R&D 100 AWARD ENTRY 2007

ElectroNeedle™

Biomedical Sensor Array

Sandia National Laboratories

2007 *R&D 100 Award Entry Form*

ELECTRONEEDLE™

Biomedical Sensor Array

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AFFIRMATION: I affirm that all information submitted as a part of, or supplemental to, this entry is a fair and accurate representation of this product.

(Signature)_____

Joint Submitter

Not applicable

Product Name

ElectroNeedle™ Biomedical Sensor Array

Brief Description

The ElectroNeedle™ Biomedical Sensor Array is a device that, when pressed against the skin, can make rapid, multiplexed diagnostic measurements in a point-of-care setting.

Product First Marketed or Available for Order

Technology research and development matured to a point that intellectual property (IP) licensing negotiations began with New Mexico Biotech, Inc., and Life BioScience, Inc., in 2006. One license was executed in January 2007 and a second one is under negotiation.

Cover: Jeb Flemming holds a test version of the ElectroNeedle™ device, Photo by Randy Montoya, Sandia National Laboratories

ELECTRONEEDLE™

Biomedical Sensor Array

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ELECTRONEEDLE™

Biomedical Sensor Array

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Product Price

Current devices are research prototypes. No commercial units have been produced. Initial commercial units are estimated to cost between $10,000 and $20,000.

Patents or Patents Pending

Patents

- United States Patent #7,132,054,"Method to Fabricate Hollow Microneedle Arrays," issued on 11/7/2006
- United States Patent Application #10/990,904, "Microneedle Electrode Array for Electrochemical Sensing," filed on 11/17/2004
- United States Patent Application #11/386,347,"Micropost Array Immunosensor," filed on 03/22/2006
- United States Patent Applicaiton #11/542,974,"Hollow Microneedle Array," filed on 10/4/2006

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Biomedical Sensor Array

Product's Primary Function

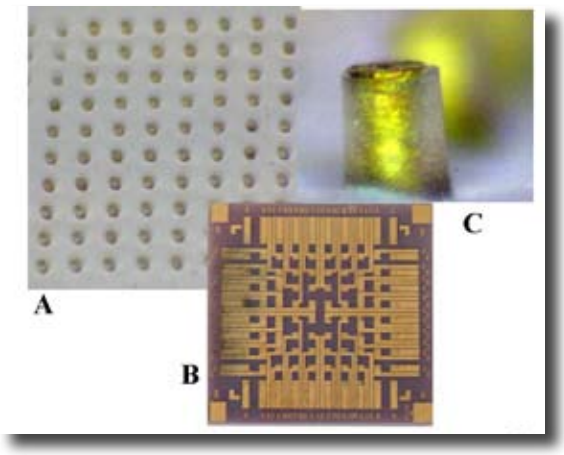

Fig. 1 Photographs of the ElectroNeedle™ device: (A) a 1 cm², 10 x 10 array of individually addressable ElectroNeedles™; (B) the backside electrical contacts; and (C) a single ElectroNeedle™, showing the protective dielectric sheath, leaving the electrode exposed only at the very tip.

Significance

A critical need exists for techniques that can measure a wide range of biomedical analytes at the point-of-care, generating an instant, comprehensive picture of a patient's health for rapid, accurate diagnosis. Sandia has addressed this need through the development of arrays of microfabricated electrochemical probes, functionalized with antibodies, enzymes, and other biological receptors immobilized on the probe tip, for use as minimally invasive diagnostic sensors. By combining electrochemical measurement techniques with well-defined recognition chemistries and an easy-to-use sensor, we can detect a range of biologically important species, including carbohydrates, electrolytes, lipids, enzymes, toxins, proteins, viruses, and bacteria, in a patient's blood or interstitial cellular fluid. This provides a painless and rapid measurement of biologically relevant molecules without having to extract fluids for later analysis.

When pressed against a patient's skin, an ElectroNeedle™ patch (Fig. 1) can detect and identify biological markers just beneath the skin's surface. Because the electrochemical analysis is accomplished *in situ*, the need to withdraw body fluid is eliminated. The height of the needles, adjustable during microfabrication, allows the biological recognition layer to be placed in intimate contact with the appropriate tissue beneath the skin's surface. For example, interstitial fluid in the epidermal layers of skin may be accessed for the measurement of small molecules such as glucose, while blood in the deeper dermal layers may be accessed for the measurement of larger molecules such as proteins.

Technical Approach

ElectroNeedle™ arrays are produced using standard microfabrication techniques — photolithography, etch, and thin film deposition. This will permit low-cost, batch production of these devices when commercialized. What makes the microfabrication unique is the microneedle material, a commercially avail-

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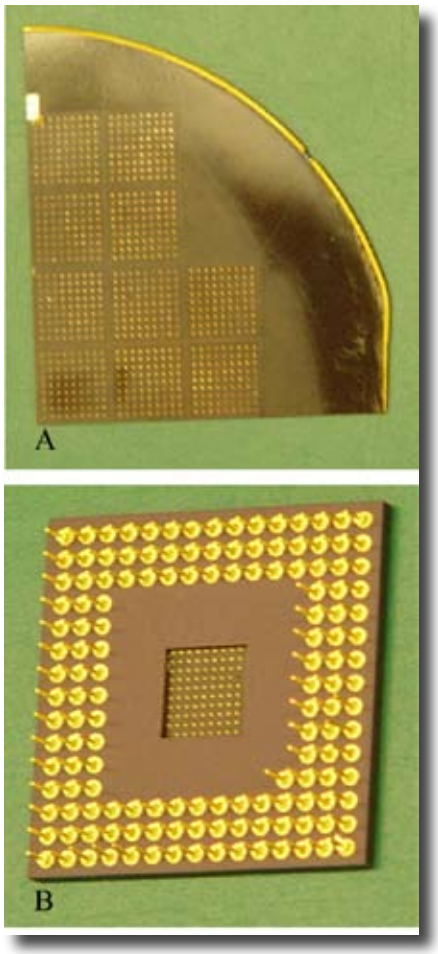

Fig. 2 Microfabricfated ElectroNeedle™ array: (A) ten sensor arrays; (B) array packaged for testing.

