DISTINGUISHING BETWEEN ASTHMA AND PNEUMONIA THROUGH AUTOMATED LUNG SOUND ANALYSIS

A Major Qualifying Project Report:

Submitted to the Faculty

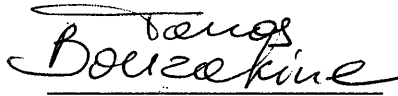of the
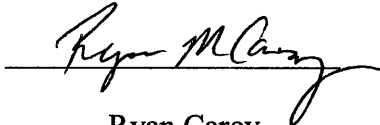
WORCESTER POLYTECHNIC INSTITUTE

In partial fulfillment of the requirements for the

Degree of Bachelor of Science

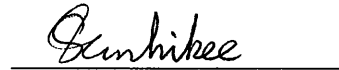by

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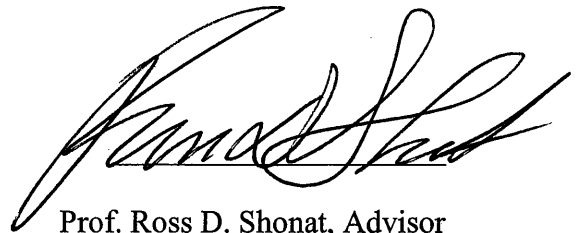Taras Bouzakine   Ryan Carey   Gladman Taranhike

Date: April 28, 2005

Approved:

1. respiratory auscultation
2. diagnosis
3. stethoscope

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ABSTRACT

This project attempts to distinguish between two pulmonary disorders, asthma and pneumonia, using automated analysis of lung sounds. Such an approach minimizes the subjectivity of diagnosis inherent to current practices by physicians. Breath sounds are recorded by a physiological microphone and hardware acquisition system, and then analyzed in software using a two stage algorithm. The first stage detects abnormal lung sounds and second stage makes a diagnosis. A clinical trial was conducted at a pediatric clinic to validate the system.

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PART I – PROPOSAL
CHAPTER 1 – INTRODUCTION

Lung-sound based respiratory diagnosis is an age-old science. For hundreds of years, doctors have been listening to the noises produced by the lungs and attempting to draw conclusions about the inner workings of the body. Laënnec's invention of the stethoscope in 1816 was a major advancement in the science of auscultation, as it was the first tool – besides the naked ear of a doctor – to aid in the process of listening and diagnosing of disease or physiological malfunction.

Since then, pulmonary sounds have become very important to the field of medicine. Their widespread diagnostic utilization by physicians demonstrates a clear need for a high level of reliability. However, since the invention of the stethoscope, very few instruments have been developed to improve lung auscultation. The most popular device remains the stethoscope, which still requires the skill of a doctor – a human interpreting the sounds of the lung, based partially on his or her own experience, and partially on arbitration, a situation that induces a substantial risk for human error during auscultation analysis and ultimately disease diagnosis (Mahnke 1). Hardly any control or benchmark exists to verify the personal observations of a physician or quantify and systematically analyze the problem on a more sophisticated level. Doctors themselves admit that the process is highly speculative (Eder, Thomas. Personal Interview. 22 Sept. 2004). Such ambiguity in the analysis sometimes leads to erroneous diagnosis and treatment. For example, pneumonia and asthma produce very similar sounds and are extremely difficult to differentiate. Further tests, such as lung x-rays, are often prescribed to further analyze a patient's condition, but such tests are time consuming and costly. Several studies have provided evidence of such approach being a widespread difficulty (Hay 1).

In contrast to the stethoscope, the field of electronics has advanced rapidly over the past century, and there has been enormous growth in many related industries (Gavriely "Foreword") that has encouraged the development of medical technologies. There has been steady progress in digital audio processing, as well as an increased understanding of the physiology of the respiratory system and how it produces sounds.

This project proposes to automate the process of diagnosis, to place it in the more objective care of programmed electronic circuitry. Specifically, the project would:

(1) begin to define a standard automated method by which respiratory ailments, particularly asthma and pneumonia, are determined from lung sounds,

(2) build a prototype device that would be tested and optimized (through a study that would have normal and diseased subjects), and ultimately

(3) allow the doctors to focus their skills on the holistic diagnosis in which humans excel, rather than the rote data processing required by lung sound analysis, an area in which the computer is superior.

The possibility of performing more sophisticated pulmonary sound analysis and perhaps diagnosis with an automated device is very favorable. Such a device could serve as a substitute for a traditional stethoscope, while affording a reduction in human error from the pulmonary diagnosis.

The ultimate goal is to create a cost effective device to decrease the cost of diagnostic healthcare. With the proposed simple structure of the device, low cost is a realistically attainable goal. A challenge for any new technology to enter the doctor's office is enormous. Current attempts to improve the traditional acoustic stethoscope have not been widely accepted by physicians.

However, a simple to use device with established diagnostic validity may have a good chance to

become popular among the healthcare professionals.

CHAPTER 2 – LITERATURE REVIEW

To become familiarized with the problem at hand and to gain a deeper understanding of the current state of the pulmonology industry, the authors examined current literature, manufacturer specifications, and historical documents for information regarding stethoscopes, general pulmonology, and digital sound analysis. The three sections of this chapter will summarize the findings about the physiology and diagnostic importance of pulmonary sounds, past and present methods of pulmonary auscultation, and trends in digital sound analysis techniques. This background information is intended for an individual with no specialized knowledge base in the field of pulmonology or signal processing. It is organized into sections that follow a probable chronological path for the respiratory signal to pass through the system.

Respiratory Sounds

During pulmonary auscultation, there are two general classes of sounds that can be heard: normal and adventitious. Normal breath sounds, originating in the trachea and bronchia, or in the lung vesicles, are generated by the unaltered ventilatory cycle. Adventitious sounds are abnormalities in the normal sound, and are usually indicative of specific abnormalities in the normal breath cycle.

Normal tracheal breath sounds

These sounds, generally recorded over the trachea, are generated by the turbulent air flow through the upper airway. Harsh in nature, their amplitude is directly related to the amount of air flowing through (and resultant turbulence in) the passages of the upper airway: the trachea, the epiglottic region, and the pharynx. Tracheal sounds cover a frequency range from approximately 100 Hz to 1.5 kHz, with the greater part of the signal below 800 Hz (Pasterkamp 979). The peaks

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and troughs in a frequency spectrum of a tracheal sound have a correlation to the airway dimensions, the gas mixture, and the body height of the subject (Dalmay 1765).

Because of the numerous factors that influence tracheal breath sounds, they can be used diagnostically in a number of different ways. For example, sleep apnea can be detected by using the sounds to determine air flow. Disorders in which inspiratory flow is obstructed can also be monitored, as this obstruction affects the tracheal sound (Pasterkamp 979).
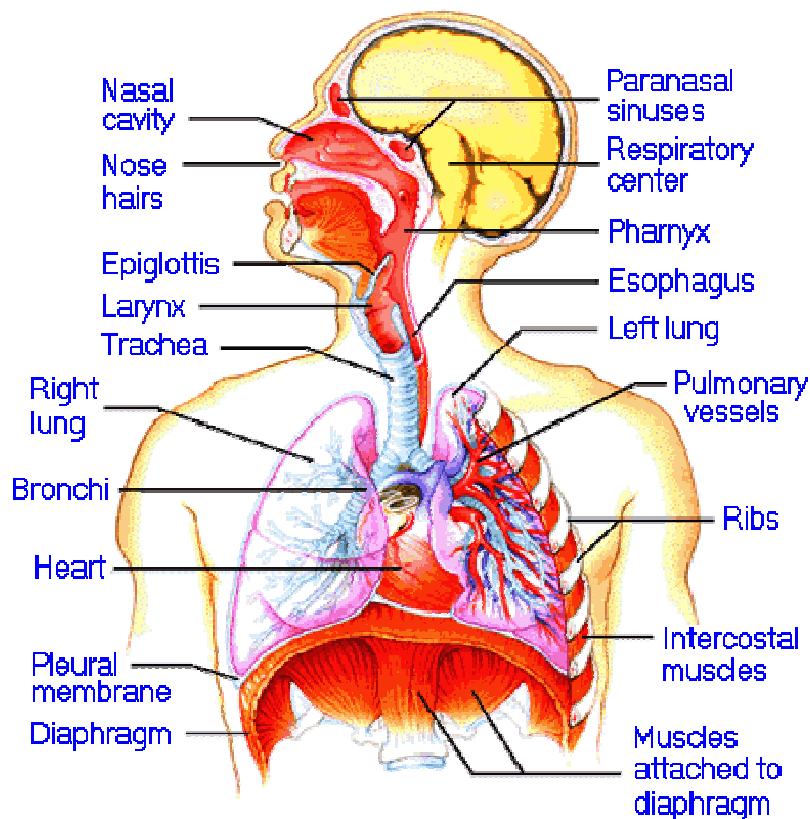
Figure 1 – Respiratory system

[Leslie Laurien, MSMI, American Medical Association]

Normal vesicular breath sounds

There are also normal breath sounds that occur throughout the lungs. These can be heard close to the chest wall. Their amplitudes vary greatly over the chest and back; but they are strongest where air flow is the highest. The exact cause of these sounds during the inspiratory stage of the

breath cycle, though not certain, has been explained by numerous theories (R.A.L.E. "Normal Sounds"). It is possible that they are produced by the redistribution of gas, or by the stretching of lung tissue during inspiration (Dalmay 1767). During expiration, the audible sounds are generated by the passage of air through central airways. An air-filled lung behaves as a low-pass filter, so vesicular breath sounds are only substantial at frequencies from zero to approximately 400 Hz (R.A.L.E. "Normal Sounds").

Due somewhat to the relationship between air flow and vesicular lung sound amplitude, it is possible to detect obstructive pulmonary disease from a definitively reduced amplitude (Pasterkamp 978). Also, a difference is propagation delays of the lung sounds traveling the same distance in different directions through the lung may suggest inhomogeneity in ventilation between parts of the lung, an indication of small airways disease (Pasterkamp 979).

Adventitious sounds

Besides inconsistencies in the propagation of the normal lung sounds, there are also several types of specific irregularities that can be heard in respiratory sounds. They are classified into two broad categories: wheezes, which are continuous and "musical", and crackles, which are discontinuous.

Wheezes

Wheezes are continuous, as their durations are longer than 80 milliseconds, and often musical, as the length allows intrinsic tones to be heard as pitches, or sinusoidal signals with frequencies generally between 100 Hz and 1 kHz. Because of this, it is fairly easy to identify a wheeze with the ear, as there are sharp peaks in the power spectrum, the intensity of which can be related to the intensity of the normal lung sound (Pasterkamp 980). Wheezes with a very low pitch are referred to as rhonchi (R.A.L.E. "Adventitious Sounds").

Wheezes are thought to be produced by the fluttering of airway walls that occurs when the air flow exceeds a certain velocity at a given passageway diameter (Pasterkamp 980). Thus, this type of sound will only occur when the air has sufficient force, and the path of the air flow has been limited in some way. It is possible to induce a forced expiratory wheeze by increasing the air flow in a healthy subject; however, the source of this type of wheeze may vary slightly from that of a wheeze triggered by a disease-related limitation of the normal flow. Asthmatic subjects, for example, often exhibit spontaneous wheezing during not only expiration, but also inspiration, a condition not reproducible in healthy subjects (Pasterkamp 980).

Wheezes can be used clinically to quantify airway flow obstruction, by determining the fraction of breathing accompanied by wheezing to normal breathing. Wheezing can also predict the existence of large airway secretions. However, caution should be used while diagnosing, as it is possible for spontaneous wheezes to be generated without any flow limitation whatsoever, and for the vibrations to be induced during tidal breathing. Also, wheezing may be absent in cases where there is obstruction of flow (Pasterkamp 980).

Crackles

Crackles, with a length of between 10 and 20 milliseconds, are thought to be produced by the sudden opening or deformation of airways. Bubble movement through fluid or secretions can also cause them (R.A.L.E. "Crackles"). Crackles are generally heard only during inspiration, and their occurrence (unlike that of wheezing) cannot be reduced by coughing (Pasterkamp 982).

The category of crackles is further divided into two types: fine and course. Fine crackles are higher pitched, and sound drier than their course counterparts. Each type of crackle is generally indicative of a particular respiratory disease (Piirilä 2140). Ultimately, crackles are perhaps the

best of the lung sounds for diagnosis: a diagnosis could depend on the timing of the crackles in the breathing cycle, their intensity, prevalence, and spatial location within the lung (Pasterkamp 982).

Coughs

A respiratory sound common to almost all respiratory diseases is coughing. Coughing is not only characteristic of being ill. It is an essential mechanism for lung defense and protection of the airway. So whether a person has a pathological respiratory condition or has healthy lungs, any danger posed on the lungs and airway may induce coughing. An effective cough starts with a large inspiratory effort, closure of the glottis, and finishes with a rapid contraction of the abdominal and chest wall muscles, coordinated with the re-opening of the glottis. This sequence creates an explosive egress of compressed air, with air speeds reaching approximately one third the speed of sound along the walls of the narrowed larger airways. The resulting "scrubbing action" along the airway walls is effective in keeping foreign bodies out and expelling anything that may be obstructive or toxic to the lungs (Gavriely, Cugell).

Although it can just be a sign of irritation, coughing is often a sign of disease in the respiratory system, and is usually more frequent and more severe when a result of disease. Disease in the lungs can cause an accumulation of mucus or an inflammation of the airways. Past studies of cough patterns in patients with lung disease have been limited to determining the number of cough episodes or paroxysms and the number of coughs per episode. Cough counts are useful, and this measurement can now be automated for determination of effect of antitussive (cough suppressive) medication and for monitoring nocturnal cough episodes in asthmatic patients (Gavriely, Cugell).

Coughs that are as a result of different ailments may have different audible acoustic characteristics (e.g. dry, productive, croup). However, these characteristics are very difficult to detect and analyze otherwise (e.g. in a digital representation). In the time domain, these sounds are a series of explosive noises. Measurements of the acoustic features of voluntary cough sounds in healthy subjects have been reported by several groups (Gavriely, Cugell). Measurements of acoustic properties of cough, duration of the cough sound, and the relationship of the sound to the time of glottic closure are some differences that may differentiate between lung diseases. For example, in a study by Piirila (46), the highest frequency components of cough sound were found to have lower amplitudes in asthmatic subjects than in chronic bronchitis subjects.

Cough sounds are easily acquired using free field microphones and can be analyzed digitally. Modified voice recognition systems have been used for this purpose in several studies and have been found to be fairly accurate (Gavriely).

Respiratory Diseases – Asthma and Pneumonia

Asthma is defined as a disease process that causes bronchoconstriction, and thus makes breathing more difficult. This condition is exasperated by allergic reactions, changes in temperature or humidity, infections of the upper respiratory system, exercise, stress, or cigarette smoke. The constriction of the respiratory paths can cause wheezing, especially when the condition is provoked by the irritants mentioned above.

Pneumonia, another respiratory disease, is caused by an infection in one or both lungs. It is often caused by bacteria or virus, or sometimes by a fungus or other organism. Certain populations (especially the very young and elderly) are prone to pneumonia infections. The symptoms are the

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same as of any other respiratory infection (fever, coughing, chest pains), but generally with pneumonia, there is also discolored fluids and sputum in the respiratory tract. Bubbles can form in the fluid, causing crackles and other sudden lung sounds. Because of the impedance of the disease on the flow of air, some wheezing may also be evident.

Evolution of the Stethoscope

The traditional acoustic stethoscope is a three-part device; it consists of a chest piece to pick up the sounds, earpieces for the user, and rubber tubing connecting the two ends. This configuration was developed in the mid-1940 and has been effectively unchanged to today. The stethoscope serves a fairly simple task – to transfer the pulmonary sounds from patient to physician – and modern technology has done little to change the acoustic properties of the device.

Figure 2 – Traditional Stethoscope

[Belgian Center for Evidence Based Medicine]

The rubber tubing of the stethoscope has a unique transfer function which predictably distorts the acoustic signal as it passes through (Figure 3). Physicians are taught to analyze the distorted sounds in daily practice. Modern advances in electronics allow for a more sophisticated approach and a cleaner signal reproduction. Thus, an electronic version of a stethoscope, implementing even a simple microphone-amplifier-speaker circuit, would be able to offer more functionality than their acoustic counterparts. There are several electronic stethoscope devices on the medical device market today, but they are not widely accepted by the practicing physicians. This unpopularity could be due to high costs, the unfamiliarity of doctors with the use of modern technology, and the modified acoustic properties of the sounds they reproduce.

Some of the products available are manufactured by brands such as Androscope, 3M Littmann, Meditron, and Cardionics (Some devices are described in Appendix B). These stethoscopes, offered at prices competitive with the traditional acoustic stethoscope, generally function as bug-for-bug compatible replacements for them, reproducing their notoriously nonlinear frequency responses. The majority of electronic stethoscopes offer at least two operating modes, akin to the tunable diaphragm on an acoustic stethoscope: the "bell" mode accentuates the lower frequencies of heart sounds, and the "diaphragm" mode accentuates the higher frequencies of lung sounds.
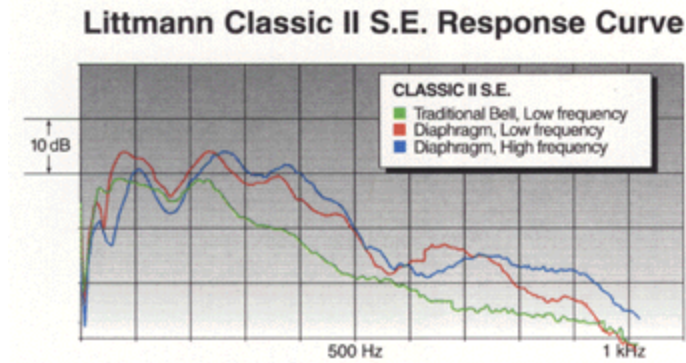
Figure 3 – Nonlinear frequency response of a Littmann Classic II Stethoscope

[3M Littmann]

Oftentimes, electronic stethoscopes offer control over the degree of amplification performed by the instrument by simply adding a volume control. Several products, such as those made by Andromed, offer additional functionality. Instead of merely duplicating the collected sound signal in the stethoscope's earpieces, they include provisions to digitally record the sound, and perhaps transfer the digitized signal to a computer or a PDA (Personal Digital Assistant). This option allows lung sounds to be displayed and even analyzed digitally. A few products do offer digital analytical functions, however none have actually realized more than a counter for the number of adventitious sounds. Even with the most advanced commercially available product, the task of diagnosis still relies completely on the human.

In addition to a number of manufacturers with advanced electronic stethoscope designs, the field is rich with patents yet to become reality. Electronic stethoscope patents range vastly in the degree of difference from the traditional stethoscope. Some offer a mere amplification of lung sounds, others allow the sounds to be digitally recorded, compared to previous records, and even visually analyzed. A number of patents draw on the device's ability to connect to a personal computer, but there are some that are meant to function as a stand-alone unit. Other domains of

patents encompass modifications to very specific parts of the stethoscope, such as the sound

pick-up head. (Table 1 details several patents related to the stethoscope.)

Table 1 – Stethoscope-related Patents

Patent #	Year	Title	Key Advances
US8591	1861	Stethoscope and Ear Trumpet	First binaural stethoscope
US693487	1902	Stethoscope	Flexible ear pieces
US3108652	1963	Stethoscope	Modern Littman design
EP0295318	1988	Electronic Stethoscopic Apparatus	Multiple auscultation recording
RU2130755	1999	Sensor of an Electronic Stethoscope	Decreased artifact noise
WO 00/2486	2000	Analytic Stethoscope	Handheld electronic device with graphical display
US6083156	2000	Portable Integrated Physiological Monitoring System	Multiple variables recorded; interfaces wit ha PC
US6324289	2001	Pick-up Head for an Electronic Stethoscope	Bell is acoustically decoupled from the pick up element
US6396931	2002	Electronic Stethoscope with Diagnostic Capability	Self contained, handheld unit with diagnostic capability
US2003002685	2003	Electronic Stethoscope	Emphasize sounds based on pathological conditions
US2003/0072457	2003	Electronic Stethoscope	Several operation modes traditional spectral properties
US2004/0096069	2004	Electronic Stethoscope	Filters audio signals; selects between band-passed inputs

Ideas can also be patented; one example is a patent filed in 2002 by Cybercare Technologies of

Boynton Beach, Florida. The document describes a generic system and method of developing a

packet based electronic stethoscope. Figure 4 demonstrates that, more than anything, the patent

resembles a flow chart of connected "black boxes".
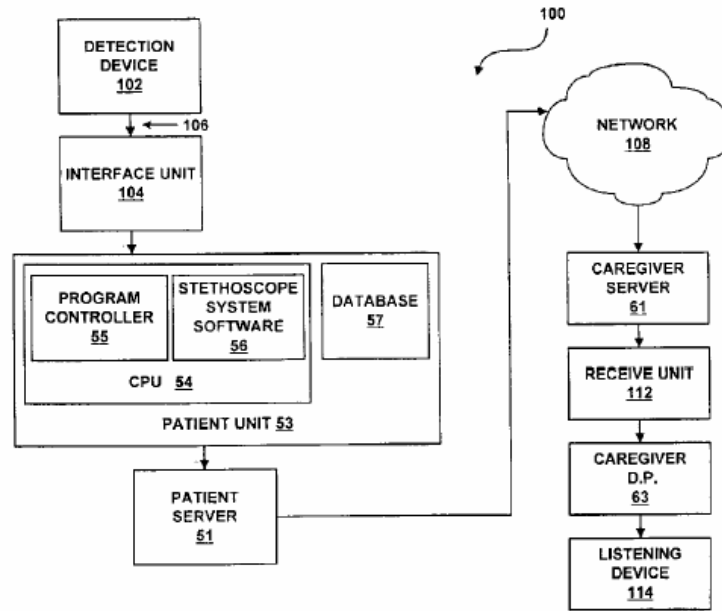
Figure 4 – Patent diagram

[US Patent and Trademark Office]

Recent research by Murphy et al has attempted to implement an automated diagnosis of pneumonia. The study is based on the premise that it is possible to make a diagnosis based on the presence of crackles in the lung sound. It used an array of microphones placed on the back to record and integrate simultaneously acquired spatial data. The conclusions indicated that auscultatory diagnosis in patients with pneumonia can be conducted by a computerized technique (Murphy 1496). Our project is similar to but also extends the work of Murphy in that we are focusing on distinguishing between asthma and pneumonia, and not just diagnosing pneumonia.

Frequency Content of Lung Sounds

Hardware filtering and frequency domain analysis are useful functions that can be implemented using electronic components. Pulmonary sounds can be filtered based on the frequency content. The main energy of lung sounds is carried within frequencies below 100 Hz (Welsby 695). Many abnormalities typical for specific lung diseases have their own specific frequency bands. For instance, wheezes usually occur at frequencies above 400 Hz and crackles occupy the bandwidth

between 750 and 1200 Hz. Based on these frequency distinctions, along with other more specific criteria, it appears possible to filter, selectively amplify, and ultimately identify specific sound patterns using automated equipment. Quantifying the process removes human error from the equation and replaces it with precise mathematical calculations. Doctors have always held a crucial part in medical diagnosis; allowing a computer to take over even a small part of pulmonary disease identification is no small or easy step for the healthcare industry.

