In Vivo $^{31}$P Nuclear Magnetic Resonance Measurements in Canine Heart Using a Catheter-Coil

Howard L. Kantor, Richard W. Briggs, and Robert S. Balaban

From the Laboratory of Kidney and Electrolyte Metabolism, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Maryland, and the Department of Radiology, Milton S. Hershey Medical Center, Hershey, Pennsylvania

SUMMARY. We have developed a new method of obtaining high resolution $^{31}$P nuclear magnetic resonance spectra from canine heart without the need for major surgery. This is done by passing an elliptical nuclear magnetic resonance receiver coil through a peripheral blood vessel into the right or left ventricle. This technique enables spectra to be obtained from a defined region of myocardium in less than 7 minutes (for the right ventricle) with a signal:noise ratio of greater than 9:1. With this catheter-coil, useful cardiac metabolic information will be obtainable, not only from specified regions of the heart, but also from various layers of myocardium. (Circ Res 55: 261-266, 1984)

$^{31}$P NUCLEAR magnetic resonance (NMR) is a valuable tool in determining the concentration and turnover of high energy phosphate compounds in various tissues, and has provided unique insights into cellular energetics (Shulman et al., 1979; Ackerman et al., 1980; Gadian and Radda, 1981; Meyer et al., 1982; Balaban, 1984). The noninvasive nature of NMR permits these measurements to be made in vivo, where neurological and endocrine feedback remains intact. These in vivo experiments can effectively be done for superficial tissues using surface coils (Ackerman et al., 1980), but internal organs, such as the heart, present difficulties with reduced sensitivity and spatial selectivity. Indeed, the noninvasive character of NMR is occasionally waived in favor of major surgery in order to place the NMR transceiver on the internal organ (Grove et al., 1980; Nunnally and Bottomley, 1981; Koretsky et al., 1983), allowing a greater signal:noise ratio and regional specificity than do external devices. New noninvasive techniques being developed are capable of sampling specific regions distant from transmitter and receiver coils, but suffer from a reduced signal:noise ratio (Hinshaw, 1976; Hoult, 1979; Bendel et al., 1980; Gordon et al., 1980; Cox and Styles, 1980; Balaban et al., 1981; Brown et al., 1982; Bottomley, 1982; Scott et al., 1982; Haselgrove et al., 1983; Haase et al., 1983; Bendall and Gordon, 1983).

We report a method of placing an NMR coil in the heart without the need for major surgery, by passing the coil through a peripheral blood vessel. We have reasoned that, in cardiac studies, it is imperative to obtain routine catheterization data to determine the physiological state of the heart, and therefore, advancing an NMR transceiver through a peripheral blood vessel, in a similar manner, would not be excessive. Using this catheter-coil, we have collected $^{31}$P NMR spectra from the right and left ventricles of anesthetized canines, without appreciable alteration of cardiovascular physiological parameters.

**Methods**

The catheter-coil consisted of a two-turn elliptical transceiver coil, 7.5 X 24 mm, in the case of the right ventricle, fashioned from copper magnet wire and insulated with polystyrene before passage through a blood vessel to the heart. A smaller coil, 3.5 X 20 mm, was used in studies of the left ventricle because of the small caliber of blood vessel used for its passage. The elongated coil shape (see Figs. 1 and 3) was necessary to permit introduction into a narrow blood vessel, while still allowing a reasonably large area of irradiation, thereby yielding an adequate signal:noise ratio.

Because this is not a common shape for an NMR transceiver coil, we have mapped its magnetic field profile at 32.5 MHz. Figure 1 is a schematic diagram of the coil which illustrates the coordinate system used for this mapping. $R_0'$ corresponds to the long axis of the coil, $r$ to the short axis of the coil. With the long axis of the coil parallel to the main magnetic field ($B_0$), a small sensing coil was used to detect the field, $B_{s/n}$, generated by the coil perpendicular to $B_0$. The sensing coil was placed at different positions, $R$, along the long axis $R_0$, and the field was measured as the coil was moved along the short axis $r$, as well as away from the face of the coil. The results of this procedure are presented in Figure 2, A-C, where three different positions of the coil along the long axis are presented: Figure 2A, at the center of the coil ($R/R_0 = 0$), Figure 2B, 60% of the way to the end of the coil ($R/R_0 = 0.6$), and Figure 2C, past the end of the coil ($R/R_0 = 1.17$).

