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The Physical Conditions of Different Organs Are Reflected Specifically in the Pressure Pulse Spectrum of the Peripheral Artery

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We try to solve the "hemodynamic inverse problem" of the internal organs in terms of the peripheral pressure pulse spectrum analysis. Side-branch organs are approximated as resonators with own natural frequencies. They are depicted not as ordinary reflection sites but as antennas that receive energy from the main artery and undergo forced oscillations with selective frequencies. Every organ also reacts back to the main artery as a secondary "small heart source" that generated harmonic forces with maximum amplitude near its own natural frequency. The whole arterial system is in a steady distributed oscillatory state that is the superposition result of encountering the forces generated by the heart and many internal organs. A "frequency matching" theory of the organ and the main artery is proposed. The Fourier components of the pressure pulse in the arterial system are related to the matching conditions of different organs. In vivo studies in kidney and spleen of rats are provided.

Key words: hemodynamic inverse problem; pulse spectrum; resonance frequency.

INTRODUCTION

The "hemodynamic inverse problem" inferring mechanical properties of an arterial system from measured input pressure and flow has been intensely investigated (e.g., Chemla *et al.*, 1998; Karamanoglu *et al.*, 1993; Kelly *et al.*, 1992; Li 2000; Stergiopulos *et al.*, 1999). Some investigators stated that all model-based methods can result from an infinite number of different arterial systems (Quick *et al.*, 2001). O'Rourke (1967) pointed out that the pulsatile power related to the axial flow is but a small fraction of left ventricular power. Instead of studing the pressure-flow relations, Karamanoglu *et al.* (1994) focused on the propagation of the pressure waves. Dai *et al.* (1985) performed an experiment to show that a disturbance in blood flow at one place can be detected in the arterial pulse waves at a distant site and discussed that noninvasive pulse diagnosis might be plausible.

Method of applying harmonic analysis on cardiovascular physiology has been amply demonstrated (e.g., Li, 2000; Mcdonald, 1974). Milnor (1989) stated that under constant conditions, the circulation behaves like a system in steady-state oscillation.

Recently, we have proposed that the whole arterial system is coupled together, and the pulsatile pressure obeys a pressure-wave equation that was derived from the radial equation of motion of the arterial wall and the fluid (Wang Lin *et al.*, 1997, 2000). When at rest, the whole arterial system is in a unified distributed oscillatory state and a steady distributed pressure pulse existing all over the arterial system. The natural frequencies of the main arterial system are matching with the heart rate in a way so that all the oscillation modes of integer multiples of the heart rate could be excited (Wang Lin *et al.*, 2003). Thus the main arterial system is a pressure reservoir or an energy reservoir. It provides harmonic force source of all integer multiples of the heart rate to all the microcirculatory system.

In this work we try to solve the "hemodynamic inverse problem" of the internal organs in terms of the peripheral pressure pulse spectrum analysis. We propose that the physical condition of different organs is embedded in

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the pressure pulse at the peripheral artery. Measurement of the peripheral pressure pulse alone could reflect some systemic information of the organs.

We have pointed out that side-branch organ not merely plays a role of reflection site, but has a resonance effect on the whole circulation (Wang Lin *et al.*, 1991; Yu *et al.*, 1994). In this study, we suggest that organs are constructed in a way that their natural frequencies coincide with some of the natural frequencies of the main arterial system. Every organ is like an antenna tuned to receive and feed back energy to the main artery. Thus "frequency matching" theory is used to illustrate how different organs interact with the main artery. Renal arteries or splenic artery was ligated in rats and the effects on the caudate arterial pressure were analyzed to confirm the proposed theory.