Digital Software Applications

After the hardware acquisition and hardware-based signal processing, the lung sound signal is converted into a digital format, and acquired by computer software. The pulmonary signal is then further filtered and analyzed digitally. The signal can also be represented in various formats, including frequency and time domain representation. Fast Fourier Transforms (FFTs) (Gavriely) and Wavelet Transforms (Kandaswamy 523) have been used to represent signals in terms of their frequencies, which can then be used to classify the sound signals into particular categories, based on the type of lung sound that they represent. Since certain categories of abnormalities are characterized by specific frequency content, successful identification is possible, but since overlap of ranges may also cause uncertainties in this process, it is prudent to recruit more decisive characteristics for classification. Computer software such as LabVIEW® and MATLAB® can be used to do such analyses.

Alternatively, several existing product packages can aid in the identification of individual adventitious sounds in a lung sound recording, instead of designing LabVIEW® or MATLAB® software from scratch to examine recordings.

- The DSP Sona-Graph is a dedicated (i.e., not computer-based), real-time, audio spectrum analysis instrument designed for high speed signal analysis and display.

- Another product, the Sonogram, is from the German Research Center for Artificial Intelligence (Deutsches Forschungszentrum für Künstliche Intelligenz, DFKI).

  - It is a tool to analyze speech and sound signals using FFTs, cepstral analysis, autocorrelation, wavelet-transformation, and a linear-predictive-coding method mostly used for speech recognition.

  - The ultimate goal of the Sonogram project is to develop a speech recognizer that works internally with Hidden Markov Models. At this time, however, only the signal analysis functionality has been implemented; it is missing many speech recognition tools (Gavriely).

Another option for adventitious sound classification is the use of Artificial Neural Networks (ANNs), which do have a precedent for use in diagnosis. ANNs are information-processing paradigms inspired by the way biological nervous systems, such as the brain, process information. They are composed of a large number of highly interconnected processing elements (suggestive of neurons) working collaboratively to solve specific problems. ANNs, like people, learn by example; one must undertake a learning process for a specific task, such as pattern recognition or data classification, before it is able to function. Artificial neural networks have a remarkable ability to derive meaning from complicated or imprecise data, and can extract patterns and detect trends that are too complex to be noticed by either humans or more conventional algorithmic computer techniques. However, because the network finds out how to

solve the problem by itself, its operation can be somewhat unpredictable, a quality not desirable for a medical standard (Stergiou 1.4).

The final function of the system may also be implemented in software. After identifying specific abnormalities in the lung sound recording, the system must determine if the annotated recording satisfactorily matches that of a known disorder, and suggest a suitable diagnosis.

The importance of pulmonary diagnostics in healthcare

The prevalent use of lung sounds in health diagnosis is clearly exemplified by the one tool doctors wears around their neck – a traditional stethoscope. Lung sounds are one of the important physiologic signals that can be examined non-invasively by doctors: the amount of clinical information that can be collected through auscultation is colossal.

According to the chairman of the Federation Internationale Pharmaceutique (Tromp), fifty percent of medications prescribed around the world are not used properly. This number is largely due to over-prescription practices common to many physicians. Professionals admit to this trend caused by a simple philosophy – it is better to be safe than sorry. For instance, antibiotics are often prescribed with the slightest chance of pneumonia. Such a simplified solution has many drawbacks – the cost of unnecessary medication and the possible futility or side-effects of needless drugs are just a few. With more sophisticated diagnosis procedures, misuse of drugs can be largely decreased: the more specific the diagnosis, the more appropriate the prescription.

Current methods of pulmonary disease diagnosis rely heavily on the interpretation of doctors. Unfortunately, subtle differences between asthma and pneumonia are not easily distinguishable by the human ear. Long experience in the medical practice will certainly eliminate much of the guesswork, but the ability to diagnose may be compromised by the deteriorating hearing of older

doctors. Aiding professionals with automated diagnostic equipment seems a good solution for the healthcare community. An automated diagnosis also allows the doctor to direct his or her attention to other aspects of patient examination. Ultimately, a nurse or a technician could use the device to take the readings and present the doctor with a completed analysis. This decreased examination time would allow the physician to serve more patients.

CHAPTER 3 – PROJECT APPROACH

This project was originally conceived by Dr. Thomas Eder, a practicing pediatrician in Worcester, Massachusetts. He envisioned technology filling a much larger role in respiratory diagnosis, a large change from the status quo use of the acoustic stethoscope, which had remained largely unchanged for decades.

After the first meeting with Dr. Eder and conducting some initial research, the original problem statement was established:

> *This project will attempt to optimize the design and manufacturability of an electronic stethoscope, as well as to increase the respiratory diagnostic functionality of the product.*

This focus was mainly brought about by an interest in determining the reason for the large discrepancy between the advancement of electronics and the actual use of new technology in pulmonary analysis and diagnosis. The initial speculation, that electronic stethoscopes may be too expensive to be widely used, brought about the formulation of the original problem statement.

Further research and a realization that the problem statement could limit the design process to a particular solution (just a modified use of the stethoscope for pulmonary diagnosis) prompted us to broaden our problem statement to encompass more generic respiratory signal analysis, and refocus on a specific problem, instead of a specific solution. The revised problem statement is as follows:

Design a low-cost respiratory signal classification system that will diagnose respiratory abnormalities, and, in particular, distinguish between pneumonia and asthma, two disorders that are commonly misdiagnosed.

Part of the project definition came from realizing the project's budget constraints. Another important modification to the definition is the emphasis on the development of a system – and not just an instrument or device. With the given objectives, it seemed best to approach the problem from a multifaceted perspective.

An additional motivation came through findings from our research that some current work had a related focus; Murphy et al are working on automated pneumonia diagnosis system (Murphy).

The first stage of the system will be dedicated to detecting and acquiring respiratory sounds. Some objectives of this sub-system are amplifying the biological signal, filtering the sounds, and converting them to digital signals. Preliminary signal processing will most likely take place in a dedicated circuit. The second stage of the system will digitally analyze the signals. This would result in classification of the signals into categories of particular abnormalities, including wheezes and crackles (sounds characteristic to various pulmonary disorders, as discussed in Chapter 2). Theoretically, by detecting the presence of such abnormalities and comparing their prevalence in lung sounds of various patients, it will be possible to make a valid diagnosis.

The idea of such a system stems from contemporary research concerning respiratory sounds. The frequency content of lung sound abnormalities has been found to vary from that of normal lung sounds. Thus, analysis of lung sounds in the frequency domain can subsequently lead to automated diagnosis. Instruments used for pulmonary sound detection and digitization are already on the market, while others are in development and research stages. Due to the apparent

prevalence of computer software performing similar applications, it was suspected that it would also prove to be the best technique to analyze signals from the lung. However, other methods were considered in the design process.

The summary above focuses on the engineering aspect of the project, based on the assumption that an automated algorithm could be used to diagnose pulmonary disorders. We assume that there exists a one-to-one correlation between combinations of abnormal lung sounds and specific disorders, for the purposes of diagnosis. Following the completion of the engineering phase, we will conduct a scientific study in a clinical setting, in which we will test the hypothesis that our system is able to diagnose pulmonary disorders accurately.

By clearly defining a method of identifying physiological disorders, we hope to substantially reduce human errors common in diagnosis using traditional instrumentation.

CHAPTER 4 – DESIGN

The process of designing the system to distinguish between asthma and pneumonia was well defined and organized, consistent with the method set forth by Dym and Little (2003). The five step process was followed as closely as possible, in order to generate the best possible system to meet the project objectives.

The first principal action in the design process was to define the problem the project was intended to solve. Several interviews and much background research helped to establish this goal, as presented in Chapter 3. The design team also visited a pediatric clinic in order to experience and evaluate the current process of auscultation. The final part of the problem definition was designation of the functions of the desired system, the constraints involved in the project, and the requirements imposed by the users.

The primary function of the system, of course, was to distinguish between the lung sound symptoms indicative of asthma and those specific to pneumonia. A number of secondary functions were accomplished to fulfill this diagnosis function, including acquiring respiratory sounds, amplifying them, and passing the sounds to the client while digitizing them. The system also had to be designed to interface with a personal computer or personal digital assistant device in order to complete some of the main functions, and for the purposes of displaying and recording the captured sounds.

Several constraints affected the design. Because of the medical use of the system, it had to meet federal medical device health and safety requirements. Due to the academic nature of this project, the system was developed and tested for less than $450 over a period of approximately 9 months.

The client and users of this system have set minimal requirements, which the final design must meet in order for it to be considered a success:

- It should acquire the audio respiratory signal with high fidelity and minimum noise.

- Any handheld elements should be lightweight.

- Any device, along with all connected accessories, should be easy for the users to transport from room to room.

- It should be of the correct proportions to be used comfortably by the users, and should not require an unreasonable amount of power so as to be unsafe for the users.

- Finally, the system should diagnose with an accuracy that exceeds current methods (i.e. a doctor's intuitive diagnosis).

The specifications presented above made up an elaborate scientific and engineering problem. Given the novelty of the project and the fact that a marketable solution for the problem had not yet been realized, prior to attempting the design, it was necessary for the team to develop a much deeper knowledge base than it currently possessed. This expertise comprised the fields of pulmonary diagnostics, audio acquisition, and digital sound processing. The findings are discussed in the Literature Review Chapter.

Needs Analysis and Specifications

Following our preliminary research and establishing of a problem statement, we began to further specify the requirements for our design. We created a nested objectives tree, as shown in Figure 5. Each of the smaller boxes illustrates a sub-objective of the objective above it.
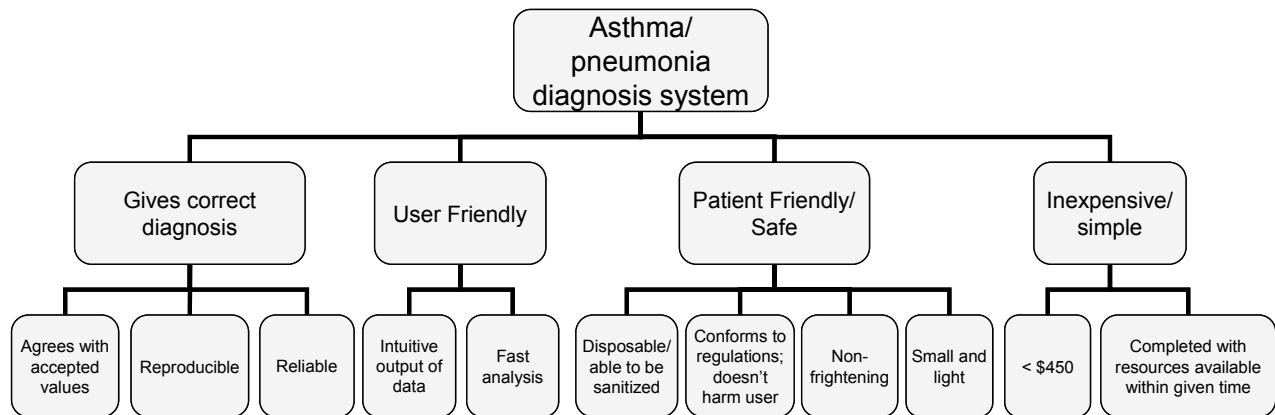
Figure 5 – Objectives Tree

These objectives were assigned percentages, based on the results of a series of pair-wise

comparison charts, shown below. For these tables, we compared each objective against each

other objective, establishing rankings for use in weighting the objectives.

Table 2 – Main Objectives: Pair-wise Comparison Chart

Objectives	Correct diagnosis	User Friendly	Patient Friendly	Inexpensive	Score
Correct diagnosis	♦♦♦♦♦	1	1	1	3
User Friendly	0	♦♦♦♦♦	0	0	0
Patient Friendly	0	1	♦♦♦♦♦	0	1
Inexpensive	0	1	1	♦♦♦♦♦	2

Table 3 – Correct Diagnosis Objectives: Pair-wise Comparison Chart

Objectives	Agrees w/ accepted	Reproducible	Reliable	Score
Agrees w/ accepted	♦♦♦♦♦	1	1	2
Reproducible	0	♦♦♦♦♦	0	0
Reliable	0	1	♦♦♦♦♦	1

Table 4 – User Friendly Objectives: Pair-wise Comparison Chart

Objectives	Intuitive output	Fast analysis	Score
Intuitive output	♦♦♦♦♦	1	**1**
Fast analysis	0	♦♦♦♦♦	**0**

Table 5 – Patient Friendly Objectives: Pair-wise Comparison Chart

Objectives	Sanitized	No Harm	Non-frightening	Small and Light	Score
Sanitized	♦♦♦♦♦	0	1	1	**2**
No Harm	1	♦♦♦♦♦	1	1	**3**
Non-frightening	0	0	♦♦♦♦♦	0	**0**
Small and Light	0	0	1	♦♦♦♦♦	**1**

Table 6 – Inexpensive/simple Objectives: Pair-wise Comparison Chart

Objectives	<$450	Completed in time	Score
<$450	♦♦♦♦♦	0	**0**
Completed in time	1	♦♦♦♦♦	**1**

The comparisons were used to generate specific weighting percentages for each objective and sub-objective, as shown in Figure 6.
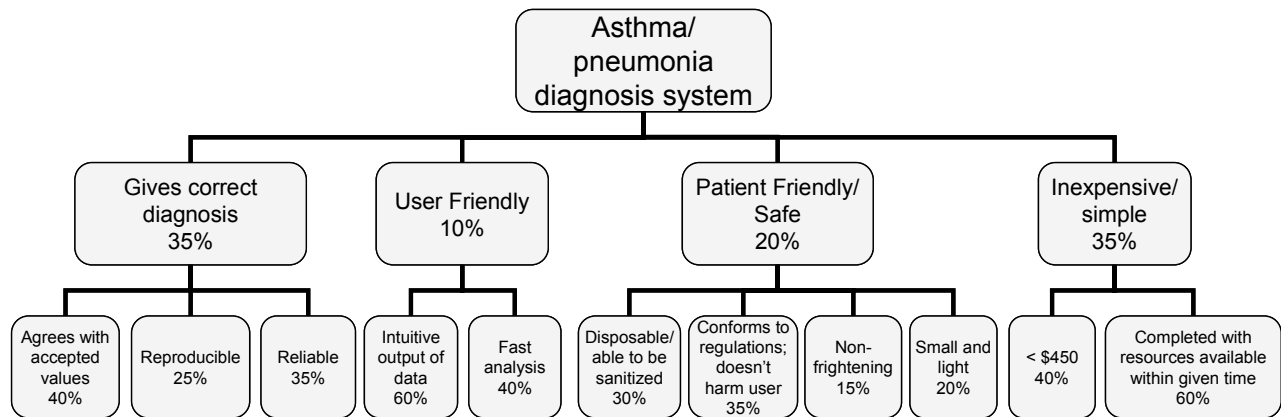
Figure 6 – Weighted Objectives Tree

To evaluate how well a design is meeting the objectives, they were clearly defined. Each objective is examined in detail below, giving an explanation for its importance and establishing a means of evaluating the designs.

Gives correct diagnosis (Objective A, 35%)

This objective means that the system is correct in reporting when a patient has asthma, is correct in reporting when a patient has pneumonia, and is correct when reporting that a patient does not have either disorder. For a medical system, giving the correct diagnosis is the primary objective. If it does not perform adequately, it does not matter how well any of the other objectives are met; the system is not acceptable. This objective is weighted at 35%, as it is more important than the lower two objectives. It is ranked equally, however, with the objective Inexpensive/Simple, as the academic nature of our project makes it just as important to be able to actually complete the design as to diagnose properly.

This objective is further divided into three sub-objectives, each having to do with giving the correct diagnosis.
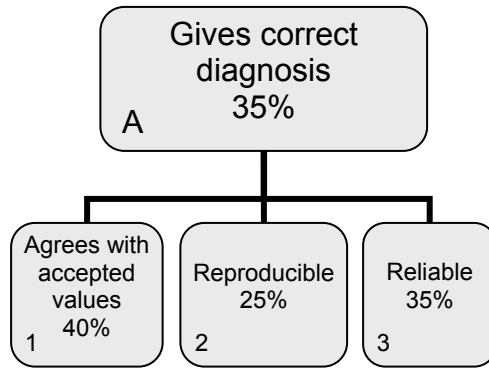
Figure 7 – Sub-objectives of Objective A

Agrees with accepted values (Objective A1, 40%)

This sub-objective is defined by the agreement of the system with an accepted diagnosis. This assumes that a definitive diagnosis can be obtained that is accepted by the medical community – this diagnosis can be through means not usually used in everyday diagnosis, or through a means that would preferably not be used (such as drug-induced response or some type of radiation imaging). This is the most important sub-objective, as it is the essence of being correct – the system must agree with what we feel is the most accurate answer we have. It is measured by comparing the system's responses (or predicted responses) with the "real" (accepted) value. The more times there is agreement, the higher the score.

Reproducible (Objective A2, 25%)

This sub-objective signifies that the system must give consistent results. That is, given the same input (i.e. the same patient), the diagnosis must be the same. Even if the system is "correct" a certain percentage of the time (and thus received a high score for the previous sub-objective), it is important that the certain percentage of correctness is high. This is measured by using the system multiple times on one patient, and scoring the system based on the correlation between the multiple results.

Reliable (Objective A3, 35%)

This sub-objective means that the system will not malfunction or wear out over time. For any medical instrument, it is important that wear-and-tear not be excessive. Lower scores were given for systems with complex mechanical moving parts or parts that would have strain put on them, as they are most prone to wear and breakage. Higher scores were given for systems without such components.

User Friendly (Objective B, 10%)

When an instrument is user-friendly, this generally means that those using the equipment work with it at the optimal ease of understanding and operation. They would have a user interface that helps them understand what the machine is doing, tells what they should do in order to have the desired output, provides a reasonable reflection of how long the machine's operations take, and finally indicates when they should actively interact with and operate the equipment. This ensures efficiency in working with the equipment and reasonably quick detection of any malfunction and the correction thereof. Usually, more user-friendly equipment triggers less anxiety and frustration in its users. When a machine is not very user-friendly, it usually requires the users to spend more time actively operating it than is needed, and may advocate unreasonable mishaps. This leads to unnecessary anxiety, frustration, and wasting of time. With other objectives having been met well, user-friendliness is not too difficult to achieve. With the use of computers, it can become very simple.
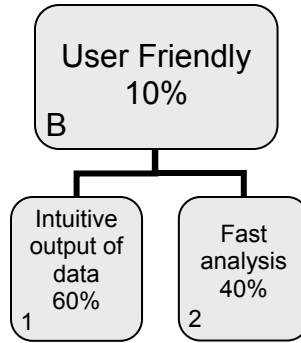
Figure 8 – Sub-objectives for Objective B

Intuitive output of data (Objective B1, 60%)

This means that when the results are being observed at the system's display, the values, changes, and trends are easily interpreted and are representative of what is actually happening. This makes it easier to understand and the results are more quickly interpreted and utilized in any subsequent analysis (e.g. diagnosis). In the case of this project, the easier it is for users to correlate displayed results and the actual condition, the greater the weight assigned to that system.

Fast analysis (Objective B2, 40%)

Any analysis that should be done (taking the current measurement, comparing it to a standard value, and understanding the implication) would be done in as little time as possible. This enables users to obtain a diagnosis quickly and to prescribe a corrective measure in a timely fashion. The less time it takes to do the necessary analyses using a particular system, the greater the weight assigned to that system.

Patient Friendly and Safe (Objective C, 20%)

The device must be patient friendly and safe for the subjects. This objective is applicable for any technology implemented in the healthcare field. The device designed to, in one way or another, improve the patient's well-being can not produce a harmful effect. The definition of *harmful* can be quite broad; it may include mild or severe physical damage to the patient or even just a sense

of discomfort – physical or mental. Effects on the patient can be immediate or delayed. The goal of the design artifact should be to minimize any such unwanted effects. In this case, a device that causes severe damage to the patient is unacceptable as a diagnostic tool – any potential benefits of using the device are negated by its harm to the patient.

The essential objective is that the overall health status of the patient does not deteriorate after the device is used. This broad definition covers any possible effects of the device. Finally, the average patient should not express emotional discomfort when the device is used. (An "average patient" is not one who will be inherently nervous by his mere presence in the doctor's office.)
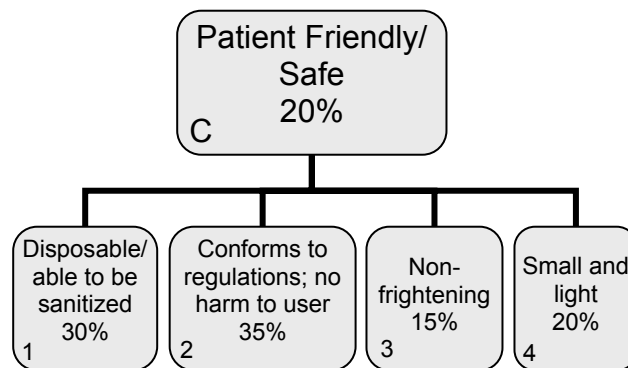
Figure 9 – Sub-objectives for Objective C

Able to be sanitized/disposable (Objective C1, 30%)

The importance of maintaining the cleanliness of patient-contacting parts of the device comes from concerns of cross-patient contamination. When multiple patients come into contact with the same device, there is the possibility of carrying bacteria or other unwanted pathogens from one patient to another. Spread of disease is certainly unwanted in a healthcare facility.

Avoiding this issue can be achieved by sanitizing the appropriate parts or replacing them with disposable components. Sanitizing can be achieved by wiping the part with an alcohol solution. As the design will be coming in contact only with the patient's skin, sanitizing with alcohol is

sufficient. The material used will dictate the ability of the device part to be sanitized. For example, plastic or metal parts can be easily sanitized with alcohol swabs. If a part is made of cloth or rubber, or is excessively large, sanitizing might be challenging.

Disposable parts ensure that each patient comes in contact with a new and clean part, thereby eliminating the need for cleaning. Almost any parts of equipment can be made disposable and replaceable. One of the few issues disposable parts introduce is additional cost. Depending on the size, shape, and material of the replaceable piece, it may be feasible to make it disposable.

Conforms to regulations; no harm to user (Objective C2, 35%)

Healthcare devices are very tightly regulated by various organizations and sets of rules. Federal Drug Administration is only one example of such control; other may include hospital specific regulations and rules set forth by local or national officials.

Conformation to all applicable standards and regulations is important for any new design. If the device fails to meet any of the rules listed above, its use is unacceptable in the healthcare setting. Designers must be sure to meet or exceed any expectations for the device.

Ensuring conformation to the rules is simply a check-list process. Once all applicable regulations are identified, the designer must simply go through the list of regulations and compare them to the device's performance. In the case of multiple regulation sources, many points of testing will likely be redundant.

Non-frightening (Objective C3, 15%)

The device must not scare the patients. This property is applicable to both adults and children. In case of pediatric applications, it likely will have to meet stricter guidelines, for children are more apt to be uncomfortable or scared by an unfamiliar device in the doctor's office. The goal of

being non-frightening is rather subjective – different people will certainly have a different reaction to the same device. As a general rule, the device should not appear overwhelming and unnecessarily large, should not produce unexpected visual stimuli, vibrations, or loud noises. A dental chair with a drill is an example of a frightening device; pulmonary diagnostics device should be much less discomforting.

