The Optimization Study on Time Sequence of Enhanced External Counter-Pulsation in AEI-CPR

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***Abstract*—To improve the aortic pressure and myocardial perfusion pressure during cardiac arrest, this study is designed to optimize sequence of Enhanced External Counter-Pulsation (EECP) for a cardiopulmonary resuscitation (CPR) technique — Active Compression-Decompression CPR coupled with EECP and Inspiratory Impedance Threshold Valve (AEI-CPR). EECP is lower-limbs compression equipment for AEI-CPR that enhanced blood regurgitation during chest decompression. Different occasion for EECP performance would bring different hemodynamic effect. A mathematical model of human circulatory system used to research AEI-CPR has been established. And then the AEI-CPR hemodynamic effect to the blood circulatory system is performed on the model. A genetic algorithm (GA) that used to find optimum sequence of the EECP is performed on the model when other parameters of external force for AEI-CPR are definite. At first, set the maximum strength of chest compression, chest decompression and lower-limbs compression at 400Nt, 160Nt and 300mmHg, respectively. Set the frequency of CPR at 100min^{-1} and the ratio of chest compression compared to LLCP at 1:1. Then, after genetic algorithm is performed on the established model, fifty groups of optimal results are obtained. The maximum coronary perfusion pressure (CPP) takes place when the EECP begin its compression at 0.2s and the interval among crural, femoral and iliac compression is 0.05s. By applying the optimization algorithm on the CPR mathematical model, the optimum sequence of the EECP could be found. And the experiment results indicate that obvious hemodynamic effect is attained when the EECP began compression at the end of chest compression.**

***Index Terms*—cardiopulmonary resuscitation, mathematical model, enhanced external counter-pulsation, genetic algorithm**

I. Introduction

Heart disease is the primary cause of mortality. Despite widespread use of cardiopulmonary resuscitation (CPR), which is an emergency medical procedure for a victim of cardiac arrest, the survival of patients recovering from cardiac arrest remains poor. One of the reasons for this situation is that the practical technique of CPR has changed little since the 1960's [1]. Most researches focus on improving the CPR technique, such as active compression-decompression CPR (ACD-CPR) and interposed abdominal compression CPR (IAC-CPR), or on devices, such as an inspiratory impedance threshold valve (ITV) attached to the airway during standard CPR [2-4]. In the 1990's, a CPR technique, which was ACD-CPR coupled with Enhanced External Counter-Pulsation (EECP) and ITV, called as AEI-CPR, was proposed [5]. Researchers claimed that AEI-CPR could improve the aortic pressure and myocardial perfusion pressure. By compressing sequentially on the lower limbs, EECP could help to augment diastolic pressure and venous return flow. By impeding intermittently aspiratory gas exchange, ITV could help to increase intrathoracic negative pressure [6]. Therefore, AEI-CPR can enhance coronary perfusion pressure (CPP) but not increase right atrial pressure during diastole. Recently, Demetris Yannopoulos et al. also investigate a CPR technique like AEI-CPR [7].

However, most of current conclusions are derived from animal experiments or studies in humans after a prolonged cardiac arrest which has lost the effective time for CPR in preserving vital organ function. Moreover, it is impossible that built a reproducible model in patients because only the seconds to minutes after the onset of

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cardiac arrest is critical [8]. Therefore, a mathematical model of AEI-CPR is established by Simulink which could simulate the hemodynamic effect in cardiac arrest [9].

The AEI-CPR differs from current methods in that it adds a device, i.e. EECP, to the lower limbs. When the chest is active decompressed, EECP produce a lower limbs compression pressure (LLCP) acting on from crus to hip sequentially to help venous return. Likewise, the IAC-CPR is also a CPR technology that incorporates alternating chest and abdominal compressions to generate enhanced artificial circulation during cardiac arrest [10]. Compared to abdomen, however, lower limbs can endure greater compression pressure, because there are many vital visceral organs in the abdomen while lower limbs are only wrapped by muscle. On the other hand, various sequence of compression acting on the lower limbs would generate various hemodynamic effects, especially diastolic CPP. As well known, the quality of CPR affects the probability of immediate survival, 24h survival, and the rate of discharge. And a study of CPR results shows that the outcome is partially determined by the deliverance push and blow, confirming the belief of Peter Safar [11].