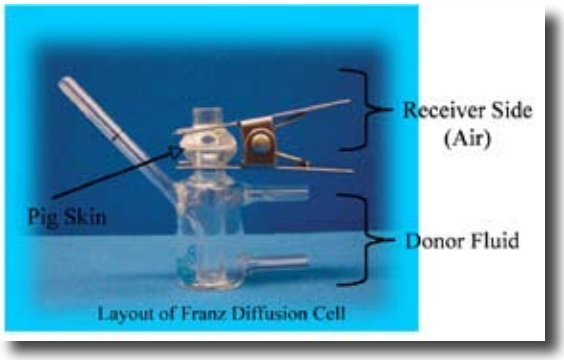

Fig. 3 Franz cell used for ElectroNeedle™ measurements in pigskin.

able glass wafer — Foturan® — that can be photo-patterned and etched to make hollow microscopic needle structures that are then filled with metal to form the sensing electrodes (Fig. 1C). These microneedles are sharp enough to be inserted into the skin but rugged enough not to bend or break. Because the metal microneedle passes all the way through the glass substrate, electrical connections are made to the back of the substrate and do not interfere with the sensing needle tip (Fig. 1B). Figure 2 shows a portion of a Foturan® wafer with ten 10 X 10 ElectroNeedle™ arrays and a single array packaged for testing.

Prior to making this technology available for licensing, we demonstrated its functionality in a laboratory setting. Tests were carried out in a Franz diffusion cell using pigskin as a substitute for human skin (Fig. 3). Using this equipment, we were able to measure glucose (Fig. 4) and quinone (Fig. 5)—electrochemically active molecules that are important to biochemical processes—through the pigskin. These results show that ElectroNeedle™ arrays are capable of measuring biologically relevant compounds in our intended application.

Naturally, there is more to a detection system than just the sensor element. Regardless of how small or capable the sensor, the balance of the system must also meet portability and performance requirements. In our case, data collection and analysis can be handled by a small, commercially available potentiostat—an instrument for controlling and measuring electric currents and voltages—built around a PDA (Fig. 6). The potentiostat is manufactured by Palm Instruments BV in the Netherlands [Ref. 1], which provides the required control and analysis software in addition to the potentiostat. We use a Hewlett Packard PDA to operate the potentiostat.

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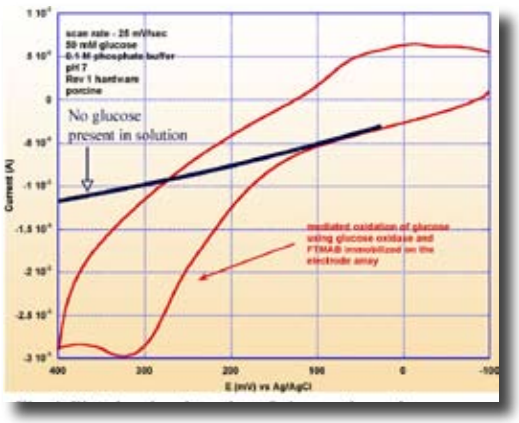

Fig. 4 Plot showing detection of glucose through pigskin.

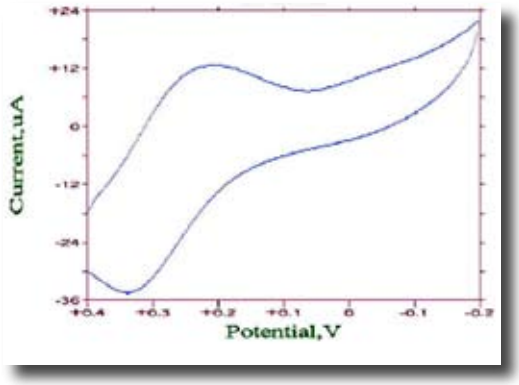

Fig. 5 Plot demonstrating detection of quinone through pigskin.

Fig. 6 Photograph of PDA-controlled potentiostat for use with ElectroNeedle™ array.

Electrochemical vs. Fluorescence Detection

Competing point-of-care technology employs fluorescence-based immunoassays for biomarker detection, in contrast to our electrochemical assays. While there are currently more fluorescence-based assays available, we have pursued electrochemical detection because of its greater potential for miniaturization. Fluorescence-based system miniaturization is hampered by the inherent requirement to convert electrical signals to optical signals and back again, while electrochemical detection avoids this conversion entirely. As an example—though not conclusive proof of the size advantage—one can compare the Abbott FreeStyle Flash® electrochemical glucose meter (1.6 in x 3.0 in x 0.8 in) [Ref 2] to the Biosite Triage® MeterPlus fluorescence detection system (8.5 in x 6.25 in x 2.75 in) [Ref. 3]. The electrochemical instrument is almost forty times smaller than the fluorescence instrument.

To successfully compete with fluorescence detection, additional electrochemical bioassays are required. To address this need, we have developed a novel electrochemically active surface functionalization technique [Ref. 3, 4, 5] that is generally applicable to biomedical detection. This process allows us to attach biological recognition sites to an ElectroNeedle™ by applying a voltage to that specific needle. This approach currently works with proteins, enzymes, and biologically relevant chemicals; demonstration of additional electrochemical assays is underway. The goal of this effort is the development of reagentless electrochemical bioassays; that is, assays that require no reagents to perform the detection other than those coated onto the tips of the ElectroNeedles™. This eliminates the need to transport and store reagents, reducing size and cost and improving convenience.