The patient response to the device can be identified by simple observation. If the patient looks uneasy, frightened, or even begins to cry – perhaps the device is not entirely non-frightening.

Small and light (Objective C4, 20%)

The device must be small and light to promote ease of use by the doctor. Bulky, heavy devices may cause physical and emotional patient discomfort, neither of which is desirable. This objective describes the overall device, as well as the parts that come in direct contact with the patient and require manipulation by the user.

Size and weight considerations are relative among the design alternatives and are meant to emphasize the superiority of one above the others. Since this is a fairly uncharted research field, no golden standard of size and weight exists – except perhaps the traditional stethoscope. The mobile parts of the device can be compared to the stethoscope. Overall, device mobility is important. If the device can be moved from room to room, the diagnosis is simpler – the device can be brought to the patient, instead of the patient going to the device.

Inexpensive/Simple (Objective D, 35%)

Usually, the simpler equipment is, the more inexpensive it is. This is mainly due to the fact that it is easier to manufacture or fabricate. Any work on production of the equipment will also done in

a shorter amount of time. The equipment being inexpensive is very important in this project as the problem statement itself requires a low-cost system.
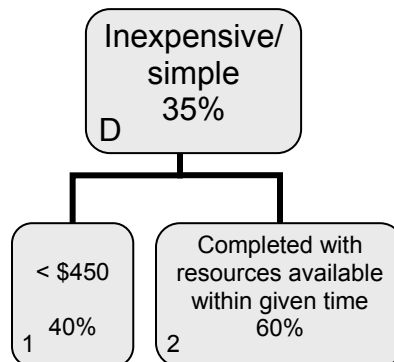
<div align="center">**Figure 10 – Sub-objectives for Objective D**</div>

Prototype costs less than $450 (Objective D1, 40%)

$450 is the allocation we had for the whole project and so in building this system, we need to stay within that budget. Decreasing the complexity of a system (by using fewer, simpler components) may decrease the expense of it. Higher scores are assigned to alternatives that are more likely to stay within the budget when produced and used in a study.

Completion within given time and available resources (Objective D2, 60%)

There were approximately 8 months available to complete this project. It was of paramount importance that we meet that target in order to consider the project a success. After considering all that needs to be done (i.e. ordering parts, assembling and synthesizing components, testing the system), systems that seem likely to take less time for development get assigned a higher score.

Alternative Designs

After establishing the objectives of the design project, and the relative importance of each, we generated a list of ideas to fulfill the objectives. They are presented in this section.

Microphone

This design consists of an acoustic microphone positioned on or slightly above the surface of the chest. The microphone would serve as a substitute for the traditional stethoscope in that it would record the sounds normally heard by users of the stethoscope. The microphone used would be able to detect sounds at the frequency and amplitude of those produced by the lungs during breathing, specifically wheezes and crackles, two adventitious lung sounds produced by pulmonary disorders.

The microphone's analog output would be amplified, converted to a digital signal, and input to a computer system. The computer would determine the frequency content of the lung sound signal, or otherwise process the sound to determine information about the occurrence and time of adventitious lung sounds. This information, when compared to a standard recording, is used to generate a diagnosis. An illustration of the system is shown in Figure 11.
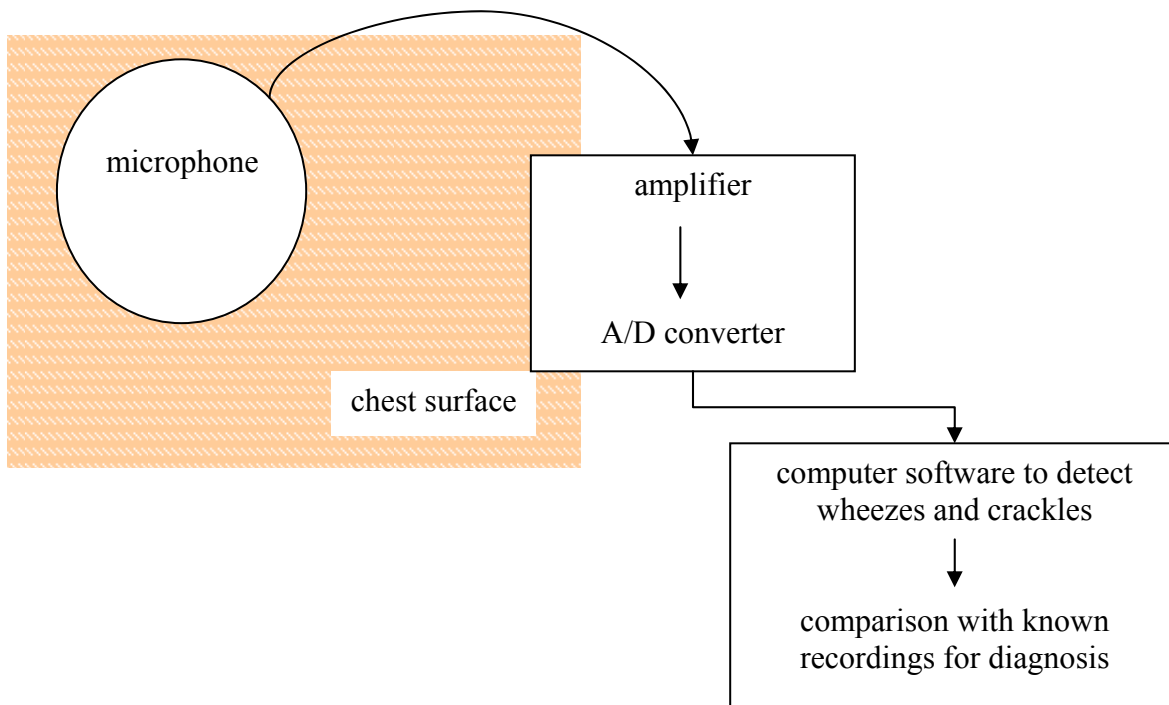
Figure 11 – Microphone Design Alternative

Vibration Sensor

This design consists of a strap wrapped tightly around the chest. Any vibrations that occur in the lungs during respiration would be recorded by a sensor in this strap. (Such sensors are known as accelerometers, as they also measure acceleration.) These vibration signals would be amplified and digitized, and then passed to a computer. Software would detect each vibration event, and annotate each event. The sequence of vibrations would be compared and contrasted with vibrations recorded from patients known to have the disorder, and the diagnosis could be generated from that comparison. An illustration of the system is shown in Figure 12.
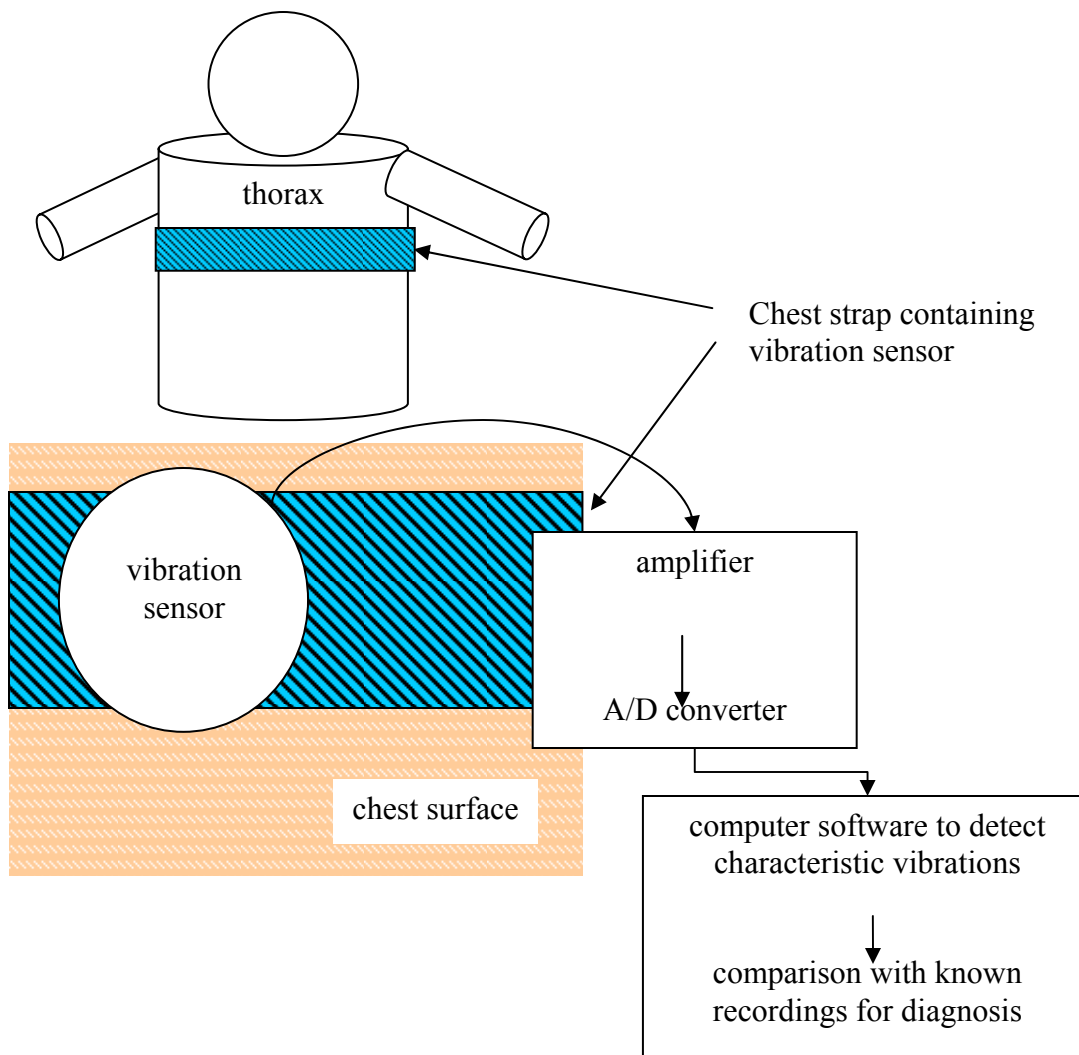
Figure 12 – Vibration Sensor Design Alternative

Cough Detection

The cough is a lung sound that has been used for a long time for diagnosis, but mainly interpreted by ear by a physician during auscultation. It is also known that there are some respiratory abnormalities that will cause someone to have a particular kind of cough (e.g. dry). These differences are very subtle to the ear, either trained or not. Digital capture of the cough sound may allow analysis and detection of important differences specific to particular abnormalities (asthma and pneumonia). An easy, low-cost way to do this is to have patients cough into a microphone and have the sound detected from either the mouth or the throat. This sound could then be processed in hardware and software, and analyzed digitally.

A representation of the system is shown in Figure 13.
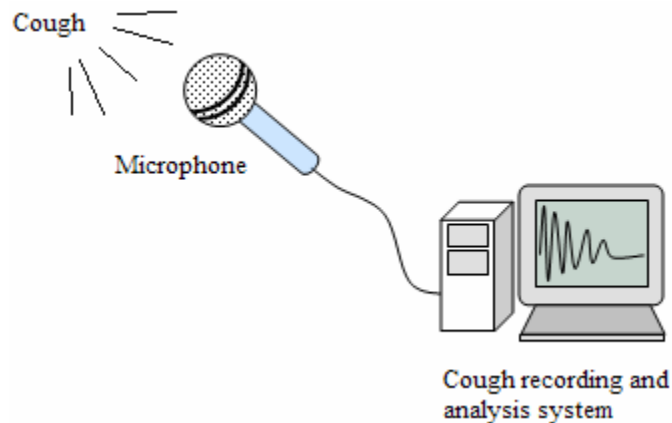
Figure 13 – Cough Detection Design Alternative

A problem that could arise with this system, especially if the sound is being detected from the mouth, is having such high intensity of air flow into the microphone. The problem with this could be that the sound would be too explosive to detect any helpful detail in the sound. A better system could still utilize the microphone, but have a barrier that would efficiently transmit the sound, but block the explosive air flow from the mouth. A representation of this new system is shown in Figure 14.
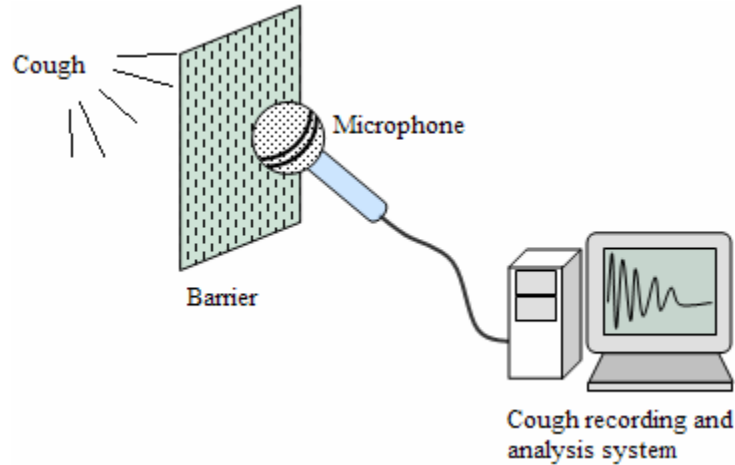
Figure 14 – Cough Detection Design Alternative with Air Blocking Barrier

This second system seems to be the better out of the two to consider in choosing a potential final design.

Air flow Detection

Another indication of disease may be a certain pattern of air flow, either from someone coughing or someone blowing as hard as they can into the apparatus. The assumption is that different respiratory abnormalities will cause people to have different air flow rates when coughing or blowing. They may have decreased flow rates if they are suffering from an ailment, and perhaps different reductions are characteristic of particular abnormalities. One technique could be to determine pressure differentials and extrapolate the air flow velocity. The apparatus would be divided into numerous smaller pipes to eliminate turbulence and ensure laminar air flow where the pressure is being measured. A pressure transducer would used, in conjunction with hardware and analysis software.

A representation of the system is shown in Figure 15.
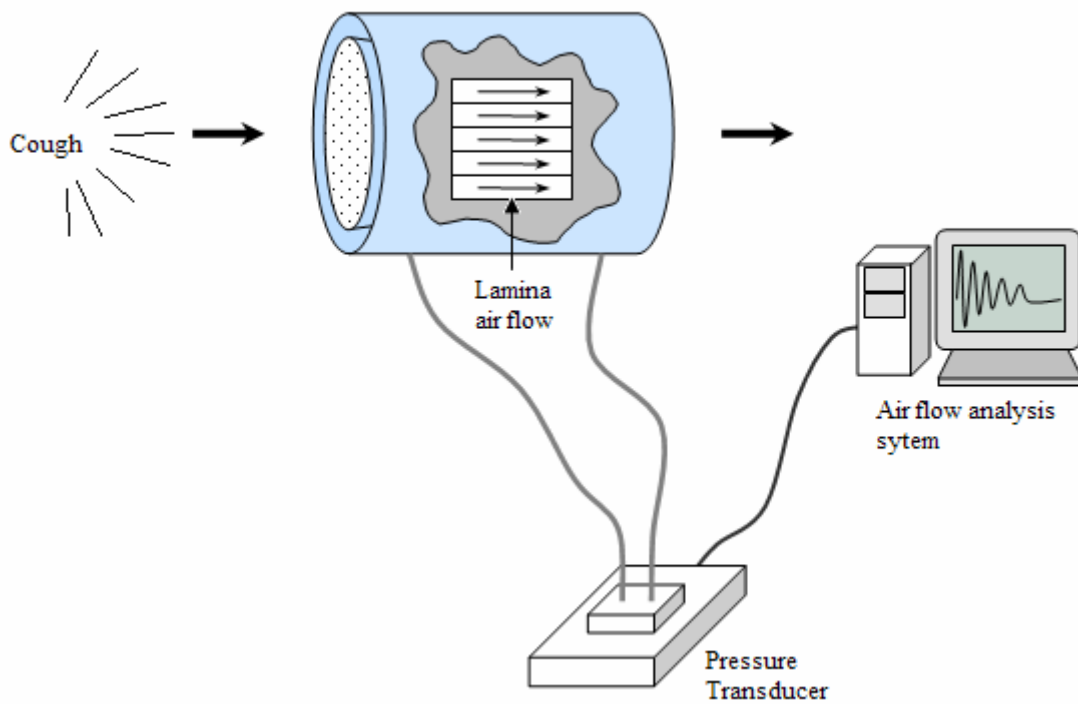
Figure 15 – Air Flow Detection Design Alternative

The apparatus could also be set up so that the path of air flow would have a turbine that would

have an audometer or a similar device to determine the speed of the air passing through. In this

case, other factors and parameters such as the torque of the turbine would need to be considered.

A representation of the alternate system is shown in Figure 16.
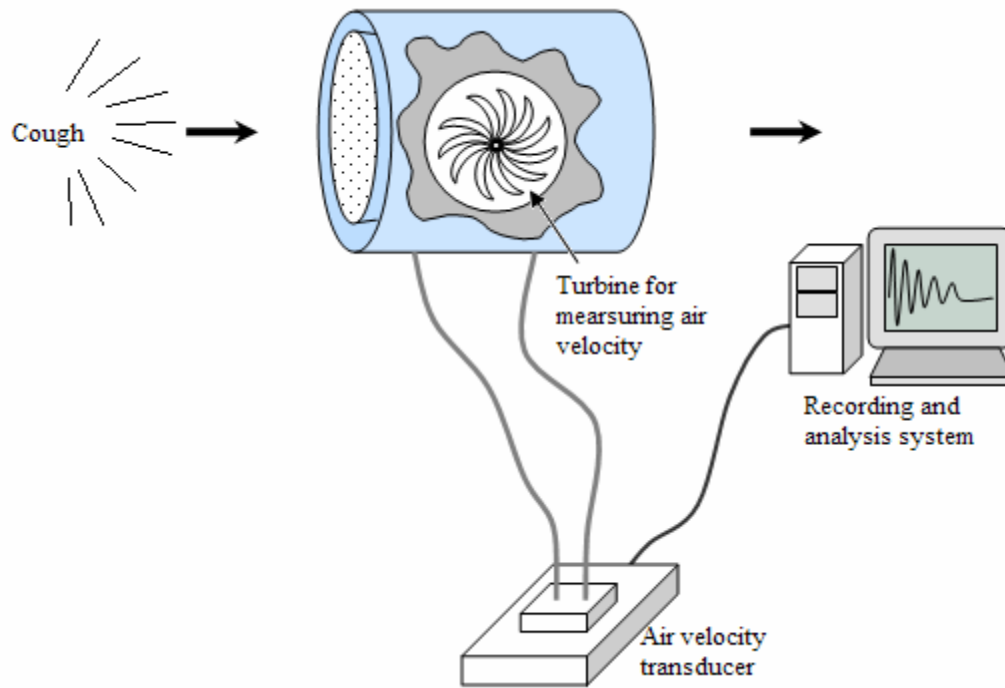
Figure 16 – A Second Air Flow Detection Design Alternative

Combination Design

A system could be made with a combination of the two parameters; sound and air flow. A

microphone could be embedded into the air-flow apparatus. A representation of the system is

shown in Figure 17.
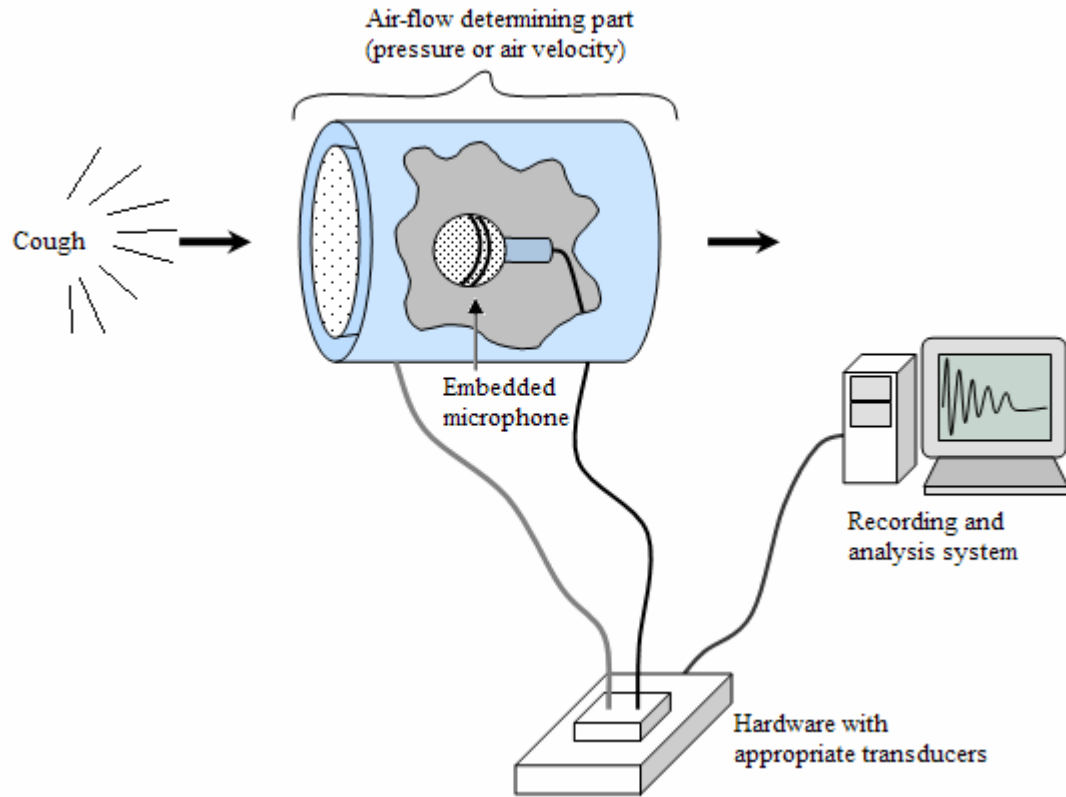
Figure 17 – Combination Design Alternative

Drug-Induced Response

Another diagnostic technique is the intentional administration of an agent to a patient to produce a mild constriction of the airways. The most common drug used in this procedure is methacholine, which affects asthma patients. After the drug is administered, vital signs are monitored and a diagnosis deduced from the patient's response, which can be seen generally between twenty and forty-five minutes. Some protocols for rapid testing exist, which allow 1the doctor to administer a similar test in approximately fifteen minutes.

The analysis of the patient's response can include air flow measurements, auscultation, and blood pressure or pulse measurements. In the case of a strong asthma condition, a bronchodilator can be administered after the test results are obtained to return the patient to a normal state.

An illustration of this alternative is shown in Figure 18.
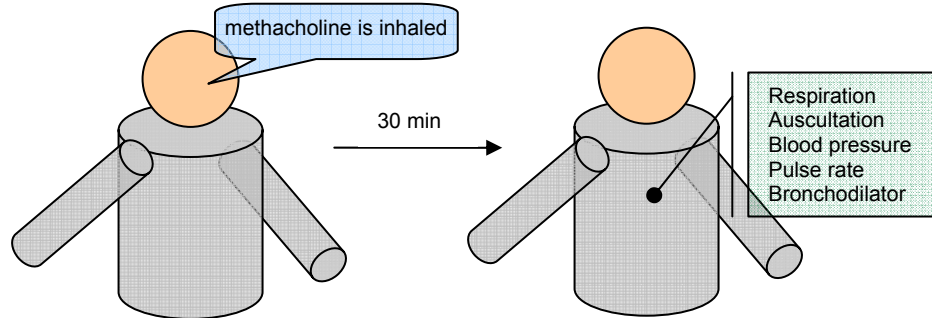
Figure 18 – Drug-Induced Response Design Alternative

Although the testing is by large harmless, there are some side effects. The patient will likely experience augmented symptoms of the lung disease (wheezing, coughing, and shortness of breath) during or immediately following testing. These symptoms can usually be cleared with the use of a bronchodilator.