To improve the hemodynamic effect of AEI-CPR, a genetic algorithm (GA) is performed on the established AEI-CPR model to find optimum sequence of the EECP when other parameters for external force are definite. In accordance with animal experiment, parameters are set as follow: the maximum strength of chest compression, chest decompression and lower-limbs compression is 400Nt, 160Nt and 300mmHg, respectively; the frequency of CPR is 100min^{-1} and ratio of chest compress to LLCP is 1:1. The duty-cycle of chest compression compared to chest de-compression is 50%. CPP is an important indicator to evaluate the quality of CPR techniques [12]. The experiment results show that the best effect of diastolic CPP occurs in LLCP applied at the end of chest compression. The optimum result of CPP is up to 50.99mmHg.

Ⅱ. MATHEMATICAL MODEL OF AEI-CPR

To research the hemodynamic effect of AEI-CPR one must not only model a human blood circulatory system but also consider the problem of mechanical coupling of the external force on the chest and lower limbs. A mathematical model for studying hemodynamic effect of AEI-CPR has been established by Simulink. It, as shown in the Fig. 1, based upon normal human anatomy and physiology, the definition of compliance (volume change/pressure change) and Ohm's Law (flow= pressure/resistance) [9, 5]. The diagram of Fig. 1 includes two parts. The first part is the blood circulatory system model contained in dot-dashed rectangle. The second part is external force performed on the chest and lower limbs expressed by round corner rectangle at the right of the diagram. Four dashed rectangles indicate control range of external force. By applying various external pressures generated by GA on the model, optimal hemodynamic effect for AEI-CPR would be found.

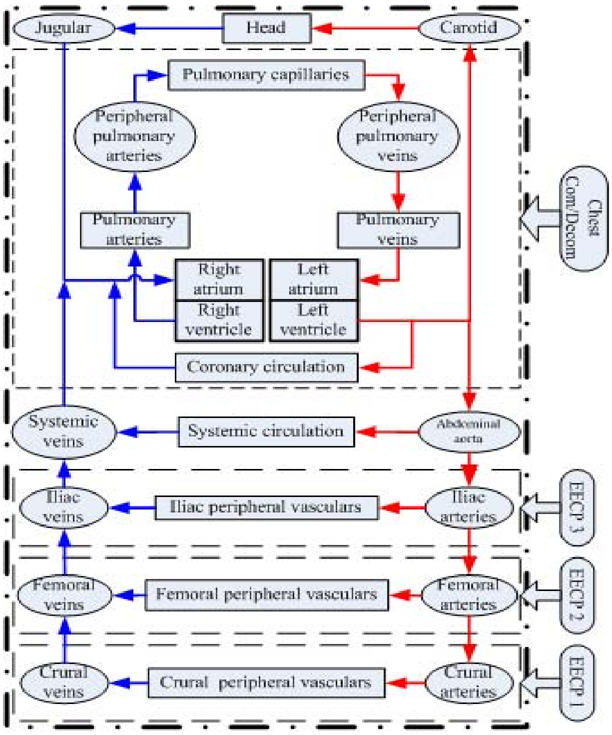
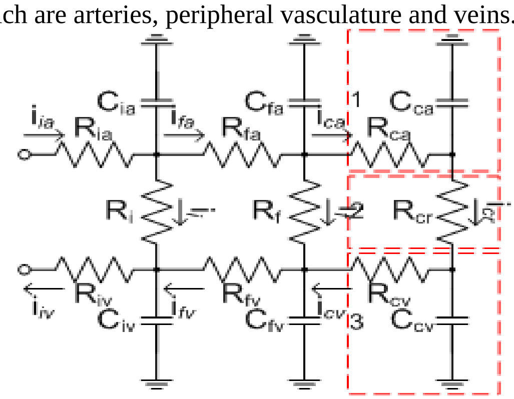


Fig. 1 Diagram of mathematical model for AEI-CPR

A. Blood Circulatory System Model

Generally, blood circulatory system model is a lumped model. According to Navier-Stokes equation and Ohm's Law, the relationship between blood pressure and blood flow is similar to the relationship between voltage and current in circuit [14]. Therefore, blood circulatory model could be simulated by an equivalent circuit. A resistance and a capacitance are used to represent blood resistance and compliance of a vascular compartment, respectively.

