Acoustic Recordings From Experimental Saccular Aneurysms in Dogs

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In an effort to isolate and characterize the emission of acoustic signals from saccular aneurysms, we made a series of invasive microphone recordings from experimental aneurysms created on the common carotid arteries of dogs using the vein pouch technique. Using a modified probe microphone, we compared recordings from the common carotid artery before creation of the aneurysm to recordings from the aneurysmal surface, both before and after clip occlusion. We then performed spectral analysis, band-pass filtering, and spectrographic analysis to compare the dominant frequency and width of the frequency range of both the aneurysmal and carotid recorded signals. The aneurysmal signals had a significantly higher dominant frequency (p<0.05) and a significantly wider frequency range (p<0.05) than the carotid signals. Aneurysmal signals recorded under conditions of systemic hypotension had a significantly lower frequency (p<0.05) than aneurysmal signals recorded under conditions of hypertension. Our results support the assumptions that acoustic signals from experimental saccular aneurysms are distinct from those of the parent vessel and that the aneurysmal signal can be characterized using passive microphone recordings.

Acoustic signals from experimental saccular aneurysms have been studied to further the understanding of the pathophysiology of aneurysmal development and subsequent rupture. Disturbances in blood flow, including vibration and turbulence, have been implicated in the formation and rupture of aneurysms by inciting mural vibration and elastin breakdown.1-4 In addition, structural fatigue and arterial dilation as a result of arterial wall vibration have been documented.5 The damaging effect of the vibration has been shown to increase when the vibrations occur at the resonant frequencies of the arterial wall.6 Advanced methods of acoustic spectral analysis can be used to examine the complicated dynamic system influencing vascular flow within and distal to the saccular aneurysms.

Aneurysmal hemodynamics have been studied to further the understanding of the pathophysiology of aneurysmal development and subsequent rupture. Disturbances in blood flow, including vibration and turbulence, have been implicated in the formation and rupture of aneurysms by inciting mural vibration and elastin breakdown.1-4 In addition, structural fatigue and arterial dilation as a result of arterial wall vibration have been documented.5 The damaging effect of the vibration has been shown to increase when the vibrations occur at the resonant frequencies of the arterial wall.6 Advanced methods of acoustic spectral analysis can be used to examine the complicated dynamic system influencing vascular flow within and distal to the saccular aneurysms.

Recent reports have examined sound emission originating from saccular aneurysms with the goal of noninvasively detecting their presence in a clinical setting.10-15 The study of aneurysmal hemodynamic and acoustic properties has had somewhat differing results. Ferguson16 used a cardiac phonocatheter to record acoustic signals from cerebral aneurysms exposed at surgery and found bruits in 10 of 17 patients. In this study, we found no sound in intracranial arteries except that transmitted from aneurysms. Ferguson1 described the bruits as a pure tone with burst patterns corresponding to the peak of systole. He attributed the failure to detect bruits in some cases to intraoperative hypotension. German and Black17 reported palpable thrills associated with experimental saccular aneurysms, whereas Stehbens18 found strong vortices within the aneurysms but an absence of thrills in his experimental work.

Using an electronic stethoscope for the noninvasive detection of aneurysms, Olinger and Wasser-
Using a modified probe microphone, Sekhar and Wasserman\textsuperscript{13} were able to record spikes, bruits, or a combination of the two in eight of 11 patients with cerebral aneurysms. In the same study, signal analysis of recordings made from two experimental saccular aneurysms in dogs revealed distinctive frequency spikes, which disappeared with aneurysmal ligation.\textsuperscript{13} Kosugi et al.\textsuperscript{10} using noninvasive cement wall microphones, found bruits with distinct peaks at 500 Hz in five of nine patients with aneurysms.

The relationship between the acoustic properties and the hemodynamics of saccular aneurysms has not been adequately established. The purpose of this work was to characterize the acoustic properties of the aneurysm to develop an understanding of the relationship between such acoustic properties and the hemodynamics. We conducted experimental studies designed to determine 1) if aneurysms emit specific sounds, and 2) if these sounds can be detected and differentiated with a passive microphone system. The acoustic recordings were performed on experimental aneurysms created on common carotid artery bifurcations in dogs.\textsuperscript{17-19}

**Materials and Methods**

We created 15 experimental saccular aneurysms surgically\textsuperscript{17-19} in eight adult mongrel dogs weighing from 11 to 20.2 kg. With the exception of one dog, we created two aneurysms per animal, one on each common carotid artery. The dogs were anesthetized with intravenous pentobarbital sodium, intubated, paralyzed with pancuronium bromide, and artificially ventilated. An intravenous line was placed in the cephalic vein for the administration of fluids and drugs. Continuous recordings of the systemic arterial pressure were made with a Statham transducer connected to a femoral arterial line.

