In addition to our activities with the IEPR, we have conducted independent investigations of this therapy and consistently observe that the benefit-to-risk ratio is high. EECP therapy is used today most often in patients who have tried many other options and have not obtained the improvements in symptom status or capacity to function on a daily basis that they are seeking. At a minimum, we recommend that it be made available on that basis to patients with Class II angina and Class II/III heart failure.

Thank you for your consideration; we look forward to your response.

Sincerely,



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January 20, 2006

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Deirdre O'Connor MS
Coverage and Analysis Group
Centers for Medicare and Medicaid Services
7500 Security Blvd.
Baltimore, MD 21244

Subject: **Comments on Proposed Decision Memo External Counterpulsation (ECP) Therapy (CAG-00002R2), posted December 20, 2005**

Dear Dr. Schafer and Ms. O'Connor:

Vasomedical, Inc., appreciates the opportunity to comment on the proposed decision memorandum (proposed decision memo) for external counterpulsation (ECP) therapy published December 20, 2005. CMS requests comment on its proposed determination that the evidence is not adequate to conclude that ECP therapy is reasonable and necessary for:

- Canadian Cardiovascular Society Classification (CCSC) II angina
- Heart Failure
  - New York Heart Association Class II/III stable heart failure symptoms with an ejection fraction (EF) of $\leq$ 35%
  - New York Heart Association Class II/III stable heart failure symptoms with an EF of $\leq$ 40%
  - New York Heart Association Class IV heart failure
  - Acute heart failure
- Cardiogenic shock
- Acute myocardial infarction

We remind CMS that our initial application only included a request for consideration of expansion to include patients with CCS Class II angina and with stable, NYHA Class II/III heart failure with an ejection fraction $\leq$ 35%. Also, references to EECP therapy pertain to external counterpulsation therapy administered with Vasomedical's proprietary ECP therapy systems.

Our specific comments include the following:

1. The evidence is sufficient to conclude that EECP therapy results in net health benefits in patients age 65 years or older with a diagnosis of stable, chronic heart failure of ischemic etiology, with an ejection fraction of ≤ 35% and symptoms consistent with NYHA class II or III, who are not adequately responding to or tolerating optimal heart failure therapy.

2. EECP therapy has demonstrated effectiveness and safety in patients with ischemic heart disease in over 50 peer-reviewed publications, and has recently been shown to be effective in patients with left ventricular systolic dysfunction and in heart failure NYHA class II and III with ischemic etiology.

3. The evidence is sufficient to conclude that EECP therapy provides net health benefits for patients with Canadian Cardiovascular Society Classification (CCSC) II angina.

4. Endpoints used in studies of EECP therapy adequately demonstrate improvement in measures of morbidity as well as symptom status and quality of life, supporting the conclusion of net health benefits from the therapy.

5. Changes in physiologic measures, such as peak VO_2, exercise duration, peripheral vascular reactivity, neurohormonal markers, indices of perfusion and cardiac hemodynamics support the conclusion that outcomes observed in patients treated with EECP therapy are primarily due to treatment effects and not to a placebo effect.

6. EECP is a highly cost-effective therapy for patients with chronic stable angina and heart failure and this information should be appropriately considered when evaluating the sufficiency of the evidence for external counterpulsation therapy.

7. Based upon consideration of the information contained in CMS' proposed decision memo and upon further analysis of the data regarding the use of EECP therapy in patients with heart failure, we are modifying our proposal for expansion of coverage for ECP to include patients as follows:

   <u>Patients age 65 years or older with a diagnosis of stable, chronic heart failure of ischemic etiology, with an ejection fraction of ≤ 35% and symptoms consistent with NYHA class II or III, who are not adequately responding to or tolerating optimal heart failure therapy.</u>

   We set forth greater detail on each of these points below.

* * *

1. **The evidence is sufficient to conclude that EECP therapy results in net health benefits in patients age 65 years or older with a diagnosis of stable, chronic heart failure of ischemic etiology, with an ejection fraction of ≤ 35% and symptoms consistent with NYHA class II or III, who are not adequately responding to or tolerating optimal heart failure therapy.**

High quality evidence from the recently concluded PEECH trial of EECP therapy demonstrates that EECP is beneficial in stable, chronic heart failure patients, NYHA Class II/III with an ejection fraction ≤ 35%, and particularly in the sub-group of patients age 65 years of age or older. CMS notes on page 5 of 31 of the proposed decision memo that:

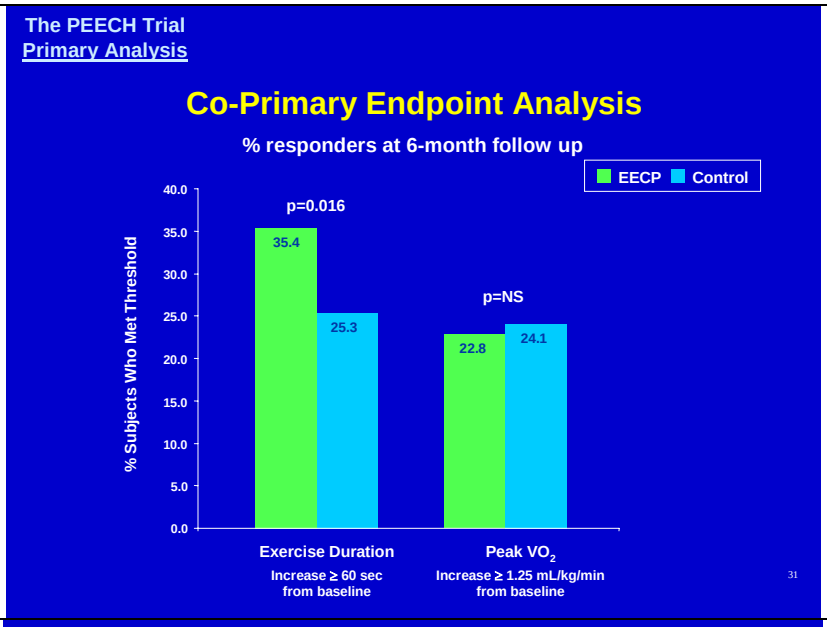
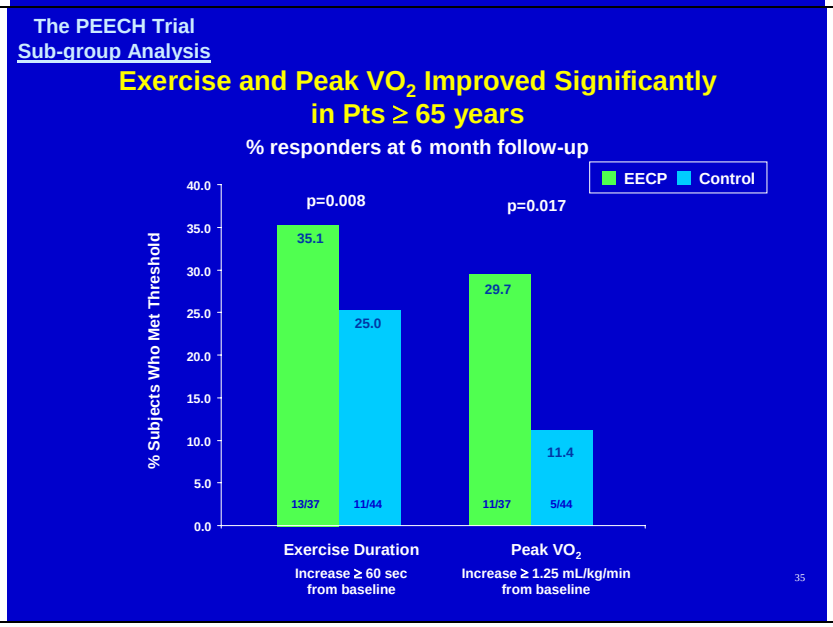
> "[r]igorous research design leads to the most convincing and dependable outcome results. A randomized trial best demonstrates the effectiveness of an intervention, serving to protect against bias . . . in the assignment process, and assuring that the degree of baseline comparability for the unobserved variable is the same as for the observed variable."

A manuscript reporting the results of the PEECH trial authored by Feldman AM, Silver MA, Francis GS, *et al* entitled "Enhanced External Counterpulsation Improves Exercise Tolerance in Patients with Chronic Heart Failure" was accepted for publication in a major, peer-reviewed cardiology journal in October, 2005, and we anticipate that it will be published soon.

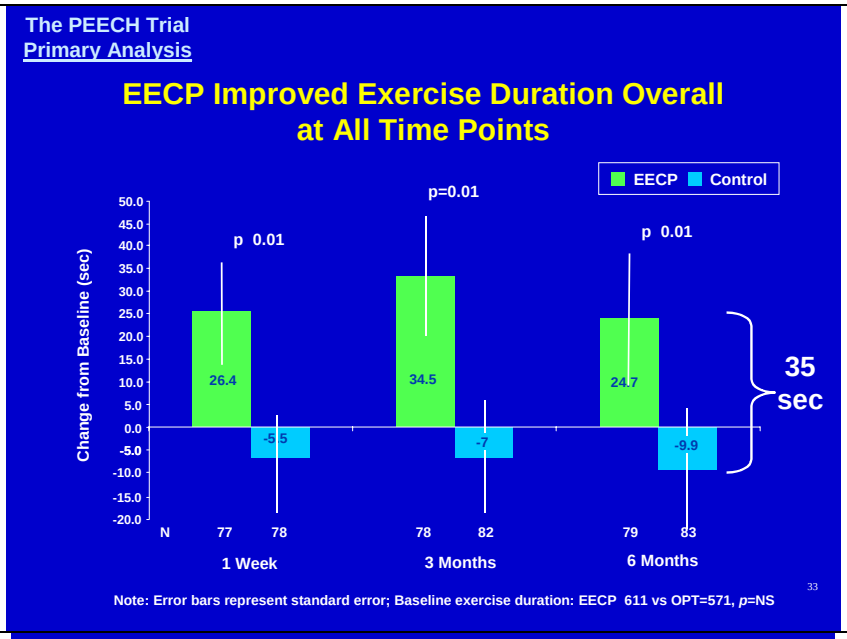
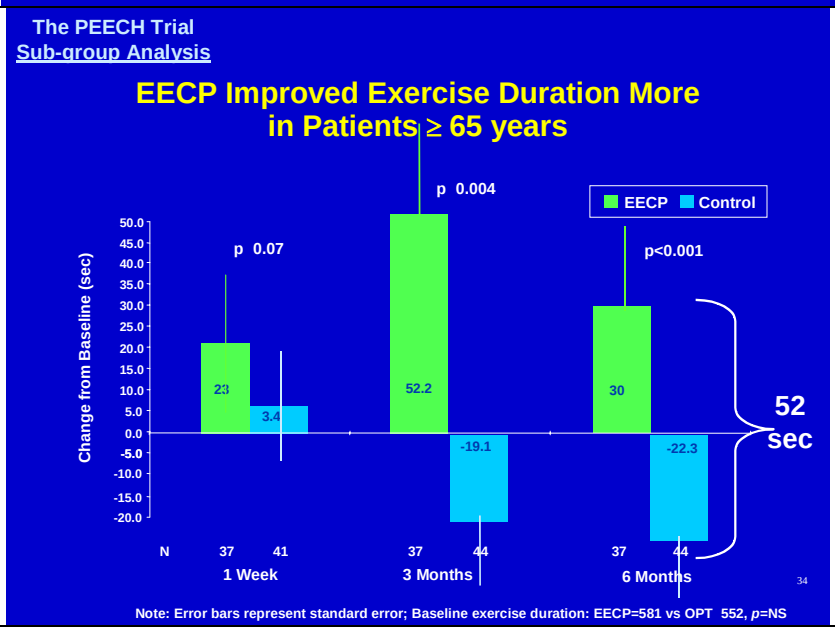
The PEECH trial was a prospective, randomized, multicenter trial of 187 patients with NYHA class II/III stable heart failure and an EF ≤ 35%, randomized to either EECP and optimal pharmacologic therapy (OPT) or OPT alone. Two co-primary endpoints were predefined: the percentage of subjects with an increase in exercise duration of 60 seconds or more and the percentage of subjects with an increase in peak VO_2 of 1.25 ml/min/kg or more, comparing results at six months follow-up to those at baseline. The trial was designed to be a positive study if either co-primary endpoint achieved a p-value < 0.025 or if both achieved a p-value < 0.05.

By the primary intent to treat analysis, PEECH was a positive clinical trial, as the between-group difference in the percentage of patients achieving the pre-specified increase in exercise duration was significant at $p = 0.016$ (Figure 1a). There was no difference detected in the percentage of subjects achieving the pre-specified increase in peak VO_2 (p = NS). Secondary endpoints for NYHA classification, exercise capacity, and quality of life were significantly improved relative to OPT alone. Additional information regarding results of the PEECH trial were provided in our initial coverage review request (page 38, *ff*), dated May 31, 2005.

Of particular note, however, are the findings from a prespecified analysis that both co-primary endpoints achieved statistical significance in the subgroup of patients age 65 or older, $p = 0.008$ for exercise duration and $p = 0.017$ for peak VO_2 (Figure 1b).

Fig. 1a: Co-Primary Endpoint Analysis in Patients Overall	
Fig. 1b: Co-Primary Endpoint Analysis in Patients ≥ 65	

Changes in the absolute values of exercise duration were significantly greater in the EECP treated group at all time points in PEECH subjects overall (Figure 2a). Importantly, however, the degree of effect was greater in subjects ≥ 65 years of age (Figure 2b).

Fig. 2a: Changes in Exercise Duration in Patients Overall	
Fig. 2b: Changes in Exercise Duration in Patients ≥ 65	

The change in the absolute values of peak VO_2 showed a trend favoring the EECP treated group at 1-week after therapy overall (Figure 3a). Most notable, though, was the degree of between-group differences in subjects 65 years of age or older. These differences reached statistical significance at 3-month and 6-month follow-up in this subgroup of patients (Figure 3b).

Fig. 3a: Changes in peak VO_2 in Patients Overall

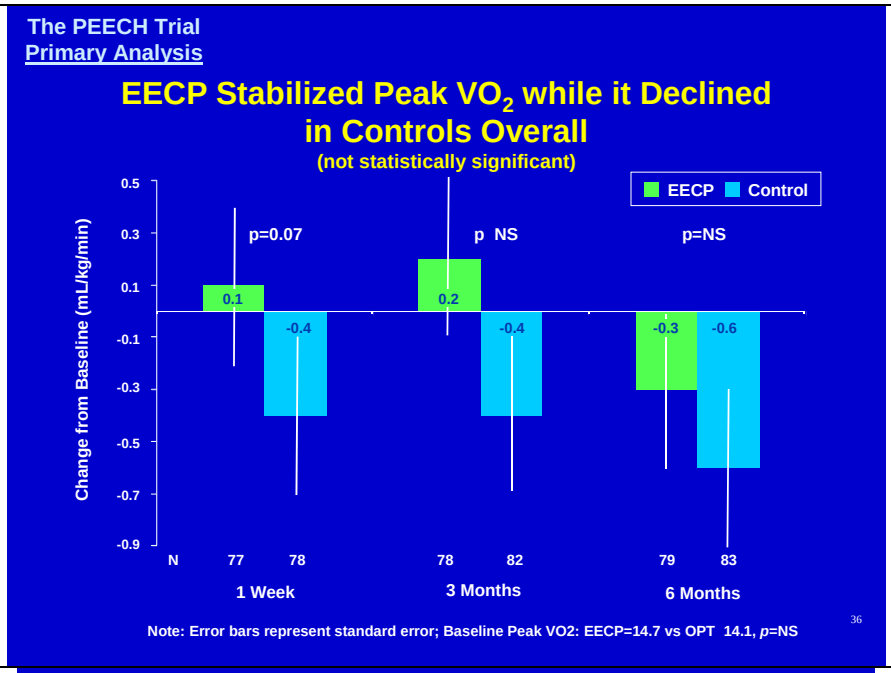
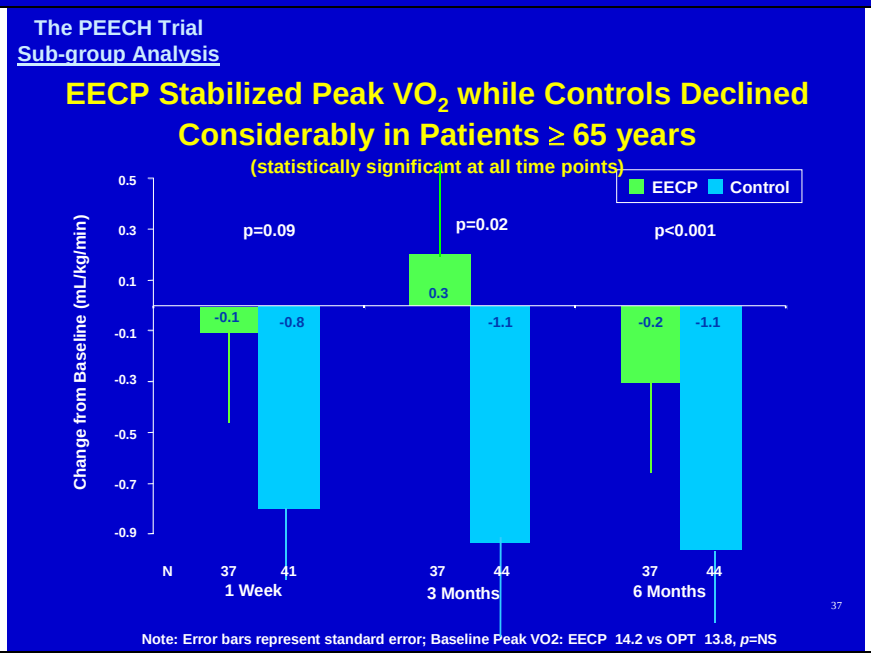


Fig. 3b: Changes in peak VO_2 in Patients $\geq$ 65



These changes are comparable to changes observed in recent heart failure trials, including those of cardiac resynchronization therapy, as shown in the comparison tables for peak VO_2 (Figure 4a) and exercise duration (Figure 4b).

