RENAL ADMITTANCE PLETHYSMOGRAPHY

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ABSTRACT

To date, admittance (or conductance) plethysmography has not been used to evaluate renal vascular dynamics. A model is proposed in which flow induced changes in renal volume occur homogeneously. Accordingly:

$$\Delta V = 3\rho L^2 \times \Delta G \quad \text{and} \quad dV/dt = 3\rho L^2 \times dG/dt$$

where ΔG is the change in conductance accompanying a change in volume (ΔV), ρ is the resistivity of the perfusate and L is the distance between the electrodes used to measure ΔG.

ΔG and dG/dt were measured in 14 dog kidneys (wt=75.7±15.3 g) perfused with a colloid perfusate (ρ=106.1±15.3 Ω-cm) using a pulsatile pump over a range of flow values (19.2-160.0 ml/min) and stroke rates (48-80). Plethysmograph pulse volume (PV-pleth) was computed from the maximum excursion of the ΔG curve and plethysmograph peak net inflow (PNI-pleth) was computed from the maximum value of the dG/dt curve. Arterial inflow and venous outflow were measured simultaneously with electromagnetic flowmeters and subtracted to provide an instantaneous net inflow signal. The peak net inflow standard (PNI-std) and the pulse volume standard (PV-std) were derived respectively from this signal and its integral.

PV-pleth and PNI-pleth respectively correlated well with PV-std (PV-pleth = 1.20 x PV-std, r=.98) and PNI-std (PNI-pleth = 1.14 x PNI-std, r=.99) for mean flow values < 115 ml/min. These relationships deteriorated somewhat at higher flows. It remains to be determined if such correlations and/or limitations exist in vivo.

INTRODUCTION

Rationale:

Renal transplant rejection is difficult to determine in the clinical setting. Nuclear renal scan studies indicate that changes in flow occur with rejection. Therefore, a method of easily and continuously monitoring changes in renal vascular dynamics during the post-transplant period might have practical application.

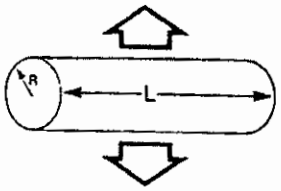
Admittance plethysmography (AP) is a method used to measure changes in limb volume and flow from accompanying changes in electrical conductivity[1]. There are no reports describing the relationship of the electrical conductivity of renal parenchyma to renal volume or flow. It is the purpose of this study to provide basic information of this type.

If meaningful information about renal vascular dynamics can be obtained with this technique, one could explore the possibility of obtaining such measurements from transplanted kidneys via insulated conductive leads placed postoperatively like temporary cardiac pacemaker wires.

Principles of Admittance Plethysmography:

A change in volume (V) of a limb segment results in a change in its conductance (G). Assuming that the segment may be modelled (fig 1) as a cylinder of length L and radius R:

FIGURE 1



$$(1) \qquad V = \pi R^2 L$$

$$(2) \qquad G = \pi R^2/\rho L$$

where ρ is the resistivity (Ω-cm). Combining (1) and (2):

$$(3) \qquad V = \rho L^2 G$$

Assuming that ΔV results from changes in cross sectional area only (i.e. L remains constant during volume changes):

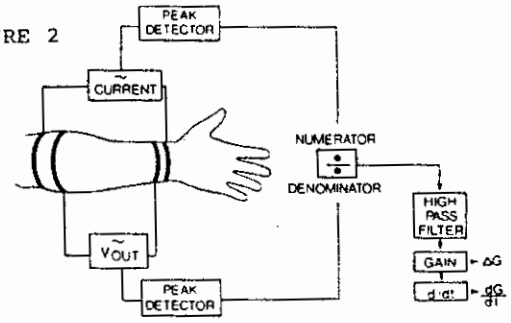
$$(4) \qquad \Delta V = \rho L^2 \times \Delta G$$

The rate of volume change (dV/dt) may be similarly computed as follows:

$$(5) \qquad dV/dt = \rho L^2 \times dG/dt$$

To implement such a system (fig.2), a sinusoidal current is injected across two

FIGURE 2



electrodes outside the segment and the voltage is measured across two electrodes at the borders of the segment. (This provides a more uniform current distribution across the segment than with a two electrode system). The amplitude of the current signal is divided by the amplitude of the voltage signal to provide a signal proportional to G. This signal is then high pass filtered to provide a signal proportional to ΔG and differentiated to provide a signal proportional to dG/dt.