Possible complications include a slight risk of collapsed lung in some patients with acute lung disease. One of the problems with drug induced tests is that adverse effects may occur hours after testing. Accordingly, such tests should only be done in limited, specific circumstances, and then only under close and careful supervision by a doctor or specially trained technician.

Respiratory Imaging

Respiratory imaging methods – such as digital tomographic x-rays, CT-scan, MRI, and normal x-ray imaging – are common for confirming a respiratory disease diagnosis, especially in questionable cases. The patient's chest cavity is photographed and various discolorations can indicate inflammation or fluid build up in the lungs. A strong drawback of imaging is the fact that it may not accurately detect pneumonia at early stages, especially if the patient is dehydrated at the time of the test. Imaging can also be prohibitively expensive, particularly when used in the clinic as a screening tool. Typical imaging techniques take 1 to 15 minutes.

The average analysis time, however, is one to two days because a radiologist is often involved; he reviews the images and sends a report back to the doctor's office.
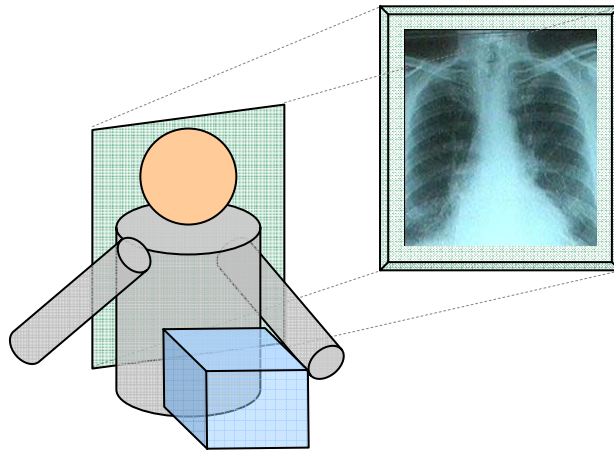
Figure 19 – Imaging design alternative, showing x-ray imaging as an example

[x-ray courtesy of BBC News]

The procedure is non-invasive. For some types of imaging, a small dose of radiation is administered to the patient, but the level is low enough to be benign unless many images are taken successively. The procedure is very common – it ranks among the most popular of all clinical diagnosis tests.

Choosing Between Alternative Designs

Each design alterative was analyzed in terms of how well it met the objectives previously established (on a scale of 0 to 5, with 0 being worst and 5 being best). The scores were multiplied by the weighting of the objective to calculate a total score for each design. The use of this method ensured that the choice was completely objective. Table 7 shows this step.

Table 7 – Using Weighted Objectives to Select Design from Alternatives						
Design Alternative:	Microph.	Chest Str.	Cough	Air flow	Drug-Ind.	Imaging
35% Gives correct diagnosis	**3.25**	**3.25**	**2.15**	**2.65**	**2.80**	**4.75**
40% Agrees with accepted values	3	3	3	3	4	5
25% Reproducible	4	4	1	3	2	4
35% Reliable	3	3	2	2	2	5
10% User Friendly	**4.20**	**4.20**	**3.20**	**3.60**	**2.00**	**2.20**
60% Intuitive output of data	5	5	4	4	2	3
40% Fast analysis	3	3	2	3	2	1
20% Patient Friendly	**4.85**	**2.40**	**4.00**	**3.50**	**2.40**	**2.90**
30% Able to be sanitized	5	2	4	4	5	4
35% Doesn't harm user	5	3	4	3	1	3
15% Non-frightening	4	1	4	3	1	3
20% Small and light	5	3	4	4	2	1
35% Inexpensive/ simple	**4.40**	**3.00**	**3.40**	**3.60**	**2.00**	**1.00**
40% < $450	5	3	4	3	2	1
60% Completed within given time	4	3	3	4	2	1
Overall Score:	**4.07**	**3.09**	**3.06**	**3.25**	**2.36**	**2.81**

All scores were assigned following in-depth research on the specific diagnostic method. In order to presume impartiality and validity of the best alternative selection, score justification for each individual design in each scoring category is outlined below.

Microphone

35% Gives correct diagnosis   3.25

40%   Agrees with accepted values   3

Because it has never been tested, it is difficult to give this method the highest score. However, it is known that sounds are produced by the lung, and that these sounds are related to the pulmonary pathology; therefore it should be a viable method.

| 25% | Reproducible | 4 |

Because sounds are fairly straightforward to collect, and unusual lung sounds will persist for some length of time, it is likely that repeating the acquisition and analysis will give an identical diagnosis.

| 35% | Reliable | 3 |

As the equipment is simply a self-contained microphone connected to an analog-digital converter, there should be little room for malfunction. However, the final product has not been designed, and it is possible that the system could have a weakness.

| 10% | **User Friendly** | **4.20** |

| 60% | Intuitive output of data | 5 |

The system would allow the care provider to both view and hear the data collected, as well as monitor each step of the process if desired. The analysis and diagnosis are displayed clearly and automatically.

| 40% | Fast analysis | 3 |

After the data collection, the software analysis should be quick, as it is likely that digital audio filtering and manipulation – fast operations on modern processors – will play a large part in the analysis. However, because the analysis is not yet fully implemented, the amount of time it takes is unknown.

| 20% | **Patient Friendly** | **4.85** |

| 30% | Disposable/Able to be sanitized | 5 |

Just like the modern stethoscope, a microphone can be quickly wiped clean with an ethanol solution, for easy cleaning.

35%   Conforms to regulations/doesn't harm user   5

Since the microphone is simply placed on the chest and used to collect sounds, normal
usage poses insignificant risk to the patient.

15%   Non-frightening   4

Again, the microphone is placed on the chest, and few patients would consider this
frightening. However, young patients do find the traditional stethoscope cold and
frightening, so the same could be thought of a microphone.

20%   Small and light   5

The component that comes in contact with the patient is a small microphone. The
analysis equipment consists of a personal computer – which could easily be a portable
computer – that can be moved without difficulty from room to room if necessary.

35% Inexpensive/ simple   4.40

40%   < $450   5

A prototype can be developed with no materials beyond a microphone that can be
acquired for less than $450, and computer equipment currently available for our use.

60%   Completed within given time   4

With the design team's expertise, we will have no problem developing an algorithm by
the completion deadline.

Vibration sensor:
35% Gives correct diagnosis   3.25

40%   Agrees with accepted values   3

Because it has never been tested, it is difficult to give this method the highest score.
However, it is known that vibrations are produced by the lung, and that these vibrations
are related to the pulmonary pathology; therefore it should be a viable method.

| 25% | Reproducible | 4 |

Because the vibrations are fairly straightforward to collect, and will be affected similarly by disorders, recording and analyzing data from the same patient, during the period when the disorder is in the same stage, should give an identical diagnosis.

| 35% | Reliable | 3 |

The equipment is not only a vibration sensor, but also a chest strap attachment that needs to be oriented properly and moved and adjusted a great deal. Malfunction seems to be an unfortunate possibility.

| **10%** | **User Friendly** | **4.20** |

| 60% | Intuitive output of data | 5 |

The system would allow the care provider to view the data collected, as well as monitor each step of the process if desired. The analysis and diagnosis are displayed clearly and automatically.

| 40% | Fast analysis | 3 |

After the data collection, the software analysis should be quick, as it is likely that digital signal filtering and manipulation – fast operations on modern processors – will play a large part in the analysis. However, because the analysis is not yet fully implemented, the amount of time it takes is unknown.

| **20%** | **Patient Friendly** | **2.40** |

| 30% | Disposable/Able to be sanitized | 2 |

A chest strap needs to be included that holds the vibration sensor in place and conducts vibrations from areas throughout the thorax. It will not be easy to clean, and needs to be securely attached to the vibration sensor, so a disposable strap is not an option.

35%   Doesn't harm user   3

It is possible that the conducting and securing straps could be adjusted improperly, and thus be able to injure the patient.

15%   Non-frightening   1

Having a large apparatus attached to oneself could very well be frightening.

20%   Small and light   3

Parts of it are small and light, but the assembly needed to conduct the vibrations is relatively large and obtrusive.

35% Inexpensive/ simple   3.00

40%   < \$450   3

This alternative design not only requires an accelerometer (vibration sensor), which should be within the budget, but also an assembly to hold it and conduct the sound.

60%   Completed within given time   3

Current research has been done on lung sound propagation and analysis, but to study lung vibrations, and use them as a basis for diagnosis, could take much additional work.

Cough:

35% Gives correct diagnosis   2.15

40%   Agrees with accepted values   3

Signals from coughs are not used much and, when compared to other signals obtained using microphones (such as having a specialized microphone placed on the chest), the signal obtained is not very clear. There isn't a standardized way of diagnosis from analyzing cough waveforms, and rudimentary techniques have not yet been very carefully assessed.

25%   Reproducible   1

Coughs in themselves are not particularly reproducible, and they are less likely to be reproducible in a manner that would make them distinguishable for ailments with similar symptoms. Cough characteristics do not only vary from individual to individual, but may vary from cough to cough in the same individual. This may create a big challenge for the consistent analysis by this system.

35%   Reliable   2

The system may be good at detecting and analyzing sound that it receives, but with the very high density of sound that can be captured by the microphone from a cough, it may be difficult to coerce a system to be able to give a diagnosis without complex functions. It makes it less reliable when the parameter being measured is less reproducible than most.

10%   User Friendly   3.20

60%   Intuitive output of data   4

When a cough sound is made and represented digitally, cough identification is not difficult. Analysis of the finer details of the cough may be less simple for the user to understand, however.

40%   Fast analysis   2

With respect to determining the number of coughs per episode and the number of episodes, that would be quite easy to count. However, to get to that point, a lot of time would need to be spent monitoring the patient. Given the explosive nature of the output signals obtained, more complex techniques would need to be used to analyze a single cough signal.

20% Patient Friendly   4.00

30%   Disposable/Able to be sanitized   4

Contact between patients and the system is not necessary and this could be interpreted as being safer for the patients. However, the symptom of which the measurements are made (coughing) is one of the most common ways pathogens are spread, so the system needs to be carefully sanitized. It should not be difficult to sanitize, however.

35%   Conforms to regulations/doesn't harm user   4

The system does not require any contact between the patient and the instrument; therefore the patients are not susceptible to much harm from it.

15%   Non-frightening   4

The part of the system that the patients would interact with, the microphone, does not seem harmful or frightening.

20%   Small and light   4

The system does not require too much equipment - only a microphone with an air flow barrier, and a computer for analysis.

35% Inexpensive/ simple   3.40

40%   < $450   4

A prototype can be built while staying within the $450 budget.

60%   Completed within given time   3

It is very possible to complete the project within the given time with this system.

Air flow:

35% Gives correct diagnosis   **2.65**

40%   Agrees with accepted values   3

Physiological measurements of air flow have been done extensively, but analyses done

with only air flow measurements do not seem to have been very common. It is not known

how well this system would produce these analyses and the subsequent diagnosis.

25%   Reproducible   3

The measurement of air flow is reproducible, but there is much variation/variability in the

parameter being measured and this could adversely affect the results given by the system.

35%   Reliable   2

Measurement of air flow is relatively easy, but an analysis and diagnosis only based on

air flow would probably not be very accurate and thus not very reliable.

10% User Friendly   **3.60**

60%   Intuitive output of data   4

The air flow can easily be measured and displayed.

40%   Fast analysis   3

The measurements can be done in real-time, but we are not sure how fast it is to analyze

and have a diagnosis output from the system. It seems like the analysis would be done in

a reasonable amount of time.

20% Patient Friendly   **3.50**

30%   Disposable/Able to be sanitized   4

The system can be sanitized and a part of it, the mouthpiece cover, is disposable.

35%   Conforms to regulations/doesn't harm user   3

The system does not seem to have anything that could adversely affect the patient.

| 15% | Non-frightening | 3 |

Having to blow through a tube and causing shortness of breath may be disconcerting for some patients.

| 20% | Small and light | 4 |

The system is reasonably small and light, including the handheld part, the transducers, and the computer system.

| **35%** | **Inexpensive/ simple** | **3.60** |

| 40% | < $450 | 3 |

This system could be built within the budget allocation. The pressure transducers would be the most costly component, as we have computers available for use.

| 60% | Completed within given time | 4 |

Construction of the system can be completed in given time period.

Drug-induced response:

| **35%** | **Gives correct diagnosis** | **2.80** |

| 40% | Agrees with accepted values | 4 |

This method is currently used by clinicians on a small percentage of all patients to confirm hard to make diagnoses. It is widely accepted as valid within the professional community and serves as a valid diagnostic tool.

| 25% | Reproducible | 2 |

Patients' response strongly depends on the amount of the agent inhaled and the effort put forth by the patients to express the symptoms of the pulmonary disorder. Also, bronchial tone is increased during the test, thereby altering the patients' normal breathing pattern.

35%   Reliable   2

This method only causes a diagnosable response in a small part of all patients and

therefore is not universal.

10%   User Friendly   2.00

60%   Intuitive output of data   2

Test results are highly interpretive and do not always lead to an unambiguous diagnosis.

Patients' responses are expressed by many various parameters and are fairly difficult to

interpret.

40%   Fast analysis   2

Additional tests are required to propagate the drug induced response into a diagnosis.

Also, some symptoms of severe pulmonary disorders do not occur until a few hours after

the test.

20%   Patient Friendly   2.40

30%   Able to be sanitized   5

Drug is administered to the patients through a specialized inhaler, which can be

disposable. Alternatively, the small inhaler can be easily sanitized.

35%   Doesn't harm user   1

Drug administration is potentially dangerous for patients with severe lung disorders.

15%   Non-frightening   1

The test is meant to produce a bronchospasm, a disease response, from the patient which

is not pleasant.

| 20% | Small and light | 2 |

This test requires multiple equipment pieces, some of which are quite large and immobile.

| **35%** | **Inexpensive/ simple** | **2.00** |

| 40% | < $450 | 2 |

The equipment and the need for a supply of medication make this method costly.

| 60% | Completed within given time | 2 |

Drug admission to patients is certainly beyond the scope of this project.

Imaging:

| **35%** | **Gives correct diagnosis** | **4.75** |

| 40% | Agrees with accepted values | 5 |

Imaging is one of the most common diagnostic tools used in the field today.

| 25% | Reproducible | 4 |

Lungs can appear slightly different from one image to another; the variance can be due to the momentary condition of the person or instantaneous lung volume.

| 35% | Reliable | 5 |

With proper analysis (by a well trained and experienced professional), imaging can reveal much information about the lung condition.

| **10%** | **User Friendly** | **2.20** |

| 60% | Intuitive output of data | 3 |

Images must be interpreted and the diagnosis may vary among professionals. High level of skill is required to analyze the results.

40%   Fast analysis   1

Professional opinion of a radiologist is necessary for complete diagnosis. Turnaround

time depends on where the radiologist is, but nonetheless requires sending information

out of the office and waiting for a response.

20%   Patient Friendly   2.90

30%   Able to be sanitized   4

No contact is made with the patient by the machine itself. Often some shielding has to be

worn to prevent unnecessary exposure to radiation, but skin contact is minimal.

35%   Doesn't harm user   3

For some types of imaging, a small dose of radiation is administered. Even though the

amount is too minute to produce harmful effect, multiple screenings multiply the risks.

15%   Non-frightening   3

The imaging machines are fairly large and the amount of precautions that must be taking

during some types of imaging can make a patient uncomfortable.

20%   Small and light   1

Imaging equipment is large and hardly mobile.

35%   Inexpensive/ simple   1.00

40%   < $450   1

Imaging machines and film development equipment (when necessary) are extremely

expensive.

60%   Completed within given time   1

Using this type of equipment is beyond the scope of this project.
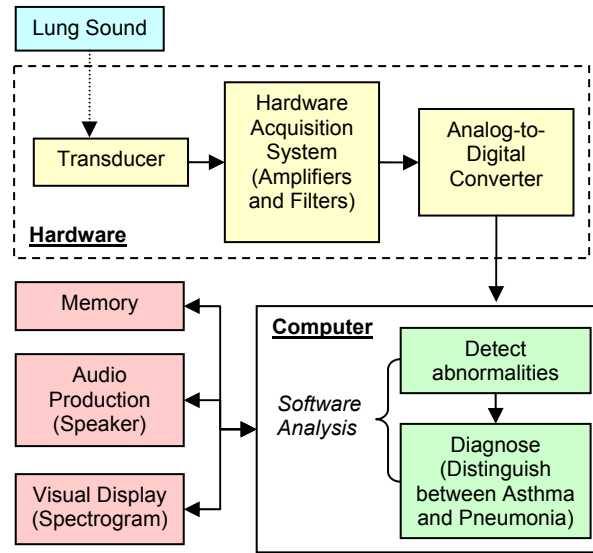
Figure 20 – Block diagram of Microphone System Design

After formally selecting the microphone design, a detailed design was created. A block diagram is shown in Figure 20. The design of both the hardware and the software stages of the system are detailed below.

Hardware Design

The first generation of the hardware design used a miniature microphone (Star Micronics MAA-03A-L back electret condenser microphone) together with a driving circuit suggested by the manufacturer's datasheet (Figure 21), amplified by a simple one-stage amplifier. The signal was fed into a computer sound card's microphone port and recorded by an open-source software package called Audacity (http://audacity.sourceforge.net/).
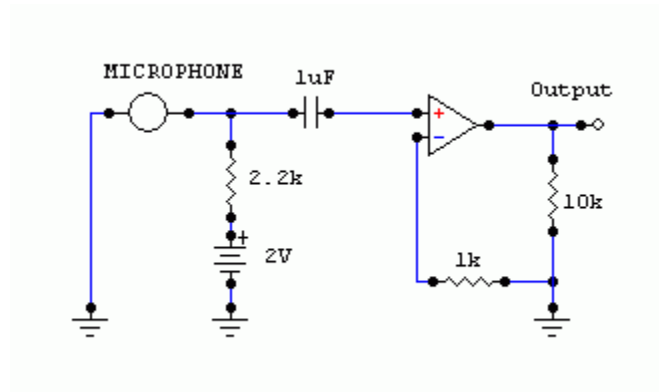
Figure 21 – Early hardware circuit design

The first set of tests focused on establishing the basic function of the assembled microphone prototype. Speech, whistling, and musical scales were successfully recorded and reproduced on the computer. During these tests the microphone was positioned at distances from the sound source ranging from only a few centimeters to approximately fifty centimeters. The sensitivity of the microphone circuit was acceptable: sounds played back on the computer exhibited little distortion from the live events. The microphone did, however, pick up the noises due to air passing directly over the pick up head; this unwanted noise was specifically noticeable during whistling close to the microphone.

Once we established our prototype's basic functionality, an attempt was made to couple the device with a stethoscope and record some pulmonary sounds. We placed the microphone into the most easily accessible part of the stethoscope, the earpiece. In theory, the sounds recorded by the system in this configuration would be identical to what a physician would hear by using the stethoscope in the traditional way. Our prediction was that sounds recorded by the prototype device would be of smaller amplitude than speech or whistling. Unfortunately, the system turned out to be completely insensitive to pulmonary sounds. The inability of the prototype to detect breathing sounds was attributed to the relatively low quality of the components used and to the

simplicity of the system. Figure 22 contrasts the recordings of the different types of sounds through the stethoscope.

(a)   (b)
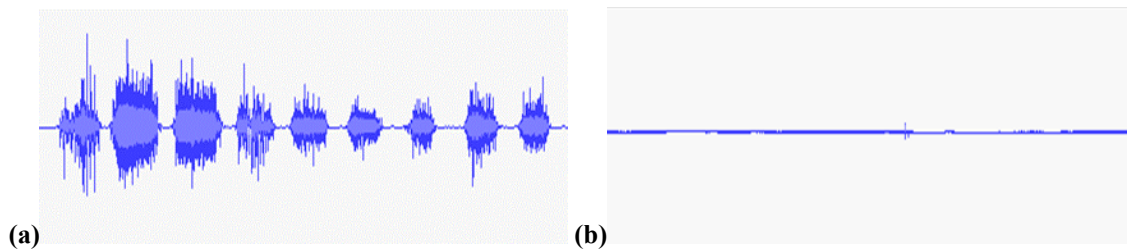
Figure 22 – Whistling sound (a) and breath sound (b) recordings made through stethoscope.

Despite the device's inability to detect pulmonary sounds, the process of building a prototype was successful in some ways. The experience of working with the microphone hardware led to the conclusion that a better design would use an integrated, commercially-available hardware package, allowing the focus of the development period to be spent on software design.

In the final design, the hardware stage consisted of a physiological sound microphone (BIOPAC TSD108) connected to a differential amplifier module (BIOPAC DA100B) and a data acquisition unit (BIOPAC MP100). This system was specifically designed to digitize physiological sounds, and included appropriate filters and analog-to-digital converters. Users also have the option to monitor the audio recording with a headset (the volume is adjustable with a knob).

Minimizing the noise detected by the microphone was a challenge, even with the commercial microphone package. Several modifications to the basic design were attempted:

- A foam padding shell was fabricated and the microphone was placed inside. This was intended to provide insulation from both room background noise and from any undue motion of the user's hands when holding the microphone. This modification was rejected, as the foam would have been in contact with the patient, and would have posed a sanitation risk. The foam padding is shown in Figure 23.

Figure 23 – Foam padding shell

- An ultrasound conducting gel was used in between the patient and the microphone, in the hope that the lung sounds would be transferred more accurately from the skin surface to the microphone. This was messy, unfortunately, and did not significantly affect the fidelity of the recorded lung sound.

- A rubber cylinder was affixed to the back surface of the microphone. This muffled much of the user motion, and did not come in contact with the patient, so sanitation was not an issue. This modification was implemented in the final design. Figure 24 shows this cylinder attached to the microphone.
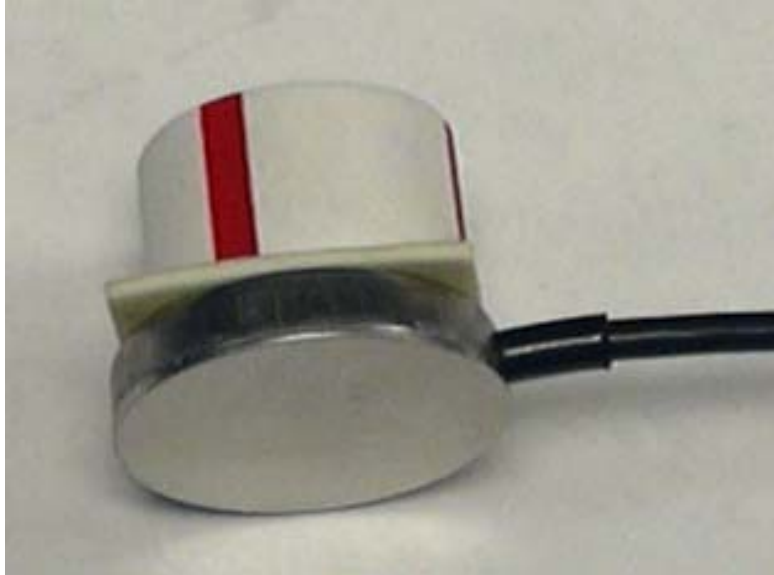
Figure 24 – Rubber cylinder handle on microphone

The final hardware acquisition system is shown in Figure 25.