THEORY

We assumed the arterial system is in a steady distributed transverse vibration state governed by a pressure-wave equation that has been derived in previous papers (Wang Lin *et al.*, 1997, 2000).

$$\frac{\partial^2 P}{\partial t^2} + b\frac{\partial P}{\partial t} + \omega_0^2 P = V_\infty^2 \frac{\partial^2 P}{\partial z^2} + \frac{2\pi r_0}{L' C_A} F_{\text{ext}} \tag{1}$$

As a first order of approximation, we simplify the arterial system as a uniform tube with length l. The position of the heart is at $z = \xi$. The external force per unit length generated by the burst of ventricular ejection can be written as $F_{\text{ext}}(z, t) = F(t)\delta(z - \xi)$. At the two ends of the tube, we assume that the blood pressures maintain their respective static values $P_0(0)$and $P_0(l)$. The response of the pressure at position z with an input harmonic force of angular frequency ω and amplitude a_ω becomes

$$P_\omega(z, t) = \sum_{n=1}^{\infty} A_n \sin\frac{n\pi\xi}{l} \sin\frac{n\pi z}{l} \sin(\omega t + \phi_n) \tag{2}$$

in which,

$$A_n = \frac{G}{\left[\left(\omega_n^2 + \omega_0^2 - \omega^2\right)^2 + b^2\omega^2\right]^{1/2}} \tag{3}$$

$$\phi_n = \tan^{-1}\frac{-b\omega}{\omega_n^2 + \omega_0^2 - \omega^2} \tag{4}$$

$$G = \frac{4\pi r_0 a_\omega}{L' C_A l} \tag{5}$$

$$\omega_n = \frac{n\pi V_\infty}{l}. \tag{6}$$

Here C_A is the area compliance of the main artery, L' is the mass per unit axial length of the arterial vessel and the adherent fluid that are oscillating transversely together. b is a damping constant, r_0 is the static radius of the vessel, and ω_0 is the residual intrinsic angular frequency of the main artery and is negligibly small for perfect matching. V_∞ is the high frequency phase velocity.

In this study, we assume that each internal organ can be lumped as one Windkessel. It receives not only the blood flow but also the harmonic force source from the main artery.

Stacy and Giles (1959) had related the input force F_i to the peripheral pressure of the organ P_{org} as

$$F_i = a'\frac{\partial^2 P_{\text{org}}}{\partial t^2} + b'\frac{\partial P_{\text{org}}}{\partial t} + c' P_{\text{org}} \tag{7}$$

On the right-hand side of the equation, the first term is the inertial effect due to the intermediate column of blood, the second term is the frictional effect due to the viscous properties of the fluid, and the third term is an elastic coupling arising from the vessel's distensible properties. Thus, every organ has its own characteristic natural frequency

$$\omega_{\text{res}} = (c'/a')^{1/2} \tag{8}$$

As the main artery offers forces of all harmonic frequencies, the organ plays as an antenna and will undergo a forced oscillation. If the natural frequency of the organ is near any of the frequency of the input force, strong response will occur. This is the familiar resonance phenomenon either in the mechanical forced oscillation system or in the RLC electric resonance circuit.

Since the main artery is connected with the organ via the side-branch artery, the organ will be acting back to the main artery (Fig. 1). In this sense, the organ behaves as a small heart that also delivers energy source to the main artery via its feedback effect. This feedback force is proportional to the pressure P_{org} of the organ, thus the organ feedback harmonic force amplitude a'_ω of angular frequency ω will also have a maximum value near the natural angular frequency ω_{res} of the particular organ.

Thus, in analogy to Eq. (2), a side-branch organ attached at position ξ_0 will give a further contribution to the pressure of frequency ω at position z of the main artery as

$$P'_\omega(z, t) = \sum_{n=1}^{\infty} B_n \sin\frac{n\pi\xi_0}{l} \sin\frac{n\pi z}{l} \sin(\omega t + \phi_n) \tag{9}$$

