

Introduction to BIOMECEC

Throughout the United States and the developed world, there is a discontinuity between outstanding biomedical research and the ability to effectively transfer these technologies into commercially viable products in the market place. In addition, in many publicly held corporations innovation has taken a back seat to meeting quarterly revenue and shareholder profit expectations. Therefore, many larger biomedical companies have turned to acquisitions and partnerships with smaller companies and universities to fuel growth and infuse new technologies into their product pipeline.

Founded in 1998, BIOMECEC's mission is to bridge that gap between early stage medical research and marketable new products. Stated simply, BIOMECEC's business model is to: a) partner with clinicians and researchers at major institutions to swiftly and efficiently develop new products that meet an identified market need and b) rapidly deploy new technologies into the marketplace that are beneficial to society. The transfer of BIOMECEC's technologies to a commercialization partner is done primarily through licensing, and OEM partnerships.

As an example of our model, BIOMECEC acquired license rights to the Micropower Impulse Radar (MIR) technology developed at Lawrence Livermore National Labs (LLNL). BIOMECEC further developed this base technology into a novel Non-Invasive Pneumothorax Detector described in more detail below.

Pneumothorax Market Overview

Pneumothorax, or collapsed lung, is a potentially serious condition that is most often caused by an injury to the chest. Due to lung recoil pressure, the pleural space is usually at subatmospheric pressure. The introduction of air into the space between the visceral and parietal pleura is known as a pneumothorax.¹ Classifications of pneumothoraxes include traumatic pneumothorax (air entering the pleural cavity following trauma), tension pneumothorax (a potentially deadly condition where air is trapped in the pleural cavity under pressure), simple spontaneous pneumothorax (caused by the rupture of a small localized alveoli), and complicated spontaneous pneumothorax (the rupture of a bullae resulting from pulmonary disease). Symptoms of pneumothoraxes vary depending on the amount of air entering the pleural space and the degree of collapse of the lung.²

Traumatic pneumothoraxes and hemopneumothoraxes are common after blunt and penetrating thoracic trauma. The North American Major Trauma Outcome study investigated the prevalence of pneumothorax and hemopneumothorax in patients sustaining major trauma. Among 15,047 trauma patients with thoracic injuries, a pneumothorax was present in 20 percent of cases, and 25 percent had a hemopneumothorax. Because a pneumothorax is often a life-threatening condition, early and accurate on-site diagnosis and treatment is critical for survival.

Current methods for diagnosing a pneumothorax (Chest X-Ray and Chest CT Scan) are not possible for emergency squads and battlefield medics, nor are they practical for long-term monitoring of critical care patients. X-rays are not ideal since the technology is expensive, non-portable, exposes the patient to ionizing radiation, and requires a trained technician to read the film. Computed tomography (CT) is considered the "gold standard," but it is time consuming and very expensive.

Detecting a pneumothorax on-site is especially important if the patient must be transported by air, because the resulting pressure drop will cause the pneumothorax to expand and could greatly exacerbate the symptoms. Furthermore, if the patient has sustained a head or chest injury requiring ventilatory support, by either bag-valve mask ventilation or endotracheal intubation, the patient will have positive pressure ventilation. It is well known that if a pneumothorax exists prior to positive pressure ventilation, without chest tube drainage a potentially fatal tension pneumothorax will develop within minutes.³

BIOMECEC's Phase I and II research has shown that MIR is a suitable technology for such a device. Being low-cost, MIR has significant potential for the military and civilian environments as well as in both the pre-hospital and acute care settings. Real-time ultrasonography has also been proposed as a low-cost portable method for diagnosing a pneumothorax. However, it has been shown that while ultrasound may be useful for localizing a known pneumothorax, it cannot be used to exclude the diagnosis, it has a high false-positive rate, and it is of no use in estimating the volume of a pneumothorax.⁴ Transthoracic impedance measurements have also been proposed, but this technique is very sensitive to noise and electrode placement and is therefore too complex for trauma field conditions.⁵ This leaves the MIR technology as perhaps the most attractive alternative for a handheld pneumothorax detection device.