Baseline recordings were made from the common carotid artery before the surgical creation of the aneurysm. Under conditions of normotension, recordings were taken by direct contact on the aneurysmal surface, and additional readings were taken serially on proximal and distal segments of the carotid artery. An aneurysm clip then was placed on the aneurysmal neck, and the recordings were repeated. In nine of the experiments, a series of sound recordings also were made under systemic hypertension induced in the animals with intravenous phenylephrine hydrochloride (Neo-Synephrine, Winthrop Pharmaceuticals, New York, N.Y.), and systemic hypotension induced by sodium nitroprusside.

The microphone recordings from the aneurysmal surface were made with a modified probe microphone (Figure 1) (model 4170, B & K Instruments, Inc., Marlborough, Mass.) with the supplementary B & K Model 2804 battery microphone power supply. The output of the microphone was connected to an acoustic aneurysm detection system,\textsuperscript{12,14} comprising a channel for the recorded aneurysmal signal and a channel for the electrocardiogram (ECG). In this system, the R wave of the ECG was used to trigger the data acquisition. The signal channel included preamplifiers, band-pass Chebyshev filters with $-3$ dB points of 100 and 1,000 Hz, and a series of low-noise amplifiers. The ECG channel consisted of a 60-Hz notch filter, amplifiers, and a logical circuit containing a peak-value detector, a comparator, and a differentiator. The sampling time delay after the R wave, the time intervals for data acquisition, and the number of epochs to be averaged for noise cancellation could be altered to maximize the quality of the recorded aneurysmal signal.

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The signal from the microphone sensor was amplified with the low-noise amplifiers of the acoustic aneurysm detector. During this process, the signal was filtered by the high-order analog Chebyshev band-pass filter to eliminate biological noise and background interference outside the signal frequency range. Recorded signals were digitized at a sampling rate of 1,706 Hz and averaged over 10 consecutive systolic periods. The average was displayed in real time on the computer. A file also was produced for off-line signal processing.

We used three methods in the analysis. 1) Classical spectral analysis with a discrete Fourier transform was used to transform the signal, after which the magnitude of the result was squared and displayed.
The relative amplitude of the signal, transformed into the frequency domain, was plotted against frequency; however, this method did not provide temporal information. 2) Spectrographic analysis, which also uses the discrete Fourier transform, was used to estimate the frequency contents of the recorded signal varying with time.20 The input signal was processed by sliding a window along the time axis at equally divided positions. Within each window, a discrete Fourier transform was performed, and the magnitude squared was plotted trace by trace, as a function of time. This method provided information about both the time and frequency of the signal. 3) The percentage of signal energy was calculated in each of 10 frequency bands, which equally divided the frequency range from 100 to 1,000 Hz. The signals filtered within the 10 bands were plotted, providing an estimation and comparison of the energy distribution of the aneurysmal signal.20 Thus, the waveforms in different frequency bands could be examined when appropriate.

Statistical analysis of the mean dominant frequency and mean frequency range (Table 1) was done with a two-tailed t test. The dominant frequencies under conditions of hypotension and hypertension (Table 2) were analyzed with the Wilcoxon matched-pair two-tailed signed rank test.21

### Results

The experimental saccular aneurysms had a mean height, length, and width (±SD) of 1.1±0.4 cm (range, 0.7–1.9 cm), 0.8±0.3 cm (range, 0.5–1.2 cm), and 0.9±0.3 cm (range, 0.4–1.1 cm), respectively. The height was measured along the log axis of the aneurysm, and the length and width were measured in axes perpendicular to the log axis, in the region of the aneurysmal sac. The mean width of the aneurysmal neck was 0.6±0.1 cm (range, 0.4–0.8 cm), and the mean diameter of the carotid artery was 0.5±0.1 cm (range, 0.3–0.5 cm).