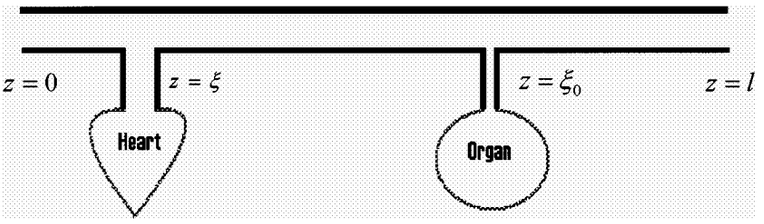

Figure 1. A sketch of the simplified arterial system with organ as a secondary small heart. l is the total length of the main arterial system. The heart is at position $z = \xi$ and the organ is at position $z = \xi_0$.

in which,

$$B_n = \frac{H}{\left[\left(\omega_n^2 - \omega^2\right)^2 + b^2\omega^2\right]^{1/2}} \tag{10}$$

$$H = \frac{4\pi r_0 a'_\omega}{L' C_A l} \tag{11}$$

Here a'_ω is the amplitude component of the feedback force generated from the organ to the main artery of angular frequency ω, and this amplitude will have a maximum value near the natural frequency of the organ, that is for $\omega = \omega_{res}$.

The response pressure amplitude of the main artery B_n (Eq. 10) due to the organ will also get a maximum value for the Nth mode if $\omega_N = \omega = \omega_{res}$, as can be seen from the minimization of its denominator and the maximization of the H through the amplitude factor a'_ω in Eq. (11). This effect should appear for every position z in the artery.

That is, the frequency matching of the organ with the Nth harmonic mode will enhance that pressure component all the way down to the peripheral artery. If the inertial or distensible property of the organ system is changed from its normal value because of illness so that its resonance frequency is shifted away from one of the angular natural frequency ω_N of the main arterial system, or the resistance of the organ system is increased, the effects will appear in the pressure pulse of the artery, and with most significant spectrum change on this particular mode. Therefore, a comparison of the pulse spectrum of a patient with that of control average taking at the same peripheral arterial position will reveal some information of the physiological properties of various specific organs via their specific Fourier components.

Here, we performed in vivo studies in rats for the extreme conditions of the kidney and spleen with either one or both of their arteries totally occluded from the main artery.

METHOD AND MATERIALS

Animal Preparation

We used a previous experimental setup (Yu *et al.*, 1994) to study the pressure pulse. Twelve male Wistar rats were taken as our subjects. Their weights were between 250 and 350 g. We divided them into two experimental groups, one for renal artery ligation and the other for splenic artery ligation. Rats were anesthetized with urethane (750 mg/kg body weight, I.P.), and their tail arteries were cannulated with an intravenous catheter (Angiocath, 22 GA, 1.00 IN, 0.9 × 25 mm, Becton-Dickinson). The catheter filled with physiological saline and heparin was connected to a pressure transducer (RP-1500 Narco Biosystem). The cannulation was done at the rat's tail about 1 cm away from the anus. The aortic blood pressure pulse was then passed through the catheter tip to the pressure transducer.

For renal artery ligation, we reached the renal arteries (*a. renalis*) from the dorsal sides of the rats' bodies, separated the fat off, and passed silk sutures under the arteries for ligation. It took about 30 min for the pressure pulse to become steady after the operation. And then we ligated the left, right, and both renal arteries in sequence. Every ligation was done in less than 3 s. The blood pressure pulses were then recorded before the ligation, during the ligation, and right after the releasing for 1 s each; 5–8 pulses were contained in each data series. At least a 15-min interval was given between two ligations.

For splenic artery ligation, we reached the lower part of splenic artery (*a. lienalis*) from the ventral side of the rats' bodies, separated the fat off, and passed a piece of silk suture under the arteries for ligation. Thirty minutes was allowed for the pressure wave to become steady after the operation. The blood pressure waves were also recorded right before the ligation, during the ligation, and after the releasing for 1 s each.

The exposed organs and the arteries were kept moist with physiological saline during the entire experiment. To study only the physical response without physiological feedback, the physiological variations such as changing of the heart beating rate or blood loss was kept to be minimum. Our criterion was that the mean aortic pressure, the diastolic pressure, and the systolic pressure should be back to the control level right after the tiding is released.

