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Biomonitoring Futures



Biomonitoring Platform Assessment

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Biomonitoring Platform Assessment

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BIOMONITORING PLATFORM ASSESSMENT

Introduction

This paper reviews current and anticipated developments in various forms of testing. The developers of these tests are very optimistic, as they should be. This report describes current test development and the potential these advances may offer. Where outcomes data is available, this paper reports on the degree of success or failure for these tests.

Enthusiasm for this mapping of current promise should be tempered by remembering past disappointments. For example, a saliva test for HER2/neu in women with breast cancer was being tested in clinical trials in 2002 with hope of FDA approval in 2003. There was a flurry of articles at that time. But there has been no further publication on these trials, and the test developer's website is no longer available. The promise, particularly if companies are seeking more investment capital or buyers, often far exceeds ultimate success.

However at least some of the tests identified here likely will prove successful. Given the right cost and usability for consumers and community health centers, these could lead to dramatically better early detection of disease and pre-disease states and support better treatment for diabetes, cancer and many other diseases. The opportunity for reducing health disparities is great enough to explore the possibilities of these potential advances.

Saliva Testing

Active research is uncovering ways to use saliva testing to diagnose and monitor health and disease states, predict progression, detect exposure to infectious, environmental and biological substances and detect microbial biomarkers. Diagnostic devices using MEMS/NEMS (microelectromechanical systems and nanoelectromechanical systems) chips, microfluidics, and multiple detection methodologies are in active development with impressive prototypes being tested. Saliva as a testing platform offers promise for real-time, painless, cost-effective disease screening that can be performed at the point of care. Tests are already available to detect alcohol, illegal drugs, various hormonal levels, HIV, failed pregnancy and other things. Researchers are looking at patterns of DNA, RNA, proteins, fatty acids, bacteria, viruses and other molecules to try to discover specific patterns that will accurately detect common diseases such

as cancers, diabetes, rheumatoid arthritis, cardiovascular disease and other diseases. It may take a few years before reliable patterns for saliva testing can be confirmed through clinical trials and regulatory approval secured. The first role of new modalities will be screening. Over time as accuracy improves it could shift into definitive diagnosis and management.

The dental community is very involved in this approach and will likely be the first group of medical professionals to use these new saliva tests to screen for common diseases during oral exams. It may be a harder sell to get physicians to accept the value of this new paradigm in diagnostic screening, but the attributes of low cost and ease of use at the point of care or in the home should be a compelling motivator – if the technology proves reliable for common serious diseases. The platform could become extremely valuable for community health centers.

SPECIFIC DETAILS:

- **Principle or Mechanism of Action:**

- The 1.5 liters of saliva a person produces daily comes from blood filtered through the salivary glands so it mirrors the blood. However, saliva concentrations of molecules are often 0.1 – 1% of that in the blood requiring more sensitive assays.

- **What it can measure:**

- DNA, RNA, proteins, bacteria, viruses, fatty acids and other molecules

- **Potential disease applications:**

- Tests developed for measuring hormones (i.e., cortisol, estrogen, testosterone, DHEA), illegal drug testing, screening for antibodies against HIV, checking identity and paternity
- Oral cancer using messenger RNA (of ~3,000 mRNAs found in saliva, 4 were part of a characteristic pattern in people with oral cancer with an accuracy of 91%)
- mRNA patterns predictive of breast cancer and diabetes
- Signature populations of ~700 mouth bacteria change with oral cancer with a particular pattern identifying 80% of cancers – researchers are incorporating more bacteria to try to improve predictive value
- A test that can simultaneously diagnose several childhood respiratory infections within minutes in the clinic
- Oral microbes can predict infection elsewhere in the body and identify specific pathogens, maybe even anthrax
- Oral signature bacterial populations may predict early diabetes (though saliva-based glucose tests have not worked)
- Predicting life-long risk of developing cavities by looking at patterns of salivary glycoproteins (bacteria that cause cavities selectively latch on to some types of glycoprotein sugar chains and are repelled by others)

- A saliva test for HER2/neu in women with breast cancer was being tested in clinical trials in 2002 with hope of FDA approval in 2003, but after a flurry of articles at that time, there has been no further publication suggesting it did not prove effective (Medic Group was doing the testing, but its website is no longer available)
 - Ovarian cancer marker CA-125 can be detected in the saliva and testing is being done – outcome unknown
 - Saliva tests for C-reactive protein, periodontal disease and osteoporosis
 - Saliva DNA testing may be used for accurately assessing how well the brain is controlling levels of serotonin, an important neurotransmitter linked to depression
- **Practicality & ease of use:**
 - Saliva testing is minimally invasive and is painless
 - Some tests have been approved for home use
 - Early on will likely be useful for screening as they will be less sensitive than standard blood sample tests. With time saliva tests could be reliable stand-alone diagnostics.
 - How tests might be used:
 - Small samples of saliva are easily collected on a swab with a sponge for testing in a device; alternatively the person could just spit in a cup (that might also be the testing device).
 - A prototype biochem lab in a cigarette-pack sized cassette using microfluidic channels can detect a particular bacterium or virus in less than one hour. Specific probes detect human antibodies for a particular pathogen, a unique protein on the bacteria's surface, or the pathogen's DNA or RNA. The resultant biomarker complexes migrate via microfluidic pathways to an area where they are scanned by a laser. Specific colors identify that a particular pathogen is present.
 - PCR testing has also been miniaturized
- **Accuracy:**
 - Accuracy over 90% for mRNA saliva test for oral cancer
- **Cost:**
 - Cost of existing drug and other tests range from a couple dollars to under \$50
 - It is unknown what tests for cancer or diabetes would cost
- **Players:**
 - Daniel Malmud, biochemist at New York University College of Dentistry worked on testing technology for 20 years and helped develop HIV test
 - David T.W. Wong at UCLA School of Dentistry developed saliva test for oral cancer
 - Charles F. Streckfus of University of Mississippi School of Dentistry is working on saliva testing for breast cancer
 - **OraSure Technologies** of Bethlehem, PA makes saliva-based drug tests and is working on new concepts
 - Paul Denny of USC School of Dentistry and **Proactive Oral Solutions** is working on salivary glycoproteins to predict life-long risk of cavities