Curves for the $B_{s/n}$ field strength are plotted for several positions along the short axis, $r$, in the dimensions of $r$, and as a function of the distance from the face of the coil, also in dimensions of $r$. The field profiles for $R/R_0$ greater than 1, indicate that $B_{s/n}$ falls off dramatically for all displacements parallel to the short axis. For $R/R_0$ less than 0.6, the field is appreciable at points which extend past...
Circulation Research/Vol. 55, No. 2, August 1984

nonmagnetic coaxial cable with two Johanson JMC 5601 variable capacitors, one in parallel, and one in series with the coil. Maximum $^{31}$P signals were obtained with 6-μsec pulses when the coil was immersed in a beaker of saline containing phosphate.

The cardiac experiments were performed on an Oxford Instruments TMR-32 magnet with a 20-cm bore at 1.89 Tesla and 32.5 MHz resonance frequency for $^{31}$P. The magnet is interfaced to a Nicolet RF console, and data are collected in the Fourier transform mode on a Nicolet 1280 computer. Shimming of the magnet was done on the tissue water resonance. Proton water linewidths of 22-45 Hz were routinely obtained. Spectra were collected in blocks of 400 scans with pulse delays of 0.75-10 seconds, and an acquisition time of 0.25 second. Resolved peaks with a signal/noise ratio of 9.4:1 for the phosphocreatine resonance were obtained in 6.8 minutes in the right ventricle, with an acquisition cycle time of 1 second. Acquisition of NMR signals from arterial blood was begun within 5 minutes after withdrawal. The canine blood spectrum was obtained in a 12-mm NMR tube on a Nicolet NT-360WB system with an 8.4 Tesla magnet, and $^{31}$P resonance frequency of 146 MHz.

We examined the right ventricle of beagles by insertion of the catheter-coil through a superficial cutdown in the external jugular vein. It was then passed, with fluoroscopic monitoring, into the right ventricle and positioned near the ventricular apex. Animals were anesthetized first with intravenous pentobarbital, then with halothane (1%)-nitrous oxide (50%)-oxygen inhalational anesthesia. Blood pressure monitoring was performed with a cannula which was passed from the femoral artery into the descending aorta, and a Swan-Ganz catheter passed from the femoral vein into the pulmonary artery. Arterial blood gas measurements were obtained to ensure adequate oxygenation and ventilation, and ECG leads were attached to detect any arrhythmias. No significant arrhythmias were noted throughout the experiment. Pulse rate (60-80 beats/min), blood pressure (115-125 mm Hg systolic), and pulmonary artery wedge pressure (10-18 mm Hg) were unchanged by the insertion of the coil in 13 dogs.

Definitions: $\alpha$-ATP, $\beta$-ATP, and $\gamma$-ATP correspond to the $\alpha$-, $\beta$-, and $\gamma$-phosphates of ATP, respectively. For ADP, the same nomenclature is used.

Results

An x-ray of the coil positioned in the right ventricle is shown in Figure 3. From multiple views on fluoroscopy during advancement, we have determined that the coil is near the apex of the right ventricle. A $^{31}$P NMR spectrum from the coil in this position is illustrated in Figure 4. Creatine phosphate (CrP) (peak C), ATP (peaks D, E, F), 2,3-diphosphoglycerate, inorganic orthophosphate, and phosphomonooesters (peak A), and phosphodiesters (peak B) were easily resolved in this spectrum. This spectrum was the average of 120 acquisitions with an interpulse delay of 10 seconds (ca. 20 minutes of collection time).
A stack plot of $^{31}$P NMR spectra collected from a coil with similar placement is shown in Figure 5. The spectra shown here were collected sequentially, and each spectrum represents ca. 6.8 minutes of data acquisition (i.e., 400 scans, 1-second interpulse delay). Similar reproducibility, as demonstrated in this figure, was found over 2 hours in 10 dogs studied.