The pressure signals were sent to a simultaneous sample and hold panel AX753 (Axiom technology Co. Ltd., Taiwan, R.O.C.) and then to a 16 bit A/D converter AX5621, which is an interface card for the personal computer. Each pressure pulse was transformed into the frequency spectra by Fourier transformation.

Data Analysis

The harmonic proportions C_n for harmonics $n = 1$–6 were calculated for each pressure pulse with the amplitude A_n of each harmonic to be normalized by its mean level (D.C. component) A_0, that is, $C_n = 100\% \times (A_n/A_0)$. The total 5–8 pulses contained in each data series were averaged. The harmonic proportions for pressure pulse right before the ligation, or the control condition, were defined as C_{0n} and those during the ligation were defined as C_{1n}. Thus the harmonic proportion changes due to ligation become $\Delta C_n = C_{1n} - C_{0n}$.

Since the amplitudes decrease rapidly with the harmonic numbers, we focused our attention only on the first six harmonics, that is, $n = 1$–6.

RESULTS

The variation of the heart rates, systolic pressure, and diastolic pressure of a group of six rats undergoing ligation of the left, right, or both renal arteries are given in Table 1. The heart rates were stable all the way through the experiment ($P < 0.90$). During ligation, the diastolic and systolic pressures changed significantly ($P > 0.99$), but they were back to the control levels right after the ligation was released. Ligation of the right, left, or both renal arteries had similar effects on these three parameters.

In Fig. 2, caudate arterial pressure pulses of one typical rat in the renal artery ligation group are given for three different stages, while those for one rat in the splenic artery ligation group are illustrated in Fig. 3. The harmonic proportions of the pressure at each stage are given aside as references.

For rat undergoing renal arteries ligation, the second harmonic proportion C_2 had dropped more than 10%, and the shape of the pressure pulses had significantly changed during the short ligation time (<3 s). For rat bearing splenic artery ligation, the first and the second harmonic proportions C_1 and C_2 almost remained the same so that the pulse shape was not changed so significantly in spite of the more than 10% change in the third harmonic C_3. For both rats, the pulse shapes were recovered immediately after release.

The average value of the harmonic proportion change ΔC_n for six rats in renal artery ligation group are depicted in Fig. 4 versus the harmonic number n. Table 2 provides the detailed statistical data. During ligation,

Table 1. The Variations of the Heart Rates, Systolic Pressure, and Diastolic Pressure in the Ligation of the Left, Right, or Both Renal Arteries Experiments

				Pair t test	
	Control	Tide	Release	C-T	C-R
Heart rate (Hz)					
Right	5.78 ± 0.20	5.84 ± 0.28	5.95 ± 0.20	ns	ns
Left	5.85 ± 0.23	5.90 ± 0.30	5.98 ± 0.23	ns	ns
Both	5.85 ± 0.28	5.84 ± 0.32	6.07 ± 0.27	ns	ns
Systolic pressure (mmHg)					
Right	117.1 ± 2.9	88.4 ± 5.6	117.0 ± 3.0	**	ns
Left	117.2 ± 3.5	87.4 ± 5.8	114.4 ± 4.6	***	ns
Both	119.9 ± 3.8	86.7 ± 7.0	119.4 ± 3.9	***	ns
Diastolic pressure (mmHg)					
Right	74.8 ± 1.7	61.3 ± 3.6	75.2 ± 2.3	*	ns
Left	75.2 ± 2.9	61.3 ± 3.7	73.1 ± 2.9	**	ns
Both	76.8 ± 2.8	62.7 ± 4.4	76.8 ± 3.2	**	ns

Note. C-T: comparison for value during ligation with control level; C-R: comparison for value after release with control level; Pair t test: probability of significant difference between two sets, ns: $P < 0.90$.
* $P > 0.99$; ** $P > 0.995$; *** $P > 0.999$.