- William Giannobile, professor of dentistry and biomedical engineering, U of Michigan School of Dentistry and director of Michigan Center for Oral Health Research (MCOHR)
 - Microchem Lab of MCOHR is manufactured by **Sandia National Laboratories**
 - National Institute of Dental and Craniofacial Research has agenda for saliva testing research and recently funded seven grants for development of saliva/oral fluid based diagnostics (<http://www.nidcr.nih.gov>)
- **Stage of development and market potential:**
 - Alcohol, drug, hormone, HIV and other saliva tests are on the market – most cost a few dollars
 - Dr. David Wong thinks a test for oral cancer might be available in 1 ½ - 2 years. Other cancers will probably take much longer
 - Dr. Wong thinks it will take about 2 years to complete the saliva roadmap and then researchers can begin looking for signatures for diabetes, rheumatoid arthritis and other diseases. Their goal is to identify genetic signatures for at least 10 common diseases by 2007
 - The test for HER/neu was in clinical trials in 2002 but apparently was not successful
 - There is proof in principle that saliva diagnostic tests might work, but it is unclear how many years it will take to perfect a specific test and get it through clinical trials and regulatory approval to get on the market – probably at least 3-5 years
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Breath Testing

Police use simple breathalyzers to confirm drunk drivers, but now technological advances permit analysis of volatile organic compounds (VOCs) that are a billion times more sensitive. Researchers have done several studies using patterns of specific VOCs to screen for diabetes, lung and breast cancer and other diseases. Early results are promising as first line screening tests. The breath collection procedures often require trained personnel and the analyzer technology is still complex, but if further testing in a wide range of patients shows clear benefit these problems will be overcome in commercial versions of the machines. The proper role in screening and therapy would need to be proven. The technology is clearly noninvasive and painless, but its cost-effectiveness must be shown before it is useful in community health centers.

SPECIFIC DETAILS:

- **Principle or Mechanism of Action:**
 - Precise assessment of very small amounts of volatile organic compounds (VOCs) in breath usually combined with analysis of patterns of compound concentration compared to unique patterns associated with disease states
- **What it can measure:**
 - Acetone which is increased in the breath in those with diabetes
 - Helicobacter pylori, the bacterium linked to peptic ulcers is detected by mass spectroscopy
 - Alcohol in the breath for drunk driving – a hand-held device quickly measures only alcohol molecules
 - Currently looking at about 400 volatile organic compounds (VOCs) – i.e., methane, pentane, benzene – in breath as markers for various diseases. Cavity ring-down spectroscopy (CRDS) detects the presence of certain gases by measuring the rate at which photons decay in a special chamber and can detect these gases at levels of less than one part per billion
- **Potential disease applications:**
 - **DIABETES** – A prototype device produced by John Plodinec and Chuji Wang analyses the acetone in a single breath to rapidly determine if a person is diabetes-free or in an early or severe stage of the disease. In 2004 they applied for a patent. They envision a device that costs \$5,000-15,000 in about 5 years (2010) that could be used for rapid screening in a clinic or at the mall. The device could also monitor effectiveness of therapy and even be used for home monitoring with results also sent to care providers.
 - **BREAST CANCER** – breast cancer is accompanied by increased oxidative stress and induction of polymorphic cytochrome P-450 mixed oxidase enzymes which affect the abundance of volatile organic compounds in the breath. A pilot study measured these changes (breath methylated alkane contour) and could distinguish between women with and without breast cancer with a sensitivity of 94% and specificity of 73.8%. The negative predictive value using this breath test was better than screening mammograms, but screening mammograms had better

positive predictive value. If large group studies confirm the results, the test could be used as a primary screen for breast cancer.

- **TUBERCULOSIS** and **PRE-ECLAMPSIA** are also being studied using this oxidative stress approach.
- **LUNG CANCER** – multiple researchers are developing methods to screen for lung cancer.
 - Serpil Erzurum of the Dept of Biopathology at the Cleveland Clinic Lerner Research Institute used a hand-sized Cyranose – an electronic nose that uses biosensor technology to produce a “smellprint” of VOCs – to show that differences in exhaled breath of cancer patients could be used for early diagnosis and monitor effectiveness of treatment. The study included 14 with lung cancer compared with 62 normal patients and yielded a positive predictive value of 66% and negative predictive value of 92%.
 - Michael Phillips did a multicenter study of 178 bronchoscopy patients (finding 87 lung cancers) and 41 healthy controls measuring 9 VOCs of oxidative stress products associated with lung cancer. The breath test was 85.1% sensitive and 80.5% specific for primary lung cancer with a 10.8% positive predictive value and 99.5% negative predictive value. Additional data presented at the 2005 American Society of Clinical Oncology meeting showed results for primary lung cancer with 81.5% sensitivity, 87.3% specificity, NPV of 99.6% and PPV of 11.6% when all 407 subjects were combined. More tests are needed to determine if these tests will be as predictive when used on patients with other cancers and chronic diseases.
- **Canine Scent Detection of Lung, Breast, Bladder and Prostate Cancer** – A just published study using dogs to sniff breath samples in a controlled randomized study (diagnosed untreated cancer patients vs. controls) demonstrated 99% sensitivity and specificity for detecting lung cancer and 88% sensitivity and 98% specificity for detecting breast cancer. Another study of dogs sniffing urine detected 41% of bladder cancers and work is also being done for prostate cancer. A study at the Florida State University Sensory Research Institute also showed that dogs could sniff out melanomas (unknown if they were detecting cancer or maybe just inflammation). These are normal dogs which are trained for several weeks using breath from cancer patients and then from normal controls. These studies show there are discriminating chemical compounds in breath for detecting cancer. The challenge is to identify the ones that most accurately predict cancer for incorporation into biomarker tests. The other option if larger trials show similar results would be to train a lot of dogs.
- Detection of **HEART TRANSPLANT REJECTION** – A FDA approved two-minute Heartsbreath test assesses oxidative stress by detecting about 200 volatile organic compounds in a single sample breath. The resulting pattern of VOCs is compared to the distinctive pattern of heart transplant rejection. The sample must be sent to the lab for chemical analysis followed by computer data analysis. The test, in many cases, can replace the invasive and expensive endomyocardial biopsy previously used to detect rejection. It also estimates the severity of rejection (mild to severe) for selecting appropriate therapy and monitoring response.
- **Practicality & ease of use:**
 - Breath tests are noninvasive, but the collection of breath and simultaneous ambient room air samples for some tests requires technical exactness. Monitoring technology is simple and fast for commercially available tests, but can be complex and time consuming for diseases under investigation. Once the technology and validity are worked out simple versions are likely to be developed.