At the frequencies used to make these measurements (> 20 KHz) biological tissue is a conductor and has no reactive component. Thus, in this context, the terms admittance and conductance plethysmography are interchangeable.

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Uses of Admittance Plethysmography:

AP has been used to measure peripheral flow indirectly by measuring the volume change which occurs in a limb segment after a venous occlusion. It has also been used to indirectly measure cardiac output from changes in thoracic conductance.

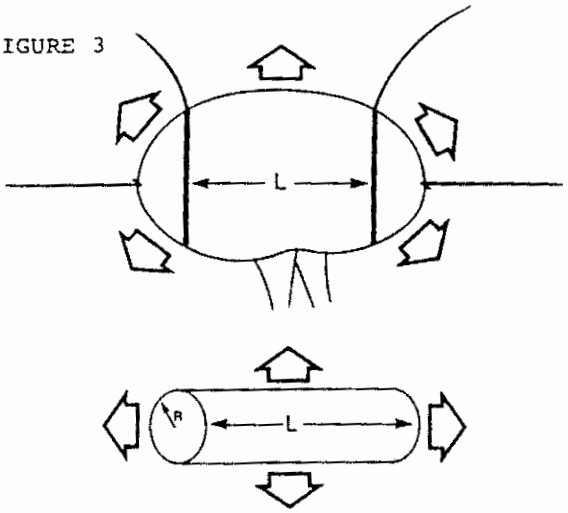
Also, phasic changes in volume may be useful in determining flow. The change in volume which occurs with each cardiac pulsation is referred to as the pulse volume (PV). dV/dt is the net inflow into the limb segment and the maximum value of dV/dt is referred to as the peak net inflow (PNI). PNI and the PV x Heart Rate product have been shown to correlate with mean limb blood flow.

We have recently demonstrated that the reproducibility of PV and PNI measurements and the fidelity of the ΔV and dV/dt curves can be substantially enhanced with selective signal averaging[2].

A Model Relating Volume Changes to Admittance Changes in the Kidney:

Whereas volume changes in the limb are constrained to the radial axis, there is no reason to make such an assumption in the case of the kidney. Grossly, the kidney appears to expand and contract homogenously. Thus, we have chosen to model the renal tissue between two circumferential inner voltage electrodes as a cylinder which expands in all directions equally (fig.3). This "homogeneous expansion"

FIGURE 3



may be expressed mathematically as:

(6) $\Delta R/R = \Delta L/L$ or $dR/dL = R/L$

We must take this into account when determining dV/dG. This may be done by expressing dV/dG as a ratio:

(7) $dV/dG = (dV/dL)/(dG/dL)$

As both V and G are functions of both R and L, both the numerator and denominator of (7) may be expanded with chained partial derivatives:

(8) $dV/dL = (\partial V/\partial L)+(\partial V/\partial R)(dR/dL)$

(9) $dG/dL = (\partial G/\partial L)+(\partial G/\partial R)(dR/dL)$

Substituting (1) and (6) into (8), (2) and (6) into (9), and (8) and (9) into (7):

(10) $$dV/dG = \frac{\pi R^2 + (2\pi RL)(R/L)}{(-\pi R^2/\rho L^2)+(2\pi R/\rho L)(R/L)}$$

This may be simplified as follows:

(11) $$dV/dG = 3\rho L^2$$

(12) or $$\Delta V = 3\rho L^2 \times \Delta G$$

Similarly:

(13) $$dV/dt = 3\rho L^2 \times dG/dt$$

Goal:

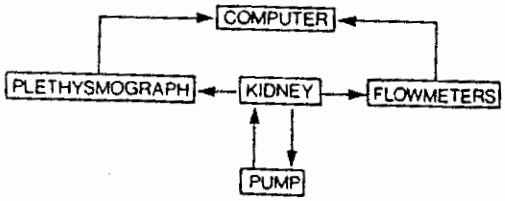
The goal of this study was to test the hypothesis that ΔV and ΔG are related as suggested in (12) and that dV/dt and dG/dt are related as suggested in (13). This was accomplished by deriving standards for PV and PNI from electromagnetic flowmeter measurements and comparing them to PV and PNI measured from the ΔV and dV/dt curves generated respectively from (12) and (13).

