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Chest 2005;128;1468-1474

DOI: 10.1378/chest.128.3.1468

This information is current as of September 16, 2005

The online version of this article, along with updated information and services, is
located on the World Wide Web at:

<http://www.chestjournal.org/cgi/content/full/128/3/1468>

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A M E R I C A N C O L L E G E O F
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Transmission of Crackles in Patients With Interstitial Pulmonary Fibrosis, Congestive Heart Failure, and Pneumonia*

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Objective: Patients with interstitial pulmonary fibrosis (IPF) often have diffusely abnormal findings on chest radiographs, making it difficult to detect evidence of superimposed congestive heart failure (CHF) or pneumonia. The goal of this study was to determine whether the crackles of IPF differed in their transmission and frequency from crackles of CHF and pneumonia in the hope of improving diagnosis and monitoring of these patients.

Methods: A multichannel lung sound analyzer was used to collect 20-s samples of sound from 25 patients with pneumonia, 17 patients with CHF, and 19 patients with IPF. We calculated a crackle transmission coefficient (CTC) by quantifying the distance a crackle spreads using a technique that cross-correlated the signal containing the highest amplitude crackle with the corresponding signal on all other ipsilateral channels: CTC, 0% = no transmission; CTC, 100% = equal transmission to all channels.

Results: Both the CTC and the crackle frequency in IPF were statistically different from that in CHF and pneumonia ($p < 0.0001$). The CTC averaged $24 \pm 5\%$ for pneumonia, $25 \pm 8\%$ for CHF, and $14 \pm 4\%$ for IPF. The crackle frequency averaged 302 ± 47 Hz for pneumonia, 311 ± 62 Hz for CHF, and 462 ± 50 Hz for IPF (\pm SD).

Conclusion: These differences in CTC and crackle frequency offer the promise of helping guide treatment in IPF patients. (CHEST 2005; 128:1468–1474)

Key words: acoustics; crackles; respiratory sounds; sound transmission

Abbreviations: CHF = congestive heart failure; CTC = crackle transmission coefficient; IPF = interstitial pulmonary fibrosis

Patients with interstitial pulmonary fibrosis (IPF) often have diffusely abnormal chest radiographic findings, making it difficult to detect evidence of superimposed congestive heart failure (CHF) or pneumonia. The crackles of these patients are commonly mistaken for the crackles of CHF. As a result, misdiagnoses are frequently made and the patients are prescribed diuretics inappropriately. In the course of studying the correlation of lung sounds with pulmonary disorders in patients at a community teaching hospital, we noticed that crackles in patients

with CHF and pneumonia were transmitted over larger area than in patients with IPF. We hypothesized that if this difference in transmission was consistent, it had the potential of providing useful diagnostic information. We therefore examined crackle transmission systematically.

MATERIALS AND METHODS

Patient Selection

Patients were selected for this study from a pool of patients who had undergone lung sound analysis as a part of a broader study of the correlation of disease processes with lung sounds patterns. To acquire patients into this study, we identified hospitalized patients and outpatients of a community teaching hospital who had a specific cardiopulmonary disease diagnosis or were considered to be normal by their caregivers. The studies are not made on consecutive patients; this is a convenience sample, and we have both the diagnoses and the lung sound analyses of 784 patients. The diagnostic category of each of the patients was that of the clinicians caring for these patients, and this was reviewed by the senior author to be sure they were consistent with established criteria.

*From Brigham and Women's/Faulkner Hospitals, Boston, MA. Supported by a National Institutes of Health small business innovation research grant (1R43HL70480–01) and a grant from Stethographics, Inc. Dr. Murphy and Dr. Vyshedskiy have financial interests in Stethographics, Inc. Manuscript received August 10, 2004; revision accepted February 16, 2005.

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Subjects were examined with a 16-channel lung sound analyzer (model STG1602; Stethographics; Westborough, MA). The lung sound analyzer was described in detail in Bergstresser et al¹ and Murphy et al.² In short, the lung sound analyzer uses electret microphones mounted in stethoscope chest pieces to record data on a personal computer. Fourteen microphones are incorporated into a soft foam microphone pad. The microphone pad is positioned on a stretcher or a plastic reclining chair positioned at a 45° angle. In this study, subjects were instructed to lie in a recumbent position on the microphone pad. Subjects were instructed to breathe deeper than normal. Typically, three to six full breaths were captured in a 20-s recording.