- Once developed they could be ideal for rapid noninvasive screening in the clinic, health fairs and in the home.
- **Accuracy:**
 - In small studies, excluding patients with multiple other diseases, the sensitivity and specificity are in the 70-90% range.
- **Cost:**
 - Single use breath alcohol detectors are less than \$3, multiuse alcohol breathalyzers are less than \$90, but evidential breath testing devices cost \$2,000-5,000 per unit and require certified personal to maintain and calibrate the machine.
 - Specific disease breath testing devices are still experimental and commercial costs have not been determined.
- **Players:**
 - John Plodinec and Chuji Wang of **Mississippi State University's Diagnostic Instrumentation and Analysis Laboratory** are working on breath analyzer to detect diabetes
 - **Picarro Incorporated** does research to detect gases at the molecular level using cavity ring-down spectroscopy
 - **Menssana Research** and CEO Michael Phillips, part of the Enterprise Development Center incubator program at New Jersey Institute of Technology developed the FDA approved Heartsbreath test to detect rejection of heart transplants, worked on lung and breast cancer, tuberculosis and pre-eclampsia tests and developed the underlying oxidative stress assessment tests.
 - Michael McCulloch, **Pine Street Foundation** did research on dogs detecting lung and breast cancer.
 - James Walker, director of **Florida State University Sensory Research Institute** did research on dogs sniffing melanoma.
- **Stage of development and market potential:**
 - Alcohol testing has been on the market for years.
 - The Heartsbreath test for detecting rejection of heart transplants is FDA approved, but with the low volume need, it may only be available in university research labs.
 - Other disease tests are still experimental. They probably could reach the market soon, but there must be clear indications for when they are most beneficial and cost-effective in screening or for monitoring therapy. That could take some time to ascertain.
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Stool Testing

Testing stool for occult blood, typically called fecal occult blood testing (FOBT), has long been the standard for screening for colorectal cancer. The newer immunochemical fecal occult blood test makes dietary restrictions unnecessary and eliminates false positives, but it is more expensive and not more effective in detecting cancer. The latest method is fecal DNA testing which detects mutations in sloughed neoplastic cells. All these stool screening tests can make a big difference by often detecting colorectal cancer at an early stage. Unfortunately, only 22% of those over 50 years old received fecal tests in the past 12 months due to low consumer acceptability with collecting the samples.

SPECIFIC DETAILS:

- **Principle or Mechanism of Action:**
 - Test stool samples for occult blood caused by bleeding colorectal cancers or products of exfoliated cancer cells
- **What it can measure:** All these tests are for screening for colorectal cancer
 - Occult blood in the stool testing is the standard screening measure for colorectal cancer
 - Immunochemical fecal occult blood tests work through antibodies that detect partial sequences of antigenic sites on the globin portion of human hemoglobin so dietary restrictions are not needed.
 - Tests for abnormal DNA from sloughed tumor cells identify APC, K-ras, p53, and BAT-26 mutations. It requires a sophisticated testing method that separates abnormal human DNA from normal human and animal DNA, then amplifies the DNA and tests it for specific abnormalities.
 - Rectal mucus test for the amount of cancer-associated carbohydrates – the ColorectAlert test by PreMD, Inc. has a sensitivity of 60% - 80% and specificity of 68% - 90% for early-stage cancer
 - Tests for mRNA and minichrosomal maintenance protein (MCM2) are being investigated
 - Tests of fecal carcinoembryonic antigen (CEA) and various fecal proteins have not been successful
- **Potential disease applications:**
 - FOBT currently is the standard screening measure for colorectal cancer

- Presence of fecal occult blood can also be due to benign polyps, arteriovenous malformations, diverticulosis and other pathology.
- **Practicality & ease of use:**
 - Easy and painless to collect stool samples, but the process is not acceptable to many people. Many tests require dietary and medication restrictions for a few days before testing to reduce the rate of false positives. Occult blood tests give near instant results when the reagent is added.
 - For DNA testing one whole stool must be collected, packed, refrigerated, and then mailed off to a central lab – limiting patient acceptance and compliance.
 - Rectal mucus is obtained during a digital rectal exam during a doctor visit and sent to the lab.
- **Accuracy:**
 - Specificity for occult blood testing ranges from 88% to 98%
 - Sensitivity for cancer of various DNA tests varies from 52% to 91%, but there are also many unexplained false positives
 - Rectal mucus – galactose oxidase Schiff test detects abnormalities in mucin structure and expression caused by cancer cells, but abnormal tests are also caused by colitis, inflammatory bowel disease and other disorders.
- **Cost:**
 - Occult blood tests are very inexpensive. The patient typically pays \$10-25
 - EXACT Sciences PreGen-26, the first commercially available stool DNA screening test cost \$795
- **Players:**
 - Bert Vogelstein at the Sidney Kimmel Comprehensive Cancer Center in Baltimore for fecal DNA testing
- **Stage of development and market potential:**
 - All these tests are now available with refinements being developed.
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Skin Testing

Skin is actually a large organ comprising about 17% of body weight, but it is not often considered for testing except for dermatologic conditions and allergen skin tests. Here are two novel skin biomarker approaches that are noninvasive and easy to obtain. One is available and the other is in early research.

SPECIFIC DETAILS:

- **Principle or Mechanism of Action:**
 - Quantitative color reaction measuring cholesterol molecules in the skin
 - Tape removal of epidermal cells for DNA or mRNA analysis for gene expression
- **What it can measure:**
 - Compounds in the skin
 - Epidermal cell gene expression
- **Potential disease applications:**
 - **CHOLESTEROL** – PREVU is an FDA approved non-invasive 3 minute point-of-care skin test for measuring skin sterol (cholesterol). Two drops of liquid on the palm result in a color change reaction which is read by a hand-held spectrophotometer (color reader). Eleven percent of the body's cholesterol is located in the skin so a high sterol reading is a reliable predictor of higher cholesterol in arteries. Studies show that skin cholesterol correlates with stress tests, carotid intima-media thickness by ultrasound, angiography, inflammatory markers and a prior heart attack. There is a demonstrated relationship with the Framingham Global Risk Score. It is a screening test useful for stratification of primary care patients according to cardiovascular risk and could potentially be used for monitoring response to therapy.
 - **PROSTATE CANCER SCREENING** - a novel skin test approach analyzes genes on the skin's surface looking for alterations in gene expression due to the cancer. A specially designed adhesive tape harvests surface skin cells. Cell DNA or mRNA is then analyzed. Prostate cancer cells produce substances that influence growth of other tissues, including skin. An ongoing study of patients at UC San Diego will analyze at least 47,000 genes and hopefully narrow that down to about 25 genes that are statistically predictive of the cancer. If successful the next step will be to see if the test can determine whether the prostate cancer is likely to be slow growing requiring only monitoring or more aggressive requiring therapy.
- **Practicality & ease of use:**
 - The PREVU sterol test is noninvasive and fast
 - Samples are easy to obtain for skin DNA testing
- **Accuracy:**
 - Not available
- **Cost:**
 - Sterol test is claimed to be “cost effective” but we were unable to find actual cost
 - Skin DNA testing requires involved laboratory testing and will likely be expensive
- **Players:**
 - **International Medical Innovations, Inc.**, maker of PREVU skin sterol test distributed through McNeil Consumer Healthcare
 - William Wachsman at UC San Diego is studying skin DNA for markers of prostate cancer

- **Stage of development and market potential:**
 - The skin sterol test is approved for use. The real question is whether it is a better screening test than serum cholesterol.
 - Tape removed skin for DNA testing appears to be as reliable as punch biopsies for skin conditions, but is in early development as a diagnostic marker for non-skin cancer and possibly other diseases.