Fig. 4a: Comparison of changes in peak VO_2 from recent heart failure trials.

PEECH Results in Context - 1

Peak VO2 data

Trial	Duration (mo)	Method	NYHA	Comparison N's	Between Group Differences 1-week mL/lg/min *p*-value	3-months mL/lg/min *p*-value	6-months mL/lg/min *p*-value
PEECH: OVERALL	9	N treadmill	II/III	EECP vs OPT 93 vs 94	0.5 (0.071)	0.6 (NS)	0.3 (NS)
PEECH: ISCHEMIC	9	N treadmill		EECP vs OPT 53 vs 54	0.8 (0.008)	0.6 (NS)	0.5 (NS)
PEECH: >= 65 yo	9	N treadmill		EECP vs OPT 37 vs 44	0.7 (0.086)	1.4 (0.02)	0.9 (<0.01)
MUSTIC N Engl J Med 2001	3		III	CRT vs OPT 67 vs 67		1.2 (0.029)	
MIRACLE N Engl J Med 2002	6	N treadmill	III	CRT vs OPT 228 vs 225			0.9 (0.009)
MIRACLE ICD JAMA 2003	6		III/IV	CRT-D vs OPT 187 vs 182			1.0 (0.04)
BB Meta analysis Eur J HF 2005	misc	Variable		BB vs Placebo 1128 vs 846			0.4 (NS)

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Fig. 4b: Comparison of changes in exercise duration from recent heart failure trials.

PEECH Results in Context - 2

Exercise Duration data

Reference	Duration (mo)	Method	NYHA	Comparison N's	Between Group Differences 1 week Seconds *p*-value	3 months Seconds *p*-value	6-months Seconds *p*-value
PEECH: OVERALL	9	N treadmill	II/III	EECP vs OPT 93 vs 94	32 (0.01)	42 (0.014)	35 (0.013)
PEECH: ISCHEMIC	9	N treadmill		EECP vs OPT 53 vs 54	41 (0.007)	52 (0.017)	46 (0.01)
PEECH: >= 65 yo	9	N treadmill		EECP vs OPT 37 vs 44	20 (0.074)	71 (0.004)	52 (<0.01)
MIRACLE N Engl J Med 2002	6	N treadmill	III	CRT vs OPT 228 vs 225			62 (0.001)
MIRACLE ICD JAMA 2003	6		II/III	CRT D vs OPT 187 vs 182			67 (<0.001)
AMLODIPINE Am Heart J 2000	3	N treadmill	II/III	Amlodipine vs OPT 214 vs 223		-13 (NS)	
BB Meta-analysis Eur J HF 2005	misc	Variable		BB vs Placebo 1128 vs 846			33 (0.045)
	misc	Treadmill					43 (NS)
	misc	Bicycle					51 (0.048)

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The excellent safety profile of EECP therapy in patients with heart failure was confirmed in the PEECH trial, as there was no difference in the occurrence of serious adverse events between study groups in patients overall (Figure 5).

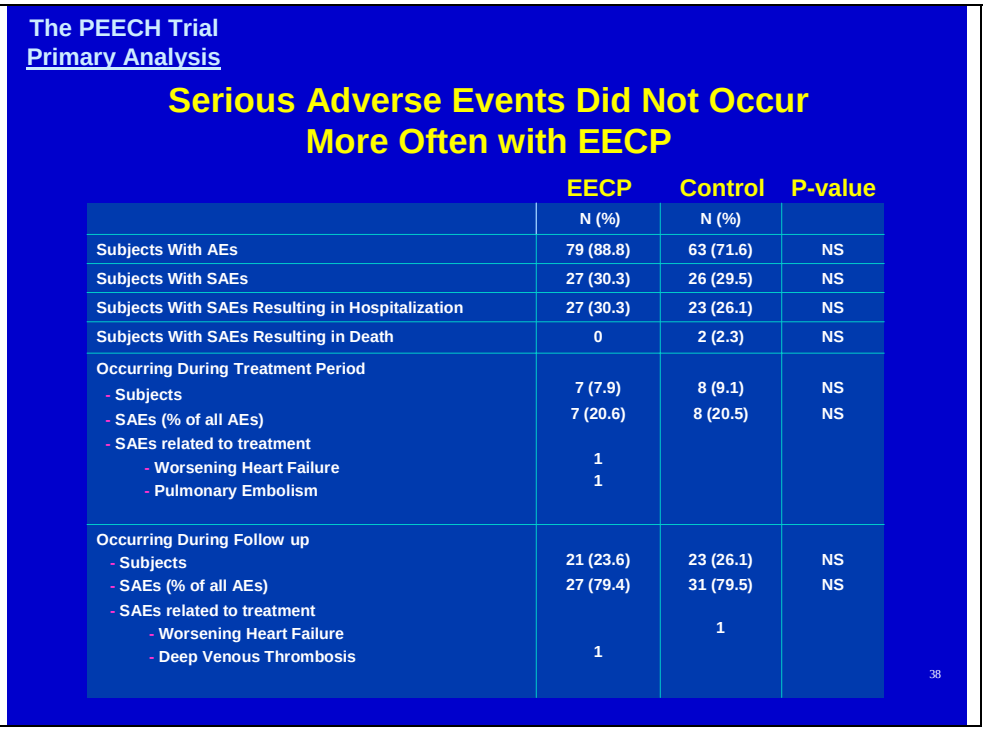


Fig. 5: Adverse Event Data in PEECH patients overall.

The data also shows that in the subgroup of patients ≥ 65 years of age, serious adverse events were rare, occurred no more often in the EECP group during treatment and less often during the 6-month follow-up period, as compared to the control group (Table 1).

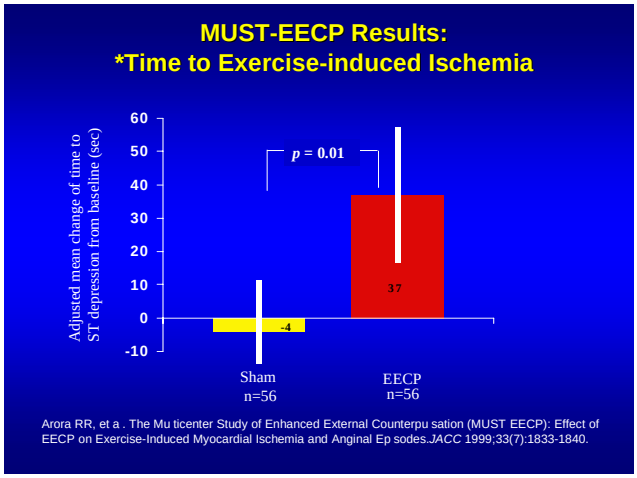
PEECH Adverse Events Summary Patients ≥ 65 years of age			
Treatment Period			
	EECP		**OPT**
Number of subjects	41		44
	Overall	EECP Related	
SAEs	5	1	4
Subjects with SAEs	5 (12%)	1 (2%)	4 (9%)
6-Month Follow-up Period			
SAEs	7	0	18
Subjects with SAEs	7 (17%)	0	15 (34%)

Table 1. Adverse Events in PEECH Subjects 65 years of age or older

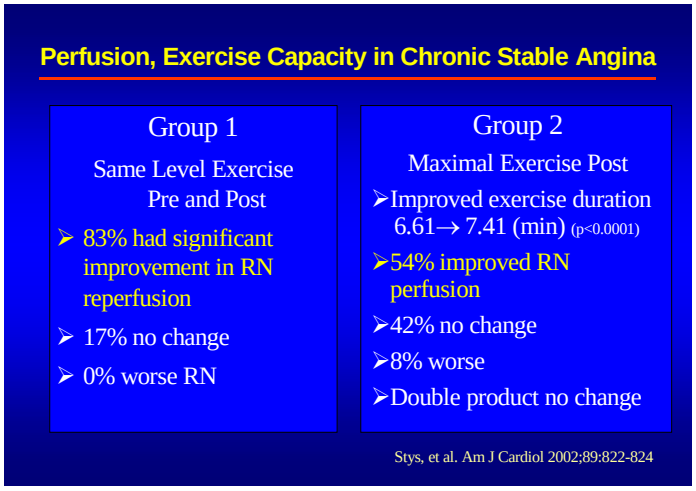
These data demonstrate that EECP therapy is effective and safe in treating heart failure patients age 65 years or older. The level of effect achieved in these patients is comparable to that obtained with other, established heart failure treatments.

2. **EECP therapy has demonstrated effectiveness and safety in patients with ischemic heart disease in over 50 peer-reviewed publications, and has recently been shown to be effective in patients with left ventricular systolic dysfunction and in patients with NYHA class II and III heart failure of ischemic etiology.**

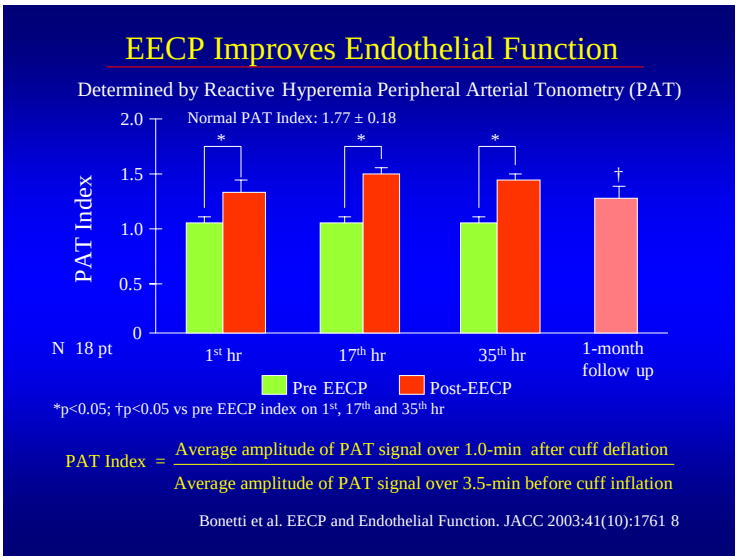
Results from the MUST-EECP trial in patients with CCS Class I, II and III angina and documented coronary artery disease clearly demonstrated that EECP therapy is effective in treating patients with ischemic heart disease as shown by the significant improvement in time to ST-segment depression observed in patients treated with EECP therapy compared with those in the sham-EECP control group.



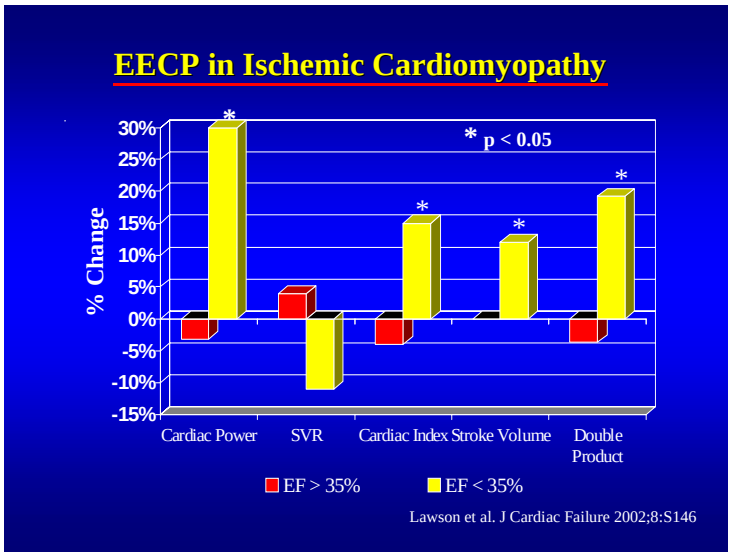
Stys *et al*, in a multicenter study using radionuclide perfusion treadmill stress tests in 175 chronic stable angina pectoris patients, demonstrated significant improvement in stress-induced myocardial ischemia in 83% of the patients with exercise performed to the same level pre- and post-EECP treatment, and improvement in 54% of the patients when maximal treadmill stress tests were used in both pre- and post treatment.



A paper published from the Mayo Clinic by Bonetti *et al* demonstrated that EECP was effective in improving endothelial cell function using an objective reactive hyperemia-peripheral arterial tonometry (PAT) technique in 23 patients with refractory angina and long-standing coronary artery disease. Endothelial function improved at one-month follow-up only in those patients who experienced clinical benefit.



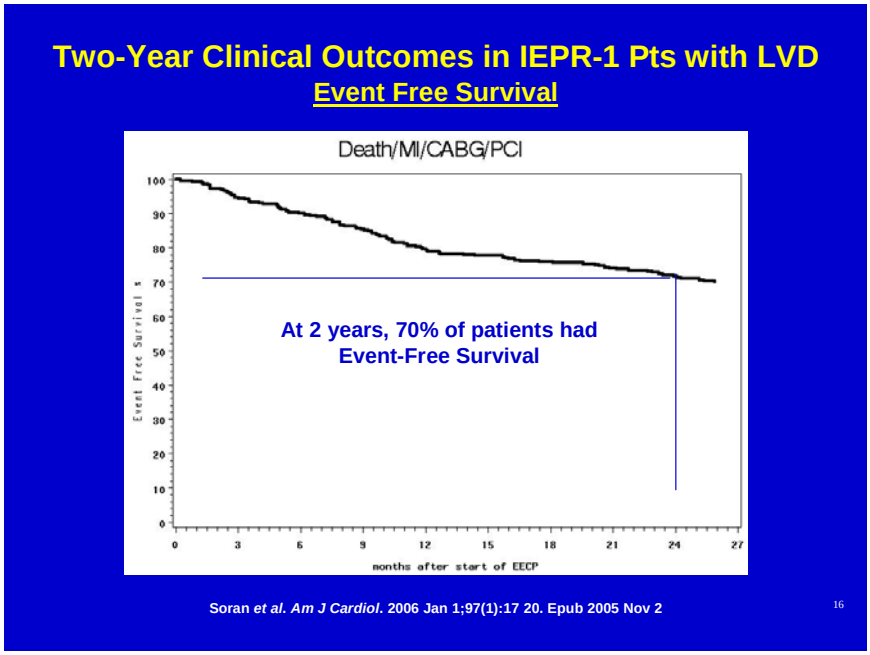
Case series studies provide insight on the selection of patients who would benefit most from a given test or treatment. In a study of refractory angina patients, impedance cardiography was used to calculate cardiac power, systemic vascular resistance, cardiac index, stroke volume and double product prior to the 1st and 35th hours of a standard 35-hour course of EECP therapy. All parameters improved significantly in those patients with ischemic cardiomyopathy and severe LV dysfunction (EF ≤ 35%) and not in those with normal ejection fraction (EF > 35%).



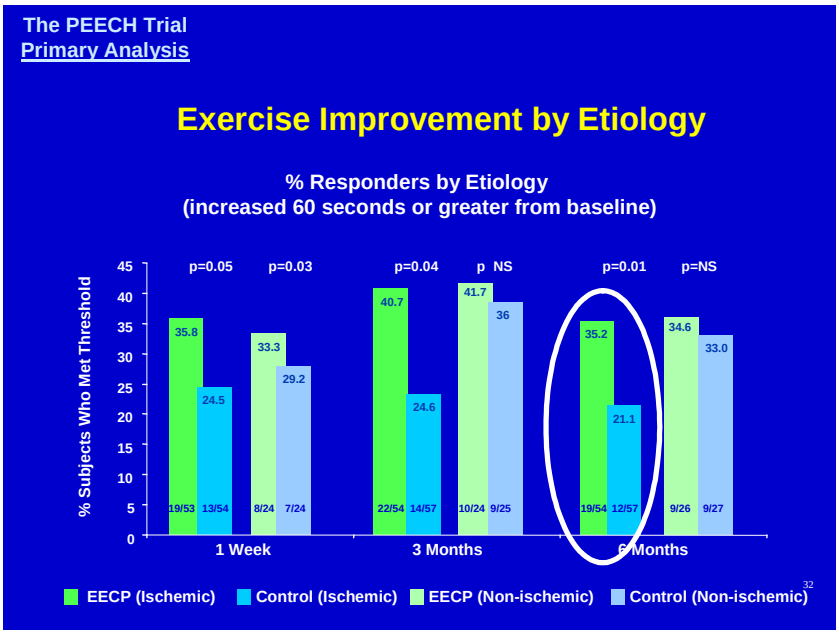
Finally, these results are further supported by the recently published results of two year follow up of a large cohort of angina patients with severe left ventricular dysfunction enrolled in the International EECP Patient Registry (Soran O, *et al*. Two year clinical outcomes after Enhanced External Counterpulsation (EECP) Therapy in Patients with Refractory Angina Pectoris and Left Ventricular Dysfunction. *Am J Cardiol* 2006;97:17-20). This paper has been previously provided to CMS in manuscript form and a reprint copy is attached as Appendix A.