BIOMECEC is in the final stages of developing a non-invasive, portable, lightweight, low-power device based on the MIR technology that can rapidly detect pneumothoraxes in the field as well as in the traditional clinical setting. BIOMECEC's device has the distinct advantages of being low cost, is portable and lightweight, and requires very little power to operate. In addition, the device requires little training and no special medical knowledge to operate. The cost of the device, estimated to be in the range of \$1000 per unit, is significantly lower than other technologies. The device will connect to a PDA via a compact flash interface. BIOMECEC expects the final device's total weight to be significantly less than one pound. Assisted by the device's software, the user will take readings at eight unique locations on the body and will receive a reading on the presence, location, and size of any pneumothorax. Another advantage is that the device will output the clinical data and results directly into the patient's digital medical record, thereby reducing medical record errors.

BIOMECE Inc.
PNEUMOTHORAX DETECTOR

Due to the large number of pneumothoraxes that result from chest trauma, coupled with the non-portable and costly current forms of diagnosis, a device such as BIOMECE's represents a significant market need. It is expected that high demand for this device will be in the area of medical air transports, ambulances and other first responders, hospital emergency rooms, and intensive care units. In addition, there is a large veterinary market for this device as x-ray is expensive and can be difficult to perform on animals. The civilian and animal market is expected to create a demand of approximately 75,000 units, thereby creating an attractive commercial market for this device.

Since a portable non-invasive pneumothorax detector is of interest to the military as well,⁶ this becomes an additional market for the BIOMECE device. Data shows that pneumothorax is the third-largest cause of fatality on the battlefield and that many deaths could have been prevented with rapid diagnosis and treatment. The military has a high level of interest in this type of device as they have been funding development of non-invasive pneumothorax detectors for the past 5 to 6 years. BIOMECE estimates that the military market would need more than 50,000 units just to equip active battlefield medics.

Technology

MIR technology has been pioneered by researchers at the LLNL.⁷ The MIR rangefinder design proposed for this project is the most sophisticated of the MIR prototypes made to date. The system accepts a standard 50-ohm matched UWB (ultra wide band) antenna and operates with a bandwidth from approximately 1 to 4 GHz. The device emits ultra-short radar pulses (<1 ns), with pulse repetition rates on the order of 2 MHz. The device utilizes the same ultra-short pulse circuitry for time gating, with a 33 gigasample-per-second transient digitizer, which allows the detection of reflective surfaces in air with spatial accuracy of approximately 5 mm. The radar's return signals are digitized and stored on a portable laptop computer or PDA. Another attractive feature of MIR is the projected manufacturing cost. Because the novel radar technology uses off-the-shelf components, the manufacturing cost for the transceiver hardware can be quite low, while outperforming conventional radar and sensor equipment costing as much as \$40,000.

MIR devices are inherently compact, lightweight (less than one pound), battery operated, robust, and portable. Since current is only drawn during the very short pulse times, the power consumption is extremely low. The power output is also very low, being generally in the range of 0.05 watts RMS (about an order of magnitude less than a handheld cell phone), and thus the device is medically safe.

The MIR technology is also ideal for trauma field use because of its insensitivity to background noise. Because of the pulsed operation of MIR based devices, the duty cycle is low and the output energy is spread over a wide band in the EM spectrum. In applications such as pneumothorax detection where the device will be used in contact with the patient, a very compact and low power MIR device can still provide a strong signal and high sensitivity.

Project Status

In the Phase I SBIR, BIOMECE investigated the feasibility of a device based on MIR technology developed at LLNL. In animal studies (swine model), we determined that pneumothoraxes as small as 30 ml were clearly detectable by the MIR device. This level of detection is important for feasibility, since it is below the threshold of clinical significance. Due to the successful outcome of the Phase I, BIOMECE was awarded a Phase II for continued development and testing.