In addition, this new technique provides an important manufacturing advantage. Because the surface functionalization process is electrically initiated, it is now possible to individually functionalize each ElectroNeedle™ in the array with a

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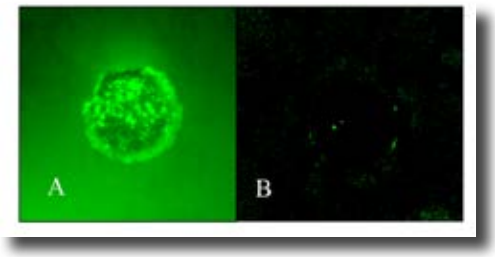

Fig. 7 Troponin detection using fluorescence immunoassay: A) false color fluorescence image of ElectroNeedle™ tip with rhodamine-tagged antibody indicating troponin capture; B) negative control.

The objective of the ElectroNeedle™ technology is to replace the need for off-site diagnostics with portable, on-site, real-time analysis of an extensive panel of biomarkers, providing the physician with an instant snapshot of the patient's health.

different assay in an automated fashion. This results in an array with many different multiplexed diagnostic tests. The automated nature of this process is particularly important given the large number of closely spaced microneedles in the array.

Although our goal is to produce an electrochemically based detection system, we have also demonstrated that the ElectroNeedle™ array can work with existing fluorescent immunoassays. Figure 7 shows an image of a single ElectroNeedle™ tip that has been treated with antibodies to bind troponin, a protein complex indicative of heart attacks. Using a Franz cell (shown in Fig. 3) containing a solution of troponin isolated by a piece of pigskin, we pressed the ElectroNeedle™ into the surface of the skin. It was then removed and reacted with a conventional sandwich assay that binds the fluorescent dye rhodamine to troponin. The fluorescence in Fig. 7A indicates the detection of troponin while Fig. 7B shows the background fluorescence of a negative control. While the particular advantage of ElectroNeedle™ arrays derives from electrochemical detection, there is certainly a benefit in the short term by being able to use existing, widely available fluorescent immunoassays. Furthermore, incorporating both electrochemical and fluorescent assays on the same multiplexed arrays provides redundant, independent detection schemes to increase confidence in the results.

Impact

ElectroNeedle™ technology has the potential to radically change the way clinical diagnostics occur. Current analytical techniques for clinical diagnostics involve the removal of blood or other fluids from a patient for analysis at an off-site laboratory, a process that is both slow and expensive. The objective of the ElectroNeedle™ technology is to replace the need for off-site diagnostics with portable, on-site, real-time analysis of an extensive panel of biomarkers, providing the physician with an instant snapshot of the patient's health. This capability will

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Where it is currently not feasible to take samples to a lab, ElectroNeedle™ technology will bring the lab to the patient.

be particularly important in emergency medical applications—including military applications—where the patient's medical history is unknown or unavailable. ElectroNeedles™ are vital in situations where the patient may be unable to respond to questions, and accurate, rapid diagnosis is essential.
Even in routine medical environments, ElectroNeedle™ technology will have a major impact on the quality of healthcare. A recent survey of physicians in technically advanced countries [Ref. 7] highlights the long wait times for diagnostic tests that many patients experience (Appendix, Item 7). Furthermore, the survey documents that test results are frequently unavailable during patients' appointments with their physicians (Appendix, Item 8). ElectroNeedle™ technology will eliminate these delays by providing a wide range of diagnostic test within the physician's office.

This technology also has the potential to significantly improve healthcare delivery in less developed regions of the world. Where it is currently not feasible to take samples to a lab, ElectroNeedle™ technology will bring the lab to the patient. The 1 cm^2 ElectroNeedle™ sensor array, coupled with the PDA-based potentiostat, will provide an easily transported, handheld, battery-powered biomedical analysis system. This system can be carried in the field by medical professionals or by relatively untrained personnel with the results reported by telephone or wireless communication to the physician. The low capital cost of this system, as compared to existing laboratory technology, and the low consumable cost (a single-use ElectroNeedle™ patch capable of making multiple measurements simultaneously) will make this system affordable worldwide and extend the benefits of modern medical science around the world.

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Two new biotechnology companies — New Mexico Biotech, Inc., and Life BioScience, Inc., — have been formed in Albuquerque explicitly for ElectroNeedle™ commercialization.

Partnerships

The significance of ElectroNeedle™ technology has been recognized by both the commercial sector and by the medical community. Two new biotechnology companies — New Mexico Biotech, Inc., and Life BioScience, Inc., — have been formed in Albuquerque explicitly for ElectroNeedle™ commercialization. One company has already licensed the IP portfolio that became available during 2006 and negotiations are underway with the second. Both companies have provided letters of support for this R&D 100 award application (see Appendix). Healthcare providers are also enthusiastic about the potential impact of ElectroNeedle™ technology. Dr. Karl VanDevender, President of the Frist Clinic, has provided a letter of support (see Appendix) that describes the benefits this technology will have on healthcare worldwide. Dr. Dominic Raj, a physician-researcher at the University of New Mexico Health Sciences Center, plans to employ ElectroNeedle™ technology in a clinical research program and has provided a support letter. It is important to point out that neither Dr. VanDevender nor Dr. Raj has a financial interest in ElectroNeedle™ commercialization. Sandia is collaborating with Dr. VanDevender and Dr. Raj to further develop ElectroNeedle™ technology to address their clinical and research applications.