This two-year cohort study included 363 refractory angina patients with a left ventricular ejection fraction ≤ 35 %. Immediately post EECP therapy, 72% of the patients improved more than one angina class, and 15.6% had no angina ($p<0.001$). At two years, 265 patients completed follow up and 55% of the patients had sustained improvement in angina class. In addition, quality of life measures using the Likert scale indicated that 58% of patients had improved quality of life post-EECP therapy compared to baseline and at 2 years follow up, 63% of patients were improved compared to baseline ($p<0.001$).

More importantly, the two-year survival rate was 83% and the major adverse cardiovascular event-free survival rate was 70% (see figure below). Objective measures of clinical outcome were assessed and 43% of patients reported no cardiac hospitalization and 81% no congestive heart failure events. These low rates of adverse clinical outcomes are notable in this cohort of patients with ischemic heart disease and severe systolic dysfunction.



Lastly, prespecified subgroup analysis on data from the PEECH trial was performed to assess response to EECP therapy in patients with heart failure due to either ischemic or nonischemic cardiomyopathy. This analysis demonstrated that patients with an ischemic etiology had greater positive responses in several parameters compared to patients with a nonischemic etiology. This difference in response is illustrated in the exercise duration data shown in the figure below.



This observation was also noted on classification of functional status by NYHA class, as between-group differences were greater in patients with ischemic etiology at all time points (one week 37.0% vs. 12.7%, $p = 0.004$; three months 34.5 % vs. 12.3 %, $p = 0.025$; six months 36.4% vs. 15.5%, $p = 0.026$, EECP vs. Control, respectively). Furthermore, quality of life was significantly improved in the ischemic subgroup at three months of follow up (-6.5 ± 3.2 for EECP patients vs. -1.5 ± 2.1 for control patients, $p = 0.046$), while differences noted in nonischemic patients did not reach significance at any time point.

These and other data demonstrate the benefits achieved with EECP therapy in patients with refractory angina unsuitable for further interventional revascularization, also in that same group of patients but with severe left ventricular dysfunction, and lastly in patients with systolic heart failure (ejection fraction ≤ 35%) of ischemic etiology and symptoms consistent with NYHA class II and III.

3. The evidence is sufficient to conclude that EECP therapy will have net health benefits for patients with Canadian Cardiovascular Society Classification (CCSC) II angina.

Clinical data supporting the use of EECP in patients with CCSC Class II angina was provided to CMS in our initial coverage request dated May 31, 2005 (see page 15, *ff*). There are several points specifically regarding the subset of CCSC class II patients that warrant further emphasis.

The results for the class II subset of patients in the MUST-EECP trial, a prospective, multicenter, randomized, double-blind study, were comparable to the results overall for patients of all anginal classes enrolled (Class I, II and III). Figures 5 through 7 (on pages 18-19 of the coverage revision request) demonstrate that as compared to controls, class II patients who underwent EECP therapy experienced increased time to ischemia on exercise and decreased frequency of angina episodes. In addition, compared to baseline, class II angina patients experienced an increase in total exercise duration, an increase in time to ischemia on exercise, and a decrease in angina episodes.

Two-Year Outcomes in Patients with Mild Refractory Angina Treatment with EECP

Analysis of results of EECP therapy according to CCS class at entry was also performed on a cohort of patients enrolled in the International EECP Patient Registry (IEPR), as discussed in the initial coverage request (see page 20, *ff*). These data are due to be published in the February 2006 issue of *Clinical Cardiology* (Lawson WE, *et al*. Two-Year Outcomes in Patients with Mild Refractory Angina Treated with Enhanced External Counterpulsation. *Clin. Cardiol*, 2006; 29). A copy of the proofread galleys are attached as Appendix B. One-hundred-twelve (112) patients had Class II angina at entry and 61% of this group had improvement of at least one angina class compared with 78% of 1,345 patients with Class III or IV angina at entry, a statistically significant difference ($p < 0.001$). A significant majority of patients with either mild or moderate-severe angina at entry were improved by at least one CCSC angina class reduction at 2-year follow-up, 70% in Class II vs. 81% in Class III/IV ($p<0.05$). Importantly, there were no significant differences in rates of major cardiovascular events (death, acute myocardial infarction, PCI or CABG) between these two groups at 2-year follow-up.

The mortality rate for the group with CCSC class II refractory angina was 4.6% and for Class III/IV was 10.8%. Other significant changes included a decrease in the number of angina episodes per week and reduction in sublingual (SL) nitroglycerin use per week in both groups immediately following ($p < 0.001$) and at two years post EECP ($p < 0.001$) compared to baseline. Quality of Life improved in 60% of Class II and 52% of Class III/IV immediately post-EECP therapy, and improvement was maintained at 2-year follow-up in 44% of Class II patients and 51% in Class III/IV, all achieving significant improvement from baseline ($p<0.001$). The study authors concluded that "The robust effectiveness of EECP as a noninvasive device, together with its relatively low start-up and recurrent costs, makes it an attractive consideration for treating patients with milder refractory angina in addition to the patients with severely disabling angina treated in current practice.

4. Endpoints used in studies of EECP therapy adequately demonstrate improvement in measures of morbidity as well as symptom status and quality of life, supporting the conclusion of net health benefits from the therapy.

Surrogate endpoints are frequently used by knowledgeable, experienced researchers as a means for conducting successful clinical trials. In their absence, clinical trials would often be impossible to complete in a timely manner. To date, there have been more than 50 peer-reviewed publications reporting clinical, quality of life, and mechanistic endpoints on patients with angina or heart failure treated with EECP therapy, including measurements of the following:

- Endothelial function
- Maximal Exercise Capacity
- Exercise Time to ST-segment depression
- Peak O_2 uptake
- Indices of Myocardial Perfusion
- Stroke Volume, Ejection Fraction
- Neurohormonal Dysfunction/Hypertension
- Symptom/Functional Status (NYHA, CCSC)
- Quality of Life

The clinical benefits associated with these surrogate markers have been documented in many studies, and the table included as Appendix C provides a summary of various surrogate endpoints used in studies of EECP therapy and cites published studies that discuss the clinical outcomes associated with these surrogate endpoints.

Two specific endpoints reported in the PEECH trial that warrant emphasis are exercise duration and peak oxygen consumption. Measurement of exercise capacity has long been recognized as a useful and important technique for the evaluation of patients with ischemic heart disease. In fact, approximately 100 years ago Einthoven originally documented changes in the ST segment of the ECG with exercise. Since then, there have been hundreds of studies that have documented the usefulness of exercise testing for outcome prediction in patients with ischemic heart disease, and the various forms of exercise testing have become a standard modality for both clinical and investigative cardiology. More information on this topic can be obtained from the ACC/AHA 2002 Guideline Update for Exercise Testing available at http://circ.ahajournals.org/cgi/reprint/106/3/388.

A recent review of exercise testing in clinical medicine[i] summarizes the literature on exercise testing and heart failure, and notes that "During the 1990s, over 40 studies were published showing that peak oxygen consumption (VO_2) was a significant univariate or multivariate predictor of risk in heart failure, and this variable is now regarded as one of the most potent markers in this condition."

Maximal exercise capacity and peak oxygen uptake continue to be valuable endpoints for clinical trials and their selection as co-primary endpoint parameters for the PEECH trial was a logical choice.

5. Changes in physiologic measures, such as peak VO_2, exercise duration, peripheral vascular reactivity, neurohormonal markers, indices of perfusion, and cardiac hemodynamics support the conclusion that outcomes observed in patients treated with EECP therapy are primarily due to treatment effects and not to a placebo effect.

CMS suggested in the draft decision memo that the placebo effect could be at least partially responsible for the outcomes reported for EECP therapy. CMS states in its analysis that "Case series do not provide evidence about whether the treatment itself directly causes the subsequent outcome, or whether some other concurrent factor is responsible for the observed outcome . . ." and "[t]he type of study . . . without a comparative control group deserves less weight . . ."

However, while it is true that observational studies generally do not support the same types of conclusions as randomized, controlled trials (RCTs), observational studies showing positive net health outcomes for EECP therapy do not stand alone. They support the results of two well-designed RCTs:

- MUST-EECP: demonstrating significant improvement in time to ST-segment depression, and
- PEECH: showing significant improvement in exercise duration and Peak VO_2 for NYHA Class II/III heart failure patients ≥ 65 years old.

Randomized controlled trials with blinded comparison of outcomes are designed to minimize bias in many forms, including the influence of a placebo effect. These RCTs of EECP therapy included so-called "hard" endpoint parameters (peak VO_2 in PEECH, time to ≥ 1-mm ST-segment depression in MUST-EECP) that are less subjective than endpoints such as anginal pain or symptom status and therefore less likely to be influenced by a placebo effect.

Furthermore, there have been several studies designed to elucidate the mechanism of action of EECP therapy that have demonstrated its beneficial effects on several physiologic endpoints, including: 1) endothelial function[ii], neurohormonal function[iii], radionuclide stress perfusion[iv], and stroke volume or ejection fraction.[v] These studies document the several physiologic effects of EECP therapy and further diminish the likelihood of a placebo effect as the major causative factor in the outcomes attributable to this treatment.

6. EECP therapy is a highly cost-effective therapy for patients with chronic stable angina and heart failure and this fact should be appropriately considered when evaluating the sufficiency of the evidence for ECP.

EECP therapy is a very cost-effective therapy for patients with stable angina and heart failure and this information should be appropriately weighed when considering expanded coverage. A detailed cost utility analysis was prepared for Vasomedical by Aequitas (an independent health care research and analysis institution) to evaluate the cost-effectiveness of EECP therapy plus guideline-compliant medical therapy for chronic stable angina. This analysis

was presented in Vasomedical's initial request for coverage expansion (see page 25, *ff*). The result of this analysis demonstrated EECP therapy to be a highly cost-effective therapy for patients with angina, yielding an incremental cost effectiveness ratio of $3,126 cost per quality adjusted life-year at two years compared to medication alone.

Furthermore, the cost of EECP compares quite favorably to the cost of other procedures used to treat patients with CAD. For example, the average procedure cost for a coronary artery bypass graft procedure is $25,500, the average cost for a percutaneous coronary intervention procedure with a stent is $13,000, and the average cost of a standard course of EECP therapy is $5,150. Patients achieving symptomatic control from EECP therapy are sometimes able to avoid these more costly procedures with resultant savings to the healthcare system.

Such cost-effectiveness also extends to the treatment of congestive heart failure with EECP. It is not uncommon for CHF patients receiving medical therapy to decompensate and require hospitalization. The hospitalization costs to the Medicare system for treating CHF are approximately $3.6 billion per year ($5,456 per discharge). Lowering the rate of hospitalizations in patients with chronic heart failure could result in a significant cost savings to the Medicare program.

One study[vi] demonstrates the potential cost benefits that could be achieved with EECP therapy in patients with chronic heart failure. Data was collected on 233 patients enrolled in the International EECP Patient Registry (IEPR) with CAD and left ventricular dysfunction (EF ≤ 40%). There was a significant reduction in emergency room visits and hospitalizations in the six month period following EECP therapy relative to the six month period prior to EECP therapy. ER visits decreased from an average of 1.9 pre-EECP to 0.17 post-EECP ($p < 0.001$) and hospitalizations decreased from an average of 1.8 to 0.25 ($p < 0.001$). Extrapolation of these data translate into a reduction of 3.1 hospitalizations per patient per year, resulting in the avoidance of $16,913 (3.1 x $5,456) in hospitalization costs per patient for an annual EECP treatment charge of $3,640 per patient, or a $13,273 net annual savings per patient. This would result in an annual savings of more than $13 million for every 1,000 heart failure patients treated. Moreover, this figure does not include the savings from the reduction of ER visits.

7. Revised Proposal for an expansion of coverage for ECP:

Vasomedical proposes the following revised expansion of ECP coverage (compared to our original request):

Patients age 65 years or older with a diagnosis of stable, chronic heart failure of ischemic etiology, with an ejection fraction of ≤ 35% and symptoms consistent with NYHA class II or III, who are not adequately responding to or tolerating optimal heart failure therapy.

Vasomedical believes that the data presented in support of this request for coverage expansion are particularly strong for patients that fit this description. While results obtained in peer-reviewed reports of clinical investigations consistently show patients with class II angina or class II/III heart failure symptoms and an ejection fraction ≤ 35% obtaining significant benefits

from EECP therapy, the strength of evidence appears to be even stronger for those patients 65 years of age or older. Results from prespecified subgroup analysis of objective measures used in the PEECH trial support this contention. EECP therapy is a safe, effective, and cost-effective treatment for these heart failure patients who have few other options.

We appreciate your timely review of the information provided herein and look forward to your response. If you have any questions, please contact me at 516-997-4600, extension 193. Thank you for your time and consideration.

Respectfully,

Thomas R. Varricchione, MBA, RRT
Vice President, Clinical, Regulatory and Quality Affairs

Appendix A

Reprint copy of "Two year clinical outcomes after Enhanced External Counterpulsation (EECP) Therapy in Patients with Refractory Angina Pectoris and Left Ventricular Dysfunction"
Soran O, *et al*. *Am J Cardiol* 2006;97:17-20

Two-Year Clinical Outcomes After Enhanced External Counterpulsation (EECP) Therapy in Patients With Refractory Angina Pectoris and Left Ventricular Dysfunction (Report from the International EECP Patient Registry)

Ozlem Soran, MD, MPH[a,*,†], Elizabeth D. Kennard, PhD[b], Abdallah Georges Kfoury, MD[c], and Sheryl F. Kelsey, PhD[b], for the IEPR Investigators

Enhanced external counterpulsation (EECP) is a noninvasive circulatory assist device that has recently emerged as a treatment option for refractory angina in left ventricular (LV) dysfunction. This 2-year cohort study describes the long-term follow-up of patients who had severe LV dysfunction that was treated with EECP for angina pectoris and reports clinical outcomes, event-free survival rates, and the incidence of repeat EECP. This study included 363 patients who had refractory angina and LV ejection fraction ≤35%. Most patients reported quality of life as poor. After completion of treatment, there was a significant decrease in severity of angina class ($p < 0.001$), and 72% improved from severe angina to no angina or mild angina. Fifty-two percent of patients discontinued nitroglycerin use. Quality of life improved substantially. At 2 years this decrease in angina was maintained in 55% of patients. The 2-year survival rate was 83%, and the major adverse cardiovascular event-free survival rate was 70%. Forty-three percent had no reported cardiac hospitalization; 81% had no reported congestive heart failure events. Repeat EECP was performed in 20% of these patients. The only significant independent predictor of repeat EECP in a proportional hazard model was failure to complete the first EECP treatment course (hazard ratio 2.9, 95% confidence interval 1.7 to 4.9). Improvements in angina symptoms and quality of life were maintained at 2 years. In conclusion, for patients who have high-risk LV dysfunction, EECP offers an effective, durable therapeutic approach for refractory angina. Decreased angina and improvement in quality of life were maintained at 2 years, with modest repeat EECP and low major cardiovascular event rates. (Am J Cardiol 2006;97:17–20)

The United States Food and Drug Administration cleared enhanced external counterpulsation (EECP) for the treatment of stable angina, unstable angina, cardiogenic shock, and acute myocardial infarction in 1995. Since then, the procedure has been widely used for the treatment of angina. Because EECP increases right ventricular filling pressure by augmenting venous return during diastole, clinicians conjectured that its use in patients who had left ventricular (LV) dysfunction and heart failure might be contraindicated. However, the arterial hemodynamic effects of EECP are similar to those of intra-aortic balloon counterpulsation, with similar diastolic augmentation and decreased afterload.[1,2] Pilot data have shown that a LV ejection fraction ≤35% is not associated with an increase in adverse events during EECP.[3] Further, EECP has proved to be safe and effective in patients who have congestive heart failure with LV dysfunction.[4] However, the long-term efficacy of EECP in patients who have refractory angina and LV dysfunction has not been evaluated. The purpose of this project was to describe the 2-year follow-up of patients who had severe LV dysfunction that was treated with EECP for refractory angina pectoris and to report the clinical outcomes, event-free survival rates, and incidence of repeat EECP.