Fig. 2 shows the equivalent circuit of lower limbs. It consists of iliac, femoral and crural part. Every part could be divided into three vascular compartments, which are arteries, peripheral vasculature and veins.



C: Compliance; R: Resistance; I: Flow
ia: iliac arteries; iv: iliac veins; i: iliac peripheral vasculature;
fa: femoral arteries; fv: femoral veins; f: femoral peripheral vasculature;
ca: crural arteries; cv: crural veins; cr: crural peripheral vasculature;
Dashed-box 1, 2 and 3 were relative to crural arteries, veins and crural peripheral vasculature, respectively

Fig. 2 The equivalent circuit of lower limbs

A vascular compartment could be simulated to a resistor paralleled with a capacitor, such as dashed rectangle 1 and 3 in the Fig. 2. Some great vessels, such as thoracic aorta, pulmonary arteries, have more compliance than their resistance, so they are simulated by capacitors. Similarly, some vascular compartments, such as capillary net, have more resistance than their compliance, so they are simulated by resistance, like dashed rectangle 2 in the Fig. 2 as shown.

In the Fig. 2, as an example, the circuits in the dashed rectangle 1, 2 and 3 corresponding to crural arteries, crural peripheral vascular and crural veins, respectively. Variable names in the Fig. 2 are defined in TABLE I. Standard values of these parameters are provided in TABLE II [9]. Other relative information of parameters of the model could be found in [13] and [15].

B. Numerical Methods of Circulatory Pressures

To model the influence of external force upon the chest in CPR, the researchers adopt a simplified scheme illustrated in the Fig. 3, in which the opposition of the chest to external compression is represented as a simple pair of spring (spring constant is k) and damper (damping constant is μ) [13]. F(t) is a time-varying external force on the chest, and it leads to the depression of sternum denoted as $x_1$cm. At the same time, the cardiac chamber is expanded $x_2$cm because of the blood filling. According to Ohm's Law, motion of the sternum in response to force F(t) is given by the differential equation

TABLE I.
NOMENCLATURE

Symbol	Definition
ia	iliac arteries
iv	iliac veins
i	iliac peripheral vasculature
fa	femoral arteries
fv	femoral veins
f	femoral peripheral vasculature
ca	crural arteries
cv	crural veins
cr	crural peripheral vasculature

TABLE II.
MODEL PARAMETERS

Resistances(mmHg/L/s)		Compliances(L/mmHg)	
Variable	Value	Variable	Value
R_{ia}	360	C_{ia}	0.00035
R_{iv}	180	C_{iv}	0.0078
R_{i}	9120	C_{fa}	0.0003
R_{fa}	400	C_{fv}	0.0063
R_{fv}	200	C_{ca}	0.00028
R_{f}	9510	C_{cv}	0.00568
R_{ca}	426		
R_{cv}	213		
R_{cr}	9812		

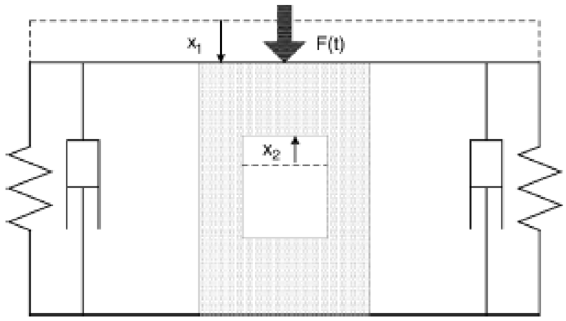


Fig. 3 Model of chest wall, mediastinal tissues, and a representative cardiac chamber

$$F(t) - kx_1 - \mu\dot{x}_1 = 0 \quad (1)$$

for sternal displacement, x_1, and velocity of displacement $\dot{x}_1$ (Here the "dot" over x_1 indicates the first time derivative). Then, instantaneous pressure versus time waveforms in each compartment of the model could be described by some difference equations [13].

When the LLCP (expressed by P_{eecp}) is performed in AEI-CPR, P_{eecp} acts as a direct pressure source. The changed pressures of lower limbs are given by equation (2)-(4), as follows.