Figure 25 – Final hardware design in clinical setting

The BIOPAC A/D converter interfaces with a computer, and is controlled by BIOPAC®'s proprietary *AcqKnowledge™* software (Version 3.7.3). This software acquires the sounds, which are then saved to disk in plain text data files. The software design section below describes the use of software to analyze these recorded sounds.

Software Design

Analyzing the lung sound signals digitally permits the use of an unprecedented number of analytical tools. Using MATLAB® (Version 7.0.1), the system is able to extract useful features from the lung sound recordings and use them to differentiate between healthy and diseased breathing patterns. In addition to producing an audible output like that of a conventional stethoscope, the system is capable of generating a visual representation of the processed data, called a spectrogram. A spectrogram of the sound of a healthy lung is shown in Figure 26. The x-axis represents time, the y-axis represents frequency, and the color represents the intensity of each sound frequency at each time in the recording. The breathing pattern is discernable, as is the fact that there are a few narrow bands of high frequency noise.
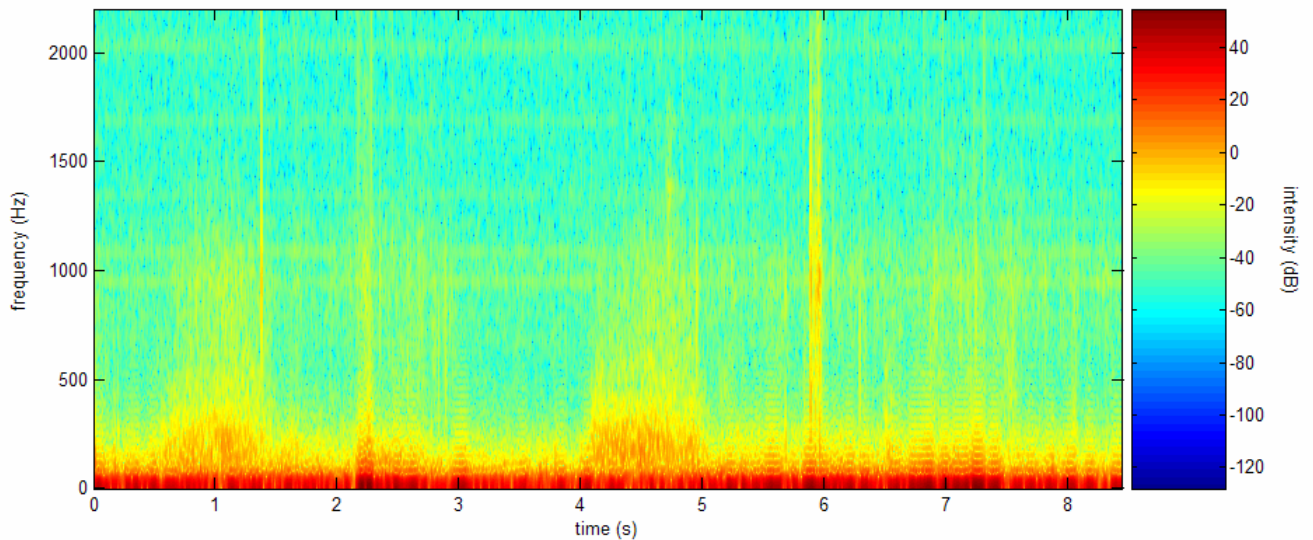
Figure 26 – Spectrogram of a generally healthy lung sound

Since asthma and pneumonia should be diagnosable by the relative amounts of wheezing and crackling (respectively), algorithms were developed to detect each of these adventitious sounds.

Crackle Detection

A spectrogram of a lung sound recording exhibiting crackles is shown in Figure 27. Crackles, as discussed in Chapter 2, are high-intensity, high-bandwidth noises lasting between 10 and 20 ms. Crackles are represented in the spectrogram as vertical red lines, and points at which crackles are detected are shown in white in the black band above the spectrogram.
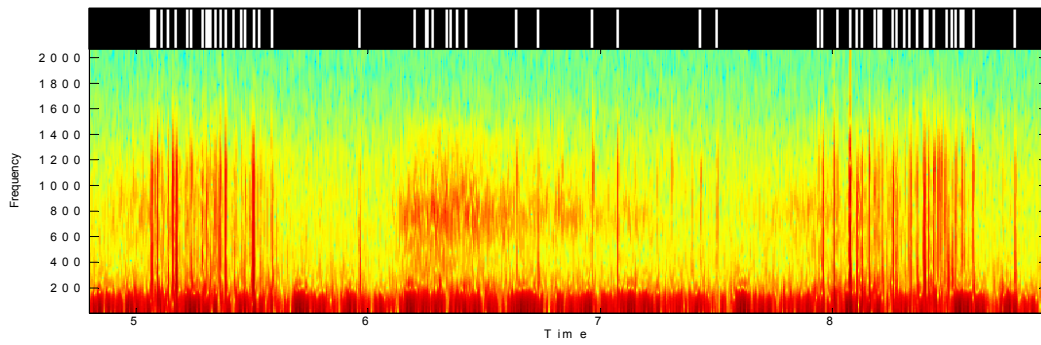
Figure 27 – Spectrogram exhibiting lung sound crackles

The algorithm functions by first creating a spectrogram. The overall intensity of the image is found, and a threshold is calculated. A filter is then used to remove all parts that are less intense than that threshold, as well as those outside the established frequency band of 200 to 1500 Hz (the frequency range in which crackles occur). Another filter then removes all components of the signal that do not have a bandwidth of at least 900 Hz. The procedure counts crackles in the remaining data by incrementing over time and searching for signals that last from 10 to 20 ms. The final step of the crackle detection algorithm is to create a *crackle ratio*, which is the percentage of the recording that contains crackles.

A flowchart is shown in Figure 28. The code for this algorithm, implemented in MATLAB, can be seen in Appendix C.
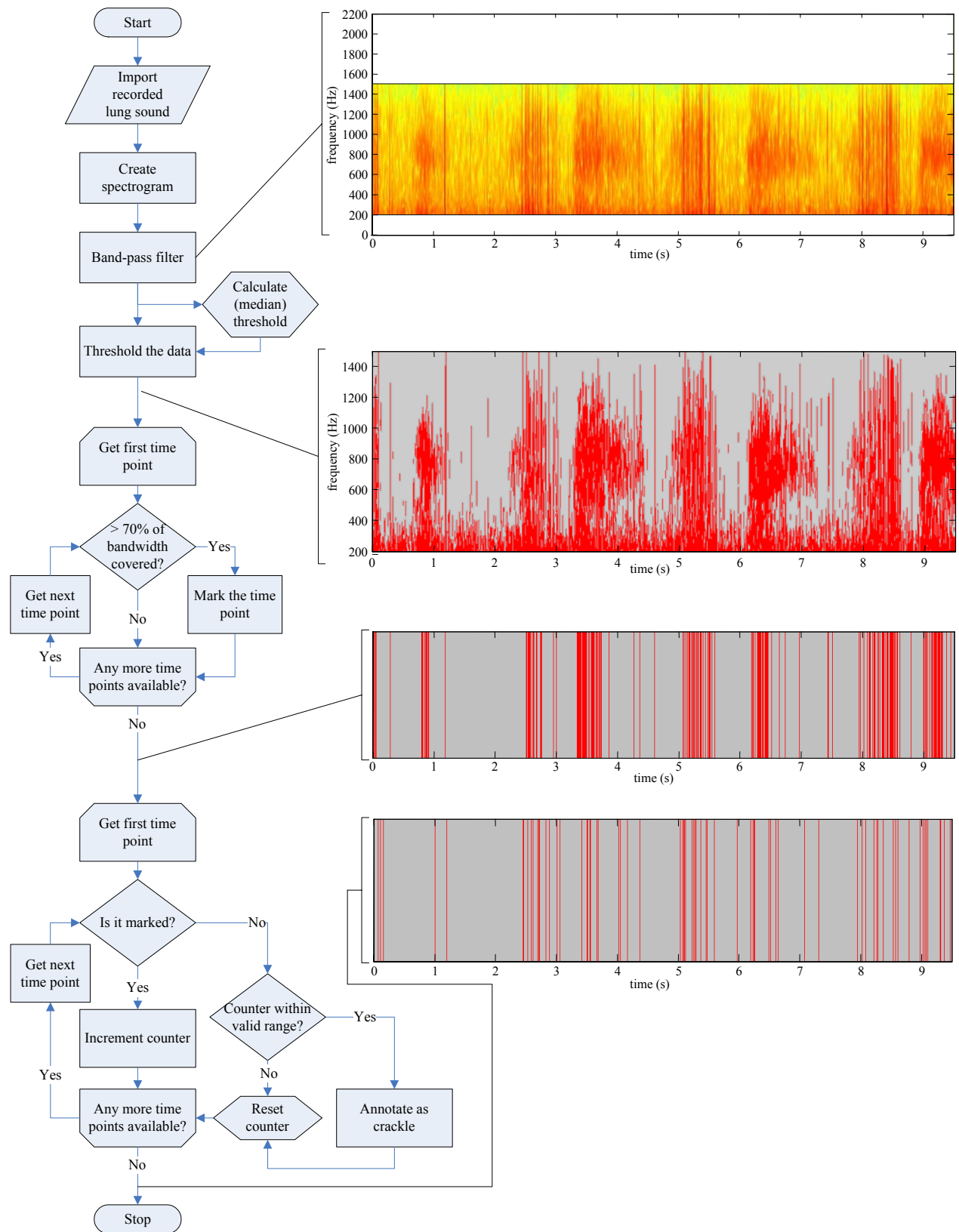
Figure 28 – Flowchart of Crackle Detection Algorithm

Wheeze Detection

A spectrogram of a wheezing lung sound is shown in Figure 29. Wheezes, as discussed in Chapter 2, are continuous, low-bandwidth, longer-lasting noises. The horizontal orange-red areas in the spectrogram are wheezes. Detected wheezes are shown in white in the black band above the spectrogram.
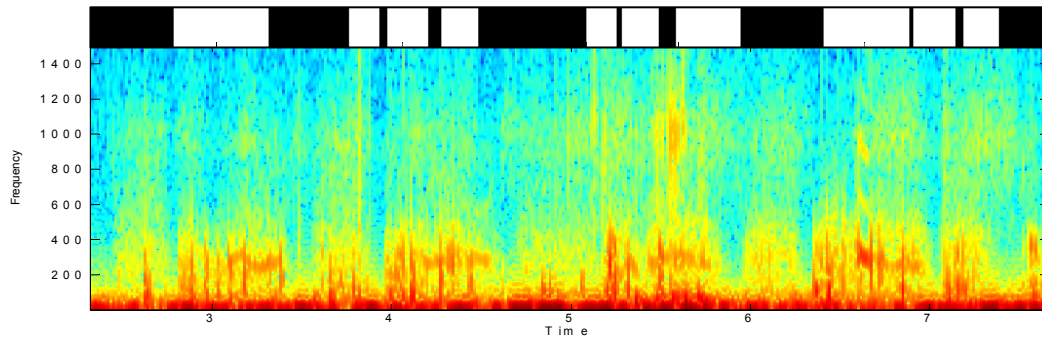
Figure 29 – Spectrogram exhibiting lung sound wheezes

Portions of the wheeze detection algorithm were modified from a method proposed by Shabtai-Musih et al (634). Like the crackle-detection program, this algorithm functions by first generating a spectrogram. The procedure then increments over time, searching for local maxima in the frequency domain at each time point. The prominence of each maximum is found by comparing its intensity to the intensities of neighboring frequencies. Trails of these maxima represent potential wheezes. The length and prominence of each trail is then calculated, and wheezes are detected when the length and prominence reach a threshold. The final step of the wheeze detection algorithm is to create a *wheeze ratio*, which is the percentage of the recording that contains wheezes.

A flowchart is shown in Figure 30. The code for this algorithm, implemented in MATLAB, is in Appendix C.
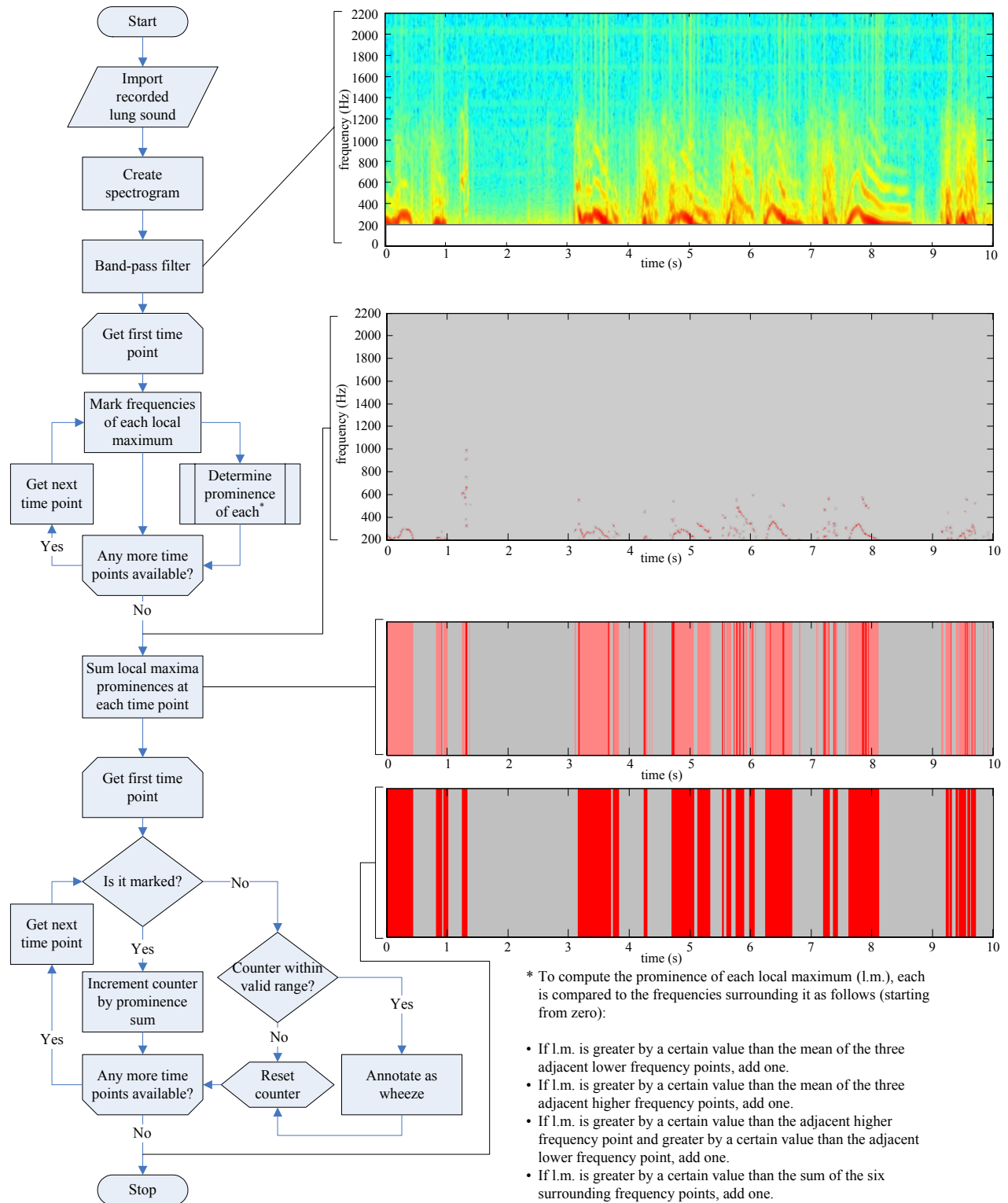
Figure 30 – Flowchart of Wheeze Detection Algorithm

Flowchart elements:

Start → Import recorded lung sound → Create spectrogram → Band-pass filter → Get first time point → Mark frequencies of each local maximum → Determine prominence of each* → Any more time points available? (Yes → Get next time point; No →) Sum local maxima prominences at each time point → Get first time point → Is it marked? (No → Any more time points available?; Yes → Increment counter by prominence sum) → Counter within valid range? (Yes → Annotate as wheeze → Reset counter → Any more time points available?; No → Reset counter) → Any more time points available? (Yes → Get next time point; No → Stop)

* To compute the prominence of each local maximum (l.m.), each is compared to the frequencies surrounding it as follows (starting from zero):

- If l.m. is greater by a certain value than the mean of the three adjacent lower frequency points, add one.
- If l.m. is greater by a certain value than the mean of the three adjacent higher frequency points, add one.
- If l.m. is greater by a certain value than the adjacent higher frequency point and greater by a certain value than the adjacent lower frequency point, add one.
- If l.m. is greater by a certain value than the sum of the six surrounding frequency points, add one.

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Spatial distribution of measurements

When the system is in use, lung sounds from approximately two full breaths are recorded at each of six locations on the subject's back. The locations are numbered 0 through 5 (Figure 31). This auscultation pattern is commonly used by physicians and allows for spatial differentiation of lung sound data. This spatial distribution is a significant constituent of the asthma and pneumonia scores and thus, the final diagnosis algorithm.

There is one exception to this procedure – when the lung sound data is collected from infants, only four recording locations are used. It has been found that there simply is not enough space on the child's back to reasonably make six different recordings. The diagnosis algorithm is slightly modified as necessary to accommodate these nonstandard recording patterns.
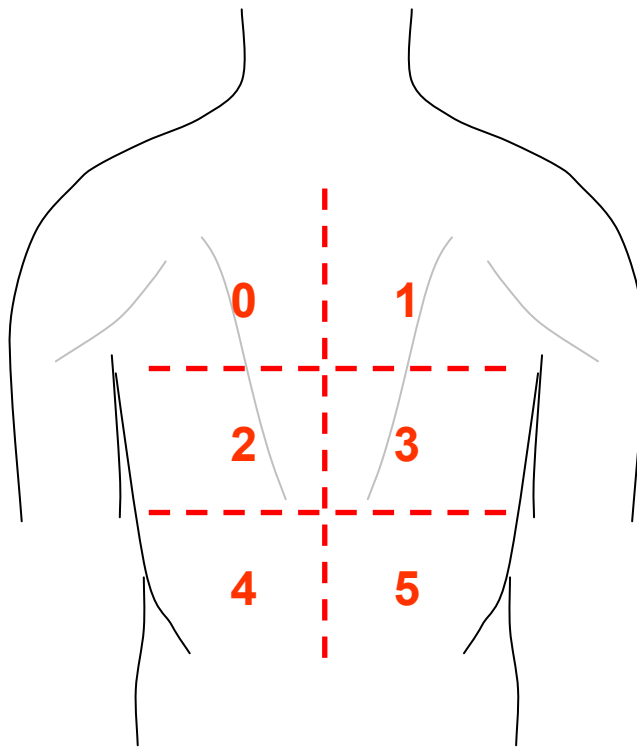
Figure 31 – Six locations of recorded lung sounds

Pneumonia and Asthma Score Assignment

The second and final stage of the software design involves the calculation of "scores" (similar to those generated by Murphy et al, 2004) for both asthma and pneumonia. The pneumonia score consists of the mean of the crackle ratios from each recording multiplied by the standard deviation of these ratios. This gives a higher pneumonia score to those who demonstrate localized problems, and a lower score to those whose problems are non-localized.

The asthma score consists of the mean of the wheeze ratios from each recording divided by the standard deviation of these ratios. This gives a higher asthma score to those who demonstrate uniform pathology.

These values are normalized to a scale of 0 to 10, in order to facilitate comparison between the pneumonia and asthma scores.

PART II – METHODS AND RESULTS
CHAPTER 5 – METHODS

Following the design stage of the device and building a working prototype, a method for

validating the final product was developed. To assess the functionality of the device, the

following hypothesis was proposed:

> *The prototype device can detect adventitious lung sounds and distinguish between*
>
> *asthma and pneumonia symptoms.*

Initially, this hypothesis was tested using freely available lung sounds recordings from the

R.A.L.E. Repository (R.A.L.E. "Adventitious Sounds"). It is necessary to note that the first

version of the algorithm for abnormal sound detection was based on the characteristics of some

R.A.L.E. sound recordings. To test the hypothesis and validate the device, the algorithm was

applied to recordings from the repository. The results were promising: crackles and wheezes

were consistently identified. Since the R.A.L.E. recordings were not originally acquired through

the hardware of our prototype, only the software portion of the device was validated in this

section.

To validate the hardware portion of the device, as well as the ability of the software to analyze

data recorded from this hardware, recordings from volunteers were collected. The first attempts

to record lung sounds with the BIOPAC® hardware were carried out on the authors of this

document. At first, a considerable amount of background noise was admitted into the recording.

Various methods of noise reduction were proposed and implemented as described in the design

chapter.

Clinical trial

In order to collect data necessary for optimization of the analysis algorithm and device validation, a clinical trial was conducted at a local branch of Fallon Clinic. The project sponsor, a pediatrician from the clinic, provided us with this ideal setting for the trial. While the primary purpose of the trial was to verify the main functionality of the system (i.e. to detect adventitious lung sounds and generate a diagnosis), the trial also provided us with invaluable feedback for our lung sound acquisition hardware and software designs, as the system was steadily used by doctors, nurses, and patients.

In order to gain approval for this trial, much preparatory work was done in efforts to adhere to Fallon Clinic's, as well as general, health practice policies and regulations. As a prerequisite for visiting the clinic and observing the pediatrician's work, we underwent training regarding Protected Health Information (PHI) and confidentiality agreements.

A Summary Form was completed, indicating the intentions, technicalities, and logistics of the study. Consent and Assent Forms were created for potential subjects in the trial. Because it was anticipated that most subjects would be minors, a parent or guardian was required to complete the Consent Form, while completion of the Assent Form was required for each subject. The study was approved by the Institutional Review Board (IRB) of Fallon Clinic. The IRB from Worcester Polytechnic Institute accepted the same forms. All three forms can be found in Appendix A.

The trial ultimately included 45 patients between the ages of 0 and 19. The device was brought to the clinic and was used for 2 months, the duration of the clinical trial. Data was periodically downloaded for analysis outside of the clinic.

Figure 32 – Clinical trial setup

Doctor Thomas Eder was the primary investigator for this clinical trial and was responsible for

subject recruitment as well as recording the lung sounds. Figure 32 demonstrates the setup of the

sound recording process as performed during the clinical trial. Dr. Eder maintained a journal for

this study where he noted the diagnosis of each patient in the study. (This diagnosis was made

based on the normal methods for diagnosing respiratory disorders, such as auscultation and x-ray

imaging.) The recordings made were used first in detection algorithm development and later to

test the device's diagnostic ability.

