# The role of Nanotechnology and Nano and Micro-Electronics in monitoring and control of Cardiovascular Diseases and Neurological Disorders

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**Abstract**

Nanotechnology has been broadly defined as the one for not only the creation of functional materials and devices as well as systems through control of matter at the scale of 1-100 nm, but also the exploitation of novel properties and phenomena at the same scale. Growing needs in the point-of-care (POC) that is an increasing market for improving patient's quality of life, are driving the development of nanotechnologies for diagnosis and treatment of various life threatening diseases. This paper addresses the recent development of nanodiagnostic sensors and nanotherapeutic devices with functionalized carbon nanotube and/or nanowire on a flexible organic thin film electronics to monitor and control of the three leading diseases namely 1) neurodegenerative diseases, 2) cardiovascular diseases, and 3) diabetes and metabolic diseases. The sensors developed include implantable and biocompatible devices, light weight wearable devices in wrist-watches, hats, shoes and clothes. The nanotherapeutics devices include nanobased drug delivery system. Many of these sensors are integrated with the wireless systems for the remote physiological monitoring. The author's research team has also developed a wireless neural probe using nanowires and nanotubes for monitoring and control of Parkinson's disease. Light weight and compact EEG, EOG and EMG monitoring system in a hat developed is capable of monitoring real time epileptic patients and patients with neurological and movement disorders using the Internet and cellular network. Physicians could be able to monitor these signals in real-time using portable computers or cell phones and will give early warning signal if these signals cross a pre-determined threshold level.

In addition the potential impact of nanotechnology for applications in medicine is that, the devices can be designed to interact with cells and tissues at the molecular level, which allows high degree of functionality. Devices engineered at nanometer scale imply a controlled manipulation of individual molecules and atoms that can interact with the human body at sub-cellular level. The recent progress in microelectronics and nanosensors crates very powerful tools for the early detection and diagnosis. The nanowire integrated potassium and dopamine sensors are ideal for the monitoring and control of many cardiovascular diseases and neurological disorders. Selected movies illustrating the applications of nanodevices to patients will be shown at the talk.

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## Introduction

Nanotechnology has already demonstrated the possibility of many advanced disease diagnosis and treatment due to its ability to provide tools for better sensitivity, specificity and reliability. It also offers the possibility to take different measurements in parallel or to integrate several analytical steps from sample preparation and detection into a single miniaturized device. The nanotechnology itself is not a single subject but rather a merging area of collective expertise in traditional sciences such as chemistry, physics, material sciences and biology. Many efforts are made to develop nanotechnology sensors and systems for healthcare applications particularly for cancer diagnosis and therapy [1], drug delivery systems [2], monitor gene expression [3], detection of brain inflammation [4] and atherosclerotic plaques [5]. Quantum dots have been able to label biological systems in vitro and in vivo, to some extent, by optical or electrical detection. This paper presents the nanowire integrated sensors on microelectrodes, which will be ideal to detect and diagnosis the cardiovascular diseases and neurological disorders.

## Cardiovascular Disease monitoring and control

In USA, cardiovascular disease is the leading cause of death. Stroke, due to cerebrovascular disorders, is the top third to claim lives yearly. Myocardial Ischemia is a condition where the myocardium, the muscular tissue of the heart, is not supplied with enough oxygen by the coronary arteries to meet their metabolic demands. Myocardium cells cannot contract properly within few seconds after the onset of ischemia. If this is not rectified by reperfusion in time, when ischemia is of sufficient severity and persist long enough, myocytes become irreversibly injured and undergo cellular necrosis. Myocardial Ischemia affects millions of people and there is a need for a biosensor that would reduce the number of fatalities result from this condition.