Examples of the analyses of the acoustic recordings made by the microphone from the aneurysmal surface and the carotid artery are shown in Figures 2 and 3, respectively. These analyses provide the time signatures (Figures 2 and 3, upper panels), the power spectra (middle panels), and the spectrograms (lower panels). A comparison of the upper panels of Figures 2 and 3 shows that, at the beginning of the sound emission, both the aneurysmal and carotid signals demonstrated a low-frequency transitional process with an increasing magnitude, after which the aneurysmal signal exhibited a vibrational pattern with a diamond-shaped magnitude envelope. In contrast, the carotid signal attenuated approximately in a decreasing exponential fashion. The narrower bandwidth of carotid signal indicates the existence of streamlined flow pattern. As shown in the middle panel of Figure 2, the major frequencies of the aneurysmal signal were located between 150 and 700 Hz, in contrast to those of the carotid signal, which had frequencies between 75 and 175 Hz (Figure 3, middle panel). In addition, the sound emission segment of the spectrogram of the aneurysmal signal (Figure 2, lower panel) had a low-high-low pattern within a systolic period, demonstrating a time-varying frequency characteristic in contrast to the sinusoidal characteristic of the sound emission segment of the carotid signal (Figure 3, lower panel).

An example of the aneurysmal signal occurring over time is shown in Figure 4, demonstrating the cyclic pattern of three systolic periods. The time interval between vibrations was approximately 135 msec. This time signature, similar to that presented in the upper panel of Figure 2, showed a low-high-low frequency pattern; however, the magnitude of the beginning vibration was larger than that in the previous example, reflecting the variation of the aneurysmal vibrational systems.

We eliminated from the analysis three sets of recordings from the 15 experiments because of electronic failure or high noise content. The microphone detected distinct acoustic signals from 10 experimental aneurysms. The recordings in which there was a failure in signal detection were contaminated with external noise, an ongoing problem inherent in the methodology.

The analytical results of the experimental recordings are summarized in Table 1. We found that the mean dominant frequency of the aneurysmal signals was 226 Hz, significantly higher (p<0.05) than the mean dominant frequency of the carotid signals (150 Hz). In addition, the mean frequency range of the aneurysmal signals was 273 Hz, significantly broader (p<0.05) than the carotid recordings, which had a mean frequency width of 151 Hz.

### Table 1. Analytical Results of Experimental Recordings

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<th>Dominant frequency</th>
<th>Frequency range</th>
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<tr>
<td></td>
<td>n</td>
<td>Mean (Hz)</td>
</tr>
<tr>
<td>Aneurysm</td>
<td>12</td>
<td>226*</td>
</tr>
<tr>
<td>Carotid</td>
<td>9</td>
<td>150*</td>
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*p<0.05.

### Table 2. Microphone Recordings of Aneurysm

<table>
<thead>
<tr>
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<th>High MAP (Mean, 162 mm Hg)</th>
<th>Low MAP (Mean, 112 mm Hg)</th>
</tr>
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<tbody>
<tr>
<td>Mean frequency (Hz) (n=6)</td>
<td>271*</td>
<td>181*</td>
</tr>
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MAP, mean arterial pressure.

*p<0.05.
An audible difference was evident between the aneurysmal and carotid recordings. The recordings from the aneurysms were higher in pitch than those from the carotid artery and exhibited a somewhat musical quality, in contrast to the drumlike sound from the carotid artery.

After clip occlusion, the characteristic aneurysmal patterns were no longer present. In addition, a critical level of mean arterial pressure (MAP) appeared to be necessary for the aneurysmal vibration to occur. Figure 5 represents the time signature of the aneurysmal signal recorded at an MAP less than 100 mm Hg. This signal did not have the aneurysmal patterns seen in the upper panel of Figure 2, recorded at an MAP of 135 mm Hg, but rather, resembled the carotid arterial patterns shown in the upper panel of Figure 3. This critical value may be specific for individual aneurysms and may vary with the shape and size of the aneurysm, as well as other mechanical parameters of the aneurysm.

We found a trend relating changes in blood pressure to variations in aneurysmal signal frequency, as shown in Table 2. In three of nine experiments, technical problems caused difficulty in obtaining quality recordings during elevation and lowering of blood pressure. In six experiments, we found that aneurysmal recordings made under conditions of hypotension (MAP=112 mm Hg) had an average frequency of 181 Hz, in contrast to the recordings
made under hypertension (MAP=162 mm Hg), which had an average frequency of 271 Hz. Based on the Wilcoxon matched-pair signed rank test, these mean frequencies were significantly different (p≤0.05).

Discussion

The production of experimental aneurysms in animals has been used with varying degrees of success to study aneurysmal flow dynamics. These methods, beginning in the 1700s with Hunter's pioneering experimental work in the carotid artery of the dog, have included mechanical injury to arterial walls, unilateral carotid artery ligation, experimental hypertension and the administration of β-aminopropiionitrile in rats, local application of toxic agents, and microsurgical techniques. The vessel walls of the vein pouch aneurysms lack the histological similarity to spontaneous aneurysms in rats or humans, but their size and shape can be varied, and they are readily accessible for sound recordings. Thus, we preferred the vein pouch aneurysm model for our work.