CHAPTER 6 – RESULTS AND ANALYSIS

The clinical trial provided invaluable feedback to the design process, in that the hardware and software could be tested in an environment very close to that in which it was designed to function clinically. Results were obtained for each of the major components of the design: hardware and software.

Hardware

Both the user (Dr. Eder) and the patients responded positively to queries regarding the ease of use and the patient-friendliness of the hardware design. Although there was no formal survey of the user perception involved in the study, the anecdotal data obtained indicate that users are satisfied with use of the system at the hardware level. Dr. Eder did not wish to use the included headset to monitor his recording, as he found it uncomfortable. (He did, however, auscultate each patient by stethoscope for the purposes of his own diagnosis.)

The functionality of the hardware system was also tested, although again not formally. Each of the recordings was reviewed both audibly and visually using a spectrogram. Little noise was found, and any that was present was generally at the very beginning or end of each recording, when Dr. Eder was presumably adjusting the position of the microphone. There was no evidence of amplitude clipping of the recorded signal, with the exception of two recordings where the infant subjects began crying, a sound which the system was not designed to record or analyze.

Dr. Eder also took part in reviewing several recordings, and noted that the recordings were accurate and similar to his stethoscope auscultation findings to the extent that he could recall.

Software

The raw recordings, as well as the results of the software analysis, are included in the accompanying CD. A sample recording and algorithm results from each class of patients are included and depicted schematically in Figure 33 (pneumonia), Figure 34 (asthma), and Figure 35 (normal respiratory health).

Subject 31 – clinically diagnosed with pneumonia

Wheeze mean: 0.0043   Crackle mean: 0.0087
Wheeze STD: 0.0038   Crackle STD: 0.0099
Asthma Score: 1.0116   Pneumonia Score: 4.4835

Figure 33 – Results from subject 31 (diagnosed with pneumonia)
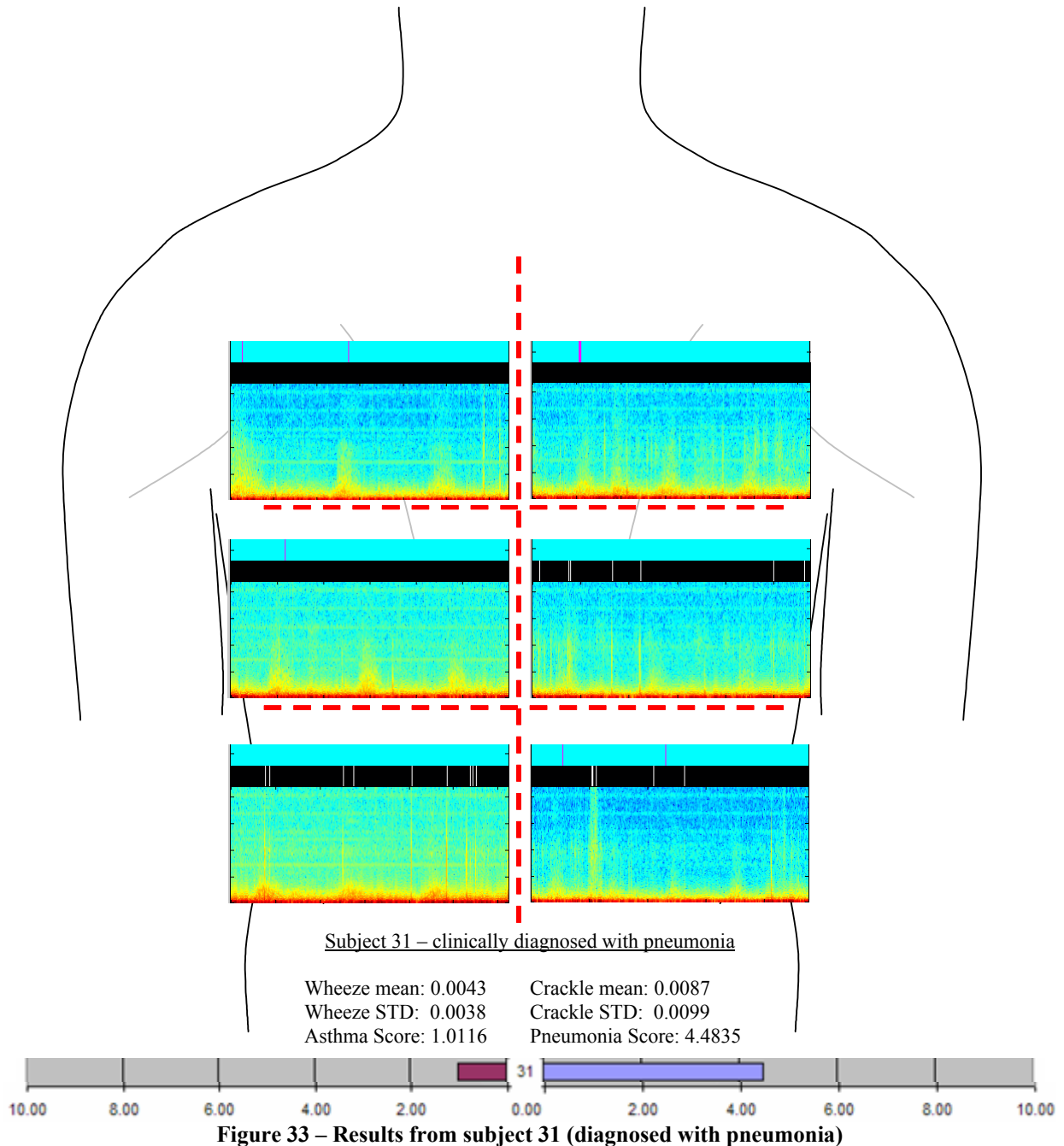
The spectrograms in each figure were generated from the recording produced in the section of the back in which the image is shown. Detected crackles are shown in white in the black bar above each spectrogram, and detected wheezes are shown in pink in the blue bar above each spectrogram. Calculated parameters are given below each group of spectrograms, and the bar at the bottom of each figure gives the asthma score (in red) and the pneumonia score (in blue).

Subject 8 – clinically diagnosed with asthma

Wheeze mean: 0.2378   Crackle mean: 0.0388
Wheeze STD: 0.1270   Crackle STD: 0.0204
Asthma Score: 9.2986   Pneumonia Score: 7.4537
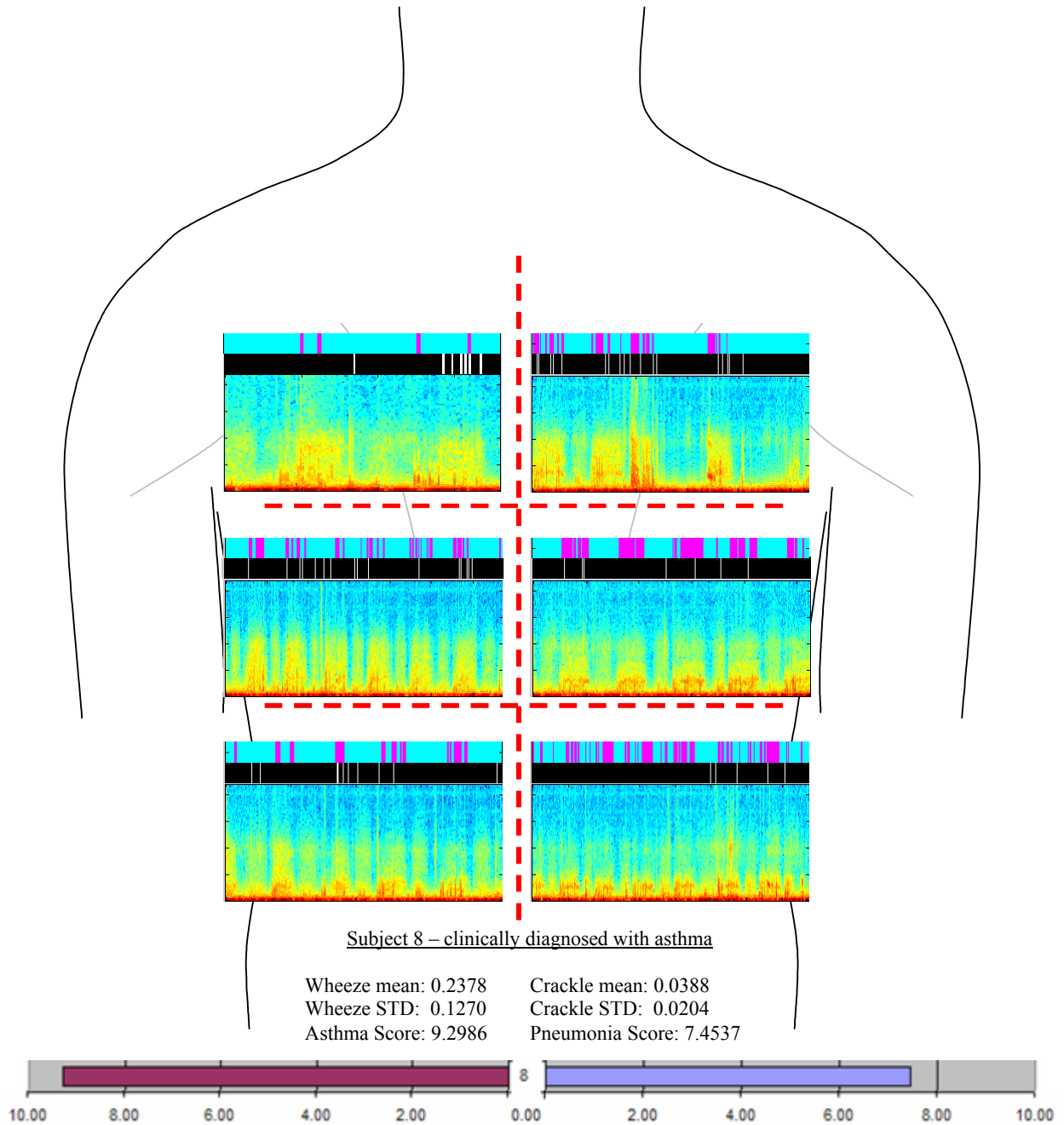
Figure 34 – Results from subject 8 (diagnosed with asthma)

Subject 5 – no clinical diagnosis - healthy

Wheeze mean: 0.0109   Crackle mean: 0.0027
Wheeze STD: 0.0220   Crackle STD: 0.0034
Asthma Score: 0.5387   Pneumonia Score: 3.5086
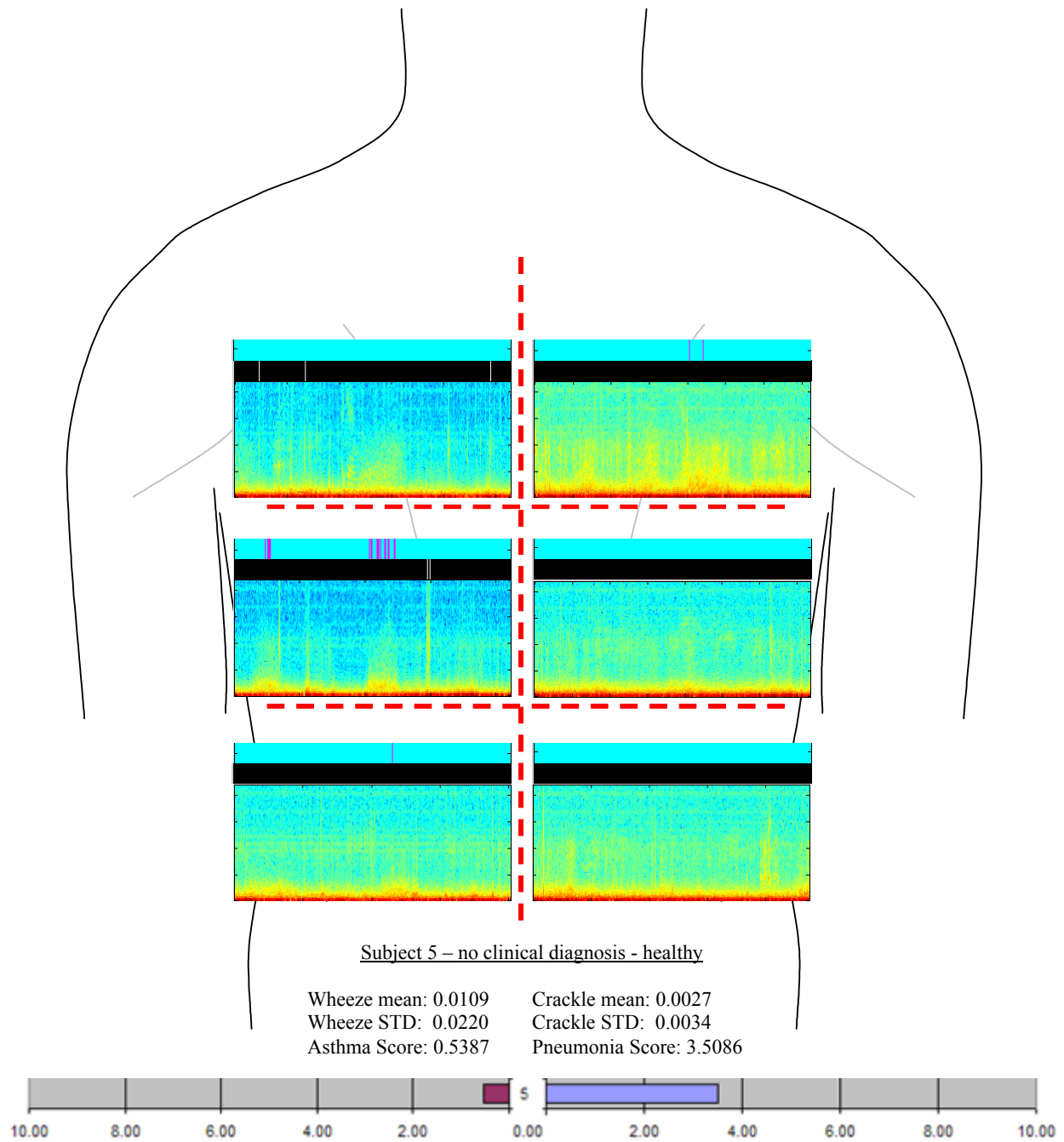
Figure 35 – Results from subject 34 (no clinical diagnosis - healthy)

The crackle and wheeze scores for each recording correlated well with qualitative judgments

from Dr. Eder's own auscultation, as well as visual scrutiny of the spectrograms produced. The

locations of the crackles and wheezes detected also correlated with a visual estimation, as can be

seen in the three sample results.

The asthma and pneumonia scores were generated for each subject by the calculation discussed in the design chapter; the scores are shown in Figure 36. The correlation between the diagnostic scores generated and Dr. Eder's qualitative diagnosis is much weaker than that for the detection stage of the software analysis.
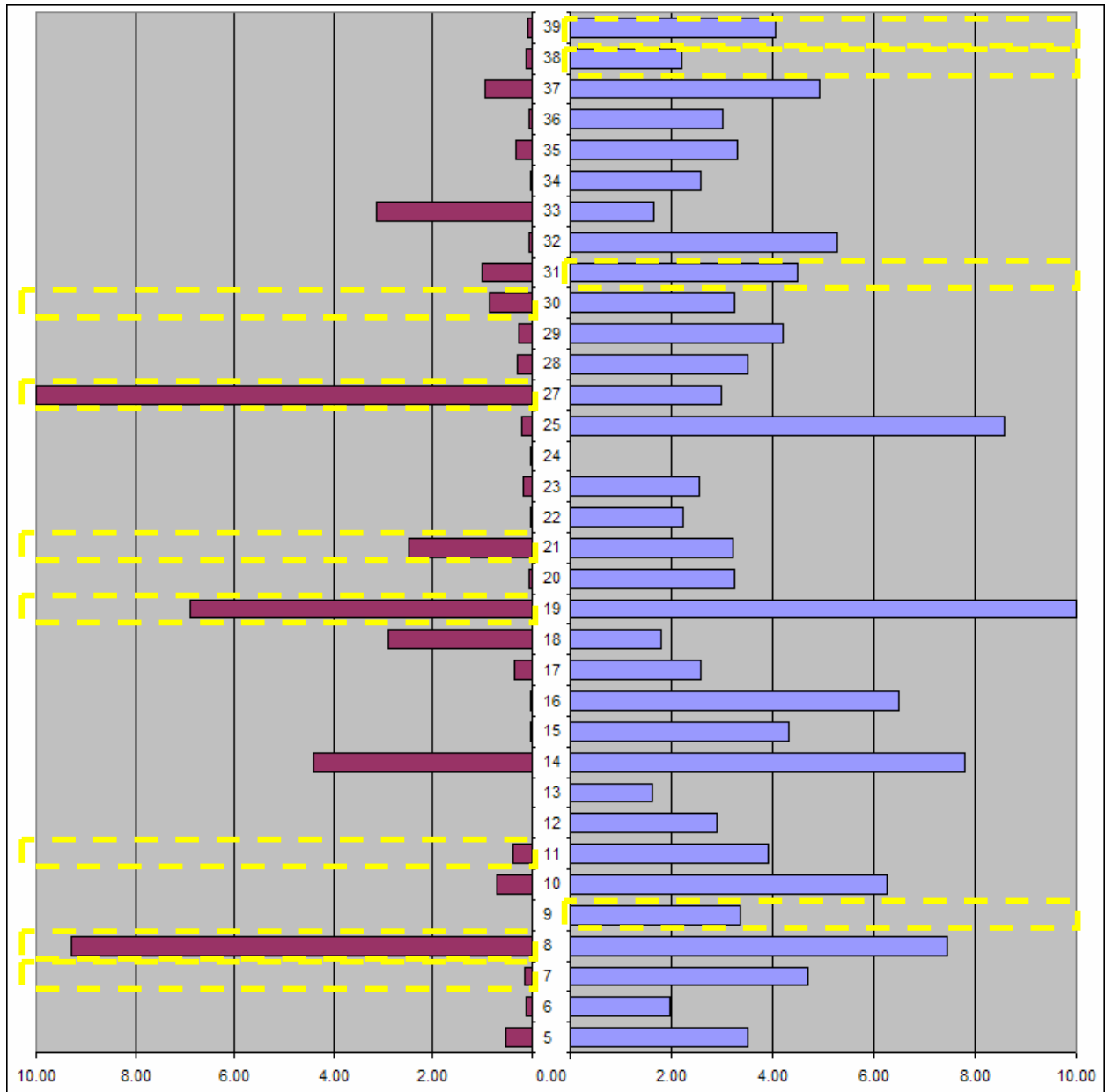
Figure 36 – Diagnostic scores. Red bars on the left are Asthma scores, blue bars on the right are Pneumonia scores. Central column identifies the study subject's number. Numbers 1-4 and 26 were test runs, and were therefore not included. Subjects that were diagnosed with asthma are indicated by yellow boxes in the left column, and those diagnosed with pneumonia are boxed in yellow in the right column.

CHAPTER 7 – DISCUSSION AND CONCLUSIONS

This project was successful in that the final device met many of the original objectives prescribed by the design process. The following summary will outline the specific objectives and how well the final device performed in each category.

Correct diagnosis:

- **Agrees with accepted values**

  This objective was not met completely by the current system. Although the detection algorithm was decidedly successful, many of the diagnostic scores generated by the system were not correlated to their associated clinical diagnoses. This casts doubt upon the initial assumption that the wheeze and crackle content of the lung sound can be used as the sole diagnostic tool for asthma and pneumonia. However, the most important contribution of this project to the field of pulmonary diagnostics was in the partial completion of this objective: the development and optimization of the algorithms to automatically recognize and classify various lung sounds.

- **Reproducible**

  Due to the limitations of the study (each subject was only seen by the doctor once, during a regular office visit) this parameter was not tested.

- **Reliable**

  During the two months spent in the clinical environment, the system did not show any signs of wear. This time period was as long as the study was able to run for; therefore, the reliability objective was met without reservations.

User friendly:

- **Intuitive output**

  The spectrograms produced by the device require minimal explanation and allow much information to be presented in a simple visual form. The final diagnosis scores signify the severity or likelihood of asthma or pneumonia in every subject. The objective of intuitive output was successfully met.

- **Fast analysis**

  Transfer of data from the acquisition system onto a computer with MATLAB® software is slightly time-consuming. Once the data have been transformed into a proper format, the analysis algorithm executes within seconds. Overall, the time required for the system to output a diagnosis is very reasonable compared to other methods currently available to a physician (i.e. x-ray imaging).

Patient friendly:

- **Sanitizable**

  The microphone can easily be sanitized. Alcohol wipes were used to clean the microphone during the clinical trial.

- **No harm**

  There is no reason to suspect any harmful effects from use of the device. During the trial period, none of the 45 subjects were injured or otherwise harmed by the study.

- **Non-frightening**

  No patient complaints were noted during the time of the trial. Following proper explanations of the study through the Assent and Consent Forms, patients of the clinic were willing to participate and did not seem to be uncomfortable or frightened by the device.

- **Small and light**

  The device has a personal computer as one of its components and the entire system was able to fit on a rolling cart (approximately 2 ft wide by 4 ft deep by 3 ft tall). A laptop computer could be used to significantly reduce the size of the system, but even in its current form, the system is easily moved from room to room.

Inexpensive/simple:

- **< $450**

  The total cost of this project was approximately $300. The majority of the cost was devoted to the purchase of the physiological microphone. The BIOPAC® equipment and the computer were borrowed from WPI, so the cost of those components is not included in the budget. The software used (AcqKnowledge® and MATLAB®) were also available through WPI.

- **8 months**

  The project began in September 2004 and was finished in April 2005, for a total duration of seven months (within the allotted timeframe).

CHAPTER 8 – RECOMMENDATIONS

By filling a specific research niche and establishing innovative lung sound analysis methods, this project opens up opportunities for continuing research. The field of automated lung disease diagnosis is very young. At the date of this publication, the authors were not able to identify any commercial products and only one research group (Murphy et al.) making strong progress towards automated diagnosis. The majority of the project objectives have been met through its design and clinical testing components. This chapter offers suggestions for expanding the project to fully meet all objectives.

A primary assumption (that the wheeze and crackle content of the lung sound can be used as the sole diagnostic tool for asthma and pneumonia) should first be re-evaluated. Although previous research has shown a correlation between adventitious lung sounds and specific respiratory disorders, it is possible that the correlation is not strong enough in some patients to serve as a primary indicator. After this step, future work should focus on algorithm improvements to the second stage (using the detected adventitious lung sounds to generate the diagnostic score). Follow-up studies can use the existing hardware and focus on improving the analytical component of the system.

A significant improvement to the device would be performing the analysis in real time. This can be accomplished by eliminating incompatibilities between BIOPAC® and MATLAB® or implementing the entire process in a package such as LabVIEW® or MATLAB®. This project attempted to use LabVIEW® in the initial stages of software development, but due to lack of expertise and time constraints, a working interface for LabVIEW® was never developed.

Hardware improvements could be made to improve the acquisition of the lung sounds. Beyond simply using a more sensitive microphone, better physiological sound isolation methods could be developed. One possibility would be to use a directional microphone to isolate lung sounds from the background noise. Another alternative would be to implement active noise cancellation. These recommendations for changes in hardware would likely elevate the cost of the system significantly, but the cost may be tolerable if the performance of the system improves noticeably.