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Blood and Serum Tests

Blood is the ideal medium for monitoring health and detecting disease. It is the body's transport system hauling nutrients, wastes, disease causing pathogens and hormones everywhere. Rapid circulation and mixing means plasma is representative of the body's chemical balance. A sample from a vein or finger stick is likely to contain a few molecules of an abnormal protein or other substance created by a disease state somewhere in the body. Sampling is easy, but the slight pain of blood drawing keeps some people away from appropriate testing. Only those with the motivation of a serious disease are willing to draw blood samples at home for monitoring. New testing technologies can detect incredibly small amounts of a substance and many devices run autonomously with high accuracy making them ideal for point-of-care and home use.

Rapid advances are being made in analyzing proteins and gene markers, often discerning unique patterns of hundreds of elements looking for characteristics consistent with disease states, especially cancers. This research is very complex and it is unknown how long it will take for effective tests to reach the market. The big challenges for clinical application are specificity for a particular disease, number of false positives and false negatives, complexity of doing the test and the cost. A good example of the problem is the PSA test for prostate cancer where a low value does not rule out cancer, benign conditions can cause an elevated value and an abnormal value doesn't tell if the cancer is indolent or

aggressively growing. The result is a lot of negative biopsies and conflict over appropriate management. There will be announcements of many promising biomonitoring tests over the coming years. The challenge for clinicians, administrators and payors will be to put these tests into proper context and selecting those that are truly valuable and cost effective.

SPECIFIC DETAILS – BLOOD TESTS IN GENERAL:

- **Principle or Mechanism of Action** – there are many technologies for evaluation depending upon the substance to be measured. Standard tests are automatically done in self contained units, and many are suitable for point-of-care or home use.
- **Sampling** – usually requires blood drawn from a vein or a finger stick. With microtechnologies, sample sizes are often a drop or even much less. Blood spot testing uses a finger prick to place a couple drops of blood on filter paper where it is dried and sent to a lab. In some cases a series of tests can be done on the sample. This is a simple, inexpensive, highly accurate way to get selected blood tests that should have wide acceptance for empowered patient self-management.

Noninvasive testing methodologies have long been needed for people with diabetes who must do multiple daily blood glucose tests. The GlucoWatch®, available in 2002, used a low electric current to pull serum through the skin for sensors on the underside of a wristwatch-like device to continuously measure glucose. However, it proved not to be practical. Other devices use microneedles, different transdermal serum technologies, implanted probes and even fiberoptic nanowires for sampling. There is even a device that shines infrared light into the sclera of the eye to record the changes in light frequencies reflecting off hemoglobin molecules in the blood (similar to the pulse oximeter). It is uncertain when a practical commercial product will become available for routine daily use, but it might still take a few more years.

- **What it can be measured:**
 - Anything circulating in the blood – electrolytes, plasma proteins, sugars and fats, blood elements such as neutrophils, pathogens such as HIV, toxins, abnormal genetic or protein products of disease, and other substances.
- **Purposes:**
 - Assess risk of developing future diseases
 - Screening for diseases
 - Determining diagnosis and subdiagnoses; identifying specific etiologies
 - Multiple uses in management of diseases – selection of therapies, monitoring progress, identifying relapses and recurrences, confirming cures and remissions
 - Prognosis
 - Important element of all aspects of biomedical research including epidemiological studies
- **Practicality & ease of use:**
 - Blood is easy to collect. Many tests are simple to perform at point-of-care or in a standard laboratory, whereas others are complex, expensive and must be mailed out to special labs.
 - The big issue is access to results. It is much more effective if the result is available when the patient is being seen by a provider, rather than trying to track down the result and contact the patient at a later time.

- **Accuracy:**
 - Most commonly used standard lab tests have high accuracy and reproducibility rates.
 - Current screening tests for cancers and other diseases tend to have high false positive and false negative rates limiting their usefulness and cost effectiveness.
- **Cost:**
 - Vary from very inexpensive to perform routine blood tests to very expensive new genetic and protein tests.
 - Even if the test is inexpensive, community health centers may find the cost of maintaining a lab with trained lab technicians beyond reach so only the most basic tests are available on site. These centers are reluctant to do screening and periodic tests that must be sent out. Even if the costs per test are moderate, it is inconvenient to track down the patients once the results have returned. If a modular testing device that is inexpensive, simple and accurate became available, it would be extremely useful in the community health clinic setting at the point-of-care. It might also be given to patients with serious chronic diseases for home self-care.

SPECIFIC DETAILS – NEW PROTEIN AND GENE BIOMARKER TESTS:

Researchers are aggressively looking for ways to assess proteins and genes in the blood to assess the risk for serious diseases, make early diagnoses before symptoms develop and help guide therapy. This is a very complex undertaking and most tests are still experimental. While the goal has been to find effective early screening tests for cancer, there usually are not enough abnormal proteins circulating in the blood to be detected until the tumor is large enough to be detected in other ways. Tests that look at genes to characterize cancers require analysis of biopsies of the cancer cells themselves. Effective screening tests may still be a few years off. Examples of current progress are as follows:

- **Genetics** – genetic variations, mostly consisting of scattered changes to single letters of the DNA code (called single nucleotide polymorphisms or SNPs), might be responsible for a disease or make a person more susceptible to getting a disease. Recent examples of research:
 - **Gene variations that increase risk** –Tests looking for specific mutations can identify higher risk individuals for close monitoring or preventive interventions. DeCode Genetics has identified a gene carried by 1/3 of Americans that might indicate added risk of type 2 diabetes. Of several variations, one appears to partially protect patients against diabetes whereas two variations increase risk. About 21% of diabetes cases could be attributed to the risky variations. The gene appears to play a role in the regulation of other genes involved in hormone secretion, but it is not an all-or-none predictor of diabetes risk.
 - **Gene patterns associated with increased risk** – “Genomic fingerprints” look at variations in dozens to hundreds of genes to find predictive patterns associated with characteristics of specific diseases for identifying high risk patients or to detect early disease. Patterns differentiating disease subsets could also help determine the most effective therapeutic option. Examples of ongoing work are genetic profiles related to predisposition to diabetes and genetic susceptibility

to kidney disease in type 2 diabetes, and proinflammatory genetic profiles that may contribute to the development and progression of cardiovascular diseases.