References

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3. http://www.biosite.com/products/meterSpecs.aspx
4. *Diazonium Functionalized Horseradish Peroxidase Immobilized via Addressable Electrodeposition: Direct Electron Transfer and Electrochemical Detection;* R. Polsky et al., Langmuir, 23, 364 – 366 (2007)
5. *Electrically Addressable Diazonium Functionalized Antibodies for Multianalyte Electrochemical Sensor Applications*; R. Polsky et al., submitted to Analytical Chemistry

Product's Primary Function

6. *Electro-Addressable Selective Functionalization in Electrode Arrays: Catalytic NADH Detection Using Aryl Diazonium Modified Gold Electrodes,* J. Harper et al., submitted to Analytical Chemistry
7. *On The Front Lines Of Care: Primary Care Doctors' Office Systems, Experiences, And Views In Seven Countries,* C. Schoen et al., Health Affairs, 25, w555 – w571 (2006); available at http://content.healthaffairs.org/cgi/content/full/25/6/w555?ijkey= 3YyH7yDwrJSoc&keytype=ref&siteid=healthaff

ELECTRONEEDLE™

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Product's Competitors by Manufacturer, Brand Name, and Model Number

Several companies are developing small, point-of-care systems for biomedical diagnosis. These range from inexpensive glucose meters for diabetes management to advanced systems for heart attack and stroke identification. These systems are characterized by small size—typically hand held and battery-powered—and minimal, if any, reagents required for analysis. An important distinction among these systems is the number of biological markers they are designed to detect. The ability to detect a range of biomarkers is critical if these systems are to provide a complete diagnostic picture of a patient.

Point-of-care competitors include:

Company	Model	Website
Abaxis Inc.	Piccolo®	www.abaxis.com
Abbott Diabetes Care	FreeStyle® and Precision Xtra	www.abbottdiabetes-care.com
Biosite Inc.	Triage® MeterPlus	www.biosite.com
HemoCue	HemoCue systems	www.hemocue.com
ZymeTx Inc.	ZstatFlu®	www.zymetx.com

Comparison Matrix

Product	Handheld?	Number of Assays/ Sample	*In Situ* Measure-ments?	Reagents Required?	Cost	Comments
ElectroNeedle™ Biomedical Sensor Array	Yes, battery-powered	50[1]	Yes	No	$10,000-$20,000[2]	
Piccolo®	No, table top instrument, 15 lbs.	Up to 14	No	Yes, included in sample chamber	Not available	
FreeStyle®	Yes, battery-powered	1	No	No	$50	Glucose only
Precision Xtra	Yes, battery-powered	2	No	No	$70	Glucose and ketone only
Triage® MeterPlus	Small, battery powered	Up to 9	No	No	$4,750	
HemoCue	Yes, battery-powered	1	No	No	$350	Hemoglobin, glucose
ZstatFlu	Small, but requires AC power	1	No	Yes	$180	Influenza

1 Potential number of assays based on existing 10 x 10 (100 element) array.

2 Estimated cost for early production model.

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How Product Improves Upon Competition

The principal characteristic that differentiates ElectroNeedle™ technology from its competitors is its high multiplexing capability—the large number of assays that can be simultaneously performed—in a readily portable package. Among the competing products, system size grows as the number of assays and functionality increases. Some competitive systems are designed for a single assay, glucose levels for example, and these are small, highly portable, and inexpensive. However, these systems do not have sufficient versatility to be used in a diagnostic setting. Systems capable of a greater number of assays, such as the Triage® MeterPlus or the Piccolo®, are more useful in diagnostic applications. These, however, are small but not necessarily handheld. Of these two, only the Triage® MeterPlus has the potential for truly being portable and it can perform only a limited number of assays at a single time. Another drawback for some competitors is the need for reagents to complete the analysis, which adds to system complexity and raises transportation and storage issues. In this environment, what distinguishes the ElectroNeedle™ technology is its potential to perform tens of assays at once in a portable, handheld instrument, ultimately without additional reagents. This will provide a sufficient number of diagnostic tests for a complete picture of the status of a patient's health. Additionally, the instrument is small enough to be carried to wherever the patient is, rather than requiring the patient, or the patient's blood samples, to be transported.

A second significant advantage that ElectroNeedle™ technology has over all of its competitors is its ability to perform *in situ* measurements. This means that not even a single drop of blood needs to be drawn from the patient because the sensors can make measurements through the skin. This capability allows for continuous monitoring of critical biochemical healthcare parameters, much like physical parameters such as blood pressure, heart rate, and respiration can be monitored currently.

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Biomedical Sensor Array

Product's Principal Applications

The ElectroNeedle™ Biomedical Sensor Array will provide rapid, on-demand, multiplexed, point-of-care biomedical assays for medical diagnosis in emergency, battlefield, and remote settings where time constraints or distance make it impractical to send the patient's samples to a conventional laboratory for analysis. It will also eliminate delays experienced by many patients and physicians in (1) waiting for diagnostic tests to be scheduled and (2) waiting for the test results. Finally, it will enable a new dimension in home healthcare, where patients can be continuously monitored and the results transmitted to a physician.

Other Applications

Although human healthcare is the principal application for this technology, the ElectroNeedle™ Biomedical Sensor Array also has equivalent veterinary applications. Rapid and low-cost disease detection in agricultural livestock will produce enormous economic impact worldwide. For example, a foot-and-mouth outbreak in 2001 cost Great Britain an estimated $15,000,000,000 (http://en.wikipedia.org/wiki/2001_UK_foot_and_mouth_crisis). An ElectroNeedle™ array designed to detect livestock diseases will allow farmers and ranchers to monitor their herds, identify infected animals before physical symptoms are apparent, contain the spread of the disease, and safeguard the food supply. Because veterinary applications do not face the same regulatory requirements as biomedical applications, we believe that ElectroNeedles™ will find their first implementation in veterinary applications.

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Summary

Improved healthcare is one of the greatest challenges we face, whether it is timely point-of-care diagnosis in the economically advantaged regions of the world, or access to advanced, affordable diagnostic tests in developing regions. The ElectroNeedle™ Biomedical Sensor Array has the potential to address both of these important needs. The ability to perform rapid, multi-plexed biomedical assays with an easy-to-use, easy-to-transport instrument will provide healthcare workers a complete picture of a patient's state-of-health when it's needed, where it's needed. This capability does not currently exist and we are aware of no technology other than the ElectroNeedles™ that has the potential to provide it.