METHODS

Subject Material and Protocol:

Fourteen kidneys (weight = 75.7±15.3 g) were harvested from 8 mongrel dogs (6F,2M, weight = 24.7±1.4 kg). Half of the kidneys were studied immediately after harvest and half after 24 hours hypothermic perfusion on a Waters pump with modified Belzer[3] perfusate at 4° C. A schematic of the experiment is shown in fig 4.

FIGURE 4



All kidneys were studied at room temperature on the Waters pump. A 15cc column of air was used to dampen the arterial waveform. The pump rate (/min) was varied from 48 to 80 in increments of 8/min. At each pump rate, the stroke volume (SV) was varied from .4 ml to 2.0 ml in increments of .4 ml. At each rate/flow setting, PV-std, PNI-std, PV-pleth, and PNI-pleth were measured as described below.

To account for variations in the conductivity of perfusate solution between batches, ρ was measured prior to each trial using a conductivity cell.

As the PV-pleth and PNI-pleth measurements reflect volume changes occurring between the circumferential voltage electrodes, whereas the PV-std and PNI-std reflect such changes in the entire kidney, all measurements were normalized to the weight of the measured segment. Segment weights were determined after measurements were completed by cutting the kidneys in the plane of the inner electrodes and weighing the middle and end segments separately.

Flow Measurements:

Arterial inflow and venous outflow were measured with 2 synchronized electromagnetic flowmeters (Carolina Medical 501) using a circumferential probe (EP-410) for the artery and an in-line probe (EP-616) for the vein. These flow signals were subtracted and then

high pass filtered (fo = Ø.1 Hz) using differential preamplifiers (Gould 13-4615-58) to generate the phasic net inflow signal (dV/dt-std). This signal was integrated with an integrating preamplifier (Gould 13-4615-7Ø) to generate the volume change signal (ΔV-std). The integrator was reset with each pump cycle.

Plethysmographic Measurements:

Plethysmographic measurements were made with a four electrode system. The two outer "current electrodes" were positioned at the poles. The two inner "voltage" electrodes were positioned circumferentially 1.25 cm in from the poles. A brief description of the plethysmograph electronics follows:

A 47 KHz, 1 mA (peak-to-peak) current is applied to the outer electrodes via an isolation transformer. The inner electrodes are connected via an isolation transformer to an instrumentation preamplifier (AD521). The amplitudes of the current and voltage signals are continuously monitored with peak detectors and the current signal is divided by the voltage signal with an analog divider (AD534) to generate a signal proportional to G. This signal is low pass filtered (fo = 26 Hz) and high pass filtered (fo = Ø.35 Hz) to generate the phasic conductance signal (ΔG) which is proportional to ΔV-pleth. This is then differentiated to produce the dG/dt signal which is proportional to net inflow (dV/dt-pleth).

Signal Processing

At a given point in time, either the ΔG and dG/dt signals or the ΔV-std and dV/dt-std signals are input to an Apple IIe computer via an A/D board (Mountain Computer). Twenty cycles are selectively averaged[4] (they must remain within the input limits of the A/D for the duration of the cycle) using a synchronizing pulse in the pump control as the gating signal.

The maximum excursion of the ΔV-std curve and the maximum value of the dV/dt-std curve are measured by the computer to respectively provide PV-std, and PNI-std. The maximum excursion of the ΔG curve and the maximum value of the dG/dt curve are measured by the computer and these values are used to respectively calculate PV-pleth, and PNI-pleth using (12) and (13).

RESULTS

Plethysmographic Pulse Volume:

The relationship of PV-pleth to PV-std at each pump rate is shown in fig 5. If all data points regardless of rate are considered, the regression equation relating these variables is PV-pleth = PV-std x 1.11 + .43 (r = Ø.965).

As shown, the slope of this family of curves decreases in the presence of both high rate and stroke volume (SV). As mean flow (MF) equals to Rate x SV, this falloff is found to occur at high values of MF. If MF values greater than 115 ml/min are excluded (fig 6) r is increased to Ø.998 (PV-pleth = PV-std x 1.19 + Ø.12).

Rate was also shown to have an independent effect on PV-pleth/PV-std slope (fig 7). Three of the MF values (76.8, 96, and 128 ml/min) occurred at different combinations of Rate and SV. If flow is held constant, an increase in rate causes a decrease in the slope in all cases ($p < Ø.Ø5$).