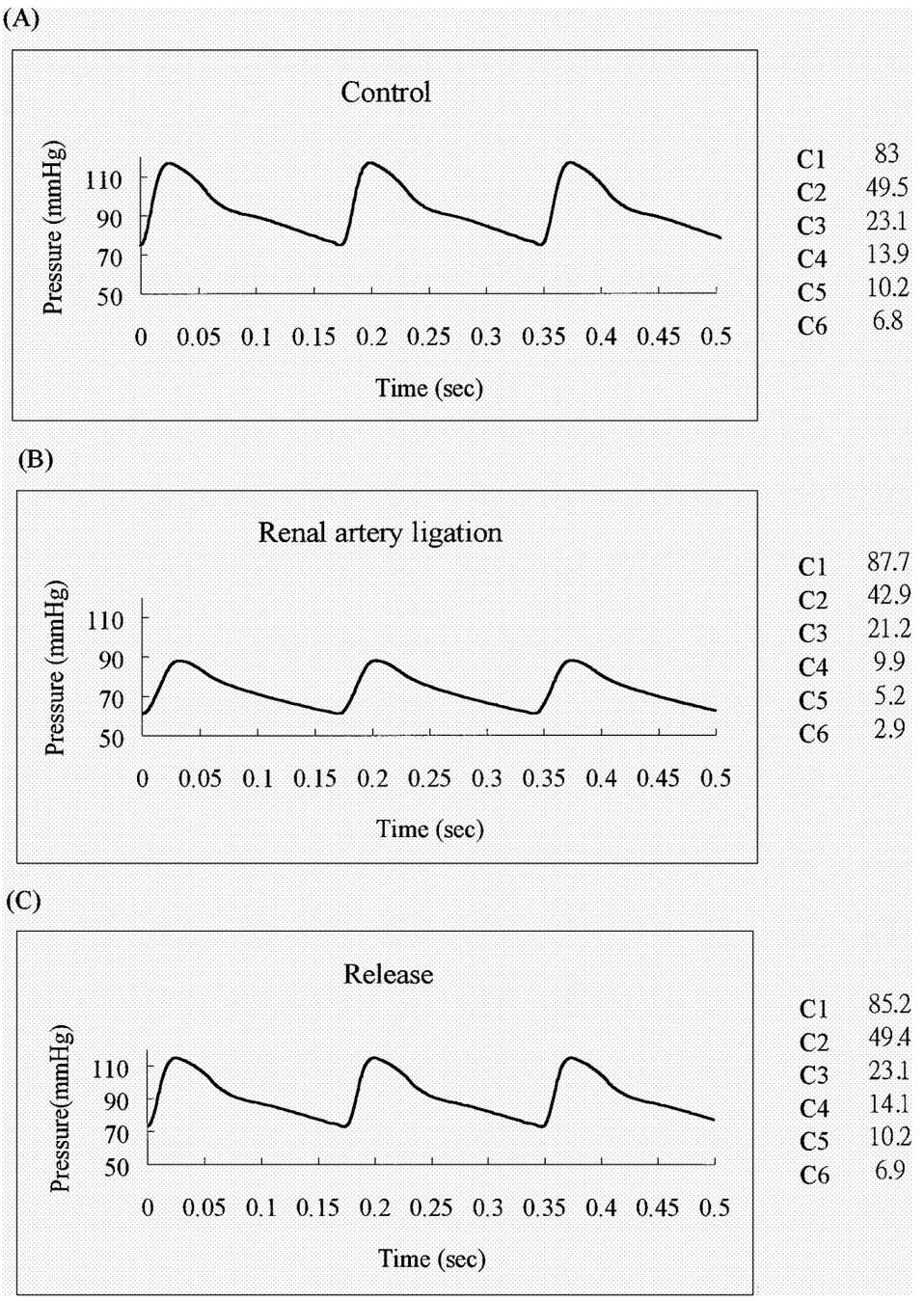

Figure 2. Pressure pulses of the three stages for one typical rat in the renal artery ligation group. The ligation time is less than 3 s. The harmonic proportions of the pressure at each stage are given aside as references.