- **Abnormal genes in established disease** – Diagnostic biomarker tests for specific abnormal genes can be used to identify subtypes of disease and help guide therapeutic decisions. Cancer is a major focus of research efforts. There are tests available that detect mutations in specific cancer genes that make them susceptible to new targeted therapies. To assess the genes in cancer cells these tests must be done on tumor tissue samples.
 - An example of a single gene test is Genzyme’s EGFR Mutation Assay. It looks for the presence of epidermal growth factor receptor (EGFR) mutations in non-small cell lung cancer patients that correlate with a successful clinical response to Tarceva® (erlotinib) or IRESSA® (gefitinib). The test costs about \$975.
 - Examples of gene pattern tests that look at a profile of 21 or 70 genes are *Oncotype DX™* and *MammaPrint®*. These microarray cancer diagnostics analyze the DNA expression profile of an individual’s breast cancer to predict likelihood of recurrence and whether chemotherapy in addition to tamoxifen would be beneficial. Both tests cost over \$3,000.
- **DNA Methylation** – DNA methylation results when a carbon atom surrounded by three hydrogen atoms attaches to cytosine within the DNA sequence, silencing the gene without changing its actual sequence. Abnormal methylation occurs early in disease, especially in cancer where several alterations are necessary for cells to evolve into cancerous ones. So far about 50 genes have been identified where methylation plays a role in cancer development. Researchers are looking for methylation patterns in biopsy specimens, serum, saliva, sputum, urine and stool to detect precancerous changes and established cancer before symptoms develop. Someday these biomarkers could be used for risk assessment, screening, confirming diagnosis, staging disease and determining the most likely beneficial therapies based upon specific cancer mutations. These biomarkers could also determine that a patient is unlikely to have cancer, avoiding invasive procedures, and if a cancer is likely to be slow growing so that radical surgery isn’t necessary. Researchers are particularly interested in bladder, breast, colon, lung, ovarian, and prostate cancers. Current testing equipment used in research is very sensitive in detecting just a few cancer cells in a specimen.
- **Mitochondrial Genetics** – Metabolic syndrome with risk factors for diabetes, hypertension, hyperlipidemia, obesity and cardiovascular disease might be triggered by genetic changes in mitochondria. Mitochondria have their own DNA (mtDNA), and as they are the power house of the cell, there is a close correlation between mitochondrial dysfunction and beta-cell dysfunction. The 16189 gene variant is found slightly more commonly in type 2 diabetes than in controls. A team at the Center for molecular and Mitochondrial Medicine and Genetics at UC Irvine is studying the genetic variations of mtDNA associated with various metabolic diseases. It is also developing biomarkers, including exploring rapid non-invasive methods potentially using infrared laser or breath analysis technologies. It is too early to tell if this research will lead to a test for screening or therapeutic decision making in metabolic disorders.
- **Pharmacogenomics** – Variations in specific genes determine how well certain drugs are metabolized and excreted by an individual. Testing guides therapeutic decisions by identifying

when a drug's standard dose should be altered or if a particular drug should not be given to that patient. This information is important for expensive or high risk medications and determining the right drug at the optimum dose immediately in a life threatening disease. Examples of recently approved pharmacogenomic tests are (1) Invader UGT1A1 Molecular Assay that detects variation in a gene affecting the metabolism of irinotecan, a colon cancer treatment, (2) the Roche AmpliChip that is used to individualize dosage of beta-blockers, antipsychotics, antidepressants and some chemotherapy drugs, and (3) the TRUGENE HIV-1 Genotyping Kit that detects variations in the genes of human immunodeficiency virus making it resistant to some drugs. In the future most patients will have a pharmacogenomic profile (like knowing their blood type today) that will be routinely checked when prescribing drugs.

- **Proteins**

- **Single protein markers** – Prostate specific antigen (PSA) is a widely used but controversial screening test for prostate cancer. Other protein markers such as carcinoembryonic antigen (CEA) for colon cancer and CA 125 for ovarian cancer are not specific enough for screening, but are somewhat helpful in monitoring the management of extensive disease. Researchers continue to look for the ideal, highly predictive biomarker for serious diseases.
 - Platelets contain proteins that regulate angiogenesis (development of new blood vessels). Therefore platelets selectively take up and preserve angiogenesis regulatory proteins secreted very early by developing cancer cells. A blood test monitoring for an increase of these regulatory proteins in platelets could provide an early indication that a cancer is developing or that a metastasis is occurring. Clinical trials are testing the predictive value of this methodology.
- **Protein profiling** – This methodology analyzes hundreds of proteins from blood or tissues with mass spectrometry and protein microarrays to identify significant changes occurring when cells progress from normal to disease. Cancer cells overproduce many proteins so a pattern of peaks and troughs, each representing the blood level of a specific protein, will hopefully detect a cancer with a high degree of accuracy. Large numbers of blood protein levels are compared between cancer patients and normal controls using sophisticated pattern recognition algorithms to discover unique “fingerprints” associated with specific early cancers. These must then be tested in large groups of cancer and non-cancer patients to determine predictive value.
 - OvaCheck®, a test for early detection of epithelial ovarian cancer, is an example of work in this area. An initial study published in *Lancet* in 2002 had a predictive value of 94%, but later efforts to confirm the methodologies and reproduce the results ran into difficulties because of complexity of the concept and minute amounts of proteins being analyzed. The FDA has declared OvaCheck to be a new medical device requiring successful clinical trials before approval. It remains to be seen whether the technology will succeed in passing this hurdle. Similar research is being undertaken by several biotech firms looking for predictive biomarker patterns for breast, lung, pancreatic and other types of cancer and a wide variety of other serious diseases. For example, researchers are seeing if protein profiling can distinguish between aggressive and indolent prostate cancers for selecting the right course of therapy.