To further validate the developed device and specifically the algorithm for diagnosis, a larger clinical trial should be conducted. There should be a shift from a young (infant to 19 years of age) population of the clinical trial to a wide range of ages, to validate the analysis and diagnosis capabilities of the system for a wider population. Also, it would be beneficial to the process of system optimization to have more subjects with pneumonia and asthma symptoms. An additional clinical trial could not only improve the design, but also improve the protocol used for recording lung sounds with the system. This would be helpful for any further use of the system, including any future commercial applications.

Future researchers can also continue the use of the clinical data acquired from this trial. During the initial stages of this project, publicly available lung sound recordings were used to validate the system. Raw data from this study can serve the same training and validation purpose for future studies. There is a plethora of information in the lung sound recordings collected in this study. Future researchers may be able to apply their own analysis algorithms to the data, in the hope of improving the analysis system designed herein, or even to detect abnormalities and diagnose disorders not considered in this study.

As it stands, our project has proven to be successful in many respects, and the technique of pulmonary diagnosis based on automated lung sound analysis is a promising possibility for widespread use in the future. Implementation of our recommendations to improve our system, combined with other research currently being conducted in the field, will help automated lung sound analysis to become a useful and commonplace diagnostic tool, lowering the cost of accurate disease identification and reducing the number of diagnostic errors.

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APPENDIX A – IRB FORMS

Contents:

Assent Form

Consent Form

Summary Form

INFORMATION AND ASSENT FORM

Study Name: Automated Stethoscope System

Sponsor: Worcester Polytechnic Institute (WPI)

Study Doctor: Dr. Thomas Eder
                    191 May St.
                    Worcester, MA 01602
                    (508) 368-7887

WHAT IS THIS STUDY ABOUT?

Dr. Eder wants to find out if a system that uses a microphone and a sound recorder can help to see if someone has lung or breathing problems, such as asthma or pneumonia. Pneumonia is when germs in your lungs cause infection. This may make it hard to breathe. This is similar to what would happen if someone had asthma. So what will be done is called a "research study."

Your Mom, Dad or Guardian will read more about the study. You can ask to read what the doctor gives them. You should talk to your Mom, Dad or Guardian about the study.

WHAT WILL HAPPEN TO ME IN THIS STUDY?

If you want to be in the study, your doctor will record your lung sounds with this system as he usually does during your checkup. He will place a microphone on different parts of your back in order to do this. This only takes about 5 minutes and it will only be done once.

If you have any questions about what will happen to you in the study, you can ask your doctor or nurse. If you do not want to do this, you can say you do not want to be in the study.

DO I HAVE TO BE IN THIS STUDY?

You do not have to be in the study if you don't want to. If you say 'Yes' now, you can say 'No' and stop later if you change your mind. No one will be angry with you if you say 'No'. The doctor will still take care of you.

WHO CAN I TALK TO ABOUT THE STUDY?

You can ask the doctor, your Mom, Dad or Guardian questions about the study any time.

ASSENT STATEMENT

Please check one box:

☐ Yes, I want to be in the study.   ☐ No, I do not want to be in the study.

_____   _____
Name of Child (Print)   Date of Birth

_____   _____
Signature of Child   Date

_____   _____
Name of Parent or Guardian (Print)   Relationship to Child

_____   _____
Signature of Parent or Guardian   Date

_____
Name of Person Explaining Assent (Print)

_____   _____
Signature of Person Explaining Assent   Date

PRINCIPAL INVESTIGATOR'S STATEMENT

I attest that I or my representative discussed this study with the above named participant and parent/guardian. This person had enough time to consider this information, had an opportunity to ask questions, and voluntarily agreed to participate in this study.

_____   _____
Signature of Principal Investigator   Date

Patient Information and Informed Consent Form for electronic recording of lung sounds

Study Name: Automated Stethoscope System

Sponsor: Worcester Polytechnic Institute

Study Doctor: Thomas Eder, M.D.
191 May Street
Worcester, MA 01602

Telephone: (508) 368-7887

You are being asked if you will approve your child's participation in a research study using an experimental (not approved by the FDA) lung sound recording system. It is your decision. Your child will also be asked if they want to take part in the study. You may decide to have your child in the study or he/she may not take part at all. If your child takes part in the study, you may remove him/her from the study at any time. In any case, your decision will not lead to any penalty or affect your child's regular medical care or any benefit to which your child is otherwise entitled. If there is anything you do not understand about the study after reading this information, please ask your child's study doctor or study staff member.

The purpose of this study is to help researchers find out if recording lung sounds using a specialized microphone and analyzing the sounds using a computer software system can significantly improve diagnosis through distinction between asthma and pneumonia. This study should not interfere with the traditional physical examination done by your child's doctor. The traditional diagnosis techniques used in the physical examination are described below and will also be discussed with you and your child by your child's doctor.

Your child will be in this study for approximately the same amount of time as your child's doctor would take using a traditional stethoscope, that is, about five (5) minutes. About sixty (60) patients at the Fallon Clinic, Inc. will be in this study; this will be the only site in the USA and Canada that will have patients participating in this study.

What will happen if you and your child decide to be in this study:

Your child's doctor will talk to you and your child about your child's health and give your child a physical exam. Your child's doctor will then listen to the child's lung sounds using the lung sound recording system.

Other Treatments

Asthma and pneumonia have very similar symptoms and, in addition to the doctor listening to lung sounds using the traditional stethoscope, many diagnoses need to be confirmed by X-ray pictures. It is hoped that this lung sound recording system will perform well enough to improve diagnosis without having to depend on X-rays as much.

Benefits

You and your child may not directly benefit from the study, but the hope is that distinction between asthma and pneumonia will be improved for the future.

Risks

There are no apparent risks for you or your child in this study.

Compensation

You will not be paid for taking part in this study.

Questions

Please feel free to ask any questions you may have about the study. If other questions occur to you later, you may ask Dr. Eder at (508) 368-7887. If at any time, during or after the study, you would like to discuss the study or your research rights with someone who is not associated with the research, you may contact the Saint Vincent Hospital/Fallon Clinic/Fallon Community Health Plan Institutional Review Board at 508-595-2205.

Confidentiality

Your child's doctor will record your child's study information on forms and have information that will be sent to Worcester Polytechnic Institute. The study sponsor will use the information to continue research and to test the automated stethoscope system. By signing this informed consent form you agree to allow this review of sound recordings from your child. All records in which your child's name appears will be kept confidential. Your child's name will never appear on any sponsor forms or in a report or publication.

By signing this form I agree to the use of my child's personal data for the purpose described in this form.

Study Funding

There is no funding

Volunteer's Statement

- ✓ I voluntarily agree to my child's participation in this study.

- ✓ I understand that the study sponsor, Worcester Polytechnic Institute, may stop the study at any time.

- ✓ I have read and understand this statement of informed consent and the risks described.

- ✓ I understand that I will receive a signed and dated copy of this consent form.

- ✓ I understand that I may withdraw my consent or withdraw my child from this study at any time.

- ✓ I have had a chance to ask questions and understand the answers given to all of my questions.

- ✓ I understand I have not waived any of my legal rights by signing this form.

▪▪

_____   _____
Signature of parent, guardian   Date

_____
Printed name of parent, guardian

_____
Relationship to study patient

****

_____   _____
Signature of person conducting informed consent discussion   Date

_____
Printed name of person conducting informed consent discussion

SAINT VINCENT HOSPITAL/FALLON CLINIC/FALLON COMMUNITY HEALTH PLAN/
RESEARCH REVIEW COMMITTEE/INSTITUTIONAL REVIEW BOARD

PROTOCOL SUMMARY SHEET FOR INVESTIGATIONS
INVOLVING HUMAN SUBJECTS

SECTION I

(must be completed)

TITLE OF PROJECT:

Automated Stethoscope System

Project #: 957

SIGNATURES:

Principal Investigator: _____   Date:
                                                     _____
                                                     Thomas J. Eder, M.D.

SVH Or Fallon Liaison: _____(none)_____   Date:
                                                     _____

(if not P.I.)

Study Personnel Information:

Principal Investigator (include institution /address/ and telephone number):

Thomas J. Eder, M.D.
Fallon May Street Clinic
191 May St.
Worcester, MA 01602
Phone: (508) 368-7887

Name of all other Fallon or Saint Vincent Hospital personnel involved in the study (i.e. physicians, nurses and other research staff):
        Sandra White, RN
        Carol Magnsen, RN
        Kathy Elloian, RN
        Susan Skonieczny, RN
        Lisa Skog, RN

SECTION I

Will residents, fellows, students, and temporary staff be involved in the study:
__Yes___ _____
        Yes   **No**

If yes, what functions will they be performing?
Students will install a lung sound recording system inside the clinic, and will collect the recorded data from the system for off-site analysis. The students do not anticipate being present during patient tests, but will train Dr. Eder to conduct the recording sessions.

Who will be responsible for ensuring that they are all properly trained?
Dr. Eder has already properly trained the students, and all procedural clearances have been arranged.

SECTION II

<p align="center">(must be completed)</p>

PHI Status:

Will "protected health information" be removed from Fallon Clinic/Saint Vincent Hospital/ Fallon Community Health Plan? (only employees are allowed to do this) to facilitate subject recruitment for this study?   No _No_ (skip to Section III)   Yes _____ (If yes, you must complete the following).
List names of employees (and their departments) allowed to take PHI off premises:

_____

_____
_____

_____
_____

SECTION III

Description of Human Subjects:

Describe how subjects will be initially identified. How will they be contacted (letter, telephone, or in person) and by whom (and where, i.e., telephone interviewer from their home, physician, coordinator from Research Office…)?

Study subjects will be recruited in person by Dr. Eder during regular office visits.

Approximately how many at our site 60   How many in total 60 (nationwide) or 60 (worldwide)

Ages : 0 to 22 years

Source of patients:

  **X   Fallon Clinic May St. Clinic – Pediatrics
            and/or
_____Saint Vincent Hospital _____ dept.
            and/or
_____clinic _____inpatient**

_____other (please elaborate)

SECTION IV

Patient Consent:

In order to use patient protected health information (PHI), staff must obtain a signed patient consent form with authorization (pre-approved by FC (Research Director) or SVH (CDRC)) attached, or receive a waiver by the IRB.

If you will be using a consent form, please complete the following and proceed to Section V.

Name of person(s) allowed to obtain consent: Dr. Eder

Will subjects include minors?   No__   Yes _X_ (A SEPARATE ASSENT FORM MUST ALSO BE

SUBMITTED)

Do you plan to obtain surrogate consent if patient is unable to give consent?   No__X__
Yes ____ If yes; why do you feel it may be necessary to obtain surrogate consent/substituted judgment?

If you will be requesting a waiver of Patient Authorization, please check here _____ , and read the following:
The eligibility criteria for a waiver are:
1)   The research could not practicably be conducted without a waiver, and
2)   The research could not practicably be conducted without access to and use of PHI.
3)   The use and disclosure of PHI involves no more than minimal risk to the patient and privacy of individuals, based on, at least, the presence of the following elements:
   i. An adequate plan to protect the identifiers from improper use and disclosure;
   ii. An adequate plan to destroy the identifiers at the earliest opportunity consistent with
      conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law; and
   iii. Adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, of for other research for which the use or disclosure of protected health information would be permitted

SECTION V
(must be completed)
Patient Information:

    1)   Where will the data be recorded?
           Dr. Eder will record patient information in a password-protected electronic database, or in a personal notebook, not accessible to any other person.

    2)   Please answer all of the following:

        i)   Where will patient's names be kept and who has access to these names?
            Names will be kept by Dr. Eder; only he will have access to them.

        ii)   How will data be encoded? (patient names, code number, patient initials?)
            Data will be encoded with a unique, arbitrary code number. Only Dr. Eder will have access to any privileged patient information (PHI).

        iii)   Where will data be kept and who has access?
            Encoded, anonymous data will be kept digitally in the computer recording system and may be accessed by Dr. Eder and the rest of the research team. This data only includes digital lung sound recordings.

        iv)   How will you protect the identifiers from improper use and disclosure?
            Only Dr. Eder will have access to any privileged patient information (PHI) or unique identifiers.

        If human subjects cannot be identified either directly or indirectly through identifiers linked to subjects, research is automatically eligible for a waiver and you may skip to section VI. All others, continue.

        v)   When will the identifiers be destroyed (must be the earliest opportunity)?   After all 60 have been enrolled. At that time Dr. Eder will destroy the list of names.

        vi)   What is the importance of this research? Explain.   To help differentiate between asthma and pneumonia

Background and purpose of the study: N/A

Describe the plan (including how long you expect research records will need to be kept):
N/A

Principal Investigator will ensure that all staff with access to the PHI will abide by the following: "No PHI collected for this research study will be reused or disclosed to any

other person or entity, except as required by law, or for authorized oversight of the research study."

_____   _____
           Principal Investigator's signature   **Date**

SECTION VI

<p style="text-align:center">(must be completed)</p>

Plan of investigation:

Please check off all types of PHI that will be collected:

_X_ **Name** (known only to Dr. Eder – used only to prevent duplicate subjects)
___**Address (street address, city, county, zip code (more than 3 digits)**
_X_**Birth date** (known only to Dr. Eder – used only to prevent duplicate subjects)
___**Telephone number**
_X_**Medical record number** (known only to Dr. Eder – used only to prevent duplicate subjects)
___***Names of relatives** (must list reason needed)
___***Names of employees**
___***Fax Number**
___***E-mail addresses**
___***Social security number**
___***Health plan beneficiary number account number**
___***Certificate/license number**
___***Any vehicle or device serial number**
___***Web url**
___***Internet protocol (IP) address**
___***Finger or voice prints**
___***Photographic images**
___***Any other unique identifying number, characteristics, or code (whether generally available in the public realm or not)**

***(must list reasons asterisked items are needed for study)**

_____

_____

_____

SECTION VI (continued)

Estimated start date: March 14, 2005

Time required to complete study: 1 Month

Inclusion criteria (include additional sheet, if necessary):

Subject falls into one of these three categories:
    Having characteristically normal respiratory health
    Having pneumonia
    Having asthma

Exclusion criteria (include additional sheet if necessary):

    Not willing to participate

SECTION VI (continued)

Describe, in detail, the plan of investigation, procedures and methods. Include procedures and forms to be collected at each visit, who will be conducting visits, interviews and/or reviewing medical records.

Subjects will be regular patients of May Street Pediatrics who agree to become part of the study by completing the consent form. Patients may be asked to join the study if, in the opinion of Dr. Eder, the sound produced by their lungs during breathing is characteristic of one of three populations: being of normal respiratory health, having pneumonia or an upper or lower respiratory infection, or being asthmatic. The study will consist of a single one to two minute lung-sound recording session for each subject, which can be conducted immediately following the subject's enrollment, or on a subsequent visit to Dr. Eder's office. In some cases, at the discretion of Dr. Eder, and with additional consent from the subject, one or two additional sessions may be conducted. (This will only occur if Dr. Eder believes that there may have been a change in the subject's health, and he or she has become a member of a different population.)

During the recording session, Dr. Eder will place a microphone, identical in size and shape to the diaphragm of a small stethoscope, on the subject's back, in six to eight positions. At each position, the subject will be asked to breathe at a steady pace slightly deeper than normal, while an audio recording is made of the sound propagating from the lungs. The procedure will be as similar as possible to standard stethoscopic respiratory auscultation.

Each recording will be labeled with only a number, with which will be associated only an age, sex, and respiratory diagnosis category (i.e. healthy, having pneumonia or a respiratory infection, or asthmatic). No personally identifiable information will leave the Fallon facility, and thus only Dr. Eder will be aware of the identity of each subject.

Will questionnaires be administered?   Yes____   No__X__   **(if yes, submit 5 copies of each)**

Will billing information or data be abstracted from medical records?   Yes_____ No_X__ **(if yes, submit 5 copies of data collection sheet)**

Will video or audiotapes be used?   Yes_____   No__X__   **(if yes, submit 1 copy)**

Will there be advertising?   Yes_____   No__X__

Please note that all advertising requires prior approval by the IRB. Fallon clinic advertising also needs approval by the communications department. Please list where advertising will be located (i.e., FC newsletter, postings at sites, Worcester telegram, radio…)

SECTION VII
Risks and Benefits:

Outline potential risks to subjects and methods of management if damage occurs:

No potential risks are identified for this study. The microphone will be sanitized before and after each use.

Outline potential benefit to subject and/or society in general:

Although there are no direct benefits to the subject, this research project will contribute to general scientific knowledge, and may ultimately lead to a better process of diagnosing respiratory disease.

Will the patient receive information about the results of the experimental procedures?

No.

Will the patient's primary physician receive information about the results of the experimental procedures?

Yes, within the May Street Clinic.

Under what circumstances will a patient be removed from the study?

At any time at which they no longer volunteer to be a participant.

SECTION VIII

Drugs:

If drugs are to be administered to subjects is the drug(s) approved by the FDA for this use?
N/A

If not, please indicate phase of study and supply the IND number: N/A

If medications are used in this trial, please explain the type of medication, its mechanism of action (if known) and how this action compares to those of the other drugs being studied as well as standard treatment.

DRUG NAMES INCIDENCE	DOSES	DRUG SIDE EFFECTS	%
N/A	N/A	N/A	N/A

Where will drugs be stored? (Please note that mass DPH regulations stipulate all drugs must be kept in a locked cabinet. Controlled substances should be dispensed through the pharmacy and kept in double locked cabinet.)   N/A

Who will administer drugs? N/A

SECTION IX

Medical Devices:

a) Name Of Device: TSD108 (Physiological Sounds Microphone), produced by BIOPAC Systems, Inc.
b) FDA Approved? _____ Yes __X__ No
C) If Not Approved: IDE#
D) _____ Significant Risk Device __X__ Non-Signif. Risk Device
 (Please Include Supporting Materials From Sponsor & Any
    Correspondence With FDA)

The Physiological Sounds Microphone was developed to use with the BIOPAC acquisition system. This system – consisting of a microphone connected to a analog-digital converter – is designed for use on humans for research and educational applications. The system is used extensively at many educational institutions, including WPI, to allow students to make non-invasive recordings of their own body sounds and bioelectric signals.

This system does not pose any significant risk to the subjects in this study.

SECTION X

Funding & Support:

Source of funding: please include name of sponsor, and explain how this project will be supported.

Worcester Polytechnic Institute is the sponsor for this study; no special funding is required.

What clinic/hospital resources will be required to conduct the study?

A single lockable room housing the computer recording system will be allocated for the study.

Personnel (include nursing, clerical, medical record, pharmacy, MIS requirements & patient accounts/billing):   the PI and some nursing staff

Equipment: none

Supplies: alcohol swaps

Who will be financially responsible for the following procedures/ office visits required for the study? Please be specific as to type and number of visit/tests(s). Please also indicate whether or not you consider these standard care.

for office visits?   Study will be conducted during regular patient office visits; therefore, no extended financial responsibilities exist.

for medications? N/A

for labs? (include number of blood & urine specimens and amount of blood to be drawn) (please indicate whether labs will be processed by PathLab or sent to a central lab).   N/A

for x-rays? N/A

for ekgs and other tests? (identify other tests) N/A

SECTION X (continued)

(must be completed)

Will health care professionals receive finder's fees for referring patients to the study? No.

Will the patient be financially reimbursed for participation? If yes, elaborate. No.

FORM REVISED 11/3/03
mc

FALLON CLINIC
RESEARCH CONFLICT OF INTEREST POLICY

SUMMARY: It is the policy of the Fallon Clinic, Inc. that its staff act in accordance with the highest ethical and professional standards in the conduct of research. This policy provides a definition of conflict of interest, investigator/staff disclosure and reporting requirements and how these conflicts will be reviewed and resolved. Any question of a conflict of interest must be resolved by the Research Department (and the IRB and Fallon Clinic Medical Director, if necessary), not the individual researcher or other staff.

DEFINITION: A conflict of interest exists when financial considerations or publication rights compromise or have the appearance of compromising one's professional judgment and independence in the design, conduct or publication of research.

The following situations are examples of potential conflicts of interest and are reportable to the Research Department:

- Any equity interest in the sponsoring company exceeding $ 10,000 or 5% ownership during the conduct of the research or within one year after termination of the research study
- Serving as a paid consultant or speaker on behalf of the sponsor
- Any proprietary interests in the products including patents, trademarks, copyrights and licensing agreements
- Any initial payments to the investigator or institution that goes beyond what is required to carry out the research study
- Any financial gain for the investigator/staff, IRB member or the institution if the study shows an outcome favorable to the research sponsor
- Any agreement with a sponsor that restricts publication or delays access to research information other than short-term delay to allow sponsor the opportunity to review any potential publications
- Any payment for services or royalties paid directly to investigators or consultants that could exceed $10,000 per year on a particular research project
- Any recruitment bonuses paid directly to the investigator or staff

POLICY APPLIES TO THE FOLLOWING INDIVIDUALS:
- All Fallon investigators conducting research at the Clinic
- Investigator's spouse, dependent or any associated entity
- All study coordinators participating in a research project
- Fallon consultants
- Other clinic or hospital staff

FALLON CLINIC SUBMISSION AND REVIEW OF DISCLOSURE FORMS

- **Research staff**: Will be required to complete and submit "Research Conflict of Interest Certification" Form, along with the Research Finance Report, to the Fallon Clinic Medical Director of Research, prior to approval of each study. Staff will also be asked to update this form annually (at the time of continuing review) for each ongoing study. The IRB Administrator will submit the forms to the Fallon Clinic Medical Director of Research. He will forward information about any potential conflicts of interest, along with his recommendation, to the Institutional Review Board. If a conflict of interest that may compromise the conduct of the study is identified, the information will be forwarded to the Fallon Clinic Medical Director who will determine whether further action will be needed
- **Other clinic or hospital staff:** Proposals for recruitment bonuses to physicians, nurses or other clinic or hospital staff must be submitted to the IRB for approval. The amount of the stipend must be in direct relationship to the time required to identify and refer appropriate patients.

DISCLOSURE TO RESEARCH SUBJECTS:

All Patient Consent Form(s) will include the following disclosure information:
- Name of sponsor
- A clause that discloses that the organization and/or staff may be compensated for participation in the study. A recommended clause is, "Fallon Clinic (include Saint Vincent Hospital if applicable) and/or the doctors involved in this trial may receive funding from the study sponsor for conduct of this research study. If you have any questions about this, please discuss them with the Institutional Review Board at (508) 852-0600, extension 33058."

FALLON CLINIC
RESEARCH CONFLICT OF INTEREST
CERTIFICATION FORM

NAME: Thomas J. Eder, M.D.

DEPARTMENT: Pediatrics

PROJECT # AND TITLE OF PROJECT: Automated Stethoscope System

NAME OF SPONSORING COMPANY: Worcester Polytechnic Institute

❑   **I HAVE NO POTENTIAL CONFLICTS OF INTEREST AS DEFINED IN THE FALLON CLINIC RESEARCH CONFLICT OF INTEREST POLICY.**

❑   **I HAVE POTENTIAL CONFLICTS OF INTEREST AS FOLLOWS (details should be included below):**

   ❑   Equity interest in the sponsoring company (that exceeds $ 10,000 or 5% ownership) during the conduct of the research or within one year after termination of the research study **(including that to my spouse or children)**

   ❑   Serve as a paid consultant or speaker on behalf of the sponsor (including spouse or children)

   ❑   Payment for services or royalties paid directly to investigators or consultants that could exceed $10,000 per year on a particular research project.