Crackles were defined in accordance with accepted criteria.^{3,4} The lung sound analyzer software automatically identified crackles in all full breaths. The validation of the use of the device as a crackle counter has been reported.⁵

We believe that the situation in which the crackles of IPF are most likely to be mistaken for those of CHF or pneumonia is when the crackles are numerous. Accordingly, only patients with a high number of crackles, *ie*, > 20 inspiratory crackles in a 20-s recording, were chosen for this study. These patients included 25 of 130 patients with pneumonia (19%), 17 of 80 patients with CHF (21%), and 19 of 19 patients with IPF (100%). Among the patients chosen for this study, the total and average numbers of inspiratory crackles analyzed are as follows: 1,529 crackles (average per patient, 61 ± 33) in patients with pneumonia, 964 crackles (average per patient, 57 ± 23) in patients with CHF, and 2,172 crackles (114 ± 52 average per patient) in patients with IPF (± SD).

Cross-correlation Technique

Figure 1, *left, A* shows the waveforms in stacked mode as recorded by two microphones located on the chest surface. The waveform shown on the top is delayed compared to the waveform shown on the bottom. The time delay between peaks (marked by triangles) is 3.3 ms. Automated calculation of time delay is best

achieved by the technique of cross-correlation. The cross-correlation function furnishes a measurement of the similarity of two signals as a function of a relative time shift. The position of the cross-correlation function peak corresponds to the time delay between the signals, and the value of the peak is an indicator of how good the match is between the two signals. Figure 1, *right, B* shows the cross-correlation function between signals shown in *left, A*. The zero time delay line is indicated by a thick vertical line. The position of the cross-correlation function peak was identified automatically (triangle). The time delay detected by cross-correlation in this case was 3.3 ms.

RESULTS

Development and Validation of the Concept of Crackle Family

The concept of “crackle families” resulted from observing the patterns of crackles as they appear on time-expanded waveform analysis. Figure 2 shows time-expanded sound waveforms recorded from a patient with pneumonia. The waveforms are superimposed on a body plot. Each waveform is positioned on the part of the body where the sound was recorded. A prominent crackle is seen on the tracing from channel 15 (indicated by a large triangle). Crackle waveforms that occur at approximately the same time are seen at all ipsilateral channels (small triangles). The crackle waveforms are shown in the stack mode in the insert in the upper right corner. We then asked the question: are these crackles independently generated or are they representations of the same event?

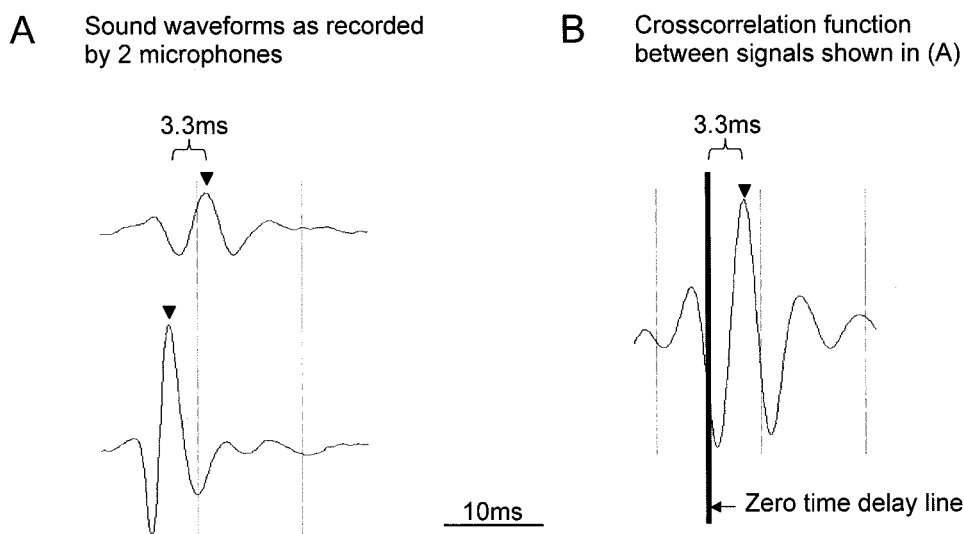


FIGURE 1. Cross-correlation technique. *Left, A*: sound waveforms as recorded by two microphones on the chest surface are shown in a stacked mode. The microphones were separated by 140 mm. The waveform on the top is delayed compared to the waveform on the bottom. The time delay between peaks (marked by triangles) is approximately 3.3 ms. *Right, B*: cross-correlation function between signals shown in *left, A*. The zero time delay line is indicated by the thick vertical line. An unambiguous peak of the cross-correlation function (triangle) corresponds to a time delay of 3.3 ms.