For the iliac arteries and vena,

$$\Delta P_{ia} = \Delta P_{eecp3} + \frac{1}{C_{ia}}(i_{ia} - i_i)\Delta t = \Delta P_{eecp3} + \frac{\Delta t}{C_{ia}}\left[\frac{P_{aa} - P_{ia}}{R_{ia}} - \frac{P_{ia} - P_{iv}}{R_i}\right]$$

and

$$\Delta P_{iv} = \Delta P_{eecp3} + \frac{1}{C_{iv}}(i_i - i_{iv})\Delta t = \Delta P_{eecp3} + \frac{\Delta t}{C_{iv}}\left[\frac{P_{ia} - P_{iv}}{R_i} - \max(0, \frac{P_{iv} - P_{ivc}}{R_{iv}})\right] \quad (2).$$

For the femoral arteries and vena,

$$\Delta P_{fa} = \Delta P_{eecp2} + \frac{1}{C_{fa}}(i_{ia} - i_f)\Delta t = \Delta P_{eecp2} + \frac{\Delta t}{C_{fa}}\left[\frac{P_{ia} - P_{fa}}{R_{fa}} - \frac{P_{fa} - P_{fv}}{R_f}\right]$$

and

$$\Delta P_{fv} = \Delta P_{eecp2} + \frac{1}{C_{fv}}(i_f - i_{fv})\Delta t = \Delta P_{eecp2} + \frac{\Delta t}{C_{fv}}\left[\frac{P_{fa} - P_{fv}}{R_f} - \max(0, \frac{P_{fv} - P_{iv}}{R_{fv}})\right] \quad (3).$$

Similarly, for the crural arteries and vena,

$$\Delta P_{ca} = \Delta P_{eecp1} + \frac{1}{C_{ca}}(i_{ca} - i_{cr})\Delta t$$
$$= \Delta P_{eecp1} + \frac{\Delta t}{C_{ca}}[\frac{P_{fa} - P_{ca}}{R_{ca}} - \frac{P_{ca} - P_{cv}}{R_{cr}}]$$

and

$$\Delta P_{cv} = \Delta P_{eecp1} + \frac{1}{C_{cv}}(i_{cr} - i_{cv})\Delta t$$
$$= \Delta P_{eecp1} + \frac{\Delta t}{C_{cv}}[\frac{P_{ca} - P_{cv}}{R_{cr}} - \max(0, \frac{P_{cv} - P_{fv}}{R_{cv}})] \quad (4).$$

In the (2)-(4), the max() function is used to represent the action of venous valves in the iliac, femoral and crural veins that prevented retrograde flow.

III. GENETIC ALGORITHM

Genetic Algorithms is a self-adaptive algorithm for global optimization searching, which coming into being by simulating evolution procedure of biology in the environments [16]. Optimization process of GA imitates biological evolution. Biological evolution depends on chromosome selection, crossover and mutation. At first, some genes of parents P(t) would be changed or mutated with some probability to generate the next generation P(t+1). Secondly, according to individual fitness, selected individual would be the next parent. According to preferred rules, a higher adaptive genetic would survive, through genetic and evolutionary constantly, to the next generation. Finally, a good individual X would reach or close to the optimal solution X^*.

A. Control Parameters

External force for AEI-CPR includes eight parameters: frequency of compression, maximum strength of chest compression, maximum strength of chest de-compression, maximum pressure of LLCP, three sequences of LLCP (leg, thigh and rump) and ratio of chest compress compared to LLCP. Applying GA to the established model, three optimum sequences of LLCP would be found when other parameters are definite. Set frequency of compress at 100/min, maximum strength of chest compression at 400Nt, maximum strength of chest de-compression at 160Nt, maximum pressure of LLCP at 300mmHg, and ratio of chest compress to LLCP at 1:1. The duty-cycle of chest compression compared to chest de-compression is 50%. Sine waveform is used to express external force for AEI-CPR on the chest and lower limbs. Time sequence of LLCP influences the changed pressure of lower limbs directly, which are $\triangle P_{eecp1}$, $\triangle P_{eecp2}$, $\triangle P_{eecp3}$.