   ❑   Other

If potential conflict of interest is indicated above, please explain why it will not impact conduct of the study.

_____   _____

Signature   Date

Fallon Clinic Financial conflict of interest.doc
12/10/2002.

APPENDIX B – ELECTRONIC STETHOSCOPES

Contents:

Andromed: Androscope Stethos

Meditron: The Meditron Stethoscope

Cardionics: E-Scope II

Andromed: Androscope Stethos

Specifications:

Supply Voltage:	3.0VDC
Supply Current:	3.5mA (typical)
Temperature:	0ºC to 50ºC (operation); -20ºC to 60ºC (storage)
Humidity:	15 to 95%RH
Altitude:	Up to 4550m
Length:	Model ST28A00: 28" (71cm) length Model ST40A00: 40" (102 cm) length
Weight:	~ 145g-165g

http://www.andromed.com

Meditron: The Meditron Stethoscope

Specifications:
- Exceptional Sound Quality
- Extended frequency settings from 20 - 20 000 Hz
- Connectable to PC for PCGs with ECG
- Easy-to-use

The Essentials of Auscultation

The Meditron Stethoscopes is based on innovative, patented sensor technology, and outperforms all other stethoscopes both in prize awarded design and sound quality.

Its sensor technology gives you the freedom to perform auscultation under the most demanding situations or in your office as usual. Listen through clothes, bandages, thick fatty tissue or fur, and still hear more and more accurately than before.

Foremost, the Meditron Stethoscopes has revolutionized the way doctors and vets can perform auscultation in their practices. Hearing, visualizing and documenting auscultation findings are now possible, with the touch of a button.

Early Diagnosis - Better Prognosis

Use the Meditron Stethoscopes, and improve your auscultation skills. Hear sounds that are present at early stages in infectious and functional diseases. This will increase your chances of making earlier and more correct diagnoses, and thereby improve your patient's prognosis.

Document your findings, analyze them and view them as PCG's with ECG on your PC. This will reduce uncertainty, save time and secure your work.

A second opinion is also only a touch away, due to a special e-mail function in the Meditron Analyzer ECG software.

Unique Features
- Exceptional Sound Quality
- 3 predefined frequency settings - tune into the sounds you wish to focus on.
  - Heart 20-600 Hz
  - Lung 200 20 000 Hz
  - Extended frequency setting 20-20 000 Hz
- Amplification of sound up to 30 times greater than conventional stethoscopes
- Connectable to PC for hearing, visualizing and documenting auscultation findings
- On/off button with timer function (3 min.)
- Adjustable ear plugs
- 2 Batteries - lifetime 200 hours 2-4 years normal usage)
- Price awarded design.

http://www.meditron.no/

Cardionics: E-Scope II

Specifications:

Maximum Output: 124 dB SPL, undistorted

The maximum volume of the E-Scope II is approximately 30x louder than an acoustic stethoscope

Audio Gain: 27 dB @ 200 Hz (SPL/SPL) Peak output for both heart and
breath sounds.

Heart Sounds: 100-240 Hz (-3dB) SPL SPL
45-900 Hz (-20 dB)

Breath Sounds: 125 to 350 Hz (-3dB)
50-2000 Hz (-20dB)

Weight: 6.2 oz

Cord Length: 38 inches from chest piece to binaural earpieces

Restart: 2 minute timer

Battery: One AAA battery can power the E-Scope II for approximately 6 months at 6 hours usage per week, or 30 uses per day.

Warranty: One year Warranty. Lifetime technical support.

http://www.cardionics.com

APPENDIX C – ALGORITHM IMPLEMENTATIONS

Source code for crackle detection:

```matlab
function crackle_ratio = cracklefind(y,Fs)
NFFT = 2048;
WINDOW = 128;
MINFRACTION = 0.6;
MAXFRACTION = 1.0;
MINFREQ = 200;
MAXFREQ = 1500;
MINTIME = 0;
MAXTIME = 9.5;
% Defining width of the crackle
widthMIN=1;
widthMAX=3;

DISPLAY_IMAGES = 0;

[B,Freqs,Times] = specgram(y,NFFT,Fs,WINDOW);
MINFREQ = sum(Freqs <= MINFREQ);
MAXFREQ = sum(Freqs <= MAXFREQ);
MINTIME = sum(Times <= MINTIME);
MAXTIME = sum(Times <= MAXTIME);

%image is B(freq,time)
specdata = (20*log10(abs(B)))';
if DISPLAY_IMAGES
    figure
    imagesc(Times(MINTIME:MAXTIME),Freqs,specdata(MINTIME:MAXTIME,:)'),axis xy, colormap('jet')
end

howbig = size(specdata);

baseline = -20;
BWdata = (specdata > baseline);

if DISPLAY_IMAGES > 2
    figure
    imagesc(Times(MINTIME:MAXTIME),Freqs(MINFREQ:MAXFREQ),...
        BWdata(MINTIME:MAXTIME,MINFREQ:MAXFREQ)'),axis xy, colormap('jet')
end
line = (mean(BWdata(MINTIME:MAXTIME,MINFREQ:MAXFREQ),2) > MINFRACTION)' .* ...
    (mean(BWdata(MINTIME:MAXTIME,MINFREQ:MAXFREQ),2) < MAXFRACTION)';

newline = zeros(size(line));

ones=0; % ones counter

for i=1:size(line,2)
    % increment the counter of pre-crackles
    if line(i)
        ones = ones + 1;
    end

    % a crackle is defined as a set width of 1s followed by a 0
    if (line(i) == 0)
        if (ones >= widthMIN) & (ones <= widthMAX)
            newline(i) = 1;
        end
        ones=0;
    end
end

if DISPLAY_IMAGES > 2
    figure
    imagesc(Times(MINTIME:MAXTIME),Freqs,line),axis xy,colormap(jet)
end
```

```matlab
if DISPLAY_IMAGES
    figure
    imagesc(Times(MINTIME:MAXTIME),Freqs,newline),axis xy,colormap('cool')
end
crackle_ratio = mean(newline);
end
```

Source code for wheeze detection:

```matlab
function wheeze_ratio = wheezefind(y,Fs)
%Spectrogram parameters:
NFFT = 2048;
WINDOW = 128;
numoverlap = 108;

DISPLAY_IMAGES = 0;

%window of interest (Hz, Seconds)
MINFREQ = 200;
MAXFREQ = 2200;
MINTIME = 0;
MAXTIME = 10;

%define length of wheezes
widthMIN=25;
widthMAX=10000;

 [B,Freqs,Times] = specgram(y,NFFT,Fs,WINDOW,numoverlap);
MINFREQ = sum(Freqs <= MINFREQ);
MAXFREQ = sum(Freqs <= MAXFREQ);
MINTIME = sum(Times <= MINTIME);
MAXTIME = sum(Times <= MAXTIME);

B = abs(B);

if DISPLAY_IMAGES
    figure
    imagesc(Times(MINTIME:MAXTIME),Freqs,20*log10(B(:,MINTIME:MAXTIME))),axis xy, colormap('jet')
end

%image is B(freq,time)
specdata = B';
peaksmap = specdata;

% %%%%%%%%VECTOR METHOD%%%%%%%%%%%
the_mean = repmat(mean(specdata(MINTIME:MAXTIME,:),2),1,length(Freqs));
column = specdata(MINTIME:MAXTIME,:) - the_mean;
variance = repmat(sqrt(1./(length(Freqs)*sum((column.^2),2))),1,length(Freqs));
column = column ./ variance;
peaks = (column > (.5*variance)) .* ((column - circshift(column,[0 1])) > 0) .* ((column - ...
    circshift(column,[0 -1])) > 0);
peakdisp = peaks | circshift(peaks,[0 1]) | circshift(peaks,[1 1]) | circshift(peaks,[1 0]);

if DISPLAY_IMAGES
    figure
    imagesc(Times(MINTIME:MAXTIME),Freqs(MINFREQ:MAXFREQ),...
        (peakdisp(MINTIME:MAXTIME,MINFREQ:MAXFREQ)')),axis xy, colormap('jet')
end

peakscore = peaks .* ((column - (circshift(column,[0 1]) + circshift(column,[0 2]) + ...
    circshift(column,[0 3])) / 3) > (2.5*variance));
peakscore = peakscore + peaks .* ((column - ((circshift(column,[0 -1]) + ...
    circshift(column,[0 -2]) + circshift(column,[0 -3])) / 3)) > (2.5*variance));
peakscore = peakscore + peaks .* (((column - circshift(column,[0 1])) > (2*variance)) .* ...
    ((column - circshift(column,[0 -1])) > (2*variance)));
peakscore = peakscore + peaks .* (((column - circshift(column,[0 2])) > (3.5*variance)) .* ...
    ((column - circshift(column,[0 -2])) > (3.5*variance)));
peakscore = peakscore - peaks .* (1 - (column - ((...
    circshift(peaks,[0 1]) + circshift(peaks,[0 2]) + circshift(peaks,[0 3]) + ...
    circshift(peaks,[0 -1]) + circshift(peaks,[0 -2]) + circshift(peaks,[0 -3])) / 6) > 0));
peakscore = peakscore + peaks .* ((column - ((...
    circshift(column,[0 1]) + circshift(column,[0 2]) + circshift(column,[0 3]) + ...
    circshift(column,[0 -1]) + circshift(column,[0 -2]) + circshift(column,[0 -3])) / 6)) ...
    > (3*variance));
peaksmap = peakscore;
%%%%%%%%%%%%%%%%%
```

```matlab
if DISPLAY_IMAGES
    figure
    imagesc(Times(MINTIME:MAXTIME),Freqs(MINFREQ:MAXFREQ), ...
        (peaksmap(MINTIME:MAXTIME,MINFREQ:MAXFREQ)')),axis xy, colormap('jet')
end

line = sum(peaksmap(MINTIME:MAXTIME,MINFREQ:MAXFREQ),2);
if DISPLAY_IMAGES
    figure
    imagesc(Times(MINTIME:MAXTIME),Freqs(MINFREQ:MAXFREQ),line'),axis xy, colormap('jet')
end

newline = zeros(size(line));
ones=0; % ones counter
prom=0;

for i=1:length(line)
    % increment the counter of pre-wheezes
    if line(i)
        prom = prom + line(i);
        ones = ones + 1;
    end

    % a wheeze is defined as a set (width*prominence) product of 1s followed by a 0
    if (line(i) == 0)
        if (prom >= widthMIN) & (prom <= widthMAX)
            %mark with a band
            for n = 0:ones
                if i-n > 0
                    newline(i-n) = 1;
                end
            end
        end
        ones=0;
        prom=0;
    end
end

if DISPLAY_IMAGES
    figure
    imagesc(Times(MINTIME:MAXTIME),Freqs,newline'),axis xy,colormap('jet')
end

wheeze_ratio = mean(newline);
end
```

APPENDIX D – DATA FROM CLINICAL TRIAL

<u>Adventitious Sounds Detection Data (First Stage of Software Algorithm)</u>

Subject	Recording	Crackles	Wheezes	MEAN & STDEV Crackles	MEAN & STDEV Wheezes
0	0	0.00735294	0	0.00173833	0.002498902
0	1	0	0.01257445	0.00285199	0.005029932
0	2	0.00154799	0.00241896		
0	3	0	0		
0	4	0	0		
0	5	0.00152905	0		
1	0	0.0052356	0	0.001736495	0.008669322
1	1	0.00204918	0.01474359	0.001920033	0.010111027
1	2	0	0.02364217		
1	3	0.00160514	0		
1	4	0	0		
1	5	0.00152905	0.01363017		
2	0	0	0.00535236	0.010064643	0.003549922
2	1	0.00498753	0.00311769	0.018852607	0.002139285
2	2	0.00462963	0.00289855		
2	3	0.00247525	0.00386698		
2	4	0.04829545	0		
2	5	0	0.00606395		
3	0	0.00660793	0.02687802	0.002170237	0.020045132
3	1	0	0	0.002682609	0.018859679
3	2	0	0.01181281		
3	3	0.00327869	0.026653		
3	4	0	0.05100539		
3	5	0.0031348	0.00392157		
4	0	0.00665188	0.02081888	0.008956057	0.028944413
4	1	0.01794872	0.02487961	0.008090522	0.01075061
4	2	0.00226757	0.04113475		
5	0	0.01879699	0.03055229	0.005897943	0.01254912
5	1	0.00506329	0	0.007786268	0.014234494
5	2	0	0		
5	3	0	0		
5	4	0	0.02580645		
5	5	0.01152738	0.01893598		
6	0	0.00821918	0	0.002740132	0.01095028
6	1	0	0.00690955	0.003421076	0.021952651

6	2	0.00516351	0.05540613		
6	3	0	0		
6	4	0	0.003386		
6	5	0.0030581	0		
7	0	0.00972763	0.00486618	0.003277062	0.004838422
7	1	0	0	0.003754429	0.004112254
7	2	0.00534759	0.00780814		
7	3	0	0.00636075		
7	4	0.00152905	0.00999546		
7	5	0.0030581	0		
8	0	0.05645161	0.05555556	0.038880633	0.237834697
8	1	0.0596206	0.20695505	0.020386559	0.12699259
8	2	0.05399568	0.22079676		
8	3	0.01939058	0.40034662		
8	4	0.03071672	0.17822839		
8	5	0.01310861	0.3651258		
9	0	0	0	0	0.015768285
9	1	0	0	0	0.018650654
9	2	0	0.02173913		
9	3	0	0.0029703		
9	4	0	0.04733219		
9	5	0	0.02256809		
10	0	0.01552106	0.00346981	0.00822094	0.004017903
10	1	0.01223242	0.0052531	0.007229477	0.002556552
10	2	0	0		
10	3	0.00611621	0.00318037		
10	4	0.01545595	0.0077332		
10	5	0	0.00447094		
11	0	0.01581028	0.00618047	0.015986892	0.015507725
11	1	0.0166113	0.00728408	0.002050173	0.015725622
11	2	0.01935484	0		
11	3	0.01587302	0.0417495		
11	4	0.01522843	0.02696273		
11	5	0.01304348	0.01086957		
12	0	0	0.00772376	0.000254842	0.00219597
12	1	0	0.00272603	0.000624232	0.003019445
12	2	0	0		
12	3	0	0.00272603		
12	4	0.00152905	0		
12	5	0	0		
13	0	0	0	0.000526615	0.000245458
13	1	0	0	0.000815853	0.000601248
13	2	0.00158983	0		

13	3	0	0		
13	4	0.00156986	0.00147275		
13	5	0	0		
14	0	0.03030303	0.02525253	0.02536623	0.019169305
14	1	0.04395604	0.02257115	0.014767527	0.009801144
14	2	0.01166181	0.00456204		
14	3	0.01554404	0.0242915		
15	0	0	0.00136302	0.001315402	0.00331651
15	1	0	0.00582319	0.002456877	0.003055749
15	2	0	0.00811771		
15	3	0.0017762	0.00277778		
15	4	0	0		
15	5	0.00611621	0.00181736		
16	0	0.00152905	0.00272603	0.002850387	0.01044568
16	1	0.00395257	0.0148423	0.001063097	0.006390739
16	2	0.00343643	0.01988178		
16	3	0.00152905	0.01226715		
16	4	0.0030581	0.00732936		
16	5	0.00359712	0.00562746		
17	0	0.01587302	0.00247934	0.005450995	0.003231405
17	1	0.0021645	0	0.00573389	0.004995137
17	2	0.0025641	0.01283079		
17	3	0	0		
17	4	0.0078125	0.0040783		
17	5	0.00429185	0		
18	0	0.05463183	0.1218425	0.011642722	0.022129497
18	1	0.0019802	0	0.021291181	0.048948038
18	2	0	0		
18	3	0.00225225	0		
18	4	0.00190114	0.00297089		
18	5	0.00909091	0.00796359		
19	0	0.05660377	0.14201183	0.031048133	0.342677602
19	1	0.04281346	0.49386642	0.01895449	0.136382453
19	2	0.03318584	0.31163435		
19	3	0.02752294	0.40208996		
19	4	0	0.24107143		
19	5	0.02616279	0.46539162		
20	0	0.00179211	0.03533371	0.00190136	0.010759027
20	1	0	0	0.002815883	0.013198852
20	2	0	0.01118568		
20	3	0.00724638	0.01284958		
20	4	0	0		
20	5	0.00236967	0.00518519		

21	0	0.01428571	0.03910615	0.015519825	0.031522077
21	1	0	0	0.013590629	0.038956196
21	2	0.03183521	0.02925688		
21	3	0.00959693	0.01140456		
21	4	0.00529101	0.00441258		
21	5	0.03211009	0.10495229		
22	0	0	0	0.000916762	0.002957652
22	1	0.00243309	0.01294745	0.001434339	0.005256909
22	2	0	0		
22	3	0.00306748	0.00479846		
22	4	0	0		
22	5	0	0		
23	0	0.00546448	0.00341491	0.003764653	0.001231842
23	1	0	0	0.004293751	0.001916596
23	2	0	0		
23	3	0.00794913	0.00397614		
23	4	0	0		
23	5	0.00917431	0		
24	0	0	0	0.001033792	0
24	1	0	0	0.001601777	0
24	2	0	0		
24	3	0.00314465	0		
24	4	0.0030581	0		
24	5	0	0		
25	0	0.00584795	0.0195003	0.005034857	0.013291095
25	1	0.00911162	0.0113879	0.003339467	0.006164969
25	2	0.00507614	0.02065131		
25	3	0	0.01349206		
25	4	0.00252525	0.00394945		
25	5	0.00764818	0.01076555		
27	0	0.07	0	0.034709783	0.030362685
27	1	0.02540835	0.02101079	0.024558753	0.040584469
27	2	0.03007519	0.01057579		
27	3	0.01335559	0.08986416		
28	0	0.01223242	0.0081781	0.00590787	0.008677807
28	1	0.00611621	0.0081781	0.004354818	0.00986802
28	2	0	0		
28	3	0.00486618	0.00380518		
28	4	0.00917431	0.02781641		
28	5	0.0030581	0.00408905		
29	0	0.01580135	0.00353357	0.00350881	0.011582373
29	1	0.00310559	0.00678952	0.006165417	0.010933012

29	2	0	0.02885482		
29	3	0	0		
29	4	0	0.02024922		
29	5	0.00214592	0.01006711		
30	0	0.02380952	0.00802292	0.006334643	0.01953557
30	1	0	0.00219419	0.011672196	0.023900631
30	2	0	0.05474934		
30	3	0.00152905	0.01317583		
31	0	0.00225225	0.00634697	0.008735558	0.004252672
31	1	0	0.00796524	0.00987123	0.003775025
31	2	0	0.00302572		
31	3	0.01767677	0		
31	4	0.02331002	0		
31	5	0.00917431	0.0081781		
32	0	0.00458716	0.00181736	0.002039777	0.00501976
32	1	0	0.00499773	0.002679563	0.003781474
32	2	0.00612245	0.00574713		
32	3	0	0.00272603		
32	4	0	0.01210428		
32	5	0.00152905	0.00272603		
33	0	0.00323625	0	0.013568502	0.02276094
33	1	0	0	0.019705635	0.054647348
33	2	0.01603206	0		
33	3	0.05166052	0.13429395		
33	4	0.01048218	0		
33	5	0	0.00227169		
34	0	0	0	0.001858498	0.002889407
34	1	0.00176367	0	0.001983854	0.00447371
34	2	0.00190476	0.00357569		
34	3	0.00542495	0.00225989		
34	4	0	0.01150086		
34	5	0.00205761	0		
35	0	0	0.01544752	0.004942132	0.029474678
35	1	0.00456621	0	0.005675549	0.035598978
35	2	0.00638298	0.0505992		
35	3	0.01376147	0.08132667		
35	4	0	0		
36	0	0	0.00447177	0.00204259	0.007740647
36	1	0.00244499	0.00612089	0.002833846	0.010174691
36	2	0.00255102	0		
36	3	0	0		
36	4	0	0.02733333		
36	5	0.00725953	0.00851789		

37	0	0.02022472	0.10892481	0.011214105	0.054972523
37	1	0.01223242	0.1138756	0.00715425	0.044505394
37	2	0.01892744	0.02371542		
37	3	0.004914	0.04221028		
37	4	0.003367	0.01789474		
37	5	0.00761905	0.02321429		
38	0	0.00810373	0	0.003644198	0.00242314
38	1	0.00458716	0	0.002649049	0.004401852
38	2	0.0030581	0.00363471		
38	3	0.0030581	0		
38	4	0	0		
38	5	0.0030581	0.01090413		
39	0	0	0	0.002293578	0.003521125
39	1	0.00611621	0.00363471	0.002927912	0.003447691
39	2	0	0.00227169		
39	3	0.0030581	0.0081781		

Scoring Data (Second Stage of Software Algorithm)

Subject	Asthma Score	Pneumonia Score	Normalized Asthma Score	Normalized Pneumonia Score
5	4.5923E-05	0.881599282	0.538730685	3.508681971
6	9.3742E-06	0.498813571	0.109970433	1.985230954
7	1.23035E-05	1.176586224	0.144334539	4.682702173
8	0.000792642	1.87282342	9.298631758	7.453660529
9	0	0.845454801	0	3.364830347
10	5.94331E-05	1.571610077	0.697220508	6.25485984
11	3.27759E-05	0.986143824	0.384500081	3.924759386
12	1.5908E-07	0.727276026	0.0018662	2.894489971
13	4.2964E-07	0.40824829	0.00504019	1.624789682
14	0.000374596	1.955823296	4.394459801	7.783992205
15	3.23178E-06	1.085334575	0.037912602	4.319529218
16	3.03024E-06	1.6345028	0.035548255	6.505166943
17	3.12554E-05	0.646910206	0.366662885	2.57464159
18	0.000247887	0.452101814	2.908011033	1.799322567
19	0.000588502	2.512622372	6.903818827	10
20	5.35401E-06	0.81514867	0.062808847	3.244214806
21	0.000210924	0.809167212	2.474390162	3.220409165
22	1.31495E-06	0.562621815	0.015425889	2.239181746
23	1.61645E-05	0.642723782	0.189628509	2.557980019
24	1.6559E-06	0	0.019425709	0
25	1.68137E-05	2.155906078	0.19724501	8.5803028
27	0.000852429	0.748135578	10	2.977509019
28	2.57277E-05	0.879386846	0.301816336	3.499876685
29	2.16333E-05	1.059394585	0.253783922	4.216290504
30	7.39392E-05	0.817366292	0.867394095	3.253040733
31	8.62307E-05	1.126527994	1.011588186	4.483475137
32	5.46571E-06	1.327461118	0.064119245	5.283170018
33	0.000267376	0.416505847	3.136635978	1.657653979
34	3.68699E-06	0.645863613	0.04325275	2.570476247
35	2.80493E-05	0.827964161	0.329051596	3.295219251
36	5.78839E-06	0.760774582	0.067904603	3.027811063
37	8.02285E-05	1.235187884	0.94117534	4.915931249
38	9.65366E-06	0.550481883	0.113248866	2.19086596
39	6.71539E-06	1.021299371	0.078779507	4.064675147