Pneumonia

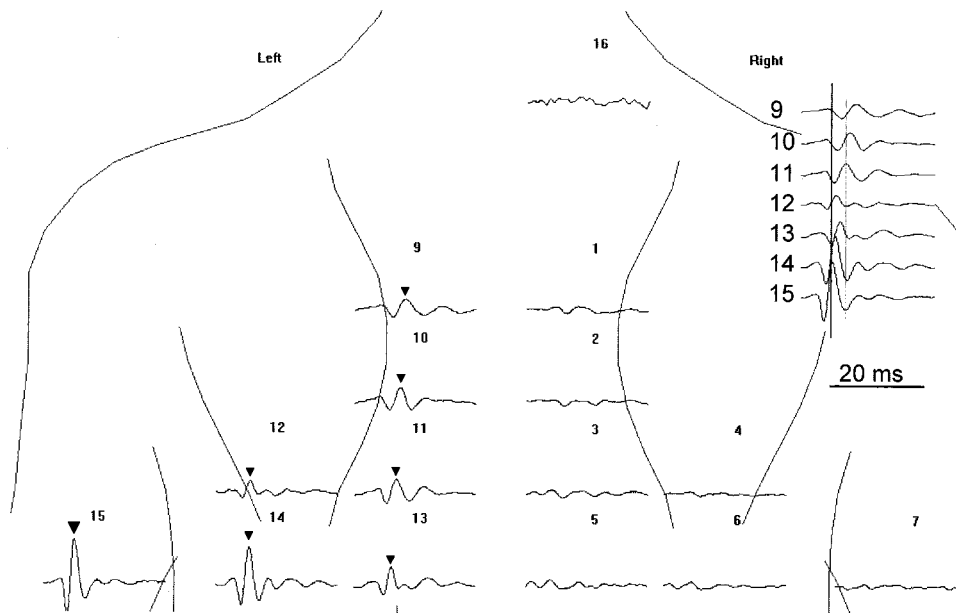


FIGURE 2. Sound waveforms of a crackle from a patient with pneumonia are shown as detected in the microphones arrayed over the posterior chest. Microphone 15 is on the lateral chest, and in this patient has the highest crackle amplitude (large triangle). The crackle is seen in all microphones over the left lung (small triangles). The crackle amplitude decreases as the distance from channel 15 increases. *Insert, upper right corner:* the crackle waveforms are shown in stacked mode to facilitate examination of arrival times at the various microphones. The crackle waveform seen in channel 15 begins earlier than the crackle waveforms in the other channels. The vertical line indicates the position of the peak in the waveform in channel 15.

Figure 3 shows six consecutive crackles as recorded by multiple channels from a CHF patient. Each group of crackles that occurred within 5 ms is marked by a frame and a letter (C, for crackle). Note that the waveforms within each group look similar to each other. The crackle waveform patterns, however, differ from one group to another. We hypothesized that crackles within each group represent the same event of airways opening and called them a crackle

family. The crackle with highest deflection is called the *mother crackle*, and the corresponding deflections at other channels are termed *daughter crackles*. This hypothesis implies that the event, which generated a crackling sound, had occurred closer to the mother channel microphone than to other microphones. Accordingly, daughter crackles are expected to be delayed in time and to have smaller amplitude compared to the mother crackle.