FIGURE 5 PV-PLETH vs PV-STD

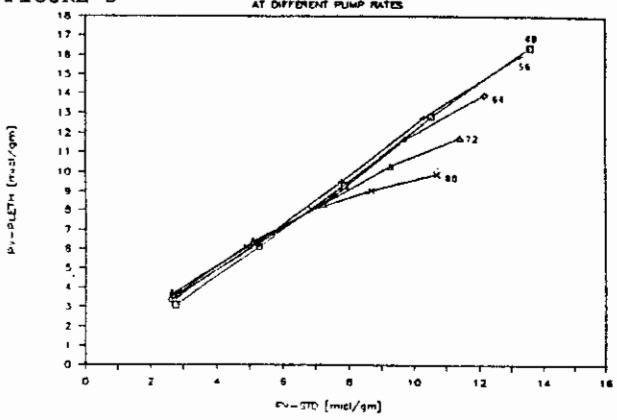


FIGURE 6 PV-PLETH vs PV-STD

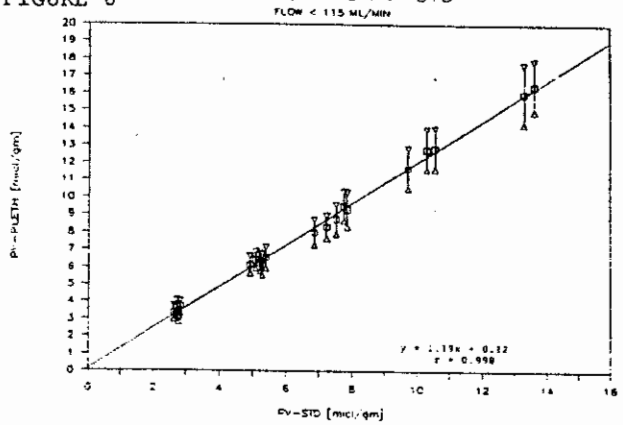
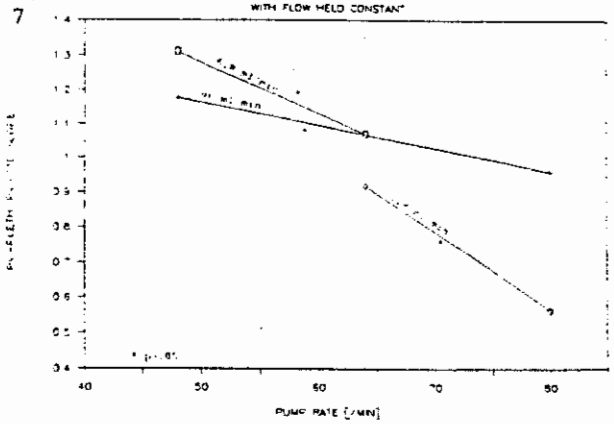


FIG 7 RATE EFFECT ON PV-PLETH/PV-STD SLOPE



Plethysmographic Peak Net Inflow:

The findings are similar for PNI (fig 8). If all data points regardless of rate are considered, the regression equation relating PNI-pleth to PNI-std is PNI-pleth = PNI-std x Ø.86 + 12.88, r = Ø.938).

As shown, the slope of this family of curves also decreases in the presence of both high rate and SV. If MF values greater than 115 ml/min are excluded (fig 9) r is increased to Ø.99Ø (PNI-pleth = PNI-std x 1.Ø8 + 3.23).

Rate is once again shown to have an independent effect on the slopes of the curves (fig 1Ø). If flow is held constant, an increase in rate causes a decrease in the slope at all 3 flow rates ($p < Ø.Ø5$).