Methods

Patient population and study: The International EECP Patient Registry (IEPR) phase 1 study began in January 1998 and enrolled consecutive patients who underwent EECP for chronic angina. More than 5,000 patients were enrolled from >100 international centers. The IEPR methods has been previously described.[3] Patients in the IEPR

The [a]Cardiovascular Institute, University of Pittsburgh Medical Center, and the [b]Department of Epidemiology, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, Pennsylvania; and the [c]Utah Cardiac Transplant Program LDS Hospital, Salt Lake City, Utah. Manuscript received March 24, 2005; revised manuscript received and accepted July 22, 2005.

The International EECP Patient Registry is sponsored by Vasomedical, Inc., Westbury, New York.

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doi:10.1016/j.amjcard.2005.07.122

Table 1
Characteristics of patients (n = 363) with left ventricular ejection fraction ≤35% before starting enhanced external counterpulsation therapy

Age (yrs)	67 ± 11
Men	78%
Previous myocardial infarction	85%
Previous coronary bypass	72%
Previous percutaneous coronary intervention	70%
Hypertension*	68%
Hyperlipidemia†	78%
Current smoker	10%
Diabetes mellitus	45%
Noncardiac vascular disease	35%
History of congestive heart failure	61%
LV ejection fraction (%)	28 ± 7

Values are means ± SD or percentages.
* Diagnosed by a physician and treated with medication and/or diet.
† Documented serum cholesterol level >240 mg/100 ml or treatment for high cholesterol level by a physician with medication and/or diet.

Table 2
Adverse events for patients (n = 363) with left ventricular ejection fraction ≤35% during enhanced external counterpulsation therapy

Death	0.8%
Myocardial infarction	0.3%
Coronary bypass	0.3%
Percutaneous coronary intervention	0.8%
Death/myocardial infarction/coronary bypass/ percutaneous coronary intervention	1.9%
Unstable angina pectoris	4.1%
Congestive heart failure	3.3%
Skin breakdown	2.5%
Musculoskeletal	2.2%

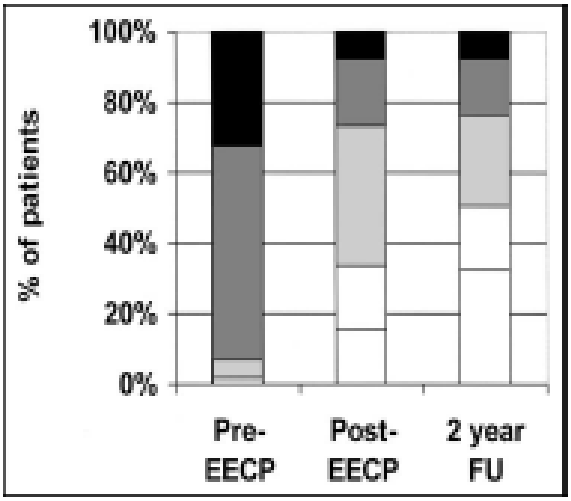

Figure 1. Angina classes 0 (*white bars*), I (*pale gray bars*), II (*medium gray bars*), III (*dark gray bars*), and IV (*black bars*) before EECP (n = 363), after EECP (n = 358), and at 2-year follow-up (FU; n = 265).

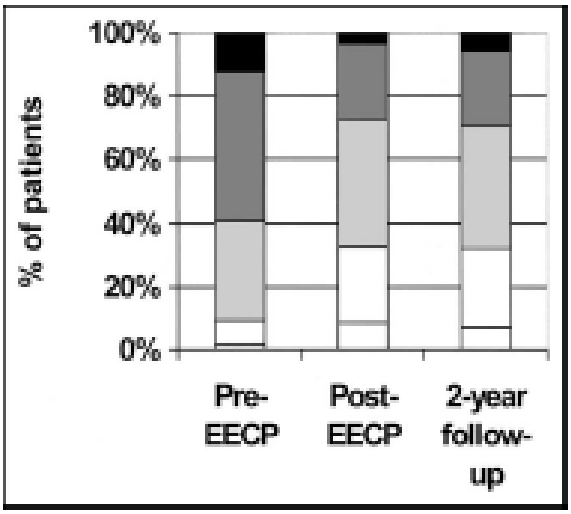

Figure 2. Quality of life rated as poor (*black bars*), fair (*dark gray bars*), good (*medium gray bars*), very good (*pale gray bars*), and excellent (*white bars*) before and after EECP and at 2-year follow-up.

were required to give informed consent, and the IEPR tracks the demographics, entry characteristics, clinical events, and outcomes of consecutive patients who undergo EECP treatment for angina, with no exclusion due to demographics, clinical status, or outcome. Canadian Cardiovascular Society classification was used to assess angina status. Quality of life was assessed by patients who used 5-point scales for health status, quality of life, and satisfaction with quality of life. At 6-month, 1-year, and 2-year follow-ups, patients were interviewed by telephone or at a clinic visit, and data concerning interim clinical events, hospitalizations, and current symptomatology were recorded. Major adverse cardiac events were specified as the composite of death, myocardial infarction, percutaneous coronary intervention, and coronary artery bypass grafting. Patient data were included only from sites with ≥85% complete follow-up.

The IEPR-generated database was queried to select the cohort of patients who underwent EECP for LV dysfunction. LV dysfunction was defined as a LV ejection fraction ≤35% as assessed by echocardiography (30%), ventriculography (58%), or gated blood pool scan (12%).

EECP therapy (Vasomedical, Inc., Westbury, New York) was administered to all patients. EECP equipment is comprised of an air compressor, a computer module, 3 sets of cuffs, and a treatment table. Systolic and diastolic pressure waves are monitored throughout treatment by noninvasive finger plethysmography. Cuffs are wrapped around a patient's calves, thighs, and lower buttocks and a computer-controlled pneumatic system acts to inflate and deflate the cuffs. Inflation and deflation are triggered by events in the cardiac cycle through microprocessor-interpreted electrocardiographic signals. A full course of therapy typically consists of 35 1-hour sessions offered once daily.

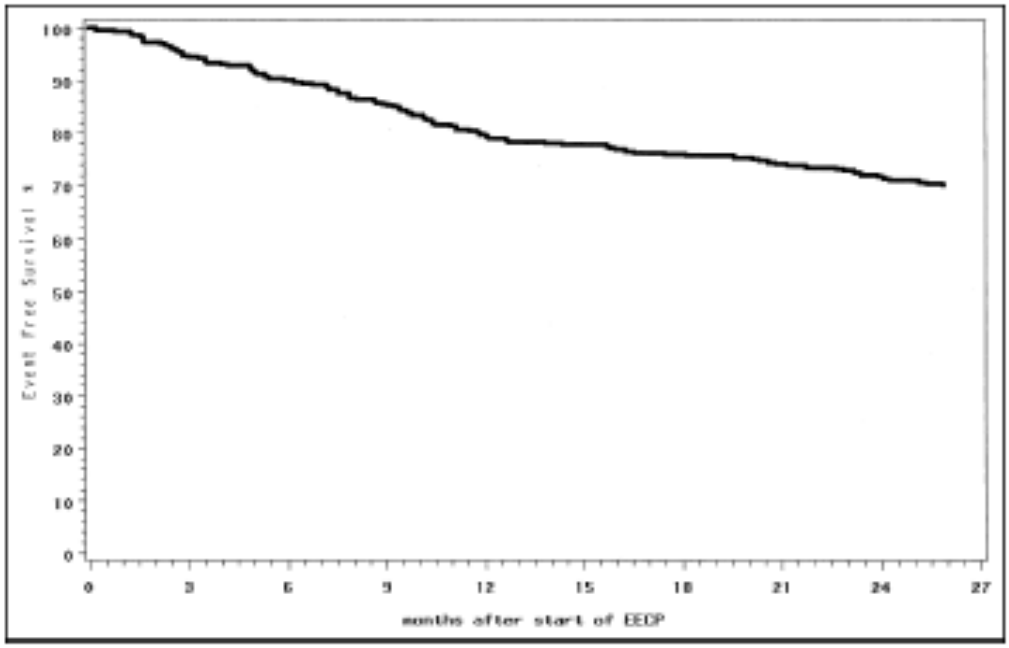

Figure 3. Event-free survival rate. Events were death, coronary artery bypass grafting, myocardial infarction, and percutaneous coronary intervention.

Statistical analysis: Baseline characteristics are presented for categorical variables as the proportion of patients who reported and as mean ± SD for continuous variables. Kaplan-Meier survival analysis was used to model follow-up events. Predictors of repeat EECP were determined with Cox's proportional hazards model. Two-tailed p values <0.05 were considered statistically significant.

Results

The IEPR included 363 patients who had angina with LV dysfunction. Patients' average duration of clinical coronary artery disease was nearly 13 years; 84% had multivessel disease and 93% were not candidates for further revascularization due to the extent and severity of disease, LV dysfunction, co-morbid conditions, previous interventions, or risk/benefit ratio. Angina was severe (class III/IV) in 93% of patients. There was a high prevalence of cardiac risk factors (i.e., 77% had a history of smoking and 82% had a family history of premature atherosclerotic cardiovascular disease) (Table 1). More than 50% reported quality of life as 4 or 5 (i.e., poor, on the 5-point scale, where 5 is worst).

On average, patients underwent an EECP treatment course of 32 hours, with 81% completing the course. Twelve percent discontinuted due to a clinical event, and 7% stopped due to patient preference. Women and those who had a history of congestive heart failure were less likely to complete the treatment course (75% of women vs 82% of men, $p = 0.15$; therapy completed by 78% of those who had congestive heart failure vs 85% of those who did not, $p = 0.08$). There was a significant difference in the rate of exacerbation of heart failure between those who did not complete treatment and had previous heart failure and those who had no heart failure (16% of those who stopped treatment vs 0%, $p = 0.05$). Major adverse cardiovascular events that occurred over the course of EECP therapy were low (Table 2).

After completion of treatment, there was a significant decrease in severity of angina ($p < 0.001$). Of the total cohort, 77% of patients decreased by ≥1 angina class, 18% had no angina, and 2% had an increase in angina class (Figure 1). The mean number of weekly angina episodes decreased by 8.2 ± 12.9 episodes ($p < 0.001$). Of those who used nitroglycerin as needed, 52% of patients discontinued nitroglycerin use after EECP. Quality of life showed a significant increase ($p < 0.001$; Figure 2).

At 2 years, 83% survived and the event-free survival rate was 70% (Figure 3). Forty-three percent had no cardiac hospitalizations, and 81% had no congestive heart failure events. Comparison of patients who showed no decrease in angina with those who showed decreased angina showed no difference in major adverse cardiovascular events at 2 years; however, those who showed no initial response reported significantly unstable angina in the 2-year period (28% vs 16%, $p = 0.02$). There was a significant difference in

Table 3
Medication use before and after enhanced external counterpulsation and at two-year follow-up

Medication	Before EECP	After EECP	Follow-up
β Blocker	71.2%	75.6%	72.6%
Calcium channel blocker	30.7%	30.4%	30.7%
Angiotensin-converting enzyme	60.5%	61.1%	52.8%
Angiotensin receptor blocker	15.5%	14.6%	11.3%
Antiplatelet	76.4%	75.2%	73.5%
Lipid lowering	75.8%	76.6%	77.7%

survival rate between those who did not complete and those who completed treatment (71% vs 85%, p <0.001). There was a sustained decrease in angina class in 55% of survivors compared with after EECP (Figure 1). Improvement in quality of life was also maintained (Figure 2).

Use of β blockers, calcium blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, antiplatelets, and hypolipidemic medication was similar at baseline, immediately after EECP, and at 2 years (Table 3).

Repeat EECP was performed in 20% of patients. Failure to complete the original treatment course was the only significant independent predictor of repeat EECP (hazard ratio 2.9, 95% confidence interval 1.7 to 4.9).

Discussion

EECP has been shown to decrease angina and stress myocardial perfusion in patients who have coronary artery disease.[4–8] Previously, however, a primary concern was that the increased venous return that resulted from EECP would precipitate an exacerbation of heart failure in patients who developed angina pectoris and had a history of heart failure with LV dysfunction. Recent reports have demonstrated that, despite depressed LV function, patients respond acutely to treatment with EECP.[4] The present results represent the largest reported long-term follow-up series of consecutive patients who had LV dysfunction that was treated with EECP for refractory angina pectoris. These patients are characterized by chronic multivessel coronary artery disease, with a high prevalence of coronary disease risk factors, severe angina refractory to medical therapy or conventional invasive revascularization, and a poor quality of life. Most patients were not candidates for further coronary revascularization. Despite this clinical profile with frequent anginal symptoms and markedly depressed LV systolic function, most patients demonstrated a significant decrease in angina and improvement in quality of life after EECP and this decrease was maintained in most patients at 2-year follow-up. Selection bias, which was minimized by reporting on patients from sites with ≥85% follow-up compliance, and survival bias may account for differences among patients who were or were not available for 2-year follow-up.

A primary limitation of this study is the lack of a control group to assess outcomes. We previously compared demographics and clinical outcomes from patients who were enrolled in the IEPR and those from patients who were in the National Health Lung Blood Institute Dynamic Registry and underwent elective percutaneous coronary intervention for refractory angina.[9] Despite an unfavorable baseline profile and risk factors in the IEPR, comparison of EECP with percutaneous coronary intervention showed an increased event-free survival rate, with a similar incidence of severe angina pectoris in patients who received EECP. EECP may offer a safe treatment option for patients who have LV dysfunction and angina pectoris. However, identifying a proper comparison group and interpreting differences in outcomes from different registries are challenges. Although difficult to perform in patients who have exhausted nearly all treatment options, a more rigorous evaluation of the effect of EECP on these outcomes will require a randomized clinical trial.

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Appendix B

Galley proof copy of "Two-Year Outcomes in Patients with Mild Refractory Angina Treated with Enhanced External Counterpulsation"
Lawson WE, *et al*. *Clin Cardiol*, 2006;29, In press

CONFIDENTIAL DOCUMENT

(Supplied under separate cover)

Appendix C

Summary of surrogate endpoints used in studies of EECP therapy
and
Studies discussing clinical outcomes associated with those endpoints

Summary of surrogate endpoints used in studies of EECP therapy and studies discussing clinical outcomes associated with those endpoints

Endpoint	Improvement with EECP therapy	Clinical Benefits
Endothelial function*	1. Significantly improved reactive hyperemia-peripheral arterial tonometry (*JACC* 2003;41:1761) 2. External Counterpulsation Therapy Improves Endothelial Function in Patients with Refractory Angina Pectoris (*JACC* 2003;42:2090) 3. A Neurohormonal Mechanism for the Effectiveness of Enhanced External Counterpulsation. The 72nd Scientific Session of the American Heart, Supplement I-832, Nov 2, 1999.	1. Vascular Endothelial Dysfunction and Mortality Risk in Patients with Chronic Heart Failure. (*Circulation* 2005;111:310-314) 2. Excess of mortality in patients with endothelial dysfunction (*JACC* 2003;41:371A) 3. Prognostic value of coronary vascular endothelial dysfunction. (*Circulation* 2002;106:653)
Exercise Time to ST-segment depression	1. MUST-EECP (*JACC* 1999;33:1833-40)	1. ACC/AHA 2002 Guideline Update for Exercise Testing. www.american heart.org. 2. Prognostic importance of a clinical profile and exercise test in medically treated patients with coronary artery disease. (*JACC* 1984;3:772-9) 3. Prediction of cardiovascular death in men undergoing noninvasive evaluation for coronary artery disease. (*Ann Intern Med* 1993;118:689-95)
Exercise Capacity	1. MUST-EECP 2. PEECH 3. Efficacy of Enhanced External Counterpulsation in the Treatment of Angina Pectoris. (*Am J. Cardiol* 70:859-862, 1992) 4. Effect of enhanced external counterpulsation on stress radionuclide coronary perfusion and exercise capacity in Chronic Stable Angina Pectoris. (*Am J Cardiol* 2002;89:822-824)	1. Exercise Testing in clinical medicine. (*The Lancet* 2000;356:1592-1597) 2. Exercise treadmill score for predicting prognosis in coronary artery disease. (*Ann Intern Med* 1987;106:793-800) 3. The prognostic value of exercise capacity: a review of the literature. (*Am Heart J* 1991;122:1423-31)
Peak VO_2	PEECH for patients older than 65 years with systolic heart failure (EF≤35%) of ischemic etiology and receiving optimal drug therapy	1. Peak Oxygen Consumption as a Predictor of Death in Patients with Heart Failure Receiving β-Blockers. (*Circulation* 2005;111:2313) 2. Impairment of Ventilatory Efficiency in Heart Failure Prognostic Impact. (*Circulation* 2000;101:2803) 3. Cardiopulmonary exercise testing for prognosis in chronic heart failure: continuous and independent prognostic value from VE/VCO_2 slope and peak