Extensive research efforts have been focused on understanding the underlying mechanisms of myocardial ischemia and developing an implantable device that would allow to continuously monitoring and early diagnosis of myocardial ischemia. Sensing extracellular potassium is a good indicator of myocardial ischemia. Within seconds after the onset of myocardial ischemia, extracellular potassium increases rapidly from 5 mM to 10-20 mM of concentrations by shrinking of the extracellular space and/or increase of passive K+ efflux from cells [6]. The mechanism of the early change in ion concentration is not completely understood.

In this paper, we present a flexible sensor with nanoelectrodes which can simultaneously measure ionic species with sufficient temporal and spatial resolution to address

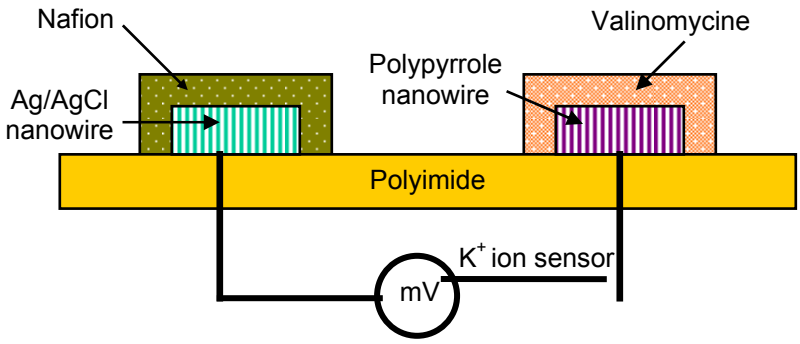
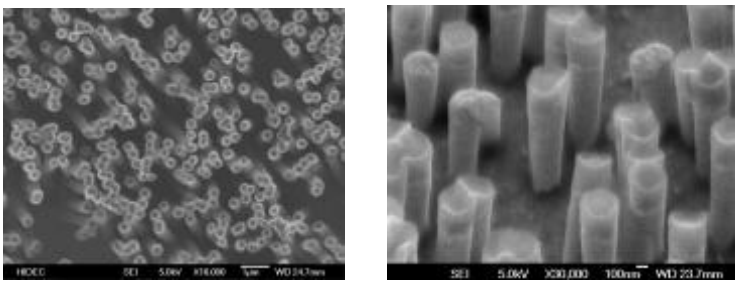



Figure 1. Schematic diagram of potassium ion sensor.

mechanisms of myocardial ischemia. In order to apply the sensor on dynamic myocardial muscle, there are several requirements such small size, mechanical flexibility to prevent tissue damage, high selectivity for other ionic species, and high sensitivity to low concentration of extracellular ions and biocompatibility. As shown in figure 1, the sensor design is based on an all-solid state biosensor which will eliminate the need for the inner filling solution usually found in traditional ion selective sensors and uniquely utilize nanowires for high sensitivity and stable potential measurement. In order to sense the potassium ions this device will use a conducting polymer nanowire. The conducting polymer nanowire made from polypyrrole acts as an ion-to-electron transducer with high sensitivity. For the ion selective membrane, valinomycin and Nafion has been chosen for the use within the cell membrane.

**Fabrication:** High sensitive potassium ion sensing is based on high aspect ratio electrodes with functional and biocompatible polymers. To start growth of polypyrrole nanowires on flexible substrates (polyimide, Upilex-25S), a conductive layer is deposited on the substrates and serves as a cathode in the electrochemical cell providing a seed layer for the growth of Au nanowires. For this purpose, a thin layer of gold with a titanium seed layer was prepared by e-beam evaporation. Then, a track etched polycarbonate membrane with cylindrical nanopores is assembled on the metal layers to function as a mold in subsequent processes. Structural and conducting polypyrrole nanorods are grown by electrochemical deposition technique on polyimide substrate. Then, functional ion exchange polymer is coated on the surface of nanorods by solution method. By changing electrochemical deposition condition and adjusting doping impurities and solid concentration in polymer solutions, it is possible to fabricate a wide variety of functional structures along the vertical and radial direction. Vertically aligned polypyrrole nanowires are shown in Figure 2.