FIGURE 8 PNI-PLETH vs PNI-STD AT DIFFERENT PUMP RATES

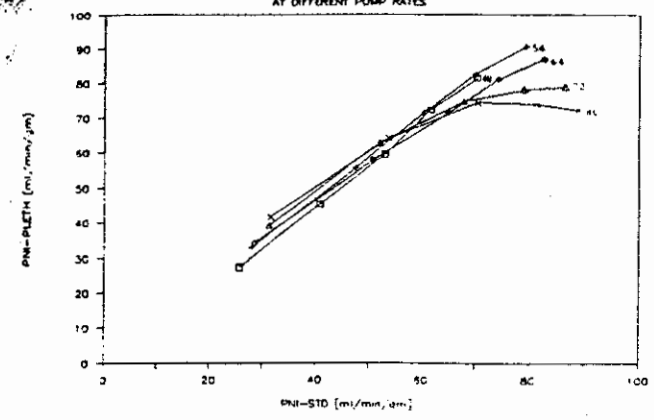


FIGURE 9 PNI-PLETH vs PNI-STD FLOW < 115 ML/MIN

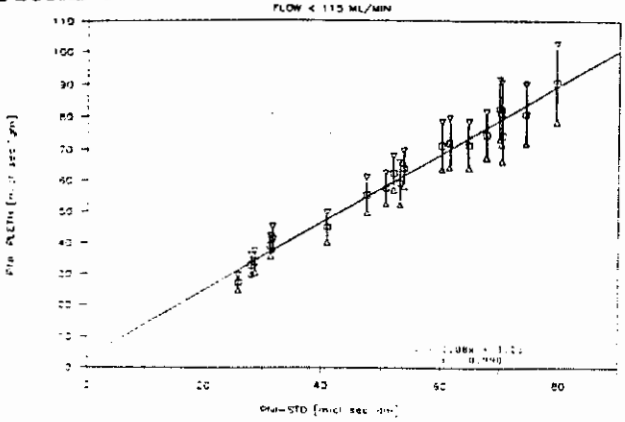
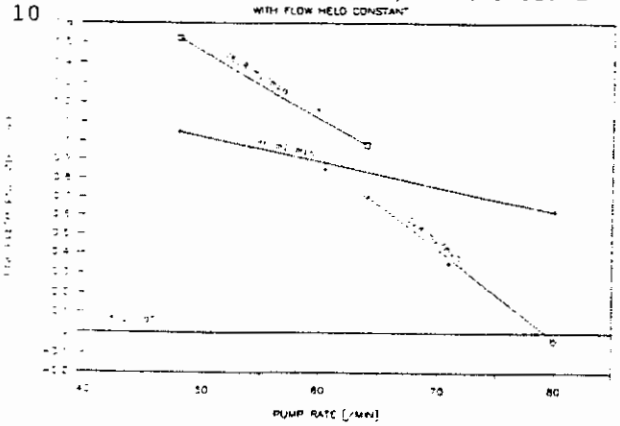


FIG 10 RATE EFFECT ON PNI-PLETH/PNI-STD SLOPE WITH FLOW HELD CONSTANT



DISCUSSION

To our knowledge, there have been no reports describing the relationship between electrical conductance of renal tissue and renal volume. In this study, we have demonstrated that over a wide flow range, phasic changes in renal volume (PV) and the maximum rate of volume change (PNI) may be reasonably predicted from changes in renal conductance using a model which assumes homogeneous geometric changes.

However, the relationship deteriorates at high pump rates, stroke volumes, and therefore mean flow values. We may speculate that the expansion of the arteriolar bed occurring at the higher flow rates and stroke volumes causes a decrease in arteriolar compliance which in turn causes a greater portion of the volume pulsation to be transmitted to the venous system, where the above mentioned geometric assumptions may no longer be valid.

The independent effect of rate is more difficult to explain. It may be due to a frequency resonance effect in which at rates greater than the resonant frequency, the vascular bed remains at a greater state of expansion, again reducing arteriolar compliance and transmitting a greater portion of the volume pulsation to the venous system.

These results must be interpreted cautiously as this experimental preparation which allows precise control of rate and flow is far from the physiologic state. The kidneys were hypothermic, denervated, and perfused with a colloid solution. It remains for further investigations to determine if such relationships and/or limitations exist in vivo.

It is also important to emphazize that flow can not be calculated directly from pulsatile changes. This can be illustrated by considering ligation of the renal vein. There would be no net flow throught the kidney although there clearly would be a measurable pulse volume.In peripheral limb plethysmography, PV x Heart Rate and PNI have been shown to correlate with MF[5]. It remains to be seen if such a correlation exists in the kidney.

As changes in flow have been shown to occur with renal transplant rejection[6], a technique which indicates relative changes in flow might be useful in indicating the early stages of rejection. If renal admittance plethysmography provides such information, it might be obtained via conductive leads placed at the time of transplant surgery and brought through the skin much like temporary cardiac pacemaker wires after open heart surgery.

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