- **Metabolites** – a new area of investigation is using advances in biotechnology to detect and interpret the small molecules (metabolites) present in the body, particularly unique molecules that can distinguish the onset of a disease like cancer from normal body functions.
- **Players:**
 - **Canary Fund** – promoting capabilities for the early detection of cancer. <http://www.canaryfund.org>
 - **Center for Molecular and Mitochondrial Medicine and Genetics (MAMMAG)** at UC Irvine looking at variations mitochondrial DNA associated with disease.
 - **Correlogic Systems, Inc.**, creators of “Hidden Patterns” diagnostic testing methodology and the OvaCheck® ovarian cancer screening test. <http://correlogic.com>
 - **Ciphergen Biosystems, Inc.** uses its SELDI ProteinChip technology to develop biomarkers for early detection and management of ovarian, prostate, pancreatic, breast, liver, lung and nasopharyngeal cancers, along with neurological, cardiovascular and infectious diseases. It is also working on measuring platelet accumulation of angiogenesis regulatory proteins secreted by very early tumors.
 - **Genomic Health, Inc.**, maker of Oncotype DX™. <http://genomichealth.com>
 - **OncoMethylome Sciences**, developers of DNA methylation biomarker tests. <http://www.oncomethylome.com>
- **Stage of development and market potential:**
 - New blood-based molecular and genetic screening, diagnostic and treatment tests for cancer and other diseases are in various stages of development and it is unclear, in spite of the hype, when they will be available, or if they will be clinically useful in everyday medicine. When they do become available, the tests currently being developed will usually be very expensive.
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Urine Testing

Urine testing was first used in ancient times for diagnosing disease. Urinalysis is useful for evaluating the urinary system and can help diagnose diabetes, hepatitis and other conditions. An example of urine chemical testing is specific hormone levels for evaluating endocrine function. Current research is looking for specific protein and genetic biomarkers in urine that could be useful in diagnosing cancers and other conditions. Urine is easily and painlessly obtainable, making it an excellent specimen source.

SPECIFIC DETAILS:

- **Principle or Mechanism of Action:**

- Anything that passes through the kidneys into the urine, including many large proteins, is available for analysis. Also tumor cells sloughed from the urinary tract can be detected.

- **What it can measure:**

- Standard urinalysis measures pH, bilirubin, glucose, ketones, hemoglobin, protein, white cells, bacteria, etc.
- Chemistry tests measure specific hormones such as norepinephrine and cortisone, electrolytes, uric acid, amylase, myoglobin, etc.
- Tumor cells and tumor markers such as CEA and CA-125

- **Potential disease applications:**
 - **Urinary track cancer** – tumor cells, or their gene and protein biomarkers, from the kidney, ureter and bladder can be detected in urine.
 - **Breast cancer** – a small study at Boston Children’s Hospital detected a protein biomarker called ADAM 12 in the urine of 94% of breast cancer patients, but only low concentrations in 15% of controls. It is highest in advanced, metastatic breast cancer. ADAM 12 may be detectable before the mammogram is positive or it may help determine whether a lesion seen on mammogram is likely malignant or benign.
 - **Multiple cancers (bladder, breast, colon, lung)** – protein biomarkers such as matrix metalloproteinases (MMPs) increase once a tumor is ready to grow. MMPs break down the extracellular matrix surrounding cells so angiogenesis can develop new blood vessels in the tumor. In theory, protein biomarkers in the urine could determine a tumor’s aggressiveness, track effectiveness of therapy and determine when a tumor reaches certain milestones such as developing a blood supply and spreading to distant sites.
 - **Ovarian Cancer** – other researchers are looking for unique serum and urine biomarkers for detecting early stage ovarian cancer to use as screening tests.
 - **Toilet for diabetes** – Toto, Ltd., a Japanese manufacturer has a ”smart toilet” that checks for glucosuria. This might be used as an initial screening test for diabetes. However, urine glucose does not correlate well enough with blood glucose for precise control of diabetes.

- **Practicality & ease of use:**
 - Urine is easily and painlessly collected and biomonitoring tests can be developed for home use. An example is the urine dipstick rapidly performing several tests that can be easily read by comparing color changes.

- **Accuracy:**
 - Qualitative accuracy is good, but variable urine dilution depending upon hydration and other factors make quantitative measurement difficult.

- **Cost:**
 - Routine urinalysis is inexpensive
 - Sophisticated protein and gene tests could be quite expensive for the foreseeable future.

- **Players:**
 - Marsha Moses, PhD, **Children’s Hospital Boston’s Vascular Biology Program**

- **Stage of development and market potential:**
 - Early development, high potential if accurate tests reach market

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Physiologic and Lifestyle Information Monitoring

Although many diseases are caused by genetic makeup, about 40-50% of our disease burden is due to poor lifestyle choices – people not taking care of themselves. Yet only 0.5% of the \$1.9 trillion U.S. health care expenditure is spent on helping people better manage their own health. Helping people change their behavior is extremely difficult. Part of the problem is not being able to manage what you can't measure. New wearable devices permit monitoring of physiological parameters that are then translated through algorithms into useful health information, such as daily energy (calorie) expenditure, amount of physical activity and duration of sleep. This information is collated over time and made available electronically to the individual and health providers in several useful formats. The net result is that people start to learn about themselves, providing a feedback loop for actions taken to improve their health. This concept is an elegant integrated system designed to provide medically accurate data through unobtrusive, noninvasive wearable sensors that are simple enough for consumer use while being relatively inexpensive to produce.

SPECIFIC DETAILS:

- **Principle or Mechanism of Action:**
 - Physiologic data is measured noninvasively and assessed by sophisticated algorithms to interpret and derive meaningful health information about the individual. The monitoring system may be a wearable device like a wrist watch, attached to the body as an adhesive patch or embedded in clothing.
- **What it can measure:**
 - Sensors might include a two-axis accelerometer (detect motion and body position), heat-flux (body heat dissipation), galvanic skin response (varies with sweating and emotional stimuli), single lead EKG (heart rate), impedance pneumography (breath rate) or electroencephalogram (brain- wave activity). Algorithms convert data into measures such as duration of physical activity, calories burned at rest or during activity, times of sleeping and awakening, heart rate, or the effects of anesthesia and sedatives on the brain. Data from additional stand-alone biomonitoring devices such as a glucometer can be wirelessly uploaded into the monitoring system computer to enhance the picture of a patient's health status.
- **Potential disease applications:**