(a) (b)

Figure 2: Images of polypyrrole nanowire sensing structures. (a) polypyrrole nanowires of 8 micron length, (b) Nafion polymer coated nanowires.

## Neurological disorders

Brain disorders including degenerative neurological disorders and traumatic injuries comprise one of the most devastating health conditions in United States. Two million people have experienced an unprovoked seizure or have been diagnosed with epilepsy, and as many as 1.8 million Americans are severely affected by dementia. Today, 4.5 million Americans have Alzheimer's disease which is projected to jump to 16 million by year 2050 unless preventive methods are developed.

Neurological diseases and disorders that bring about a disturbance in the control of movements, voluntary or involuntary, are grouped together as Movement disorders. The problem is not of paralysis, or loss of pyramidal or corticospinal control of movement, but of disturbance of the resting or activated function of the motor system. The problems involve an alteration in the ability to initiate movement, the status of the muscular tone and tremor. The movement disorders are influenced by many drugs notably neuroleptics, dopaminergic and cholinergic drugs.

This paper aims to understand the common disorders, their clinical presentation and the role of functional surgery in treating these disorders. Functional Neurosurgery involves the surgical destruction or chronic excitation of a part of the brain as treatment of a physiological or psychological disorder. There has been a recent resurgence of interest in surgery for Parkinson's disease, essential tremor and other neurodegenerative disorders. This has been largely due to improved understanding of functional anatomy of the basal ganglia and development of neurophysiological, neuroimaging and neurosurgical techniques and the incomplete efficacy of current anti-Parkinsonian drugs when taken chronically in a significant number of patients.

Various neurological disorders that are currently treated by functional Neurosurgery include Parkinson's disease (PD), essential tremor (ET), dystonia, multiple sclerosis and Huntington disease.

Parkinson's disease is a progressive neurological disorder that results from degeneration of neurons in a region of the brain that controls the movement of the nerve system. This degeneration crates a shortage of the brain signaling (neurotransmitter) known as dopamine, causing the movement impairments that characterize the disease. Dopamine is a chemical messenger responsible for transmitting signals between the substantia nigra and the next 'relay station' of the brain, the corpus striatum, to produce smooth, purposeful muscle activity. Loss of dopamine causes the nerve cells of the striatum to fire out of control, leaving patients unable to direct or

control their movements in a normal manner. Parkinson's disease was first formally described in 1817 by James Parkinson, a British Physician who published a paper on what he called as 'an essay of the shaking palsy'. However th disease has probably existed for many thousand of years. Its symptoms and potential therapies were mentioned in the Ayurveda, the system of medicine practised in India, as early as 5000 BC, and in the first Chinese medical text, Nei Jing, which appeared 2500 years ago.

The four primary symptoms are tremor or trembling in hands, arms, legs, jaw and face; rigidity or stiffness of the limbs and trunk; bradykinesia or slowness of movement; and postural instability or impaired balance and coordination. Occasionally, the disease also causes depression, personality changes, demetia, sleep disturbances, speech impairments, or sexual difficulties. The tremor is the major symptom for many patients and it has a characteristic appearance. Typically, the tremor takes the form of a rhythmic back-and forth motion of the thumb and forefinger at three beats per second. This is sometimes called 'pill rolling'. Tremor usually begins in a hand, although sometimes a foot of the jaw is affected first.

PD increases dramatically with age, with an overall prevalence of 20.5/100000. Onset under 30 years of age is rare, 4-10% have onset before 40. In the U.S.A. ~200/100000 (0.2%) are in the 70-80s age group. In other countries (Iceland, India, Scotland, Australia) the prevalence is 1,000-2,000/100K (1-2%). The mean age of onset is around 60 years.

Clinical and laboratory evidences have proven that lesions in the substantia nigra lead to bradykinesia and tremor. In PD the dopamine content of the substantia nigra, putamen and caudate nucleus are low. This leads to an increased inhibitory activity at the globus pallidus which causes the inhibition to initiate movement.