ELECTRONEEDLE™

Biomedical Sensor Array

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Appendix

1: Letter of Support, New Mexico Biotech, Inc.
2: Letter of Support, Life BioScience, Inc.
3: Letter of support, Karl VanDevender, M.D.
4: Letter of Support, Dominic Raj, M.D.
5: *Sandia Lab News* article
6: Sensors Online article
7: Physicians Survey results, Exhibit 5 (from Ref. 7)
8: Physicians Survey results, Exhibit 3 (from Ref. 7)

Appendix Item 1

new mexico biotech, inc.

February 9, 2007

To Whom It May Concern:

Considering the incredible advances that healthcare has seen in the past century—antibiotics, immunizations, open heart surgery and organ transplantation—it is equally amazing that the technology for drawing blood has not changed appreciably since its inception. Needle phobia (Journal of Family Practice, Dr. James Hamilton, 1995) is a well-documented phenomenon that affects over 10% of the population and results in the avoidance of healthcare services and in many cases premature death. Needle sticks in some patients cause a drop in blood pressure, known as a vaso-vagal response.

The interest in replacing painful needle sticks for blood sampling is evidenced in the more than 500 existing patents for microneedles—needles that are so small as to avoid stimulating the nerve endings responsible for sending pain signals to the brain. Unfortunately, this approach has not been successful as the viscosity of blood makes it difficult to draw through a needle that is small enough to avoid triggering a pain nerve ending.

ElectroNeedle® technology represents a break-through because it has achieved the holy grail of the painless needle stick while bypassing the viscosity problem by creating an instantaneous biochemical reaction at the tip of the needle/post after it is inserted into the patient's epidermal or dermal layer of the skin. The genius of ElectroNeedle® technology is that it not only avoids a painful needle stick but it does so with a post that can be *durably* scaled to allow for varying penetration depths into the skin.

ElectroNeedle® technology will impact an enormous array of healthcare settings, including but not limited to:

- home testing
- self-monitoring of care
- primary care physician's office
- hospital critical care units
- emergency departments
- academic labs
- public health departments

As one example physicians, using ElectroNeedle® technology, will be able to obtain the results of routine blood tests *during* the course of the office visit. This will fundamentally change the patient experience in the physician's office to be more patient-centric and more productive. Combined with the power of decision support software, the diagnostic process will be shortened and targeted therapies introduced in rapid fashion.

Patients and their practitioners will be so enamored with this new approach to blood testing that it will be hailed as one of the great medical advances in the twenty-first century and I fully support Sandia National Laboratory's application for the R&D 100 award.

Sincerely,

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January 27, 2007

Editor
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2000 Clearwater Drive
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Re: R&D 100 Awards

To Whom It May Concern:

We are submitting this memorandum in support of the Sandia National Laboratories developed ElectroNeedle® Biomedical Sensor Array. We believe that this technology has the ability to drastically change the way point-of-care diagnostics and disease management is conducted. The painless sampling offers a much needed solution for repeated patient self-management techniques, such as glucose measurements, and the multiplexed diagnostic capabilities may potentially revolutionize the way general health monitoring occurs at both the first responder and clinical level. Life BioScience Inc. founding members include two of the initial inventors of this technology, Jeb Flemming and Colin Buckley. Life Bioscience Inc. anticipates completing a licensing arrangement with Sandia National Laboratories for this powerful technology.

Kind Regards,

Blake Ridgeway

The Frist Clinic
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February 19, 2007

Editor
R & D Magazine
2000 Clearwater Drive
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RE: R & D 100 Awards

To Whom It May Concern:

I am writing this letter in support of Sandia National Laboratories' ElectroNeedle® Biomedical Sensor Array (EBSA) Technology.

I was introduced to the concept of EBSA Technology at Thanksgiving 2005 during a visit with my cousin, Pace VanDevender, who is an officer at the Sandia National Laboratories in Albuquerque, New Mexico. Subsequently I visited Sandia National Laboratories on two occasions to learn more about this remarkable technology.

I am a practicing physician in internal medicine in Nashville, Tennessee. I am President of The Frist Clinic in Nashville. This clinic was founded in 1938 by the father of former Senate Majority Leader, Bill Frist. I am also a Professor of Clinical Medicine at Vanderbilt University Medical Center.

I have practiced medicine in India, Nepal, and several African countries. It is clear to me that EBSA will provide a new level of care in emerging countries.

It is also clear to me that this technology is very critical to our national security. It can be used for screening vaccine status at borders, screening for potential epidemic producing diseases, and monitoring human exposure to high risk infections. I believe that it can also help provide enhanced security in inadequately secured biomedical labs in developing countries such as Indonesia and Malaysia.

It is also clear to me that this technology can be used for monitoring human food sources and for screening swine, poultry, beef, fish, and other animals. Given that approximately 80 % of patient visits in the United States are made primarily for laboratory blood analyses, it follows that technology of this sort can reduce medical cost in a dramatic way in our own country.

It is my belief that EBSA Technology represents a significant advance towards enabling all the peoples of the world to have access to basic healthcare.

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February 19, 2007
RE: R & D 100 Awards
Page 2

Over the past 30 years I have not encountered a new technology with such potential wide application. I am proud to support the efforts of Sandia National Laboratories in their ElectroNeedle Biomedical Sensory Array development. I see this as having a universal application to promote good health and to provide comfort to all mankind. Therefore, I fully support the nomination of ElectroNeedle Biomedical Sensory Array for the R & D 100 Award.

Sincerely,

F. Karl VanDevender, M.D.

FKV/sln

THE UNIVERSITY OF NEW MEXICO ♦ HEALTH SCIENCES CENTER
SCHOOL OF MEDICINE

Department of Internal Medicine
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Pope L. Moseley, M.D., M.S.
Professor and Chair

February 8, 2007

Editor

R&D Magazine

To Whom It May Concern:

I am writing this letter attesting the significance and versatile clinical applicability of the innovative "The ElectroNeedle® Biomedical Sensor Array" technology. The transition of this technique from conception to the prototype form was carefully planned seeking input from researchers and clinicians. This micro-technique incited not only intellectual curiosity, but also unbridled anticipation because of its limitless potential both in the area of research and in clinical practice. While I am a physician-researcher, I will confine myself to describing the clinical potential of this invention.