In the Phase II SBIR to be completed by the end of 2005, BIOMECE, working with LLNL, has further optimized the MIR characteristics of the device and antenna for depth of field, power, and MIR beam angle. BIOMECE has generated a body simulation phantom in order to test the device on simulated pneumothoraxes and to develop the data acquisition system and GUI on a laptop for clinical study.

BIOMECE continues to optimize the signal analysis algorithms using human data collected at clinical sites. We are acquiring scans on human subjects to correlate the MIR measurements to chest X-Rays. Currently the device is showing an 84.375% correlation on 32 patients. An important ongoing aspect of development is the miniaturization of the device in order to make data collection easier and more reliable.

The device, already highly portable, uses a laptop with data acquisition hardware, an MIR pulse/receive unit with an antenna, and some interface electronics. A smaller device, which is currently a focus of development, consists of a Pocket PC (PDA) with a compact flash data acquisition card and an MIR pulse/receive unit with an antenna. The final device is envisioned to be the MIR antenna attached to a Pocket PC (PDA) via a custom interface compact flash card that contains both the MIR pulse/receive unit and the data acquisition hardware.

This project has been supported in part by the National Institute of Health's Heart, Lung, and Blood Institute's SBIR program. Current clinical data is being collected with the laptop version of the device in the trauma centers of two hospitals in Metro Detroit. The goal is to provide the clinical sites with a PDA-based version of the device later this year for continued testing.

Clinical Protocol

The current clinical protocol has the clinicians identify patients that potentially have a pneumothorax. While the patient is waiting for the confirming X-Ray or CT-Scan results, the clinician approaches the patient to obtain informed consent. Once the

BIOMECE Inc.
PNEUMOTHORAX DETECTOR

consent is given, the clinician uses the BIOMECE non-invasive pneumothorax detector to collect the MIR data by placing the antenna at 8 defined locations on the patient and taking two readings at each location (one at full inhalation, and one at full expiration). The MIR data is automatically stored on the computer's hard drive without a diagnosis provided. The clinicians periodically send the MIR data to BIOMECE for processing with our proprietary algorithm. BIOMECE then correlates the algorithm results with the radiographic results obtained from the clinicians. The correlation analysis reviews presence. Additional analysis is done to determine if location (left or right side) and size of the pneumothorax can be ascertained. While we are currently collecting data for both inhale and exhale, we do not expect this to be necessary in the final device.

Clinical Study Patient Results Summary

Detroit Sinai-Grace Hospital: Dr. Robert Dunne, MD, Clinical PI	Detroit Receiving Hospital: Dr. Phillip Levy, MD, Clinical PI
14 Patients:	18 Patients:
9 without a pneumothorax	16 without a pneumothorax
5 with a pneumothorax	2 with a pneumothorax
78.57% (11 of 14) Correlation with Radiographic Results	88.89% (16 of 18) Correlation with Radiographic Results
3 false positives	1 false positive
0 false negatives	1 false negative

Conclusion

BIOMECE has developed a working prototype of a non-invasive pneumothorax detector utilizing MIR technology licensed from LLNL. BIOMECE has developed a laptop version of the MIR signal acquisition electronics and software, which has been delivered to two clinical sites. BIOMECE has also developed algorithmic MIR signal analysis software implemented in C# to determine whether a pneumothorax is present. The laptop version of the pneumothorax detector has to date been used to collect data on 32 patients with an 84.375% correlation. We are continuing our development efforts by developing a simplified, hand held, PDA based device that integrates the MIR signal collection hardware and software with the signal analysis algorithm to provide a real-time indication of the presence or absence of a pneumothorax.

By the end of our Phase II project, BIOMECE will have developed a non-invasive pneumothorax detector that consists of a MIR pulse/receiver box and antenna that interfaces with a Pocket PC via a compact flash data acquisition system. We will have collected data on up to 100 patients (40 with the laptop version and up to 60 with the PDA version). We will have developed an algorithm written in C# that will be capable of real-time data analysis on the PDA to provide a pneumothorax outcome.