		VO2. (*Eur Heart J* 2000;21:154-61)
Radionuclide Stress Perfusion Studies	1. Exercise Capability and Myocardial Perfusion in Chronic Angina Patients Treated with Enhanced External Counterpulsation. (*Clinical Cardiology*. 2003 Jun;(26):287-290) 2. Effects of Enhanced External Counterpulsation on Stress Radionuclide Coronary Perfusion and Exercise Capacity in Chronic Stable Angina Pectoris. (*Am J of Cardiol* 2002 Apr 1;89(7):822-824) 3. Enhanced External Counterpulsation Improved Myocardial Perfusion and Coronary Flow Reserve in Patients with Chronic Stable Angina; Evaluation by 13N-Ammonia Positron Emission Tomography. (*Eur Heart J* 2001 Aug;22(16):1451-1458)	1. Contributions of nuclear Cardiology to Diagnosis and Prognosis of Patients With Coronary Artery Disease. (*Circulation* 2000;101:1465-1478) 2. Incremental value of prognostic testing in patients with known or suspected ischemic heart disease: a basis for optimal utilization of exercise technetium-99m sestamibi myocardial perfusion single-photon emission computed tomography. (*JACC* 1995:26:639-647)
Stroke Volume, Ejection Fraction	1. Enhanced External Counterpulsation Improves Systolic Function by Echocardiography in Patients with Coronary Artery Disease. (*Heart Lung*. 2005 Mar-Apr;34(2):122-125) 2. Benefit of Enhanced External Counterpulsation in Coronary Patients with Left Ventricular Dysfunction: Cardiac or Peripheral Effect? Heart Failure Society of America, The 6th Annual Scientific Meeting, Boca Raton, Florida, USA, Sept 22-25, 2002.	1. Variables predictive of survival in patients with coronary disease. Selection by univariate and multivariate analyses from the clinical, electrocardiographic, exercise, arteriographic, and quantitative angiographic evaluations. (*Circulation* 1979;59;421-430) 2. Predictors of mortality and mobidity in patients with chronic heart failure. (*Eur Heart J* 2006;27,65-75)
Neurohormonal Dysfunction / Hypertension	1. Beneficial Effects of EECP on the Renin-Angiotensin System in patients with Coronary Artery Disease. European Society of Cardiology, Sept 1-5, 2001, Stockholm, Sweden. 2. Effect of Enhanced External Counterpulsation on Circulating and Tissue Angiotensin II in Experimental Myocardial Infarction. The Heart Failure Society of America, Sept 9-12, 2001, Washington, DC, USA.	1. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for 1 million adults in 61 prospective studies. (*The Lancet* 2003;360:1903-1913) 2. Expert consensus document on angiotensin converting enzyme inhibitors in cardiovascular disease. The Task Force on ACE-inhibitors of the European Society of Cardiology. (*Eur Heart J* 2004;25:1454-1470)
Symptom/ functional class improvement (NYHA,CCSC)	1. PEECH. 2. Two-Year Outcomes After Enhanced External Counterpulsation for Stable Angina Pectoris. (from the International Patient Registry [IEPR]). (*Am J Cardiol*. 2004 Feb	1. Prognostic impact of demographic factors and clinical features on the mode of death in high-risk patients after myocardial infarction--a combined analysis from multicenter trials. (*Clin Cardiology* 2005

	15;93(4):461-464) 3. Benefit and safety of enhanced external counterpulsation in treating coronary artery disease patients with a history of congestive heart failure. (*Cardiology* 2001;96:78-84)	;28(10):471-478) 2. Prospective validity of measuring angina severity with Canadian Cardiovascular Society class: the ACRE study*****
Quality of Life	1. PEECH 2. Effects of Enhanced External Counterpulsation on Health-Related Quality of Life Continue 12 Months After Treatment: A Substudy of the Multicenter Study of Enhanced External Counterpulsation. (*Journal of Investigative Medicine.* 2002 Jan;50(1):25-32) 3. Psychosocial Effects of Enhanced External Counterpulsation in the Angina Patient: A Second Study. (*Psychosomatics*. 2001;42(2):124-132)	4. Association Among SF36 Quality of Life Measures and Nutrition, Hospitalization, and Mortality in Hemodialysis. (*J Am Soc Nephrol* 12:2797-2806, 2001) 5. Risk and Benefits of optimized medical and revascularization therapy in elderly patients with angina – On-treatment analysis of the TIME trial. (*Eur Heart J* 2004;25,1036-1042) 6. Health-Related Quality of Life as a Predictor of Hospital Readmission and Death Among Patients with Heart Failure. (*Arch of Internal Med* 2005; 165:1274-1279)

*http://www.ucl.ac.uk/peg/publications/Hemingway_CanJCardiol2004%20CCS.doc

References

[i] Ashley, et al., Exercise testing in clinical medicine. Lancet Vol 356, November 4, 2000 1592-1597.

[ii] *See* External Counterpulsation Therapy Improves Endothelial Function in Patients with Refractory Angina Pectoris (JACC 2003;42:2090); Significantly improved Reactive hyperemia-peripheral arterial tonometry (JACC 2003;41:1761)

[iii] A Neurohormonal Mechanism for the Effectiveness of Enhanced External Counterpulsation. The 72nd Scientific Session of the American Heart, Supplement I-832, Nov 2, 1999; Beneficial Effects of EECP on the Renin-Angiotensin System in Patients with Coronary Artery Disease. European Society of Cardiology, Sept 1-5, 2001,Stockholm, Sweden; Effect of Enhanced External Counterpulsation on Circulating and Tissue Angiotensin II in Experimental Myocardial Infarction. The Heart Failure Society of America, Sept 9-12, 2001, Washington, DC, USA.

[iv] Exercise Capability and Myocardial Perfusion in Chronic Angina Patients Treated with Enhanced External Counterpulsation. *Clinical Cardiology.* 2003 Jun;(26):287-290; Effects of Enhanced External Counterpulsation on Stress Radionuclide Coronary Perfusion and Exercise Capacity in Chronic Stable Angina Pectoris. *Am J of Cardiol.* 2002 Apr 1;89(7):822-824; Enhanced External Counterpulsation Improved Myocardial Perfusion and Coronary Flow Reserve in Patients with Chronic Stable Angina; Evaluation by 13N-Ammonia Positron Emission Tomography. Eur Heart J. 2001 Aug;22(16):1451-1458.

[v] Enhanced External Counterpulsation Improves Systolic Function by Echocardiography in Patients with Coronary Artery Disease. Heart Lung. 2005 Mar-Apr;34(2):122-125; Benefit of Enhanced External Counterpulsation in Coronary Patients with Left Ventricular Dysfunction: Cardiac or Peripheral Effect? Heart Failure Society of America, The 6th Annual Scientific Meeting, Boca Raton, Florida, USA, Sept 22-25, 2002.

[vi] Soran, The Impact of EECP Treatment on Emergency Room Visits and Hospitalization. Presented at the European Society of Cardiology Congress 2005 Stockholm, Sweden.

CARDIOMEDICS

January 19, 2006

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Dear Dr. Phurrough:

We are, of course, disappointed in CMS' proposed Decision of December 20, 2005, on our formal request for coverage for ECP for the treatment of (a) NYHA Class II-IV stable congestive heart failure (CHF), (b) acute myocardial infarction (Acute MI), (c) cardiogenic shock (CG Shock) and (d) CCSC class II stable angina (Angina) and a revision of the criteria for coverage of ECP for CCSC class II-IV Angina. As you know, we withdrew our request for coverage for Acute CHF.

Coverage For Stable Angina

Our request for a revision of the criteria for coverage for CCSC class III-IV Angina was not addressed in CMS' Decision of December 20, 2005, nor did CMS address Vasomedical's request for an even wider change in the criteria for coverage for ECP in the treatment of CCSC class II-IV Angina.

We believe the demonstrated success of ECP in the treatment of CCSC class II Angina, as well as in CCSC classes III and IV Angina, as seen in our 58 patient Angina paper[1], papers by Lawson et al showing one year[2] and three year[3] sustained benefit from EECP in Angina Pectoris by pre and post thallium-201 stress tests, Vasomedical's MUST Study, and the widespread support of ECP seen in the responses submitted during the initial public comment period, warrants the addition of CCSC class II Angina and a revision of the criteria for coverage of ECP for CCSC class II-IV Angina, as set forth in the first full Paragraph on Page 6 of our letter to CMS of June 23, 2005.

While, for the sake of brevity, we cited only our 58 patient Stable Angina Study[1] in our letter to CMS of June 23, 2005, requesting coverage of ECP for CCSC class II Stable Angina and a change in the criteria for coverage of ECP for CCSC Class II-IV Angina, a number of other papers have been published demonstrating the benefit of ECP in treating Stable Angina, which support and validate our 58 patient Stable Angina Study[1] and our request for coverage of ECP for CCSC class II Angina and a change in the criteria for CCSC class II-IV Angina.

In a paper by Lawson et al[2], 18 patients with chronic angina, despite surgical and medical therapy, received 36 hours of ECP on an EECP device. Treadmill thallium-201 stress tests prior to the ECP therapy and one year later showed a complete resolution of ischemic defects in 12 (67%), a reduction in 2 (11%) and no change in 4 (22%), with 14 (78%; $p<0.01$) showing a significant decrease in myocardial ischemia, as well as significant increases in exercise duration and double product.

In a follow-up paper by Lawson et al[3] on the above described patients, stress thallium testing at three years in 10 patients, who were available for follow-up and were event-free during the three year period, 8 (80%) showed preservation of the benefit of the 36 hours of EECP, and 2 (20%) reverted to baseline. The tests were read by independent reviewers.

These two papers[2-3] justify our and Vasomedical's request for coverage of ECP for the treatment of CCSC class II Angina and either our or Vasomedical's request for a change in the criteria for coverage of ECP in the treatment of CCSC class II-IV Angina.

In a paper by Lawson et al[4], 33 patients with stable angina were separated into 26 (79%) Responders who, at 5 years after 35-36 hours of ECP, had a decrease in radionuclide stress perfusion defects and 7 (21%) Nonresponders who had no radionuclide improvement, compared to radionuclide stress perfusion tests prior to the 35-36 hours of EECP. During the 5-year period, 8 patients had cardiac events requiring hospitalization and 3 died. Overall, 21 of the 33 subjects (64%) were alive at five years without cardiovascular morbidity or the need for repeat vascularization. This five-year survival rate justifies coverage of ECP for CCSC class II Angina and either our or Vasomedical's request for a change in the criteria for coverage of ECP for the treatment of CCSC Class III-IV Angina.

In the sections of this letter relating to Coverage of ECP for the Treatment of Stable CHF, Acute MI and CG Shock, you will find papers that demonstrate the effect of ECP on diastolic and systolic pressure, cardiac output, and other parameters of different early ECP devices applied in different manners, and the benefits of repetitive application ECP, through the opening and development of collaterals, the release of endogenous angiogenic growth factors and the increase in capillary density in the infarct area. Please review these references with respect to the coverage of ECP for the treatment of CCSC class II Angina and the change in criteria for coverage of ECP for CCSC class II-IV Angina requested in this section.

In light of the above, we hope CMS will take a favorable stance on our formal request to expand coverage of ECP to the treatment of CCSC class II Angina and to revise the criteria for coverage for CCSC class II-IV Angina, as set forth in the first full Paragraph on Page 6 of our letter to CMS of June 23, 2005, or in Vasomedical's proposed NCD Form, as the myocardial revascularization benefits of ECP should be made available to the population of Angina patients we requested, such coverage is reasonable and necessary, and no such coverage presently exists.

<u>Coverage for Stable CHF</u>

While we understand CMS gives greater weight to randomized, controlled clinical studies than to retrospective data, the two are not mutually exclusive. In our 127 patient CHF paper[5], <u>all</u> of the NYHA Class II-IV CHF patients, who also suffered from a co-morbidity of CCSC class III-IV Stable Angina, who were serially treated with ECP at all of the six participating sites were included in our 127 patient CHF paper[5]. Bias can be introduced in both randomized, controlled clinical studies and retrospective studies by the selection of patients to be included or if the reporting is not rigorously enforced.

Cardiomedics' personnel traveled to each participating Investigator's site to be certain that all NYHA Class II-IV CHF patients with CCSC class III-IV Stable Angina treated with ECP at each site were included and to assure that the reporting was rigorous. Knowing the quality of Vasomedical's Investigators, we are sure the same rigorous reporting was enforced by them.

We conceived the Graduated Pressure Regiment to avoid excessive preload, which ECP produces at 1.5:1 to 2:1 D/S Ratios, which have been shown in a paper by Suresh et al[6] to be optimal in the treatment of Angina. Such high D/S Ratios are known to cause adverse effects in CHF patients, including exacerbation of CHF symptoms, increased mortality and morbidity and premature withdrawal from the therapy. We had planned to cite four papers on the adverse effects seen in CHF patients from EECP therapy[7-10]. However, to save CMS time in the review process, we decided to cite only the paper by Lawson et al[8], and we did not include papers[7, 9 & 10]. Since we had already scanned the references, which is a slow process, we did not have time to re-number and scan them again, and also correct the reference numbers in the text of this letter. **Please excuse the absence of reference[7] below**.

We will appreciate your taking the time to particularly note the Lawson et al paper[8]. The study described in the Lawson et al paper[8] makes it clear why the clinical results in CHF seen with Vasomedical's EECP device, at uniformly high D/S Ratios, differ so widely from the clinical results in CHF seen with our ECP System, under our Graduated Pressure Regimen. We believe the Lawson et al paper[8] also makes it obvious why Vasomedical chose to not include fragile NYHA class IV CHF patients in their PEECH Study.

Our clinical results in CHF deserve CMS covering ECP for the treatment of NYHA Class II-IV CHF, and we can find no better reason than the Lawson et al paper[8] for including the limitation on coverage of ECP for the treatment of NYHA Class II-IV CHF "to the use of ECP devices under a Graduated Pressure Regimen that have demonstrated in a clinical study, published in a peer-reviewed cardiology journal, mortality in the year following the ECP therapy of 2% or less and a reduction in hospital admissions in the year following the ECP therapy of 80% or more, compared to the prior year," as we requested in our letter to CMS of June 23, 2005, and are repeating herein.

We treated NYHA class IV CHF patients in our 127 patient CHF study[5], even those in the average 1.32:1 High D/S Ratio Group because, under our Graduated Pressure Regimen, the D/S Ratios were started at very low levels and were gradually increased in stages over the 35-hour, seven week course of ECP Therapy. If our Graduated Pressure Regimen had not been conceived, our Investigators, like Vasomedical's, would not have treated fragile NYHA class IV CHF patients at uniformly high D/S Ratios, in light of the adverse events seen in the Lawson et al paper[8].

Please excuse the absence of references 9-10.

In a recent paper by Soran O et al[11], which was published in January 2006, two-year registry data on 363 patients with refractory angina pectoris and left ventricular dysfunction, followed for six months, showed that 72% of the subjects improved from severe to no or mild angina, the survival rate was 82%, the MACE-free survival rate was 70% and 43% had no cardiac related hospitalization.

However, the Soran et al paper[11] mentions 81% of the subjects had no reported congestive heart failure events, but fails to describe the adverse CHF events that occurred in 19% of the subjects. Also, this paper mentions that only 78% of the subjects with congestive heart failure completed the course of EECP therapy, but does not describe the reasons for the

22% who dropped-out. As a result, this two-year paper[11] supports our position that different ECP devices used in different manners produce different results, as this paper shows EECP, applied at high D/S Ratios, results in adverse events and premature withdrawals in a significant percentage of CHF patients, such as seen in the above cited Lawson et al paper[8]. In our 127 patient CHF study[5] of ECP, under our Graduated Pressure Regimen, there were no adverse events or withdrawals from the ECP therapy.

In its Decision of December 20, 2005, CMS mentioned the lack of the range of the D/S Ratios in our 127 patient CHF paper[5]. You will see in the third paragraph of the middle column on Page 148 of our 127 patient CHF paper[5], we listed the range of each of the above average D/S Ratio Groups. You will note the range of the Low D/S Ratio Group was 0.4:1 to 0.99:1, and the range of the High D/S Ratio Group was 1.3:1 to 1.6:1.

In its Decision of December 20, 2005, CMS also mentioned the need for a study to compare our D/S Ratios and Regimen to Vasomedical's. The answer to CMS dilemma in viewing these conflicting protocols is, in the High D/S Ratio Group, under our Graduated Pressure Regimen, mortality in the year following the ECP therapy was 8.82%, whereas in the Low D/S Ratio Group, mortality in the year following the ECP therapy, under our Graduated Pressure Regimen, was only 1.85% ($p<0.0001$). Our 127 patient CHF paper[5] provides the comparison CMS suggests, without subjecting CHF patients to the adverse effects of a High D/S Ratio EECP Therapy without a Graduated Pressure Regimen. The difference in outcomes speaks for itself.