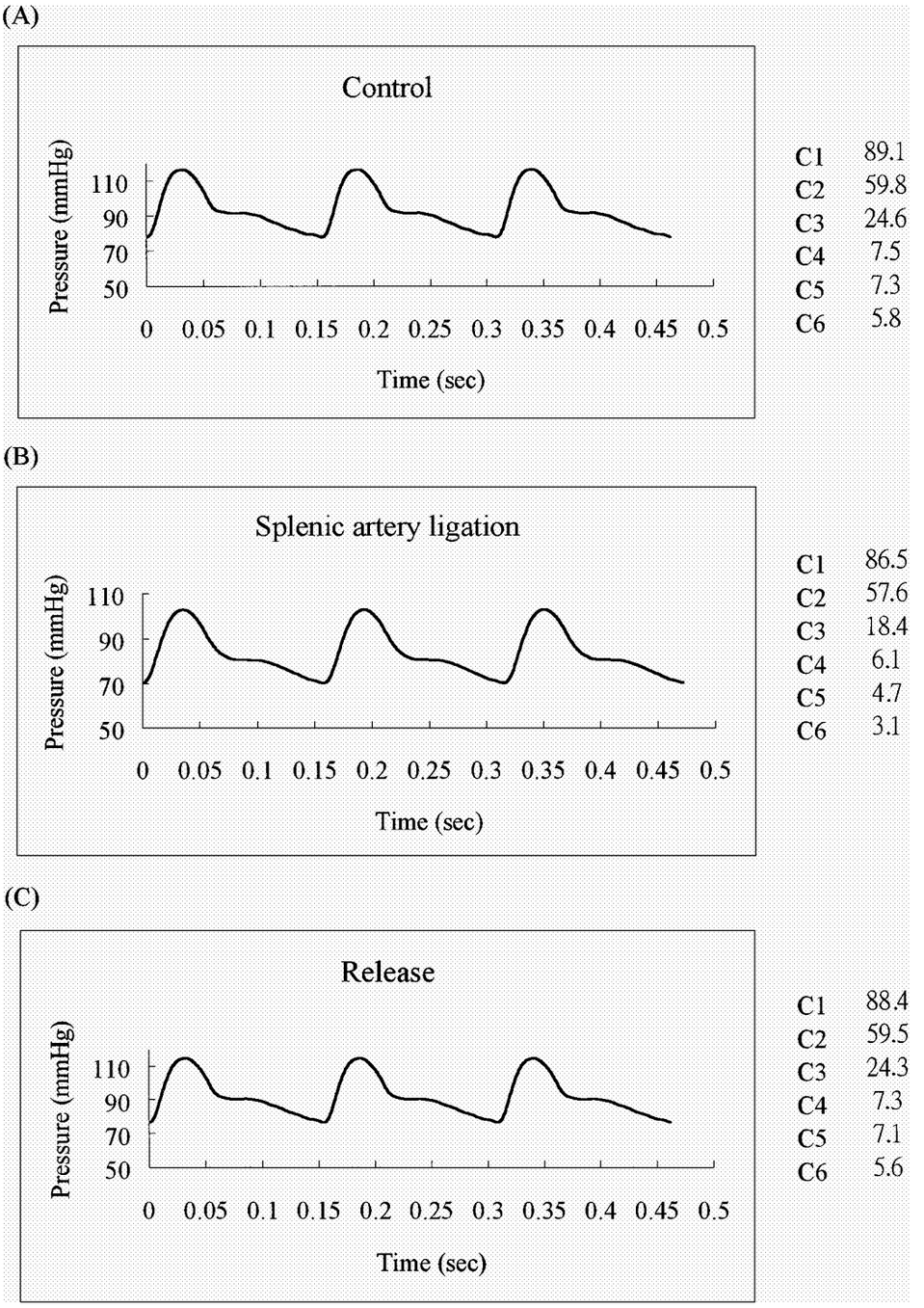

Figure 3. Pressure pulses of the three stages for one typical rat in the splenic artery ligation group. The ligation time is less than 3 s. The harmonic proportions of the pressure at each stage are given aside as references.