Next Steps

BIOMECE is continuing the development of the Non-invasive Pneumothorax Detector into a commercialized device. The major steps involved in completing this development for non-military applications include further miniaturization of the electronics, completion of the transition to a PDA based device, final algorithm development, and an expanded clinical study. For battlefield and military applications, we will integrate our system with the Battlefield Medical Information System Tactical (BMIST) platform developed by the U.S. Army's Telemedicine and Advanced Technology Research Center (TATRC), and optimize the system for specific military requirements, including the need to function through Kevlar body armor or under the blades of a helicopter.

- 1 Miniaturize the MIR pulse/receive and digitization circuits to fit in a compact flash slot on a PDA.**
BIOMECE has considerable experience in circuitry miniaturization. In order to achieve the final form factor of a compact flash card for the MIR pulse/receive and digitization circuitry, BIOMECE will employ multi-chip-modules (MCM), utilizing the die of the chips currently used on the surface mount boards. This will allow us to fit the components in the compact flash slot of the PDA, or on a small PCB attached to the compact flash. This will allow the entire device to be hand held, and weigh significantly less than one pound.
- 2 Enhance the PDA algorithm software to provide real-time location and size of a pneumothorax.**
As we continue to acquire clinical data, we are revising the signal analysis algorithm to optimize pneumothorax detection. Additional development will be needed to transition the software for the miniaturized MIR circuitry, complete the port to the PDA environment, and implement the final data analysis algorithm and display in real time.
- 3 Validate the system in an expanded clinical study.**
Once the product development modifications have been made and functionally tested, BIOMECE will return to our clinical collaborators and perform an additional clinical study to validate the system. This study will focus upon making sure the

BIOMECE Inc.
PNEUMOTHORAX DETECTOR

device meets the clinician needs and on validating the diagnostic accuracy. We envision including several EMTs as well as the Emergency Department Clinicians in this study.

4 Integration with the BMIST system to create an electronic trauma triage system.

BIOMECE will integrate our pneumothorax device with the BMIST system developed by TATRC. Since our device will already be PDA based, this will be a natural transition. The BIOMECE device will output clinical data and results in XML format to easily integrate to the BMIST and provide additional diagnostic information. Additionally, testing will need to be conducted and circuit design and packaging optimized such that the pneumothorax detector will function properly in a battlefield environment. BIOMECE envisions the device to be used in Tactical Field Care, prior to evacuation of the victim, and therefore will work through Kevlar body armor, or within the noisy environment of a helicopter evaluation unit.

In addition, BIOMECE has performed initial testing to determine the use of the device to detect and monitor the heart beat of a patient. For the military application, this could be an additional function of the device that could be integrated into the BMIST system, to help assess patient stability.

¹ *The Merck Manual of Diagnosis and Therapy*, Sixteenth Edition, Berkow R., Ed., (Merck Research Laboratories, Rahway, NJ, 1992).

² Rosen, *Emergency Medicine*: 1998. 521-527.

³ Roberts and Hedges, *Clinical Procedures in Emergency Medicine*, 1998.

⁴ Siström C.L., Reiheld C.T., Gay S.B., Wallace K.K., "Detection and Estimation of the Volume of Pneumothorax Using Real-Time Sonography: Efficacy Determined by Receiver Operating Characteristic Analysis", *Am J Roentgenol* **166**(2), 317-321 (1995)

⁵ Noack G., Freyschuss U., "The Early Detection of Pneumothorax with Transthoracic Impedance in Newborn Infants", *Acta Paediatr Scand* **66**(6), 677-680 (1977).

⁶ Ling G.S.F., Day B.K., Rhee P., Ecklund J.M., "In Search of Technological Solutions to Battlefield Management of Combat Casualties", in *Battlefield Biomedical Technologies*, Homer H. Pien, Editor, Proceedings of SPIE Vol. 3712, 1-9 (1999).

⁷ Mast J., Azevedo S., Haddad W., Ng L., Burnett G., "Micropower Impulse Radar Technology and Applications", *LLNL Report UCRL-ID-130474*, 1998.