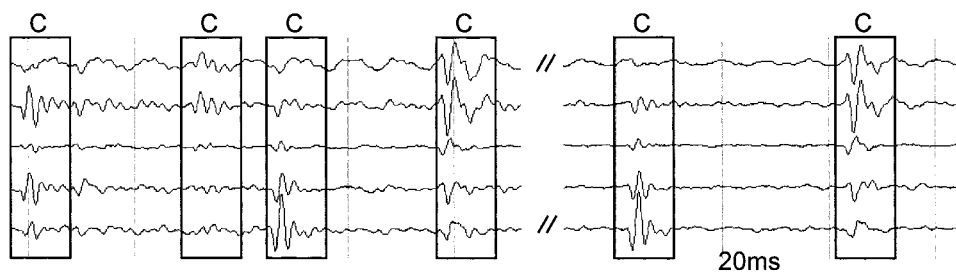


FIGURE 3. Consecutive crackles as recorded by multiple channels in a patient with CHF. Each crackle family is marked by a frame and by the letter C. The waveforms of daughter crackles are very similar to the waveform of their respective mother crackle. Crackles from different families show noticeable variation in waveform patterns.

Consider again the crackle family in Figure 2. The insert shows waveforms in stacked mode to facilitate examination of arrival times at the various microphones. The crackle waveform seen in channel 15 (the mother crackle) begins earlier than the crackle waveforms in the other channels. To quantify the time delay between mother and daughters, the signal containing the crackle with the highest amplitude (the mother crackle) was cross-correlated with the corresponding signals on all other ipsilateral microphones (daughter crackles) as explained above. Figure 4 shows the analysis of the crackle family shown in Figure 2. Figure 4, *top*, A illustrates the time delay between the mother crackle and daughter crackles as a function of distance between the microphones. The time delay increases nearly linearly with increased distance. The correlation between time delay and distance was 0.97. In all three disorders, the correlation between the time delay and distance was statistically significant: 0.53 for pneumonia ($p < 0.005$), 0.51 for CHF ($p < 0.005$), and 0.45 for IPF ($p < 0.005$). We conclude that in most crackle families, the crackle with the highest amplitude (the mother crackle) occurred earlier than the daughter crackles, and channels further away from the mother channel received the signal later than the channels closer to the mother channel.

The daughter crackle amplitude was expressed as a percentage of the mother crackle amplitude by calculating the ratio of the peak of the cross-correlation function to the peak of the mother crackle autocorrelation function. This ratio characterizes the degree of sound transmission from the sound source to the corresponding microphone on the chest surface. We call this *ratio transmission coefficient*. By definition, the mother transmission coefficient is always 100%. The daughter transmission coefficient has a value of 0% in the absence of any transmission and 100% when sound is transmitted equally to the daughter and mother channels. Figure 4, *middle*, B shows transmission coefficient as a function of distance from the mother channel. The transmission coefficient decreases linearly with increased distance. The correlation between transmission coefficient and distance was -0.94 . In all three disorders, the correlation between the transmission coefficient and distance was statistically significant: -0.75 for pneumonia ($p < 0.005$), -0.77 for CHF ($p < 0.005$), and -0.78 for IPF ($p < 0.005$).

Figure 4, *bottom*, C shows the transmission coefficient as a function of time delay. The correlation between these two parameters was -0.88 . In all three disorders, the correlation between the transmission coefficient and time delay was statistically significant: -0.46 for pneumonia ($p < 0.005$), -0.46 for CHF ($p < 0.005$), and -0.43 for IPF ($p < 0.005$).