$^{31}$P NMR spectra with interpulse delays of 10 seconds, as shown in Figure 4, were collected in order to obtain information on the relative peak intensities. Using the curve-fitting routine supplied with the Nicolet Magnetics software for Lorentzian line fitting, we calculated a CrP:ATP ratio of 1.7 (range 1.5–1.9, in four animals) using the $\beta$ peak of ATP for the calculation. This is in agreement with the value of 1.6 for open-chest coil placement in rats (Grove et al., 1980). For perfused hearts, values between 1.2 and 1.6 have been noted, depending on the perfusion medium and the type of preparation (Matthews et al., 1982; Ingwall, 1982).

To determine the contribution of blood phosphorus compounds to the heart spectrum, we examined the $^{31}$P NMR spectrum of well-oxygenated canine blood immediately after withdrawal. In Figure 6, we note that there is a large pair of peaks corresponding to the phosphates of 2,3-DPG, whereas there are much smaller resonances for ATP. The 2,3-DPG:ATP ratio was greater than 20:1, using the $\beta$ ATP to estimate the ATP content. If the peak corresponding to peak A in Figure 4 were totally produced by 2,3-DPG, then the ATP in blood could account for no more than 5% of the observed ATP resonance intensity. The previously stated CrP:ATP ratio, therefore, is representative of the right ventricular myocardium.

The metabolic state of the left ventricle may be
FIGURE 6. A canine blood $^{31}$P NMR spectrum collected at 147 MHz. The pulse width is 22 $\mu$sec (ca. 80°), with an acquisition time of 1.02 seconds and a delay time of 10.0 seconds. Two hundred scans were collected, and a line broadening of 15 Hz was applied. Peak assignments are: peak A, phosphates at the 3 and 2 positions of 2,3-DPG; peak B, orthophosphate; peak C, phosphodiesters; and peaks D, E, and F are the phosphates of ATP as described in Figure 4.

more interesting than that of the right ventricle, noting its greater contribution to cardiac work, and we show in Figure 7 that $^{31}$P NMR spectra can be similarly obtained from the left ventricle with a catheter-coil. This spectrum was obtained with a 1-second pulse delay, rather than the 10-second delay used in Figure 4 because of the reduced signal:noise ratio in the CrP and ATP resonances, and the desire to minimize data acquisition time. It is understood that the different conditions of data acquisition do not permit comparison of spectra from the right and left ventricle, nor quantification of the relative concentrations of phosphorus compounds in the left ventricle. Note that a tall peak corresponding to 2,3-DPG is present (with some contribution from inorganic orthophosphate and phosphomonoesters).

FIGURE 7. A $^{31}$P NMR spectrum obtained from the left ventricle of a beagle, using a 2-turn 3.5 mm $\times$ 22 mm catheter-coil. Eight thousand scans were collected with a 1-second interpulse delay. Peak labels are as described in Figure 4. Line broadening of 20 Hz was applied.

This probably is a result of slightly greater displacement of the coil from the myocardium, compared to the right ventricle studies. The contribution of blood to the observed ATP resonance is, however, still minimal, based on the size of the 2,3-DPG in this spectrum. If the coil is displaced from the cardiac wall in the left ventricle, longer pulse widths may eliminate the blood signal near the coil, as previously used to eliminate the skin and tissue near an external surface coil (Balaban et al., 1981). In preliminary studies, we have found that increasing the pulse width to 20–30 $\mu$sec will reduce the 2,3-DPG signal, supporting the contention that the cardiac wall is displaced from the coil face by our present coil placement technique in the left ventricle.