Differently constructed ECP devices, used at different pressures and timings or under different regimens, have been shown to produce conflicting results. For example in an early paper by Langou RA et al[12], one early "ECP" device used on humans undergoing cardiac catheterization, sequenced ECP (as in our ECP system) was shown to increase the ratio of diastolic pressure to 1:1 (typically 67:1), to increase cardiac output by 17%, greater than typically seen with the use of an IABP, and increase coronary flow by 25%, with the conclusion that the ECP device is an excellent cardiac assist device.

However, in an early paper by Solignac A et al[13], a different "ECP" device produced only a mean increase in diastolic pressure of 13% and no effect on coronary flow or oxygen need was seen, with the conclusion that ECP was of doubtful value in the treatment of Angina. In another early paper by Loeb HS et al[14] a different "ECP" device produced an increase in mean diastolic pressure of only 8 mm Hg, coronary sinus flow was not increased and oxygen need was not reduced, expressing the same doubtful conclusion of Solignac et al[13].

While the "ECP" devices cited in these papers[12-14] and others available in the literature were constructed differently, functioned differently and pressure was applied in different manners, they were all "ECP" devices, according to the FDA. The ECP devices cited in the above three papers[12-14] and others utilized a variety of constructions, some with an inflatable lower body suit, cuffs on the calves and thighs, cuffs on the calves, thighs and buttocks, cuffs on the calves, thighs and upper arms, cuffs inflated sequentially, cuffs inflated simultaneously and bladders in a casing that enclosed both the calves and thighs, as well as other variations. Some of the devices used round, square, very large, very small and variously shaped bladders. It is no surprise that the clinical results differed from one device to another.

Only in our 127 patient CHF paper[5] were the D/S Ratios started uncommonly low and gradually increased in stages over the 35 one-hour, seven-week course to ECP therapy. It is no surprise that the clinical results differed from one manner of application to another.

Recognizing the mechanical differences between our ECP System and Vasomedical's EECP Device, the different levels of pressure applied and the manner in which we increase the pressure and D/S Ratio in stages under our Graduated Pressure Regimen, it should be no surprise that our clinical results are different from Vasomedical's and no head to head comparison of our ECP System under our Graduated Pressure Regimen with Vasomedical's EECP System is needed to reconcile the differences.

Also, in the bottom line on Page 17 of CMS' Decision, of December 20, 2005, CMS states the incidence of hospitalization was not shown by NYHA CHF Class. To the contrary, Table VI on page 151 of our 127 patient CHF paper[5] is titled "Average Number of All-Cause Hospitalizations by New York Heart Association (NYHA) Class". As you will note, in the Low D/S Ratio Group, under our Graduated Pressure Regimen, for which we are seeking coverage, all cause hospital admissions in the year following ECP, compared to the year prior to ECP, was reduced in each of the three NYHA CHF Classes: by 88.5% in Class II ($p<.0154$), by 87.8% in Class III ($p<.0001$) and by 84.0% in Class IV ($p<0.0154$).

Incidentally, we should call your attention to a printer's error in the p value for the difference in hospitalizations in NYHA Class II CHF in the Mid D/S Ratio Group in Table VI of our 127 patient CHF paper[5]. The correct p value is <0.02.

In addition to the significant reduction in mortality seen in our 127 patient CHF study[5], the cost of our ECP therapy will be more than offset by the reduction in hospital admittances. What better justification for coverage of ECP for the treatment of NYHA Class II-IV CHF, administered under a Graduated Pressure Regimen, than a statistically significant reduction in mortality and a statistically significant reduction in hospital admissions is reasonably necessary for CMS to render a favorable decision on coverage for ECP for NYHA Class II-IV CHF, with the limitation on coverage we requested?

Finally, in the last paragraph on Page 17 of CMS' Decision of December 20, 2005, CMS questions why there were differences in the number of patients in the figures reported for mortality and the number of patients in the figures reported for LVEFs and NYHA CHF Class in our 127 patient CHF paper[5]. This is easy to explain. To be conservative, we reported on all cause hospitalizations of all of the patients in the three Groups, living or dead, which included seven terminal hospitalizations, whereas the data on LVEFs and NYHA CHF Class were reported on only the survivors, as was cited in the text of the paper.

Obviously, to report on the LVEFs and incidence of hospitalization at one year after 35 hours of ECP, the patient had to be alive at the end of the year. Had we reported on the incidence of hospitalizations of only the survivors, the number of hospitalizations of the survivors in the year following ECP would have been reduced by the terminal hospitalizations, and the reductions in hospital admissions would have been more significant. However, we felt presenting the data, as we did, better reflected the actual incidence of hospitalization resulting from ECP under our Graduated Pressure Regimen.

Also, with respect to our 127 patient CHF study[5] being a retrospective analysis of registry data, we understand CMS recently granted coverage of a left ventricular assist device (LVAD) for the treatment of Acute MI with Shock, based upon AbioMed's registry data on just 50 patients, with the data showing a reduction in mortality to 40%, versus the typical mortality in CG Shock of 80%, and with the native hearts of 70% of the survivors having regained function. We believe CMS' decision was well justified by the excellent data cited above. However, the 50 patients in the LVAD's registry is less than the number (54) in the Low D/S Radio Group in our 127 patient CHF Study[5] under our

Graduated Pressure Regimen, and the 40% reduction in morality in AbioMed's group was smaller than the reduction in mortality in our 127 patient CHF study[5]. Our request for coverage of ECP for the treatment of NYHA Class II-IV is entitled to the same favorable decision.

For the above cited reasons, we again repeat our formal request for coverage of ECP for the treatment of NYHA Class II-IV Stable CHF and we respectfully request that coverage of ECP for NYHA Class II-IV Stable CHF be limited to the use of ECP devices, under a Graduated Pressure Regimen, which have demonstrated in a clinical study, published in a peer-reviewed cardiology journal, a reduction in mortality in the year following the ECP therapy to 2% or less and a reduction in hospital admissions in the year following the ECP therapy of 80% or more, compared to the year prior to the ECP therapy, as set forth in our letter of June 23, 2005 and September 15, 2005, as such coverage is reasonable and necessary, and no such coverage presently exists.

We understand CMS prefers to make coverage decisions on medical devices on a generic basis. However, medical devices are constructed and used differently and are not the same as unique chemical entities, like drugs, each of which must be separately clinically tested and approved for sale by the FDA. While applying the limitation on coverage we requested for a medical device is unusual, "substantial equivalence" is not a sufficient standard to assure that CHF patients will benefit equally from different ECP devices used in different manners.

The aforementioned mortality and hospital admission criteria that we requested be included in the limitation on coverage of ECP for NYHA Class II-IV CHF are reasonable and necessary to assure that only ECP devices providing significantly improved net health outcomes are covered. We believe these criteria will prevent the waste of taxpayer money that would occur if Medicare was to pay for the use of ECP devices that provide little or no tangible improvement in net health outcomes and have been shown to produce significant adverse effects. Setting a new precedent that assures a significant improvement in patient outcomes and avoids the waste of taxpayer money is not only well worth the effort, it demonstrates sound fiscal management of Medicare's funds and assures improved health outcomes for Medicare beneficiaries.

Coverage for Acute MI and CG Shock

In CMS' Decision, with respect to our request for coverage for Acute MI and Cardiogenic Shock, CMS said medical therapy has advanced since the time of our randomized, controlled, 258 patient Acute MI paper[15], which was published in 1980. While it is true that medications have changed since the time of this study, all of the Acute MI patients in both the ECP Treatment and Control Groups received optimal medical therapy, including antiarrhythmic drugs, diuretic agents, digitalis, vasodilator drugs and propanolol, a beta blocker, as well as analgesics and sedatives. To be sure, Plavix, Rheopro and other new drugs did not exist at the time of this study. However, had they existed and been employed in this study, mortality in both the ECP Treated patients and the Controls would, presumably, have been reduced.

Since this was a randomized, controlled clinical study, designed to eliminate or minimize bias and any placebo effect, and with both the ECP Treated patients and the Controls receiving optimal medical therapy, such as it was at the time, it would be reasonable to conclude that ECP contributed substantially to the 56% reduction in mortality between the 14.7% mortality in the 116 Controls and the 6.5% mortality in the 108 patients who received 4 or more hours of ECP within 24 hours of the onset of their Acute MI symptoms ($p<.05$).

The very basis of randomized, controlled clinical trials of devices is to make concomitant medical therapies uniform for both the Treatment and Control Groups, so the contribution of the new device to any difference in results between the two groups can be seen. To dismiss the contribution of ECP to the 56% reduction in mortality shown in our Acute MI paper[15], by characterizing the medical therapy applied to both groups as "old", is patently incorrect.

Also in our 258 patient Acute MI paper[15], care was taken to assure that the ages, sexes, medical histories and severity of the Acute MI in the controls in this study were comparable to those of the ECP treated patients, and the paper states "there was no significant difference in pharmacologic therapy." The above-cited paper[15] also makes the following statements:

"The validity of this study was supported by rigorous implementation of protocol, randomization procedure, data acquisition and analytic methods."

"Outcome was consistently favorable in all ECP treated groups."

"The most critical factor determining the clinical course of patients hospitalized with Acute Myocardial infarction is infarct size, because cardiac pump failure, the major cause of mortality in this setting, is the result of extensive cardiac damage." (You will see referenced papers demonstrating ECP's ability to limit or reduce infarct size later in this letter.)

"mechanical circulatory assistance may have an important role in early application to control myocardial damage before hypertension and cardiac pump failure develop."

"external pressure counterpulsation produces considerable augmentation of diastolic blood pressure, a critical determinant of coronary blood flow."

and "experimental studies suggest that external pressure counterpulsation may increase collateral flow to ischemic myocardium."

The degree of attention to detail in the above cited paper[15] is illustrated by the authors providing the reason for each and every patient in the Intent to Treat cohort's exclusion from the study (including their not meeting the protocol's requirement for a Killip Class II Acute MI, not having received the ECP therapy within the prescribed time from the onset of symptoms, etc.). Many papers do not explain the difference between the Intent to Treat cohort and the number of patients reported upon or simply provide a generalized description of the reasons for the difference. This attention to detail adds to the credibility of this paper's results. The Soran et al paper[11] is a good example of the lack of detail in some papers mentioned above. This is obviously not the case in our 258 patient Acute MI paper[15].

The earlier version of our present ECP System used in the aforementioned 258 patient Acute MI study[15] employed only two sets of cuffs about the calves and thighs. Fortunately, this ECP device was able to create D/S Ratios only up to about 1:1 and commonly produced D/S Ratios of 0.8:1. The maximum pressure allowed in the FDA clearance of this earlier ECP System was 250 mm Hg, and it was typically used at less than 200 mm Hg, whereas the maximum pressure under the FDA clearance for our present ECP System, with a separate buttocks cuff, is 300 mm Hg.

However, the amount of pressure used to produce the initial Low D/S Ratios under our Graduated Pressure Regimen in our 127 patient CHF paper[5] were typically 70-90 mm Hg. High 1.5:1 to 2:1 D/S Ratios typically require pressures of 250 to 300 mm Hg. As a result, the hearts of the Acute MI patients in our 258 patient Acute MI Study[15], having suffered damage due to the

infarct, did not have to labor to overcome excessive preload. Had this not been the case, we believe mortality in this study would have been significantly higher.

We understand that less than half of the hospitals in the United States have catheterization laboratories able to provide PTCA procedures, and we understand that CABG surgery is presently offered by only somewhat more than half of the hospitals in the United States. **(As used herein, "PTCA" means PTCA with or without stents.)**

As a result, persons suffering an Acute MI or CG Shock that arrive at a hospital without PTCA or CABG facilities should receive 4 hours of ECP (8 or more hours for CG Shock patients) and be stabilized before being transferred to a facility with PTCA and/or CABG capabilities, as traffic in metropolitan markets and the distance of rural hospitals from metropolitan markets subjects these patients to an inordinate risk of death due to irreversible myocardial damage that can occur within hours in infarct cases.

The same applies to Acute MI and CG Shock patients that arrive at a hospital with PTCA and/or CABG capabilities and who are amenable to such procedures. Even a few hours of ECP before a PTCA or CABG procedure can help stabilize the patient and have been shown to increase perfusion of the myocardium, which can reduce or limit the infarct size[12, 17].

This also applies to Acute MI and CG Shock patients who are admitted to a hospital with PTCA, CABG and IABP capability, but are not amenable to a PTCA, CABG or IABP procedure, who, for religious or psychological reasons, are not willing to undergo a PTCA, CABG or IABP procedure or who, in the opinion of a cardiologist or cardiovascular surgeon, even if amenable to a PTCA, CABG or IABP procedure, could benefit from ECP. Such patients should be entitled to receive the life saving benefits of our non-invasive ECP System, such coverage is reasonable and necessary, and no such coverage presently exists.

In a paper by Strobeck JE et al[16], you will note on page 3 of the paper, the refusal of a patient to undergo a repeat CABG procedure and, later, his refusal to undergo catheterization for an angiogram to confirm the progression of disease in his right coronary artery. If he was being cared-for by a general practitioner in a rural area, without a cardiologist or cardiovascular surgeon to prescribe ECP, which is required by the present criteria for coverage, he would have not had the benefit of ECP. Refusal of patients to undergo an invasive procedure, even when counseled by a cardiologist to do so, is not unusual.

Medicare beneficiaries, whether they live in a rural area or not, have the right to refuse any invasive procedure, and they should be entitled to coverage of whatever therapy would help them, whether they are amenable to an invasive procedure or not. They should be entitled to elect ECP for the treatment of Acute MI or CG Shock, as well as ECP for the treatment of NYHA Class II, III or IV CHF and CCSC class II, III or IV Angina, as coverage of ECP for these conditions is reasonable and necessary, and no such coverage exists.

In the late 1970's, at the time of the aforementioned 258 patient Acute MI Study[15], the second, important benefit of the repetitive application of ECP was not recognized, as the existence and function of angiogenic growth factors was largely unknown. We now know that repetitive one-hour ECP treatments release endogenous angiogenic growth factors causing, over time, the creation of capillaries and revascularization of the myocardium.

In a paper by Huang W et al[17], an increase in capillary density of 30% ($p<0.01$) was created by 2.33 hours of ECP in the ischemic area of the hearts of 8 dogs by ECP following the ligation of a coronary artery, whereas no increase in capillary density was seen in the hearts of

the 6 control dogs following ligation of the corresponding coronary artery. It is noteworthy that no increase in capillary diameter was seen in either group, confirming that ECP's cardiogenesis effect is primarily the creation of capillaries. As defined by Shaper (Circl Res, 1996; 79:911-919), "angiogenesis" is the creation of capillaries, whereas "arteriogenesis" is the widening of existing arteries, which was not seen in this paper[17].

As we discussed at our meeting with CMS on December 14, 2005, PTCA and CABG procedures open blockages in the major coronary arteries and permit blood flow downstream through existing arteries to the capillary beds in the myocardium. While ECP can force blood around blockages in the coronary arteries and open the collaterals in acute ischemia, ECP has little or no cardiogenesis effect upon large, heavily muscled coronary arteries or their immediate branches. The benefit of the repeated application of ECP in patients with chronic ischemia is due to angiogenesis and the creation of new capillaries[17] to revascularize the heart. ECP is complimentary to, and is not an alternative to PTCA or CABG procedures. The combination of ECP and PTCA or CABG produce more complete revascularization of the heart muscle than either therapy alone.

Bypass surgery and PTCA are not perfect, and some Angina and Acute MI patients may continue to experience Angina after the CABG or PTCA procedure. Even a small amount of Angina in such patients is said to be an ominous portender of future problems. Repeating PTCA and CABG surgery is expensive and, sometimes, a second CABG procedure is contraindicated by the patient's condition, scar tissue, adhesion of the pericardial sack to the heart, etc. Angina and Acute MI patients, following CABG surgery or PTCA, should be entitled to the myocardial revascularization benefit of ECP's creating angionenesis and capillary growth.

With respect to our 20 patient study of ECP in the treatment of CG Shock[18], the contribution of ECP to the 230% increase in survival in CG Shock during the hospital stay and the following month to 35%, versus survival at the time of 15% ($p<0.01$), cannot be ignored. In fact, even with improved IABP devices and today's new drugs, we understand survival in CG Shock is still only about 20%. Any therapy that can reduce mortality in a condition with such high mortality certainly needs to be available to critically ill people.