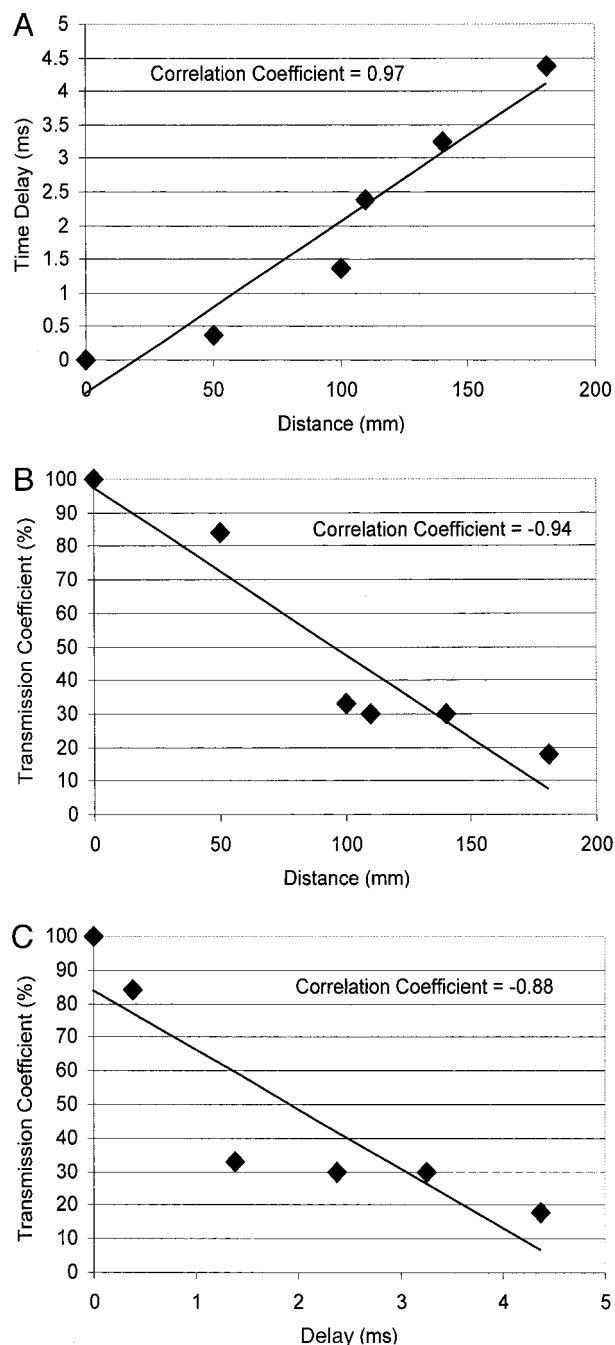


FIGURE 4. Daughter crackles have smaller amplitude and are delayed in time compared to the mother crackle. This Figure analyzes the crackle family presented in Figure 2. *Top*, A: time delay between mother crackle and daughter crackles from Figure 2 as a function of distance between microphones (correlation coefficient = 0.97). *Middle*, B: daughter crackles amplitude or transmission coefficient as a function of distance from the mother channel (correlation coefficient = -0.94). *Bottom*, C: daughter crackles transmission coefficient as a function of delay from the mother channel (correlation coefficient = -0.88).

Development of the Crackle Transmission Coefficient

The development of the crackle transmission coefficient (CTC) came about as a result of observing

the apparent differences in crackle transmission among different crackles observed on time-expanded waveform analysis, and then developing a method to quantify these differences. In the patient with pneumonia (Fig 2), the crackling sound was transmitted throughout a considerable area on the chest. In contrast to the crackle in the patient with pneumonia, the crackle in the patient with IPF was transmitted over a much smaller area (Fig 5). Notice the prominent crackle on channel 5 (indicated by a triangle, Fig 5). The crackle barely stands above the background noise at channels 1, 2, 3, 4, 6, and 7. As a rule, crackles in patients with CHF and pneumonia are transmitted over an area approximately 10 cm in diameter. In general, the crackles of IPF are transmitted over a smaller area than the crackles of CHF and pneumonia. We rarely observed significant crackle transmission to the contralateral lung in any disease.

To quantify the difference in transmission between crackle families, such as that shown in Figures 2 and 5, each crackle family was assigned a CTC. The CTC was calculated by averaging transmission coefficients of all daughter crackles. The CTC has a value of 0% in the absence of any transmission (only mother can be observed) and 100% when there is equal transmission to all ipsilateral channels. In the

example in Figure 2, the CTC equals 31% and daughter crackles can be observed on all ipsilateral channels. In the example in Figure 5, the CTC equals 1% and no daughter crackles can be distinguished from the background. We were usually able to visually identify daughter crackles on the ipsilateral channels in families with a CTC of $\geq 5\%$.

Average inspiratory CTC and average crackle frequency were calculated for every patient in the study. Inspiratory CTC averaged $24 \pm 5\%$ for pneumonia, $25 \pm 8\%$ for CHF, and $14 \pm 4\%$ for IPF. The differences in CTC between IPF and CHF and between IPF and pneumonia were statistically significant ($p < 0.0001$). Inspiratory crackle frequency was also different: the frequency averaged 302 ± 47 Hz for pneumonia, 311 ± 62 Hz for CHF, and 462 ± 50 Hz for IPF. The differences in frequency between IPF and CHF and between IPF and pneumonia were statistically significant ($p < 0.0001$).