This method is capable of detecting and quantifying a wide range of electrolytes and molecules of diverse physico-chemical properties precisely and provides information in a dynamic manner in diverse body compartment; a physician's dream and patent's boon. This technique is most useful in some of the most vulnerable population such as children and most disabled in whom it is most difficult to obtain blood samples to analysis and modulate therapy accordingly. This probe as proposed provides a painless and rapid measurement of biologically relevant molecules without having to extract fluids for later analysis. It is likely to prove invaluable in emergency situations such as electrolyte imbalances in which prompt diagnosis and management can be life saving.

While the potential for this electroneedle is innumerable, some applications will have significant impact on patient management and also profound economic implications:

(1) Dynamic biochemical data is vital in the management of medical emergencies such as diabetic ketoacidosis and dysnatremia.

(2) This has potential application in the management of life threatening sepsis, by providing preliminary information about the infecting organism and hence modifying therapy.

(3) In acute coronary syndrome, information regarding the change in cardiac enzymes is vital in planning the management, this probe is likely to provide such information.

Other non-life threatening, yet very important applications include:

(1) Cross-match and HLA typing in transplants.

(2) Modified to study the serology, it will be useful in diverse conditions including those in the management of rapidly progressive glomerular diseases.

(3) In patients with end-stage renal disease patients, diabetes mellitus and management of patients in the intensive care unit and emergency department, this technique when available is likely to contribute significantly to the appropriate and painless and rapid management of the patients.

I sincerely believe that this technique, when widely available, will revolutionize the management and aid prompt and appropriate care for the patients. If you have any questions, please do not hesitate to contact me.

Sincerely

Dominic Raj MD, DM
Associate Professor of Medicine
Department of Internal Medicine
Division of Nephrology
University of New Mexico

Sandia National Laboratories

NEWS RELEASES

FOR IMMEDIATE RELEASE
August 2, 2005

ElectroNeedles may provide diabetes patients a painless way to check blood glucose levels

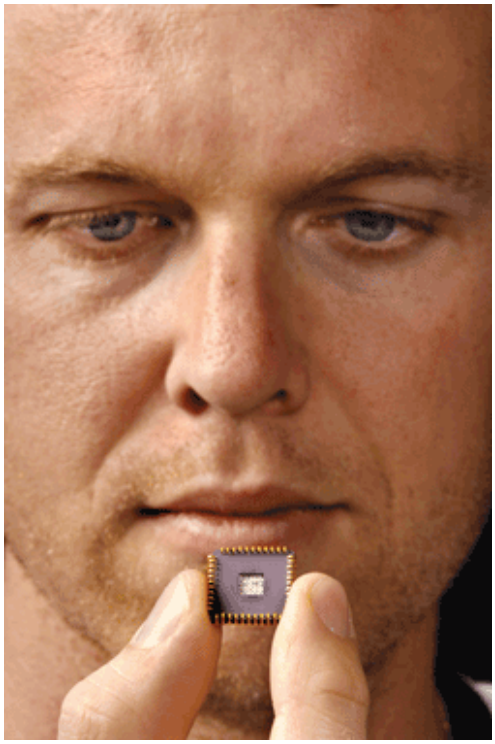
Micron-sized µPosts can also diagnose heart attacks by sensing proteins

Albuquerque, N.M.— Two tiny devices recently developed by researchers at the National Nuclear Security Administration's Sandia National Laboratories could mean the elimination of blood drawing by diabetes patients to test glucose levels or by medical personnel to determine if someone is having a heart attack. Test results would be instantaneous.

The two arrays of micron-sized needles operate similarly by penetrating painlessly into the skin. Arranged in varying numbers on a small patch, the needles can measure molecules inside the body, eliminating the need to withdraw blood from a patient.

One device is ElectroNeedles, micron-sized electrodes capable of measuring molecules such as glucose that can donate or accept electrons (redox behavior). The other is µPosts, micron-sized posts that have the potential of painlessly measuring proteins and other macromolecules, including protein markers released during a heart attack, using optical measurements. The platforms complement each other and together create a diagnostic suite capable of detecting many important biological markers.

"The tiny ElectroNeedles, expected to be constructed of cheap throw-away plastic, would not only make glucose testing simple and painless, but would significantly cut the diagnostics time involved in protein analysis," says Jeb Flemming, Sandia project leader. "Because the analysis is done inside the body, the need to withdraw body fluid is eliminated, and because the needles are so small the measurements are painless."



JEB FLEMMING, project lead for the ElectroNeedle platform, holds a test version of the device. The prickly parts are in the center of the package. A

Flemming and fellow researchers David Ingersoll and Carrie Schmidt came up with the idea for the ElectroNeedles and µPosts while working on a Sandia-funded Bio-MicroFuel Cell research project where Flemming investigated harvesting sugars from living plants and animals. Some of that internal money funded early ElectroNeedle and µPost work.

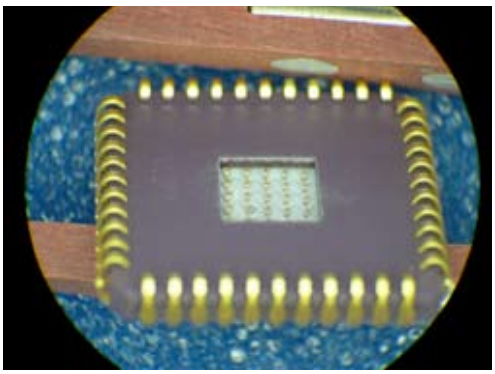
production version could be even smaller and simpler. (Photo by Randy Montoya)
Download 300dpi JPEG image
(Media are welcome to download/publish this image with related news stories.)