As mentioned earlier in the section of this letter regarding coverage of ECP for Stable Angina, CMS' recent coverage of an LVAD for Acute MI with Shock (CG Shock), based on 50 patient registry data with a reduction in mortality to 40%, coverage of ECP for the treatment of Acute MI and CG Shock is equally justified. Our 258 patient Acute MI study[15] was randomized and controlled and demonstrated a reduction in mortality of 56% in 108 patients, versus 116 controls ($p<0.05$), and our 20 patient CG Shock study[18] showed a 230% increase in survival from 15% to 35% ($p<0.01$), almost equal to the 40% survival with AbioMed's LVAD, to which modern drugs contributed, but could not by themselves produce such a reduction in mortality. Accordingly, coverage of ECP for Acute MI and CG Shock should be granted.

For the sake of brevity, in our letter to CMS of June 23, 2005, we cited only our 20 patient CG Shock Study[18]. However, several other published papers demonstrated the comparability of ECP to the IABP and mentioned ECP's non-invasive, fast and easy-to-apply advantages[13,19-21], as described in the following paragraph.

In addition to the paper by Langou RA et al[13], in other papers by Wright PH[19], Cohen LS[20] et al and Watson JT et al[21], ECP devices were shown to compare favorably with intra-aortic balloon pump (IABP) devices. In some parameters, these early ECP devices did not perform as well as IABP devices, and in some parameters these early ECP devices performed better than

IABP devices. The ability of ECP devices to increase venous return (which IABP devices cannot do) and the non-invasive nature and fast, easy application of ECP devices as additional benefits were cited in these papers[13,19-21].

As mentioned in some of the above papers[13,19-21], many Acute MI patients undergoing CABG surgery die when removed from cardiopulmonary (heart-lung) bypass machines, and many Acute MI and CG Shock patients undergoing IABP therapy die when IAB catheter must be removed. The ability of ECP devices to wean patients off cardiopulmonary bypass (heart/lung) machines is another reason why ECP should be covered for the treatment of Acute MI, and the ability of ECP devices to wean CG Shock patients off an IABP should justify coverage of ECP for CG Shock. Gradually increasing the D/S Ratio under our Graduated Pressure Regimen allows patients to be weaned from heart-lung bypass and IABP devices without creating excessive preload and forcing the heart, weakened by the infarct, to work harder.

Also, as demonstrated in a paper by Applebaum et al[22], ECP increases both cerebral and renal flow by 22% and 19%, respectively. While the long-term persistence of the effect of ECP on cerebral and renal flow is not known, in critically ill Acute MI and CG Shock patients, the application of ECP during the critical "life and death" period would provide life-saving support for these patients. This further justifies coverage of ECP for Acute MI and CG Shock.

In addition, unlike the IABP, ECP provides venous return, reducing systolic pressure, the work-effort of the heart and its oxygen need. And, when the cuffs deflate, the arteries in the buttocks and legs are partially empty, reducing the resistance to pumping blood out of the left ventricle and further reducing the work-effort of the heart and its oxygen need. As a result, we believe these benefits of ECP, under our Graduated ECP Regimen at low D/S Ratios, contributed substantially to the significant reduction in mortality shown in our 127 patient CHF study[5], the 56% reduction in mortality shown in our 258 patient Acute MI study[15], and the 240% increase in survival shown in our 20 patient CG Shock study[18].

Considering our 258 patient Acute MI Study[15], our 20 patient CG Shock Study[18], CMS' recent coverage of a LVAD for the treatment of Acute MI with Shock, based upon retrospective data, the other papers cited herein and the explanations provided in this letter, we repeat our request for coverage of ECP for Acute MI and CG Shock, with coverage being limited to the use of ECP devices under a Graduated Pressure Regimen that demonstrated in a clinical study, published in a peer-reviewed cardiology journal, a reduction in mortality during the hospital stay to 7% or less in Acute MI and an increase in survival during the hospital stay and the following month to 30% or more in CG Shock, as requested in our letter of June 23, 2005, as such coverage is reasonable and necessary, and no such coverage presently exists.

Copies of some of the papers available electronically are attached hereto. A number of the referenced papers are not available for electronic transmission and would present very large files if scanned and transmittal electronically. We'll send them with this letter and see if it goes through. In any case, we will express a hard copy of this letter and all of the referenced papers, including those attached hereto, some of which may be underlined to denote particular information, along with one or more CDs containing all of the referenced papers, including those attached electronically hereto.

We trust another review of our CHF[5], Acute MI[15] and CG Shock[18] papers, along with the newly referenced papers and the information provided in this letter, will enable CMS to cover ECP for the treatment of CCSC class II Stable Angina, revise the criteria for coverage of ECP for CCSC class II-IV Stable Angina, and cover ECP for the treatment of NYHA Class II-IV Stable

CHF, Acute MI and CG Shock, with coverage for these three latter conditions being limited to the use of ECP devices under a Graduated Pressure Regimen, which have demonstrated in clinical studies, published in peer-reviewed cardiology journals, reductions in mortality (and hospital admissions in CHF) per the criteria we requested herein and in our letters to CMS of June 23, 2005 and September 15, 2005.

Very truly yours,

/s/ Marvin P. Loeb

Marvin P. Loeb, Sc.D.
Chairman and CEO

Attachments: Cited Papers

c.c. Isabel Dunst
Sheree Kanner
Monique Nolan

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December 23, 2005

Pamela Douglas, MD, FACC
President American College of Cardiology
c/o Rebecca Kelly
Director, Regulatory Affairs
American College of Cardiology
9111 Old Georgetown Road
Bethesda, MD 20814

Re: Expansion of EECP Reimbursement Coverage

Dear Dr. Douglas,

As one of the pioneering institutions for EECP therapy in the United States, Stony Brook University Hospital has witnessed many benefits with the use of this therapy beyond its current indications for Class III/IV refractory angina patients. We would like the ACC to reconsider its position in regard to expanding EECP's reimbursement coverage in light of the following factors:

1. Research data from the MUST-EECP Trial and from the international EECP Patient Registry (IEPR) shows benefits in patients with CCS Class II angina as well III & IV. Stony Brook participated in the MUST-EECP trial as the data coordinating center, and we also are part of the Registry.

2. A randomized, controlled clinical trial (the PEECH trial), plus on-going registry studies, and personal observation of patients who have undergone EECP support the proposal that expanded coverage can significantly benefit patients with heart failure by improving their symptoms, functional status and quality of the life. Patients barely able to ambulate before starting treatment often enjoy dramatically improved quality of life. Stony Brook University Hospital also participates in this trial

3. Nearly 80% of patients with angina without heart failure have noted a significant reduction in their symptoms. Anginal events are reduced and require a higher level of activity to be initiated. Most patients require less medication, even as their exercise tolerance improves.

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STONY BROOK
STATE UNIVERSITY OF NEW YORK

4. Perhaps most importantly EECP is a noninvasive out-patient procedure, it can be repeated, carries very little risk to patients, and it achieves its benefits in patients who already are on optimally tolerated medical therapy.

5. Since several laboratories have identified possible physiologic mechanisms to explain how EECP works, we doubt the affects are related primarily to placebo effects.

Sincerely,

Peter F. Cohn, M.D.
Professor of Medicine,
Chief of Cardiology, Emeritus

cc: Jyme Schaefer, MD
Deirdre O'Connor, MS
Coverage & Analysis Group Centers for Medicare & Medicaid Services
7500 Security Blvd
Mail Stop C1-09-06
Baltimore, MD 21244

OCONNOR, DEIRDRE E. (CMS/OCSQ)

From: Dolina, Elaine L. (CMS/OCSQ)
Sent: Thursday, February 16, 2006 4:32 PM
To: OCONNOR, DEIRDRE E. (CMS/OCSQ)
Subject: ECP Comment

Deirdre-
This comment was submitted on the main CMS site through the RightNow Q&A tool:

I am commenting on the review of external couterpulsation to protest that it is not being extended to congestive heart failure treatment. the PEECHES study has clearly shown EECP to be effective in improving the level of functioning for patients with CHF. By decreasing the readmission rate EECP has also shown it can be cost effective for treatment of CHF. Please reconsider this decision in light of the studies of improved patient care and cost benefit. Eugene Moffett,M.D.

SURESH N. GADASALLI, M.D., F.A.C.C.
CONSULTIVE CARDIOLOGY
(432) 580-8686
ABIM BOARD CERTIFIED INTERNAL MEDICINE, CARDIOVASCULAR DISEASES
AND INTERVENTIONAL CARDIOLOGY (CAQ)

January 5, 2006

Jyme Schafer, M.D.
Coverage and Analysis Group
Centers for Medicare and Medicaid Services
7500 Security Blvd.
Mail Stop C1-09-06
Baltimore, MD 21244

Dear Dr. Schafer,

Vasomedical, Inc. has been working with CMS over the last several months to increase awareness of the benefits of **EECP therapy** for treating angina and congestive heart failure including reduction in symptoms, improvements in the ability to exercise, and improved quality of life as have been reported in numerous investigations including the recent PEECH Trial.

We are disappointed by the proposed CMS decision not to expand reimbursement coverage of **EECP therapy.** We believe the breadth and quality of clinical evidence supporting the use of **EECP therapy** in patient with congestive heart failure, including the PEECH study results clearly demonstrates the significant benefits of this therapy. We will continue our efforts to provide the clinical evidence to support the use of this noninvasive option for treating cardiovascular disease and are confident that we can work with CMS to secure expanded coverage.

Sincerely,

Suresh N. Gadasalli, M.D., F.A.C.C.

SNG:dk

THE HEALTHY HEART CENTER
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Joseph M. Branconi, MD, FACC

Kim French, MS, ARNP
Laura Webb, PA-C

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Administrator

WWW.HVCBDOCS.COM

January 10, 2006

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Please contact me at (941) 761-4448 if you have any questions or require assistance with any of the links noted above.

Sincerely,

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Sincerely,

Enrique Rivera, MD,
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Sincerely,

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Please contact me at (941) 761-4448 if you have any questions or require assistance with any of the links noted above.

Sincerely,

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December 20, 2005

Steve Phurrough, M.D., MPA
Director of Coverage Analysis Group
7500 Securty Blvd
Baltimore MD 21244

RE: EECP

Dear Dr. Phurrough:

I understand Medicare will not cover EECP for heart failure with severe to moderate LV dysfunction. This decision is interesting as the recent PEACH trial showed, very effectively, that patients' symptoms were markedly improved. I find it interesting that coronary angioplasty is being performed more and more for symptoms related to congestive heart failure and to angina that is not disabling. I have seen bypass surgery be performed for congestive heart failure when there is no clear evidence that this works. At the same time, Medicare has paid for this.

EECP treatment would be a fraction of the cost and, if it prevented one hospitalization, would be well worth the small expenditure of a 35 course treatment of EECP.

It is a shame when decisions are based on economic reasons rather than clinical reasons especially when treatment, which is affective, is also low cost.

I would hope that you could reconsider this. I do understand the importance of strictly regulating those patients that receive EECP so that the same issues that have occurred in bypass surgery and, more recently, coronary angioplasty, would not be repeated; namely, procedures being performed for questionable indications.

Sincerely,

James P. O'Neil, M.D., F.A.C.C.

JPO/ivh
cc: Administrative File: CAG-00002R2
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Marcel Salve, M.D., NPH
Director, Division of Medical and Surgical Services
7500 Security Blvd
Baltimore MD 21244

Diedra O'Connor
Policy Analyst
7500 Security Blvd
Baltimore MD 21244
CMS
Washington, D.C.

DD: 12/20/2005 / DT: 12/21/2005

Jan. 16, 2006

Jyme Schafer, MD
Deirdre O'Connor, MS
Coverage and Analysis Group
Centers for Medicare and Medicaid Services
7500 Security Blvd.
Mail Stop C1-09-06
Baltimore, MD 21244

Re: EECP Coverage

To Whom It May Concern:

As an interventional cardiologist, I have opportunity to prescribe ECP therapy for my patients that are unable to benefit from surgical intervention and are not responding adequately to medications. In the past 2 years that our hospital has offered ECP therapy we have had approximately 50 patients complete the treatment schedule.

The majority of these patients show positive benefits from the treatment. Patients experience both physical and emotional improvement after receiving therapy that improves their quality of life. The antidotes related to me on follow-up visits range from being able to climb a flight of stairs without stopping for chest pain to "You've given me my life back." A consistent comment is, "Why did I have to wait until I was this bad, to get this treatment?"

I would recommend extending ECP coverage to include Class II angina pectoris and CHF. Given the PEECH research and trials, and the experience of my patients', I believe the positive benefits and cost effectiveness are evident.

I am not associated with the ECP therapy department of our hospital nor do I have any conflict of interest with the manufacturers.

Sincerely,

Jay Ambrose, MD

Independence Cardiology Associates, P.C.

C. David Akin, MD, FACC
G. William Pogson, MD, FACC
Paul R. Chu, MD, FACC
Sarat C. Pachalla, MD, FACC
Jenny Glazier, RN, Med-Surg CNS, Preventative Cardiology
Janette Rector, RN, BC, FNP

January 16, 2006

Jyme Schafer, M.D.
Coverage and Analysis Group
Centers for Medicare and Medicaid Services
7500 Security Blvd
Mail Stop C1-09-06
Baltimore, MD 21244

RE: Proposed coverage decision

Dear Sirs:

We have used external counterpulsation therapy now for approximately five years. We have found it quite efficacious for people with untreatable angina.

The data now supports its use also in patient with refractory left ventricular dysfunction.

This class of patients have limited options and a very poor longterm outcome.

The "PEECH" Trial gives strong indication that EECP will be significantly helpful for this group of people and I would encourage your consideration for coverage for patients with congestive heart failure as well.

I appreciate your consideration.

Thank you,

David Akin, M.D.
DA:nmc

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FAX. (718) 597-7939

January 6, 2006

CMS
Jyme Schafer, M.D.
Deirdre O'Connor, M.S.
Coverage and Analysis Group
Centers for Medicare and Medicaid Services
7500 Security Blvd.
Mail Stop, C1-09-06
Baltimore, Md. 21244

Dear Dr. Schafer and Ms. O'Connor:

My office and my patients are very disappointed by the proposed CMS decision not to expand reimbursement coverage of EECP therapy.

The PEECH study clearly demonstrates the significant benefits of EECP therapy in treating patients with angina and CHF. This results in a reduction in symptoms, improvement in the ability to exercise, and improved quality of life.

It is hard for us to understand why external counterpulsation cannot be used for CCSC class II angina and NYHA class II/III stable heart failure with an EF of less than 35% --- when the patients themselves, almost without exception--- testify that their quality of life is so much improved with just being able to do "normal" things such as walking to the mailbox, climbing a flight of stairs, carrying groceries, and not feeling drained and fatigued.

We do hope that your office will reconsider expanding reimbursement coverage for EECP therapy based on the PEECH trial and the testimony of thousands of patients who have "come back to life."

Sincerely,

Robert M. Potenza, M.D.

OCONNOR, DEIRDRE E. (CMS/OCSQ)

From: Richard Ryder [rar@cardioassoc.com]
Sent: Thursday, January 12, 2006 9:53 AM
To: OCONNOR, DEIRDRE E. (CMS/OCSQ)
Subject: EECP

I am a cardiologist who has been doing EECP even before Medicare paid for the proceedure. I also have a subspeciality in heart failure as the past director of the heart failure program at the Brody School of Medicine. I would like to have the opportunity of offering EECP to patients with angina who are not failures with angioplasty. As I am sure you are aware there is no data to support the use of angioplasty to prolong life except in the presence of for acute myocardial infarction or acute coronary syndromes. The relief of symptoms can be achieved with EECP with much less cost and risk. Also, the heart failure population is very much in need of additional options to improve their lives. This group needs additional therapy.

Richard Ryder MD
Cardiology Associates
30 Harrison St #250
Johnson City, NY 13790

William P. Algary, M.D., F.A.C.C., Retired
Charles D. Ross, M.D., F.A.C.C.
Morris E. Williams, Jr., M.D., F.A.C.C.
Lawrence W. Freeman, M.D., F.A.C.C.
Michael W. Payne, M.D., F.A.C.C.
Gregory W. San, M.D., F.A.C.C.
Douglas S. Head, M.D., F.A.C.C.
Brad M. Simpson, M.D., F.A.C.C.
Ned D. Freeman, M.D., F.A.C.C.

UPSTATE CARDIOLOGY, P.A.

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John E. Cebe, M.D., F.A.C.C.
Steven D. Johnson, M.D., F.A.C.C.
Jon M. Bittrick, M.D., F.A.C.C.
Barbara A. Morán-Faile, M.D., F.A.C.C.
A. Thomas Siachos, M.D.
Christopher H. Smith, M.D.
Kathryn M. McFadden, PA-C
Sandra W. Lowe, MS, RNCS, FNP
Diana M. Harper, MSN, RNCS, FNP

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January 10, 2006

Jyme Schafer, M. D.
Deirdre O'Connor
Coverage and Analysis Group
Center for Medicare and Medicaid Services
7500 Security Boulevard
Mail Stop C1-09-06
Baltimore, Maryland 21244

Dear Dr. Schafer and Ms. O'Connor:

As a physician involved in prescribing EECP® over the last few years I have been impressed with its efficacy in improving angina pectoris, as well as improving symptoms of congestive heart failure. I certainly would like to see EECP® expanded to patient's who have New York Heart Association Class II, III and IV angina, as well as class II and III symptoms of congestive heart failure because I think this would be a great benefit to many patient's with their overall well being.