- **Weight loss and controlling weight** – monitor exercise, total calories burned a day, calorie intake (computerized food diary), real-time daily calorie deficit or excess to provide an accurate picture of activity and impact on calorie balance for the patient. This can reinforce healthy patient behavior and provide valuable information to a professional providing coaching.
 - **Diabetes management** – lifestyle changes to increase activity and lose weight have been shown to prevent prediabetes from progressing in 58% of patients, adequately manage early disease without medications and improve outcomes in more advanced cases. Sensors can keep track of activity and calories burned (as noted above). Additional information such as blood glucose, blood pressure, EKG readings and weight can be captured by other monitoring devices and wirelessly added to the monitoring system for a comprehensive computerized picture of ongoing health status. The system provides feedback to reinforce patient behavior and assist providers in disease management.
 - **Level of anesthesia** – monitoring of brain-waves can directly tell whether anesthesia is deep enough for the patient to be unconscious and free of pain during surgery.
 - **Effectiveness of a central nervous system drug** – normally it takes 4-6 weeks of trial and error to determine if a newly administered anti-depressant drug is effective and select the optimal dose. A simple brain-wave reader with sensors periodically strapped to the forehead can determine efficacy in about a week.
 - **Rehabilitation or subjects working in extremely stressful environments** – monitoring of vital signs can track progress or level of risk.
 - **Research projects** where continuous “free-living” physiologic data is needed to correlate with other experimental parameters.
 - **Mental state, health status, other conditions** where information derived from physiologic parameters assists management. For instance, researchers are investigating whether brain wave patterns can detect Alzheimer’s disease before clinical symptoms are apparent.
- **Practicality & ease of use:**
 - Unobtrusive, noninvasive wireless sensors can be worn all day without discomfort and systems are easy for patients to use. Data is wirelessly collected, interpreted and displayed in easy to understand formats.
 - **Accuracy:**
 - Accuracy is continually improving as more data helps refine algorithms. For instance, the SenseWare® and bodybugg™ armband devices by BodyMedia provide 92% accuracy for total calories burned.
 - **Cost:**
 - BodyMedia’s armband device is about \$300 and could go down to \$100 with increased volume and mass marketing.
 - **Players:**
 - Astro Teller, PhD, CEO and John (Ivo) Stivoric, Chief Technology Officer at **BodyMedia, Inc.** <http://www.bodymedia.com>
 - **WEALTHY, the Wearable Health Care System** <http://wealthy-ist.com>

- **Aspect Medical Systems** the maker of BIS™ technology for brain wave monitoring; device is incorporated into multiple vendor patient monitoring systems. <http://www.aspectmedical.com>
- **Stage of development and market potential:**
 - BodyMedia devices have been on the market for a couple years. Their capabilities and accuracy are continually being upgraded. The 2006 version of the SenseWear Armband® will have a single lead EKG sensor for heart rate in addition to accelerometer, heat flux, galvanic skin response, skin temperature and event stamp.
 - WEALTHY, a European consortium has been designing a garment that has embedded sensors incorporated into textile fibers to continuously monitor vital signs and uses mobile phone signaling to transmit data or alert emergency medical services. It is still undergoing development.
 - Aspect Medical Systems' BIS™ brain-wave monitoring technology was approved by the FDA in 1996 for assessing level of consciousness during anesthesia. It hopes to win FDA marketing approval for using brain-wave monitoring for assessing antidepressant drugs by the end of 2008.
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Imaging Tests

Imaging technologies have progressively improved. Now they are digital for easy transfer of images and hand-held portable devices exist for ultrasound and even CT scans for use in clinics. Progressive advances are constantly changing the cutting edge of screening and diagnostic tests for breast, colon and lung cancer, but standard tests usually remain the most cost effective for community health clinics. The big breakthrough though is noninvasive molecular imaging that visualizes and measures normal as well as abnormal cellular processes at molecular or genetic levels of function. This provides the ability to detect the presence of a disease such as a specific cancer, earlier and more accurately, rapidly shows whether a therapy is working, and detects asymptomatic recurrences.

SPECIFIC DETAILS OF STANDARD ANATOMIC IMAGING FOR CANCER:

- **Breast Cancer**

- There are two key components of molecular imaging. The first is the **imaging probe** which zeros in on the specific target of interest and is then visualized by a special scanning method. A specific receptor site is identified that is associated with a target molecule that characterizes the disease process under study. A molecular imaging agent is developed that binds specifically with that receptor site, and then it is labeled with a radioactive substance or other methodology that allows detection by the imaging device. Once administered to a patient, the probe locates and binds to target molecules in high enough concentration to be detected by the imager. The concept is simple, but the development process is complex. Currently there are over 500 probes with many more to come.
 - The second component is the **imaging modality**. Currently there are three noninvasive, in vivo imaging technologies that can provide spatial and temporal dimensions of understanding.
 - **Radionuclide imaging devices** can visualize very low concentrations of radionuclide probes in real time and provide quantitative information, but provide low image resolution.
 - **PET (Positron Emission Tomography) scan** – uses positron emitting radioisotope probes and is becoming popular for research and clinical applications.
 - **SPECT (Single Photon Emission Computed Tomography) scan** – probes use isotopes emitting gamma rays that are detected by a gamma camera to create the scan.
 - **Radionucleotide imaging combined with CT or MRI** – provides functional imaging with high anatomic definition for precise location of the pathology.
 - **MRI (Magnetic Resonance Imaging) scan** – uses paramagnetic-labeled probes which require large doses and sometimes overwhelms the system being investigated. The image is of high resolution.
 - **Optical Imaging** – uses fluorescent or bioluminescent probes that emit radiation in visible or near-infrared wavelengths, which are scanned by optical cameras. As light penetrates only a few millimeters of tissue the technology is limited to the skin, breast and internal cavities where a remote camera probe can be placed.
- **What it can measure:**
 - Proteins, genes, pathogens, and other molecules that are associated with physiological processes and diseases can be visualized. Quantitative measures can be made in some cases.
 - **Potential disease applications:**
 - **Diagnostic Imaging**
 - Detect disease or even predisease early before there are any symptoms
 - Differentiate reversible from irreversible damage in heart attacks and strokes; identify benign from malignant cancers
 - Evaluate all organs for metastatic cancer
 - Rapidly determine effectiveness of therapy allowing quick substitution if it is not working
 - Follow-up for early detection of recurrences
 - Estimate disease prognosis