It wasn't until they hired Colin Buckley, a medical student from the University of New Mexico Medical School, that the team realized the significance of their invention. "Colin gave us a much-needed insight into the medical diagnostic field," says Flemming.

The team realized that the tips of each of the ElectroNeedles and µPosts could be coated with a biologically active layer capable of measuring concentrations of specific lipids, proteins, antibodies, toxins, viruses, and carbohydrates (such as glucose). Using the ElectroNeedles and rapid electrochemical methods for analysis, a measurement can be made in a few seconds. Likewise, using coated µPosts to capture proteins and other non-redox behaving molecules, optical measurements can potentially be made in less than a half hour.

"Multiple chemical platforms, such as µPosts, will change medical diagnostics by giving the physician a greater understanding of the health of the patient in a shorter amount of time than standard laboratory analysis used today in medicine," Buckley says.

The arrays may be configured in a variety of formats - larger or smaller to accommodate different applications.



Closeup of ElectroNeedle (Media are welcome to download/publish this image with related news stories.)

The ElectroNeedles and µPosts can be tailored in size to sample in different portions of the skin. For example, they can be made shorter to measure small-molecular-weight compounds such as glucose in the upper layer of the skin, or they can be made longer to measure larger molecules in the blood, such as Troponin I, a key protein released when a person has a heart attack.

"Today if someone goes to an emergency room with chest pains the doctor assesses the patient's condition based on their symptoms. In order to accurately diagnose a patient the doctor has to take a blood sample, which is typically sent to an off-site laboratory for analysis," Flemming says. "The person usually has to wait six hours to get confirmation on whether they have elevated Troponin I levels indicating they have had a heart attack."

With a µPost test a doctor would know within a couple of minutes of a patient's arrival at the emergency room if the patient has elevated Troponin I levels, as most of the diagnostics can take place inside an ambulance during a patient's trip to the hospital.

"There would be little to no pain associated with this," Flemming says. "The only thing the patient would feel is a slight itching."

ElectroNeedles and µPosts now exist as a prototype and are made of Foturan®, a glass-like material. The intent is to ultimately mass-produce them from an inexpensive plastic.

The devices have been used to measure glucose and Troponin I within pig skin, with the next step to test them on pig skin with blood.

The technological advances at Sandia have led to several patents pending.

Sandia is a multiprogram laboratory operated by Sandia Corporation, a Lockheed Martin company, for the U.S. Department of Energy's National Nuclear Security Administration. Sandia has major R& D responsibilities in national security, energy and environmental technologies, and economic competitiveness.

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Sandia technical contact: Jeb Flemming, (505) 844-2230, jhflemm@sandia.gov

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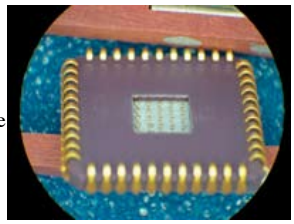
Help for Hide and Heart

Oct 1, 2005
By: Stephanie vL Henkel
Sensors

Part of the misery of being diabetic is having to prick your finger or arm for glucose-level testing. And haste *prevents* waste when it comes to diagnosing a heart attack. Sandia researchers led by Jeb Flemming are developing diagnostic tools—ElectroNeedles and µPosts—that could benefit both diabetics and heart patients. Other members of the research team include Sandia's David Ingersoll and Carrie Schmidt, and Colin Buckley, a medical student at the University of New Mexico Medical School.



ElectroNeedles (photo, with needles in package center) are micron-sized electrodes capable of measuring glucose and other molecules that can either donate or accept electrons (redox behavior). Configured in arrays, the needles penetrate the skin painlessly and take a glucose measurement *inside* the body, without drawing blood. Rapid electrochemical analytical methods produce readings in seconds.

µPosts take advantage of optical technology to measure proteins and other macromolecules, including the elevated troponin I levels associated with certain types of heart attack. The procedure is painless, and the analytical results are available in <30 min. after the patient's arrival in the ER because most of the diagnostics can be handled in the ambulance en route. Compare this scenario with conventional diagnostic techniques that require drawing a blood sample and sending it to the lab, a protocol that can mean six hours of waiting.

Short Takes

The MicroNeedle and µPost platforms are mutually complementary. The tips of both devices are coated with a biologically active layer that measures concentrations of specific lipids, proteins, antibodies, toxins, viruses, and carbohydrates (e.g., glucose). Their size can be custom-tailored for different areas of the patient's skin—shorter for diabetes testing and longer for larger molecules in the blood such as troponin I.

The prototype ElectroNeedles and µPosts are fabricated of Foturan, a glass-like material. The market versions are expected to be made of an inexpensive, disposable plastic. Thus far they have been tested for measuring glucose and troponin I in pig skin, with additional testing with blood to follow.

Contact Jeb Flemming, Sandia National Laboratories, Albuquerque, NM; 505-844-2230, jhflemm@sandia.gov , www.sandia.gov.

EXHIBIT 5
Access Experiences And Office Hours Among Primary Care Physicians In Seven Countries, 2006