Discussion

In these studies, we demonstrated that $^{31}$P NMR spectra can be collected from the right and left ventricles of the heart. In the right ventricle, we were able to collect spectra in 6.8 minutes with a signal:noise ratio of greater than 9:1. In the left ventricle, the signal:noise ratio was much worse, with a minimum acquisition time on the order of 20 minutes. We have only studied the left ventricle in three animals, and believe that the poor signal:noise ratio is due to difficulty in coil positioning with respect to the myocardium, as suggested by the large 2,3-DPG peak and our preliminary pulse width experiments. Further work is required to obtain the same signal:noise ratio as in the right ventricle, although—in principle—this should be obtainable. This might be accomplished by gating the NMR acquisitions to the heart beat (i.e., collecting the signal when the coil is adjacent to the heart wall) or...
Kantor et al. / In Vivo 31P NMR Using a Catheter-Coil

with more experience in coil placement in the left ventricle.

The catheter-coil technique differs from other methods of obtaining cardiac NMR spectra in two important respects. First, it is less invasive than thoracotomy, at the same time permitting a large coil-filling factor which should improve the signal-to-noise ratio. The noninvasive techniques under current development, such as the sensitive point method (Hinshaw, 1976; Bottomley, 1982; Scott et al., 1982), topical magnetic resonance (Gordon et al., 1980), chemical shift imaging (Hoult, 1979; Cox and Styles, 1980; Bendall et al., 1980; Brown et al., 1982; Haselgrove et al., 1983; Haase et al., 1983), and surface coil focusing (Balaban et al., 1981; Bendall and Gordon, 1983; Bendall and Aue, 1983) are probably reduced in sensitivity in comparison to the catheter-coil, due to smaller effective coil-filling factors. Second, as we have shown in the field profile analysis, the catheter-coil can sample a region 3-4 mm from the face of the coil. Thus, internal placement of the coil permits the study of the subendocardium rather than the full thickness of heart muscle, and may permit variation of the depth examined through alteration of the pulse width (Balaban et al., 1981; Bendall and Gordon, 1983; Bendall and Aue, 1983). Because of the higher sensitivity of the subendocardium vs. deeper tissues to ischemia, as well as other pathological processes (Braunwald, 1984), this technique offers some advantages over previously used NMR techniques in studying clinically relevant problems.

This technique is hampered by the need to enter the vasculature surgically in order to obtain spectroscopic information. The present procedure also does not include a method of coil fixation to ensure maintenance of position. Although some movement could occur during drastic changes in heart rate or work output, no movement was detected during these steady state experiments, as judged by both x-ray images and NMR spectra. Even if more severe protocols did result in coil displacement, the relative intensities of the peaks would still reflect the metabolic state of the particular chamber under study. Both of these problems can be overcome with the use of collapsible coils enabling percutaneous advancement, and the development of coil fixation, not unlike those used in endocardial pacemakers. In addition, significant improvement in signal-to-noise ratio may be obtained by using a large transmitter coil (around the outside of the animal) and the catheter-coil for a receiver only. This would maintain its spatial localization and provide a more homogeneous B1 field. Such changes will increase the ease of performing experiments, and improve the applicability of the catheter-coil technique to medically relevant problems.

We have demonstrated that it is possible to obtain in vivo high resolution 31P NMR spectra from defined regions of both the left and right ventricles without the need for major invasive surgery. With only slight modification, this technique should be applicable to the study of other internal organs.

We thank Carole Mancuso, Joyce Minnich, and Drs. William White, Randolph Patterson, John Doppman, and Delwin Buckhold for their helpful advice and technical assistance.

Address for reprints: Robert S. Balaban, Building 10, Room 6N-307, National Institutes of Health, Bethesda, Maryland 20205.

Received November 28, 1983; accepted for publication May 25, 1984.

References

the isolated, perfused rat heart. Biochim Biophys Acta 720: 163–171
Scott KN, Brooker HR, Fitzsimmons JR, Bennett HF, Mick RC


INDEX TERMS: Nuclear magnetic resonance • Heart • Metabolism
In vivo 31P nuclear magnetic resonance measurements in canine heart using a catheter-coil.

H L Kantor, R W Briggs and R S Balaban

doi: 10.1161/01.RES.55.2.261

_Circulation Research_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1984 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/55/2/261

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation Research_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation Research_ is online at:
http://circres.ahajournals.org/subscriptions/