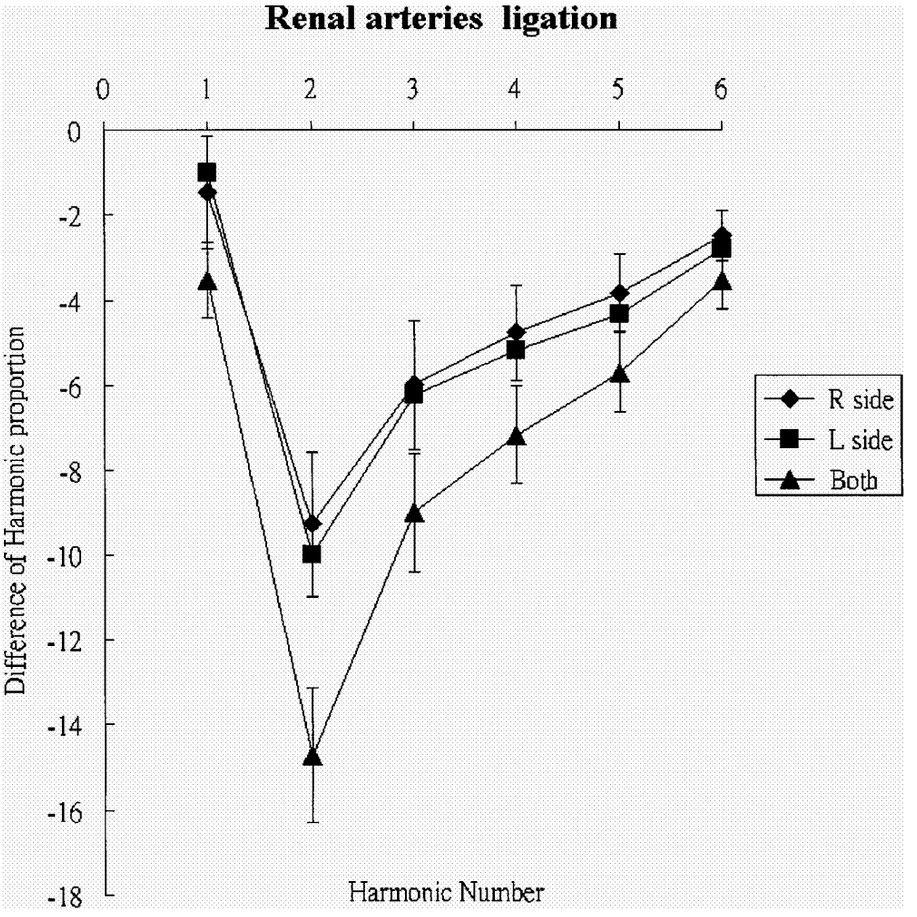

Figure 4. The average values of the harmonic proportion change ΔC_n for six rats in renal artery ligation group versus the harmonic number n. Standard error bars are also provided for the right renal artery ligation set and the both renal arteries ligation set.

the harmonic proportions of the aortic pressure pulse have a maximum dropping for the harmonic number $n = 2$. The average effects during the right-side or the left-side renal artery ligation are not significantly different, but the average effect during both renal arteries ligation is somewhat larger than the one-side effect.

The average value of the harmonic proportion change ΔC_n for another group of six rats undergoing splenic artery ligation is illustrated in Fig. 5 for harmonic number $n = 1$ to 6. Table 3 provides the detailed statistical data. A maximum dropping appears at the harmonic number $n = 3$ during the splenic artery ligation.