Relationship Between Frequency and Crackle Transmission Coefficient

The crackles of IPF were observed to have higher frequency than those of either pneumonia or CHF. We wondered whether this frequency difference was a factor in the differences observed in transmission.

Interstitial Pulmonary Fibrosis

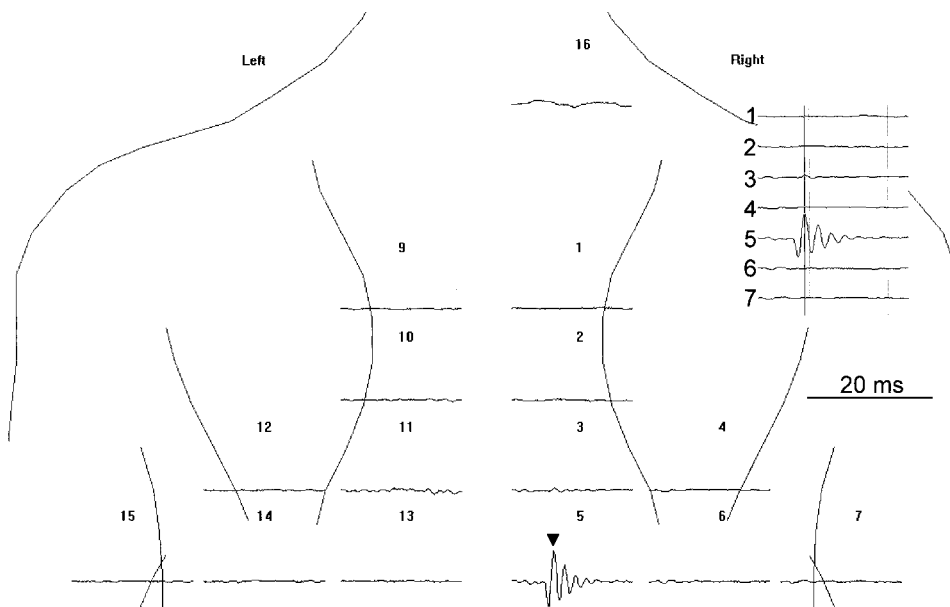


FIGURE 5. Sound waveforms of a crackle from a patient with IPF are shown as detected in the microphones arrayed over the posterior chest. The mother crackle is recorded on channel 5 (triangle). No daughter crackles can be distinguished from the background. The crackle transmission coefficient calculated for this crackle family equals 1%. *Insert, upper right corner:* The crackle waveforms are shown in stacked mode.

To address this question, we studied the relationship between CTC and crackle frequency. Figure 6 shows CTC as a function of crackle frequency from a patient with CHF. Note that CTC is decreased at higher frequency. The line fit in Figure 6 has the slope of $-0.07\%/Hz$. This corresponds to a 7% decrease in CTC for every 100-Hz increase in frequency. This observation was noted in the majority of patients. CTC decreased with increased frequency in 91% of patients with pneumonia (slope = -0.03 ± 0.02), in 88% of patients with CHF (slope = -0.03 ± 0.02), and in 63% of patients with IPF (slope = -0.01 ± 0.02). We conclude that crackles with higher frequency are usually transmitted over a smaller area of the chest. The differences in slopes between IPF and CHF and between IPF and pneumonia were statistically significant ($p < 0.005$).

We then calculated mean CTC and mean inspiratory crackle frequencies for every patient (Fig 7). Consistent with our previous observations, CTC decreased at higher frequency. Comparison of IPF crackles to those of CHF and pneumonia yielded a new observation: at a given frequency, the mean CTC was greater in patients with CHF and pneumonia than in patients with IPF. This observation is consistent with the hypothesis that lungs of patients with CHF and pneumonia are better transmitters of sound.

DISCUSSION

In this study, we have described criteria that differentiate IPF patients from CHF and pneumonia patients on the basis of crackle transmission and frequency. Crackles in IPF patients had a strong tendency to be of higher frequency than the crackles

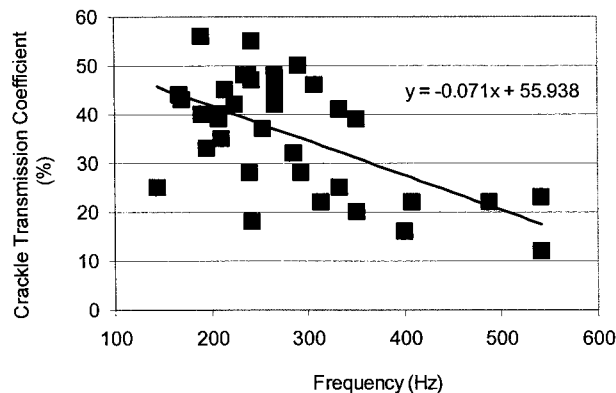


FIGURE 6. Crackle transmission coefficient of inspiratory crackles as a function of crackle frequency from a single patient with CHF. Each marker represents a single crackle family.