We did not fully investigate the relationship of aneurysmal vibration and critical MAP because of the complexity of the system, yet it appeared that the vibrational system required a sufficient driving force to function. With the exception of two cases of low-intensity bruits, Ferguson was unable to record aneurysmal bruits when MAP was less than 50 mm Hg. He also found that the amplitude of the bruits varied directly with MAP. Kosugi et al found that the group of patients with strong, clear bruits had slightly higher blood pressure than those with faint or no bruits; however, this difference was not statistically significant. This relationship between critical MAP and aneurysmal vibration requires further study. Velocity of blood flow within an artery may also have a critical relationship to the production of aneurysmal sounds.

We have found a trend relating changes in the blood pressure to the frequency of the aneurysmal signal. Under conditions of low MAP, the mean aneurysmal signal frequency was lower (similar to the carotid arterial signal frequency) than it was under conditions of high MAP.

We discovered that the mean dominant frequency of the acoustic signal from the aneurysm was significantly higher than that from the carotid artery. We believe, however, that the group average for the aneurysmal dominant frequency is biased slightly toward the lower frequency range. This bias was possibly due to the random error in data acquisition using the synchronous averaging technique.

There is also disagreement in the literature as to whether the phenomenon of aneurysmal vibration is due to turbulent flow, resonance, vortex shedding, or a hydrodynamic whistle mechanism. Olinger and Wasserman postulated that aneurysms act as Helmholtz resonators, suggesting that several mechanisms could be driving the resonating system. The musical quality of the aneurysmal recordings in this study also has been observed in previous studies. These vibrations were described as high-pitched, pure tones with a musical quality, with the mean dominant frequency of 460 or 500 Hz. Aaslid and Nornes disputed the contention that the turbulent sounds recorded from the aneurysms by Ferguson could be a pure signal. Roach studied blood flow inside aneurysms using a Perspex model of a dog aortic trifurcation. By using frequency analysis, she found that the frequency peak was a function of flow rate and suggested that eddies were shed from the aneurysm origin. In support of Ferguson and others, we found the aneurysmal signal to be a significantly predominant tone illustrating a maximal burst pattern at the peak of systole. Nonetheless, we attribute the vibration not to turbulence (as did Ferguson), but to a resonance phenomenon because there were sound emissions at one or two frequencies, which varied with blood pressure.

It should be pointed out that musical murmurs have been reported not only from aneurysms, but also from cerebral blood vessels in spasm, after the
aneurysms have been clipped, or without aneurysms at all. It is important to note that the musical sounds recorded here were under normal flow conditions; therefore, these sounds cannot be attributed only to an increase in blood flow beyond a critical velocity.

The generation of vibrations by biological membranes is dependent on their elasctance, which equals the Young's modulus of elasticity multiplied by the wall thickness. Thus, given the same stimulus, different vibrations are likely to be produced by the following: 1) a thin-walled aneurysm, 2) a thick-walled aneurysm, 3) the wall of an artery, and 4) the wall of a vein. Because any single aneurysm is likely to have different wall thicknesses and other pathological alterations in different areas, the same aneurysm may vibrate at different dominant frequencies under different conditions. Therefore, our vein pouch model has certain limitations while trying to replicate the in vivo situation.

We evaluated the various methods of signal processing used in these studies and found the spectrographic analysis superior to the power spectral analysis on the entire data stream, yielding higher detection sensitivity and demonstrating signal frequency variation over time. As in many biological sounds, the frequency characteristics of the aneurysmal signal were found to be time variant. We believe that improvements in sensitivity and a reduction in variability can be made by replacing the probe air microphone with a hydrophone of the type used in the noninvasive patient recordings with the acoustic aneurysm detection system.

In summary, our results show that acoustic signals from experimental aneurysms are distinct from the parent vessel and that the signal can be characterized by analysis of passive microphone recordings. The implications of this are of great importance for two reasons. First, further studies of this nature can be beneficial in determining the genesis of acoustic signal emission from aneurysmal lesions. The study of the generation of such signals and their relationship can lead to an understanding of the pathophysiology of aneurysmal formation and rupture. In addition, these preliminary studies in experimental saccular aneurysms have provided guidelines for the characterization of aneurysmal signals to be used in the detection and differentiation of intracranial aneurysms in noninvasive tests.

Acknowledgments

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