- **Therapeutic Imaging** - A targeted therapeutic delivery mechanism combines a molecular probe with a drug or other therapy so the treatment is concentrated in the tumor with low toxicity to normal tissues.
 - **Basic and clinical research** – molecular imaging has a huge role in understanding normal physiology, discovering targets for therapeutic interventions, facilitating development and clinical trials, and as part of regulatory approval process.
- **Practicality & ease of use:**
 - These technologies are still in an early stage of development and require equipment and expertise that is only available in research centers and major medical centers. Imaging probes are usually administered intravenously. Their role in practical clinical medicine is still being created and validated.
- **Accuracy:**
 - They are highly specific in identifying particular physiologic processes and diseases, but resolution and quantitative information is still less than desired in many applications.
- **Cost:**
 - Expensive:
 - CT scan – \$450-\$700
 - MRI scan – \$700 - \$900
 - PET scan – \$2,000 - \$6,000
- **Players:**
 - Big radiology companies – GE, Siemens, Philips
- **Stage of development and market potential:**
 - Molecular imaging is progressively being used in clinical medicine, particularly for the diagnosis and management of cancer. However, the expense of equipment and staff limit its use to larger medical centers and imaging centers. Its use will grow exponentially as new indications are verified, equipment costs decline and more medical centers add them.
 - In the future technologies will be much more capable, portable with ease of use in the clinic and dramatically reduced in price. They will be relied upon for early diagnosis, extent of disease and rapidly verifying the benefit of specific expensive therapies.
 - Routine use in community health clinics will likely be a long way off unless the cost effectiveness of treating common severe diseases such as lung or breast cancer is so great as to justify the expense of doing molecular imaging studies.
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Miscellaneous Testing

- **Analysis of Breast Nipple Aspirate Fluid to Detect Breast Cancer**
About 80% - 85% of breast cancers originate in mammary ducts. Nipple aspirate is obtained during a routine physical and sent to the lab where the amount of cancer-associated sugar is determined creating a numeric breast cancer test value. Pilot studies are underway on the PreMD Breast Cancer Test. http://imimedical.com/products_breast.htm.
- **Noninvasive glucose tests**
 - **Infra-red analysis of glucose in scleral capillaries** – A patient would hold a device the size of a cell phone up to her eye for infra-red radiation technology to shine on vessels in the sclera (white part of the eye). The right wave-length would interact with glucose molecules in blood flowing through these tiny vessels and reflect light back in proportion to the amount of glucose in the blood. Oculir is advancing beyond the proof of concept study to a clinical trial for potential approval. John Burd is CEO of Oculir, Inc. Reference: Blood Sugar Readings in a Painless Blink of the Eye. Newsweek, January 16, 2006, p 87.
 - **Non-invasive glucose monitoring of tear fluid** – This is a contact lens that has a special area at the bottom which changes color depending upon the glucose concentration in tear fluid. Blood has 15 times the concentration of glucose as tear fluid, but the ratio remains constant over a wide range. When glucose levels change there is a few minute lag time before tear fluid catches up. The device uses a photonic soft hydrogel glucose-sensing material which changes color across the full spectrum from infrared to blue depending upon the glucose concentration. The patient can estimate blood sugar at any time by just holding a special compact mirror up to the eye and compare the colored spot on the contact to a color code chart around the mirror. It is under development by Glucose Sensing Technologies of Pittsburgh.
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- **Gyroscope Biosensor for Detecting Cancer**

The biosensor has a disk less than 1/10 millimeter in diameter coated with special patterns of DNA or proteins which will bind with specific cancer markers. The disc vibrates electronically in two modes. If a marker binds to the surface the uneven weight will change the frequency of the vibration which can be measured to determine the mass of the protein. From this the protein particle associated with the specific cancer can be accurately identified. The technology might also be used to screen for pathogens.

Sources:

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- **Behavioral Biomonitoring and Remote Home Biomonitoring**

Many companies are now developing biomonitoring and assistive devices, primarily for permitting elders to safely live at home. But these technologies can also be used to measure compliance in taking medications and even as part of systems to coach healthy behavior. There are ways to continuously monitor a patient for level of depression. They can be designed to assist patients in self-managing their health or to provide useful data for controlled clinical trials for drug regulatory approval. It is reaching the point that biomedical engineers can create a monitoring device for any activity that is important to measure. For instance a “smart bed” can assess amount and quality of sleep, vital signs and body weight. Motion sensors in a house can measure activity, assess gait and detect a fall. Devices in the kitchen can tell if a person is eating properly and whether food preparation is sanitary. Smart devices, maybe using radio frequency identification tags, can monitor whether the subject is taking pills properly and can remind him if he forgets.

These technologies can be useful in assisting patients play a major role in self-management of chronic diseases such as diabetes, asthma and congestive heart failure. This approach requires moderate to significant up front costs, depending upon the sophistication of devices used, but can save money in the long run by preventing expensive complications and early death.

Examples of Players:

- MIT AgeLab
- Honeywell HomMed, LLC
- Intel Proactive Health Research Lab
- Medical Automation Research Center at the University of Virginia
- University of Rochester Center for Future Health – Smart Medical Home
- Georgia Institute of Technology
- Motorola’s iDEN Subscriber Group
- GE Industrial Systems
- Panasonic Telecare Solutions

The Ideal Test for Consumer Health Monitoring

What might be ideal characteristics for consumer health monitoring? A recent request for proposals from NineSigma, a global “sourcing” service where companies can request high-tech innovations, on behalf of a large consumer packaged goods company gives a good perspective of what is desirable in future biomonitors for point of care and consumer use. NineSigma is seeking proposals for novel non-invasive biological sensing technologies for disease states that would be appealing to consumers and sold over-the-counter. Criteria include:

- Does not require a biological sample (totally non-invasive) – skin would be ideal
- Easy to use, inexpensive, appropriate for consumers
 - Cost must be in line with other consumer over-the-counter diagnostics
- Predictive for internal disease state or health condition monitoring
 - Preferably can be used to detect multiple disease states
 - Examples of areas of interest
 - Cardiovascular health
 - Poor blood circulation
 - Renal function
 - Diabetic maintenance
 - Fetal monitoring
 - Menopause progression
 - Reproductive health (women and men)
 - Nutrition
- Qualitative or quantitative, but have the ability to become quantitative in the near term
 - Similar accuracy, sensitivity and false positive/negative rates compared to existing consumer-based diagnostic methods
- Examples of possible approaches:
 - Fluorescence or near infrared (NIR) optical sensors
 - Novel skin-based or skin-associated biomarkers
 - Algorithm development for existing optical biosensors to improve reliability
 - Non-optical biosensing approaches
 - Non-invasive optical approaches to metabolite detection
 - Consumerization of existing non-invasive biosensor methods
- Be approvable by FDA for consumer use
- Technology mature enough to be ready for clinical trials within three years
- Ideally be protectable via patents in the US

Beyond this impressive list of characteristics being sought in the market place, other criteria for consumer biomonitoring that would make it even more useful in managing health include:

- Passive monitoring with wearable device
- Electronic device that stores data and can transmit it wirelessly to health providers and electronic health records
- Electronic interface able to provide electronic mentoring or coaching for the user