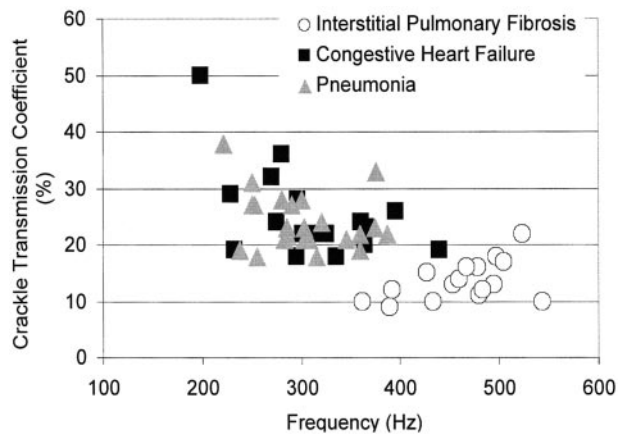


FIGURE 7. The mean crackle transmission coefficients as a function of mean frequency. There is a strong tendency for the data points of the CHF and pneumonia patients to be toward the upper left of the graph and IPF patients to be toward the lower right.

of CHF and pneumonia as has been reported.⁶ The higher-frequency crackles of IPF patients in this study were transmitted through the chest to a much smaller degree than crackles in CHF and pneumonia patients. The smaller degree of crackle transmission in IPF patients may be a consequence of decreased sound transmission of higher-frequency sounds. The lung is recognized to be a low-pass filter. Transmission of sound input at the mouth has been shown to be inversely proportional to sound frequency.^{7,8} Further, crackle transmission in this study was inversely proportional to crackle frequency in all three pulmonary disorders studied. Since the crackles of IPF have higher frequency than those of either pneumonia or CHF, the frequency difference may be one factor in the differences observed in crackle transmission. Another possible explanation is that the fluid content in the lungs of patients with CHF and pneumonia may be greater than that in the lungs of IPF patients. This difference in fluid concentration may be responsible for transmission differences. Indeed both factors may be operative.

This study was based on the assumption that crackles occurring within 5 ms are of the same crackle source, and belong to the same family of crackles. It is possible that this assumption is incorrect. An alternative hypothesis is that in CHF and pneumonia there are multiple sources of similar crackles and hence higher CTC values. The lower values of CTC in IPF according to this hypothesis may be explained by the possible occurrence of fewer crackle sources in IPF. However, we find no evidence to support this alternative hypothesis. We believe it to be an unlikely explanation for the following reasons: (1) It is not likely that there are

fewer crackle sources in IPF as crackle counts in IPF patients average considerably higher than they do in other diseases. (2) It is also not likely that crackles occurring within the same 5 ms are not of the same family in most instances.

The reasons for believing that crackles occurring within 5 ms are of the same crackle source is based on several factors. First, the waveforms of daughter crackles are very similar to the waveform of their respective mother crackle, while crackles from different families usually show noticeable variation in waveform patterns (Fig 3). Second, within a 5-ms interval, the crackle with the largest amplitude (mother crackle) is almost always the earliest in timing. Third, the decrease in amplitude in the daughter crackles is almost always associated with a corresponding increase in time delay. Finally, the channels that are farther away from the mother channel exhibit greater time delay and decrease in amplitude. In summary, crackle families behave in a manner consistent with the assumption that a single crackle event was transmitted to ipsilateral channels and also with the assumption that the mother channel is closest to the crackle sound source.

The marked differences that characterize IPF patients from the other two conditions monitored in this study provide evidence that acoustical analysis could be a helpful guide in the management of such

patients. These observations suggest that more definitive studies should be done to evaluate the clinical utility of these differences in crackle transmission.

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