B. Algorithm Description

The fitness of the organism for survival is the maximum CPP in the diastole. CPP is an important indicator to evaluate the quality of CPR techniques, because it illustrates the blood flow perfuse into coronary artery to ensure the heart's blood supply. The non-random selection is done to maximize diastolic CPP. Before performing GA on the established model, some constraints must be set. At first, set T=(t_1, t_2, t_3) at optimized sequence, where is the time that EECP performs compression on the leg, thigh and rump, respectively, in a CPR period. Secondly, according to compressing frequency which is 100/min, the range of t_1, t_2 and t_3 is 0.1s ~ 0.45s. Thirdly, it must be $t_1 \leqslant t_2 \leqslant t_3$. Finally, set the objective function at

$$f(T) = \max(CPP_{diastolic}) \quad (5).$$

The steps of GA of the sequence are as follows:

(1) According to constraints above, generate a random initial sequence T, and set counter n=1;

(2) Run the AEI-CPR model and compute f(T);

(3) Randomly select three factors of T, and according to constraints to mutate them, and then get a mutant or modified sequence, T';

(4) Run the AEI-CPR model and compute f(T');

(5) If f(T') < f(T'), then set T=T', n=1; otherwise, reserve T, and n=n+1;

(6) If n>50, then stop optimizing and the optimal sequence is T; otherwise, go to step 3.

That is, when a time sequence T is not displaced by other new time sequence T' for 50 times, an optimal result would be obtained.

IV. RESULTS

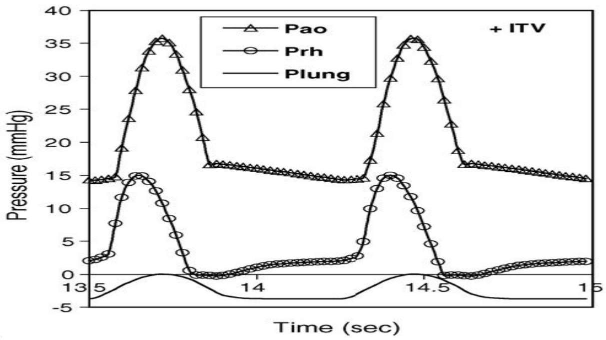
The blood circulatory system model has been established using MATLAB/Simulink. Its fixed-step size is 0.0001s, and the initial pressure of all organs' compartments is 5mmHg. The simulation time is 70s. Fig. 4 shows that the simulating result is in accordance with the reference data. Fig. 4 (a) is the reference data, and Fig. 4 (b) is the simulating result. In the Fig. 4, Pao represents the pressure of thoracic aorta, Prh represents the right atrial pressure, and Plung represents the pressure in the lung.

Genetic algorithm is performed on the mathematical model, and 50 groups of result are obtained. TABLE III lists five groups of results which generates the best effects of diastolic CPP.

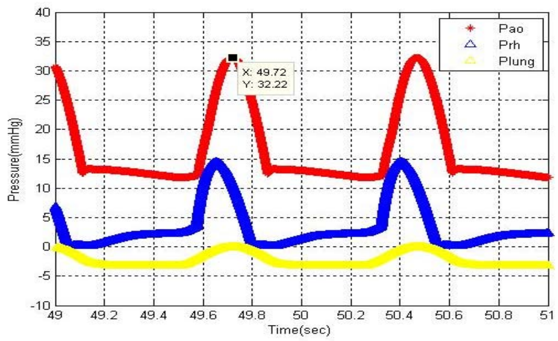
In the TABLE III, the third sequence of LLCP generats the maximum diastolic CPP. Fig. 5 shows the experimental result when time sequence of LLCP is 0.2s, 0.25s, 0.30s on the leg, thigh and rump, respectively.