Certainly EECP® therapy in the past has allowed a great increase in activity in many patients and improved their quality of life. Symptoms of walking and independent daily activities certainly improves with this therapy, as well as a decrease in the frequency of chest pain.

Please consider expanding the indications for EECP® to include angina patient who also are afflicted with congestive heart failure symptoms.

Sincerely yours,

Michael W. Payne, M. D., F.A.C.C.

MWP/llr

DICTATED NOT READ

Medical Health Center

January 6, 2006

Jyme Schafer, MD
Deirdre O'Connor, MS
Coverage & Analysis Group
Centers for Medicare & Medicaid Services
7500 Security Blvd. – Mail Stop C1-09-06
Baltimore, MD 21244

Dear Dr. Schafer & Ms. O'Connor,

This letter is written as a part of the public comment feedback regarding the proposal to not expand coverage for EECP therapy for patients with Class II angina or Class II or III congestive heart failure. As a practicing Board Clinical Cardiologist with Board Certification in Cardiovascular Medicine & Interventional Cardiology, I feel comfortable saying that the majority of patients that are being treated with EECP today are in Class II or III congestive heart failure and many of the angina patients would officially be classified as Class II stable angina.

As you probably know, the New York Heart Association Class IV congestive heart failure refers to a group of patients who are terminally ill with heart failure and are usually spending most of their days in a hospital. The typical outpatient who receives EECP and, in our experience benefits from EECP, is a Class II or III CHF patient. Providing coverage to Class II or III CHF patients would really just be an acknowledgement of what is actually going on in the real world of medicine. It would also allow us to reasonably bring a safe and proven effective therapy to a much larger pool of patients (Class II and III NYHA CHF patients) than the relatively small pool of terminally ill NYHA Class IV patients and for a more rational cost effective use of the scarce supply of health care funding.

With respect to the Class II angina question, the issue, I don't think, is as clear-cut. The biggest distinction between a Class II and Class III angina patient is often just a matter of judgment and there is a large, gray area between the two categories. It is very easy to turn a Class II patient into a Class III patient through selective

presentation of their symptoms and so, I believe, that many of the Class III patients being treated with EECP today are probably Class II patients, but it would be difficult to prove it. Therefore, I'm just suggesting that allowing coverage for Class II patients would just be an acknowledgement of an existing reality and would not change the situation except to bring the Medicare reimbursement fee system into line with existing clinical practice.

Theoretically, there is a cost benefit argument here too, since an EECP patient would be expected to use fewer anginal medications and would cost society less in the long run.

Sincerely yours,

Mark M. O'Connell, M.D., FACC
MMO/ht
T: 1/10/06

8 Form letters of Support

CLASSIC CITY CARDIOLOGY, P.C.

Susan Kreher, M.D., F.A.C.C. • Masih Uddin, M.D.
1500 Oglethorpe Ave., Ste. 300-B
Athens, GA 30606

Tel: 706.543.8444

Fax: 706.543.5656

Jyme Schafer, M.D.

Deirdre O'Connor, M.S.
Centers for Medicare and Medicaid services
Mail Code#: S2-02-08
7500 Security Boulevard
Baltimore, Maryland 21244-1850

Subject: Enhanced External Counter Pulsation Therapy.

Dear Dr. Schafer and Ms. O'Connor,

My cardiology practice has offered EECP therapy for the last 18 months to patients with angina, who have not been able to undergo revascularization. Often times these patients also have severely decreased left ventricular systolic function. After 35 one-hour sessions of EECP therapy, these patients often have significant improvement in overall sense of well being, reduction in angina, and fewer incidences of congestive heart failure. It is frustrating for me to see the vast number of patients with heart failure, who currently are not eligible for EECP therapy because of nonpayment. This therapy is significantly less expensive than a biventricular pacemaker/defibrillator and as much more physiologic.

My office did nuclear perfusion scans before and after EECP therapy and many times the patient had significant improvement in the overall myocardial perfusion and also some improvement in ejection fraction with EECP therapy. The positive changes are known to last more than 18 months and can be repeated if patients have more symptoms.

I would request that you reconsider your decision not to cover congestive heart failure as an indication for EECP given the very positive results seen in patients who have angina and severe decrease in LV systolic function. In

my mind, this is a much more cost-effective treatment than cardioverter defibrillators, which cost over $60,000 for one patient compared to EECP, which is less than $7000 for one patient.

Thank you for reconsidering this important treatment for the patients with heart disease.

Sincerely,

Susan K Kreher

Susan Kreher, M.D., F.A.C.C.
1500 Oglethorpe Avenue, Suite 300-B
Athens, Georgia 30606
SK/rai

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Allan E. Sosin, M.D.
Founder/Medical Director

Koren Barrett, N.D.
Naturopathic Doctor

Julie Kahn, N.D
Naturopathic Doctor

Jyme Schafer, M.D.
Deirdre O'Connor, MS
Coverage and Analysis Group
Centers for Medicare and Medicaid Services
7500 Security Boulevard
Mail Stop C1-09-06
Baltimore, MD 21244

January 13, 2006

Dear Dr. Schaefer and Ms. O'Connor,

What follows is the story of a patient with ischemic cardiomyopathy who paid out of pocket for external counterpulsation therapy.

A 54-year-old man was seen in September, 2005 with complaints of extreme shortness of breath and exercise intolerance along with severe edema. He had a history of quadruple cardiac bypass surgery performed in December, 2003 subsequent to a myocardial infarction. He had been experiencing increasing shortness of breath and lack of energy as well as swelling of his legs and abdomen. He was awakening at night with shortness of breath. On examination blood pressure was 135/95, weight 233 pounds. The heart was irregularly irregular with a rate of 130 per minute. There was marked neck vein distention. He had a strong left ventricular heave. Point of maximal impulse was 3 cm lateral to the nipple at the anterior axillary line. There was a grade 3/6 systolic murmur of mitral insufficiency. Extremities revealed four plus bipedal edema..

Echocardiogram revealed markedly reduced ejection fraction in the range of 20%. BNP was 1040.

He was treated with diuretics and an angiotensin receptor blocker. After discussion he was started on therapy with external counterpulsation. He had a total of 35 treatments delivered over seven weeks. It he lost 25 pounds. His edema completely resolved. Exercise was markedly enhanced and his symptom of nocturnal dyspnea disappeared. He was able to sleep on one pillow.

Repeat laboratory studies revealed that his BNP had declined to 450.

I informed the patient today that Medicare and Medicaid had decided not to approve external counterpulsation therapy for the treatment of congestive heart failure. He

responded that he thought that was a bad decision. He stated that he was feeling better than he had in many months, and was happy that he did not have to undergo invasive or dangerous procedures. He considered external counterpulsation therapy a natural treatment with enormous benefit and no risk. He also commented that this decision must have been influenced by the drug companies, and by parties who stood to benefit from invasive cardiac procedures. He could not understand why such an effective and safe therapy would be denied to so many people, when cardiac catheterization, pacemakers, defibrillators, and bypass surgery are all paid for.

As a physician who has used external counter pulsation for the treatment of patients with congestive heart failure as well as angina, I urge you to reconsider your decision, and approve payment for external counter pulsation therapy.

Sincerely yours,

Allan Sosin

Allan Sosin M.D.

Oxford Valley Cardiology Associates, P.C.
Ranga A. Rao, M.D., F.A.C.C. • Ramesh K. Adiraju, M.D., F.A.C.C. • Srinivas S. Alvi, M.D., F.A.C.C.
Jennifer L. Swope, MSN, NP-C
370 Middletown Blvd. ■ Oxford Square - Suite 510 ■ Langhorne, PA 19047 ■ (215) 750-6566 ■ Fax (215) 750-7288

To Dr's Tyme Schafer and Deirdre O'Connor:

I am a EECP therapist at oxford valley Cardiology in Langhorne Pennsylvania. I have been doing EECP treatments for 4½ years now. I have seen how much it has helped our patients over the years. We have had patients C severe chest pain, get the treatments and are amazed how much it has helped their chest pain. They take alot less nitro, or stop it all together. I have patients tell me how great it is to go threw the day and not get chest pain. It has also helped to give alot of our patients more energy, to be able to live a better quality of life. I have seen these treatments help so many of our patients over the years.

I think it is so important to get an expansion of Medicare reinbursement for EECP for our patients. I believe these treatments can help alot more patients if their insurance will cover it.

Debbie Barnett

Veda Adams, EECP Therapest

I'm writing to tell you that
the EECP Treatment has helped
alot of patients, I sent letters
out to patients for them to send
back. This very important to
us and patients a lot of
them suffer from this and reimbursement
will help, if they need any
records showing results and
how many times they came
I can show it by asking
my supervoss at work
any questions call me at
732-247-7444 - ext 154.

Sincerely,
Veda Adams

New Brunswick Cardiology
Somerset, NJ 08873

EECP® Heart Center of Kansas

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January 6, 2006

Jyme Schafer, MD
Deirdre O'Connor, MS
Centers for Medicare & Medicaid Services
Mail Code: S2-02-08
7500 Security Boulevard
Baltimore, MD 21244-1850

Subject: Enhanced External Counterpulsation (EECP) Therapy

Dear Dr. Schafer and Ms. O'Connor:

I am a Registered Nurse who has served my community as the EECP Clinical Coordinator for the EECP Heart Center of Ks since our start up in May of 2001.

Recently, I became aware that the proposal to expand coverage for Medicare beneficiaries for EECP Therapy was denied and that you are seeking public comment on the proposed determination. Please allow me to share with you some of my experiences as an EECP health care provider.

First of all the bulk (27 years) of my nursing career has been entrenched in the cardiac field. I began in the 1980's as a Surgical Intensive Care nurse in a unit extending post-op care to patients who received bypass surgery and valve replacement. Our unit's average census made up 12-14 post-op heart patients on a daily basis. I also had the privilege of assisting in the initial setup of our local Transplant team, both as a retrieval nurse and a transplant team member. For the next 12 years I worked in Coronary Care settings spanning our nation; i.e. Kansas, California, Illinois, and Indiana.

My intention is not to bore you with my resume; I am trying to point out my vast experience in the care of Cardiac patients, while expressing the extreme need for EECP Therapy.

In 2000 I was approach by a local Cardiologist about setting up an EECP Clinic. He provided me with a vast amount of research requesting that I look into the procedure from a clinical aspect and from a potential business aspect. I will admit I was suspicious of a Non-Invasive procedure due to my vast experience on the Invasive side working not only in post-op settings but in Heart Catheterization Labs.

What I discovered was an effective Non-Invasive procedure which offered patients an option, in many cases the only option they had left. I also discovered that from a business aspect EECP was not and I repeat was not a money maker.

I am blessed to work for a Cardiologist who is more concerned about the quality of his patients' lives than his income. Our EECP Clinic opened with the full knowledge that it would not make a profit for many years but most importantly we would be able to provide an inexpensive treatment for our most severely ill patients that actually worked.

Nothing frustrates a health care provider more than to be forced to tell a patient; "I'm sorry but there are no more procedures we can safely provide. You have made all the lifestyle changes we've requested, your medications have been maximized, and the most I can suggest is limiting your daily activities to prevent your symptoms."

My patients represent a population who has chest pain on a daily basis. In many cases they are unable to do simple activities such as cooking a meal, bathe, get dressed, walk out to the mailbox, or climb a flight of stairs without suffering from chest discomfort, fatigue, and shortness of breath.

Can you place yourself in their situation?

Since 2001 we have improved the quality of over 600 lives in the state of Kansas with EECP Therapy; however there are many more patients with CCSC Class II angina and NYHA Class II/III stable heart failure with an ejection fraction of less than 35% who could benefit from this inexpensive therapy if the proposal to expand coverage for Medicare beneficiaries was passed.

It is a well known fact that heart related disorders eat up the majority of health care cost in the United States. The number of admission on a daily basis for heart patients remains staggering.

The number of patients that are told there are no options left makes me want to cry!

EECP Therapy truly changes the quality of my patients' lives. In some cases they are able to return to work, be removed from the transplant list, travel, play with their grandchildren, go out to dinner with family and friends, reduce their hospital admissions, in short do the things we take for granted.

Please reconsider your recent decision and expand the coverage for Medicare beneficiaries providing more persons with the opportunity to have their life back.

Sincerely,

Linda Rae Rolfe, RN
EECP Clinical Coordinator
EECP Heart Center of KS

Southwest Heart

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G. Mason Garcia, MD, FACC, FCCP
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C. James De Sando, Jr., MD
Joseph Chambers, MD, FACC, FCCP, FSCAI
Billie Froning RN, MSN, A/GNP
Maureen Middleton, RN, MSN

Southwest Heart Research
Ken Peart, Manager
Jennifer Stein, RN
Beth Conrardy, RN
Denise Wieland, RA
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Nuclear Department
Alysia Waid, CNMT

EBCT/DEXA
Alicia Bubala

Tuesday, December 27, 2005

Jyme Schefer MD, Deidre O'Connor MS
Coverage & Analysis Group
Centers for Medicare and Medicaid Services
7500 Security Blvd.
Mail Stop C1-09-06
Baltimore, MD 21244
Re: Comment on EECP coverage

Dear Jyme and Deidre:

As an experienced EECP therapist of several years I received a notification from Vasomedical regarding the no change in expansion of EECP coverage for Class II angina and NYHA Class II/III CHF will be authorized at this latest review. For my experience, the earlier patients get this therapy the better! *It should **NOT** be considered a last resort treatment.* Patients do better the sooner they get in for treatments before all major arteries are so clogged up even EECP does not have that much impact on their health. Why wait until the patient is so far gone that treatment is finally authorized when they can get treated earlier and have better outcomes? In my experience, a patient's life span will increase with earlier treatment. The more collateral circulation they have the better their chance of survival if a major cardiac event occurs in a major coronary artery. Less hospital stays, less cost to the public, better quality of life is achieved with early stage EECP treatments. EECP is cheaper, non-invasive, than repeating expensive bypass surgeries. I urge you to consider authorizing EECP at earlier stages of coronary artery disease.

Best regards,

Janet Browne
EECP Therapist
Southwest Heart

January 4, 2006

Center for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244

To Whom It May Concern:

I am convinced from personal observation of patients who have undergone ECP that such expanded coverage will significantly benefit patients and be cost effective. I am an advanced registered nurse practitioner practicing in ECP therapy. I have been very impressed with the benefits of this therapy. I have used ECP on numerous CAD patients who also suffer from CHF, and have noted improvement in their heart failure as well as the chest pain. I believe that many elderly patients would be better served by receiving outpatient ECP rather than being hospitalized for CHF treatment, angiography, or high-risk revascularization procedures. I am very supportive of expanded coverage for ECP for patients who have Class II, III or IV angina, not readily amenable to revascularization and for patients with stable congestive heart failure with an ejection fraction of 40% or less. Thank you for your consideration of this matter.

Sincerely,

Bonnie Kimble MSN,ARNP

OCONNOR, DEIRDRE E. (CMS/OCSQ)

From: Claire McGrorey [cmcgr@comcast.net]
Sent: Friday, January 20, 2006 4:54 PM
To: OCONNOR, DEIRDRE E. (CMS/OCSQ)
Subject: EECP Therapy

Dear Ms. O'Connor,

I have a friend who had EECP treatment and is alive, kicking and feels better than he has in a long time. I have followed EECP advances ever since.

I have read countless testimonials on CMS's database site regarding EECP therapy. The positive comments far outweigh the few negative ones.

I sincerely hope those at CMS who analyzed the earlier data and who are currently examining the peer review articles are doing so objectively.

Invasive cardiac procedures are big business for surgeons, hospitals, insurance companies and huge medical product companies like Guidant and Boston Scientific.
I worry that again greed has become the motivating factor here. Instead of allowing for a more affordable alternative and clearly beneficial treatment that has improved so many people's lives who have previously tried the traditional, invasive treatments often more than once with often temporary.limited benefits, CMS appears to choose to ignore the data instead of truly listening to the testimonials of practitioners and cardiac patients who have used the EECP treatment. A big red flag! Dr. Douglass, the
president of the American College of Cardiology and some of her members have a lot to lose from their pocketbooks. We have been hearing about it in the news all too frequently these days. Good science and medicine deserves the right to move forward. It is CMS's ethical responsibility to be open to the strong evidence put before you and your colleagues. EECP works. Your decision impacts the health of many thousands of people each year. I believe CMS's approach to medical treatment is to use the least invasive forms of treatment first and only if those are unsuccessful does CMS approve of more invasive forms of treatment. Am I right?

Sincerely,

Claire McGrorey
Villanova, PA