	AUS (%)	CAN (%)	GER (%)	NET (%)	NZ (%)	UK (%)	US (%)
Office hours							
Does your practice have office hours to see patients at the following times?							
Some early morning hours (before 8:30 a.m.)	43[b,c,d,e,f]	27[c,d,e,f,g]	80[d,e,f,g]	85[e,f,g]	37	33[g]	40
Some evening hours (after 6:00 p.m.)	52[c,d,e,f,g]	48[c,d,e,f,g]	74[d,e,f,g]	4[e,f,g]	38	39	38
Some weekend hours	76[b,c,d,e,f,g]	38[c,d,f,g]	24[d,e,f,g]	2[e,f,g]	39[f,g]	5[g]	47
None of these	14[b,c,e,f,g]	34[c,d,f]	7[d,e,f,g]	13[e,f,g]	34[f]	40[g]	29
Does your practice have an arrangement where patients can be seen by a doctor or nurse if needed, when the practice is closed, not including ER? (percent yes)	81[b,c,d,e,f,g]	47[c,d,e,f,g]	76[d,e,f,g]	95[e,f,g]	90[g]	87[g]	40
How often do you think your patients experience the following?							
Difficulty paying for prescriptions							
Often	15[b,c,d,e,g]	24[d,f,g]	23[d,f,g]	7[e,f,g]	27[f,g]	13[g]	51
Sometimes	64[b,c,d,f,g]	56[c,e,f,g]	35[d,e,f,g]	55[f,g]	62[f,g]	48	43
Rarely/never	21[c,d,e,f,g]	18[c,d,e,f,g]	42[d,e,g]	36[e,g]	11[f,g]	39[g]	5
Difficulty paying for care other than prescriptions							
Often	27[c,d,e,f,g]	25[c,d,e,f,g]	35[d,f,g]	12[e,g]	39[f]	14[g]	42
Sometimes	59[b,c,f,g]	51[c,d]	36[d,e,f,g]	61[e,f,g]	54	50	51
Rarely/never	14[b,c,d,e,f,g]	22[c,e,f,g]	29[e,f,g]	26[e,f,g]	7[f]	35[g]	7
Long waiting times for diagnostic tests							
Often	6[b,d,e,f,g]	51[c,d,e,f,g]	8[d,e,f]	26[f,g]	28[f,g]	57[g]	9
Sometimes	39[c,d,e]	39[c,d,e]	16[d,e,f,g]	49[f,g]	53[f,g]	36[g]	42
Rarely/never	55[b,c,d,e,f,g]	9[c,d,e,f,g]	76[d,e,f,g]	23[f,g]	19[f,g]	6[g]	48
Long waiting times for elective surgery or hospital care							
Often	69[c,d,e,f,g]	70[c,d,e,f,g]	9[d,e,f]	51[e,f,g]	85[f,g]	62[g]	9
Sometimes	26[d,e,f,g]	24[d,e,f,g]	27[d,e,f,g]	42[e,f,g]	14[f,g]	35	34
Rarely/never	4[c,e,g]	4[c,e,g]	66[d,e,f,g]	7[e,f,g]	1[f,g]	2[g]	56

SOURCE: Commonwealth Fund International Health Policy Survey of Primary Care Physicians, 2006.

NOTES: Reading from left to right starting with Australia (AUS), the letter indicates significant differences with the country or countries to the right, as indicated ($p < .05$). For unweighted N, see Exhibit 1.

[b] Different from Canada.

[c] Different from Germany.

[d] Different from the Netherlands.

[e] Different from New Zealand.

[f] Different from the United Kingdom.

[g] Different from the United States.

EXHIBIT 3
Coordination Of Care: Primary Care Physicians' Reports On Experiences In Seven Countries, 2006

	AUS (%)	CAN (%)	GER (%)	NET (%)	NZ (%)	UK (%)	US (%)
During the past 12 months, how often have your patients experienced the following?							
Problems because care was not well coordinated across multiple sites or providers							
Often	5[f]	5[f]	5[f]	5[f]	4[f]	15[g]	5
Sometimes	35[b,c,d,e,f]	41[c,f,g]	16[d,e,f,g]	41[f,g]	45[g]	50[g]	32
Rarely/never	60[b,c,d,e,f]	51[c,f,g]	78[d,e,f,g]	52[f,g]	51[f,g]	34[g]	60
A patient's medical record/clinical information was not available at the time of scheduled visit							
Often	4[b,d,f,g]	10[c,d,e]	3[d,f,g]	1[f,g]	2[g]	7[e]	8
Sometimes	24[b,c,d,g]	31[c,d,e]	8[d,e,f,g]	15[e,f,g]	25[g]	29	32
Rarely/never	72[b,c,d,f,g]	56[c,d,e,f]	89[d,e,f,g]	83[e,f,g]	72[f,g]	64[g]	58
Tests or procedures had to be repeated because findings were unavailable							
Often	1[b,d,f]	3[c,d,e]	1[d,f]	<1[f,g]	1[f]	3	2
Sometimes	9[b,c,d,e,f,g]	17[c,d,f]	3[d,e,f,g]	7[e,f,g]	13[f]	24[g]	14
Rarely/never	89[b,c,d,e,f,g]	78[c,d,e]	95[e,f,g]	92[e,f,g]	86[f]	73[g]	82
When you refer a patient to another doctor, for what percentage of patients do you get information back about the results of the referral?							
Almost all	76[b,c,d,e,g]	62[c,e,f,g]	68[d,e,f,g]	61[e,f,g]	82[f,g]	75[g]	37
Most	19[d,e,g]	22[d,e,f,g]	21[d,e,f,g]	35[e,f]	14[g]	18[g]	33
About half or fewer	5[b,c,g]	15[d,e,f,g]	11[d,e,f,g]	4[g]	3[f,g]	7[g]	28
After patient has been discharged, how long does it take to receive a full discharge report from the hospital?							
Less than 48 hours	10[b,c,d,e,f,g]	3[e,g]	4[e,g]	5[e,g]	29[f,g]	4[g]	14
2–4 days	21[b,c,d,f,g]	6[e,f,g]	7[e,g]	7[e,g]	19[f,g]	10[g]	25
5–14 days	40[b,c,e,f,g]	28[c,d,f,g]	35	35	34	34	34
15 days or more, or rarely receive a full report	28[b,c,d,e,f,g]	58[c,d,e,g]	53[e,g]	48	18[f,g]	52	23
15–30 days	16	33	37	40	13	36	11
More than 30 days or rarely receive full report	12	25	16	9	5	18	12

SOURCE: Commonwealth Fund International Health Policy Survey of Primary Care Physicians, 2006.

NOTES: Reading from left to right starting with Australia (AUS), the letter indicates significant differences with the country or countries to the right, as indicated ($p < .05$). For unweighted N, see Exhibit 1.

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