DISCUSSION

From the in vivo study of rats, we found that with ligation of one or two of the renal arterial systems, the second harmonic component of the pressure pulse at caudate artery is reduced significantly. Ligation of the splenic artery makes a peak decrease in the third harmonic component of the pulse. From our resonance theory, we would deduce that the natural frequency of the rat's kidney is nearly twice of the heart rate while the spleen organ of rat has a natural frequency nearly triple of its heart rate. Noordergraaf *et al.* (1979) pointed out there is a similarity principle in mammalian hemodynamics (see also Li, 1996). Thus, we might predict same frequency mapping of

Table 2. The Average Values of the *n*th Harmonic Proportion Change ΔC_n for Six Rats Undergoing Right, Left, or Both Renal Arteries Ligation

n	ΔC_n (Left artery)	ΔC_n (Right artery)	ΔC_n (Both arteries)
1	-1.02 ± 3.20	-1.47 ± 3.40	-3.52 ± 2.18
2	-10.00 ± 4.21	-9.28 ± 2.36	-14.72 ± 3.87
3	-6.22 ± 3.68	-5.98 ± 1.81	-9.00 ± 3.46
4	-5.17 ± 2.73	-4.75 ± 1.37	-7.15 ± 2.82
5	-4.32 ± 2.23	-3.82 ± 1.17	-5.68 ± 2.30
6	-2.8 ± 1.40	-2.48 ± 0.76	-3.53 ± 1.62

Table 3. The Average Values of the *n*th Harmonic Proportion Change ΔC_n for Six Rats Undergoing Splenic Artery Ligation

n	ΔC_n (Splenic artery)
1	0.996 ± 3.36
2	-1.20 ± 1.18
3	-4.46 ± 1.77
4	-2.10 ± 1.00
5	-1.74 ± 0.97
6	-1.45 ± 0.85

the organs with the harmonic components of the pressure pulse for all mammals. To make an accurate mapping of all internal organs to their respective harmonic frequency components of the pressure pulse needs much more in vivo study of different mammals and many pathological statistics in human being.

Organs not only play roles of reflection sites, but also have resonance feedback to the main arterial system. Quick *et al.* (2001) once suggested that mammalian arterial system is not constructed to minimize reflection per se, but instead, to minimize the effect of reflection.

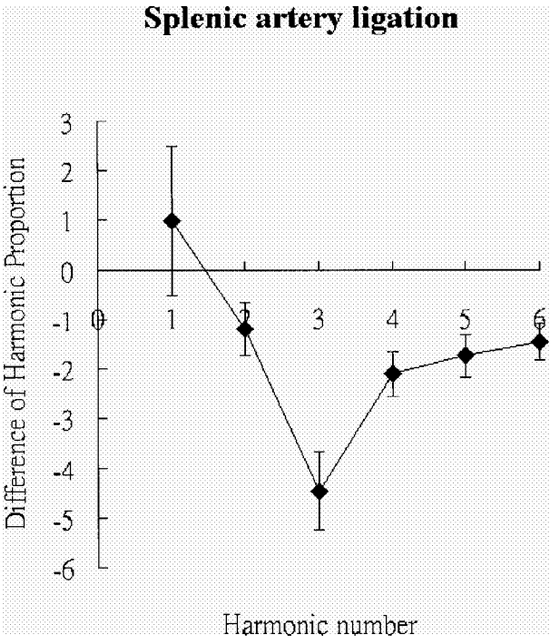

Figure 5. The average value of the harmonic proportion change ΔC_n for six rats in splenic artery ligation group versus the harmonic number n.

We conclude that the organ is constructed to meet the resonance requirement so that it will not only consume smallest amount of energy but also facilitate the energy transfer to the peripheral artery. It is because of this brilliant design that the left ventricle needs to provide only 1.7 W of power to support the circulation of blood in the whole human body (Milnor, 1989).

"Frequency matching" might be the basic rule for spontaneous body regulation from the point of view of energy saving. Illness of the internal organs resulted with hypertension or irregular heart rate might be indirect effects of a self-tuning to fulfill the best frequency matching or maximum energy saving. Therefore, the principle of therapy should be based on finding the main cause of the mismatch.

If we could diagnose and cure small mismatch of the organ before the body has a strong feedback tuning, many chronic diseases could be prevented. Pressure pulse spectrum analysis might provide one way to achieve this goal.

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