TABLE III.
RESULTS OF GENETIC ALGORITHM

No.	Time of leg	Time of thigh	Time of rump	CPP
1	0.384	0.391	0.393	50.49
2	0.487	0.493	0.492	45.17
3	**0.200**	**0.250**	**0.300**	**50.99**
4	0.486	0.490	0.494	45.20
5	0.411	0.417	0.429	47.05



(a) Reference data



(b) Simulating result

Fig. 4 Reference data and simulating results

Fig. 5 includes five charts. The first chart expresses external force waveform of AEI-CPR performed on the chest and lower limbs. The broad-brush waveform expresses the external force on the chest, which positive value is chest compression and negative value is chest decompression. Its unit is Newton (Nt). The other three waveforms in the first charts are compression pressure on the leg, thigh and rump. Their units are mmHg. All external force waveforms are expressed by trapeziform waveform for in accordance with animal experiments and clinic. The second chart expresses the thoracic aortic pressure. The third chart expresses right atria pressure. The fourth chart expresses CPP, which is the difference of aortic pressure and right atria pressure. These three units are mmHg. The fifth chart expresses blood flow of aorta. Its unit is Liter (L). According to Fig. 5, diastolic CPP can be enhanced and arrive at maximum during middle of chest decompression. Moreover, when EECP starts compression on the crus at the end of chest decompression, the aortic blood flow can increase about 0.06L. It ensures that plenitudinous blood flow can be send to brain.

V. CONCLUSION

The present results suggest that it might be better to begin with LLCP at the end of chest decompression, and the interval of time of LLCP is about 0.05s. These results are in accordance with the parallel animal experiments and the data published before.

CPR is very important to a patient who endures cardiac arrest. Applying the mathematical model for CPR, several of experiments could be executed on the model repeated, and could guide clinical operations better.

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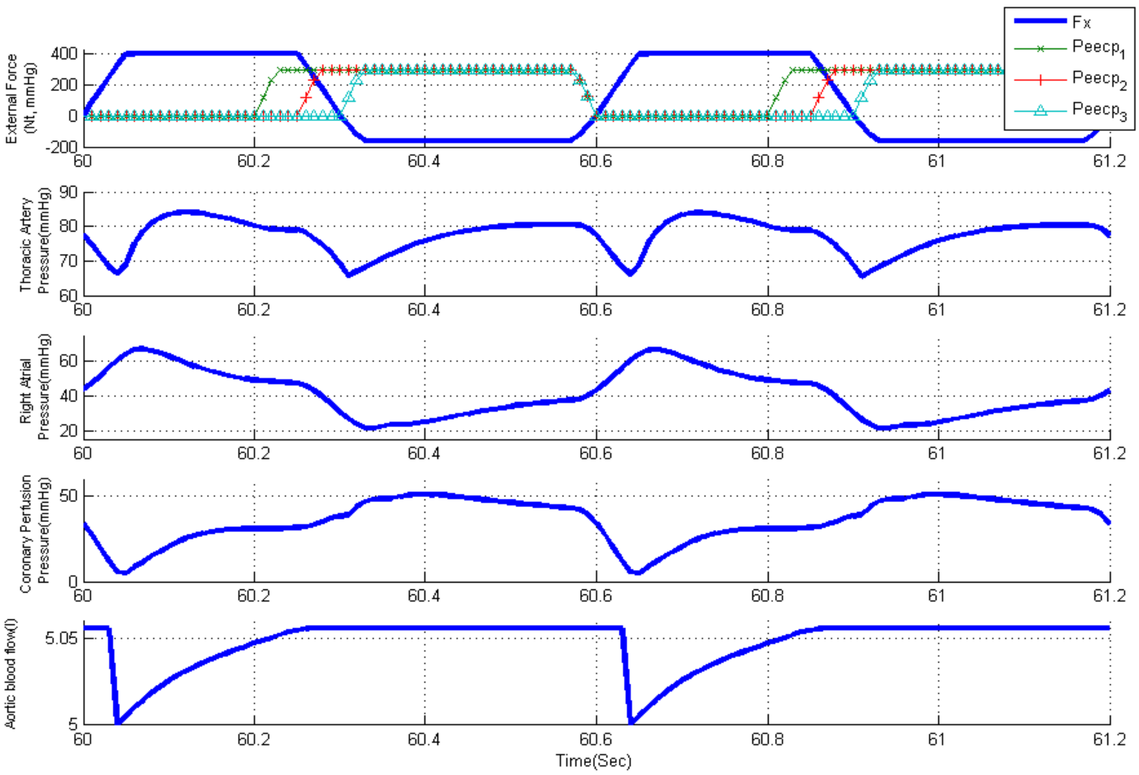

Fig. 5 Result of Optimal Time Sequence of LLCP

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