Genetic Factors contribute to 10% of PD in those who have onset of symptoms before 50. Alpha-synuclein (AS) is a ubiquitous neuronal protein of unknown function that may have a role in synaptic vesicle transport or recycling. Overexpression of AS in animal models leads to dose-dependent neurodegeneration, with special susceptibility of dopaminergic cells in the substantia nigra.

Dietary factors implicated are a decrease in the vitamin and antioxidants in certain types of diets. Environment factors as seen by an increased incidence in rural areas may be due to dopamine neuron toxins fond in some pesticides. MPTP, rotenone and Parquat are few of the chemicals that have been proven experimentally to induce PD by selective destruction of the dopaminergic cells in the substantia nigra

## Clinical Features

A loss of 60% of nigral neurons with 80% depletion of striatal DA is required before symptoms of PD develop. The onest is insidious and asymmetric. The first symptom is ***tremor*** that is usually at rest in the form of a Pill-rolling movement that is somewhat decreased with purposeful movement. ***Bradykinesia*** is slowness in initiating movement. Muscular ***rigidity*** is felt on passive movement of joints in the form of a smooth resistance or superimposed ratchet-like jerks(Cogwheel rigidity). Postural instability occurs late. Mental manifestations include depression, bradyphrenia (slowed thinking) and dementia .

**Tremor:** In the early stages of the disease, about 70% of people experience a slight tremor in the hand or foot on one side of the body, or less commonly in the jaw or face. It appears as a 'beating' or oscillating movement and is regular (4-6 beats per second). Because tremor usually appears when the muscles are relaxed, it is called "resting tremor." This means that the affected body part trembles when it is at rest and not doing work and often subsides with action. The tremor often spreads to the other side of the body as the disease progresses, but remains most apparent on the original side of occurrence.

**Rigidity:** Rigidity or increased muscle tone means stiffness or inflexibility of the muscles. Normally muscles contract when they move, and then relax when they are at rest. In rigidity, the muscle tone of an affected limb is stiff. Rigidity can result in a decreased range of motion. For example a patient may not swing his or her arms when walking. Rigidity can also cause pain and cramps at the muscle site.

**Bradykinesia:** Bradykinesia is a slowing of voluntary movement. In addition to slow movements, a person with bradykinesia will likely also have incompleteness of movement, difficulty in initiating movements, and arrests of ongoing movement. Patients may begin to walk with short, shuffling steps (festination), which, combined with other symptoms such as loss of balance, increases the incidence of falls. They may also experience difficulty making turns or abrupt movements. They may go through periods of "freezing," which is when the patient is stuck and finds it difficult to stop or start walking. Bradykinesia and rigidity can occur in the facial muscles, causing a "mask-like" expression with little or no movement of the face. The slowness and incompleteness of movement can also affect speaking and swallowing.

**Secondary symptoms**

Secondary symptoms of Parkinson's disease may include Speech changes, Loss of facial expression, Micrographia (small, cramped handwriting), Difficulty swallowing, Drooling, Pain, Dementia, or confusion, Sleep disturbances, Constipation, Skin problems, Depression, Fear or anxiety, Memory difficulties and slowed thinking ,Sexual dysfunction, Urinary problems, Fatigue and aching and Loss of energy .

## Indications for Surgery

The following have been identified as selection criteria for Surgery: at least 5 years from the onset of symptoms, patients severely disabled by idiopathic Parkinson's disease despite optimal medical treatment, but sensitive to L-dopa, and exclusion of severe cognitive or psychiatric disorders.

Stereotactic neurosurgery for the treatment of Parkinson's disease (PD), targets the subthalamic nucleus (STN) and the globus pallidus internus (Gpi). The ventralis intermedius (Vim) nucleus of the thalamus is targeted for ET. Following target selection, procedures include the generation of lesions or the placement of deep brain stimulating electrodes in the selected target.

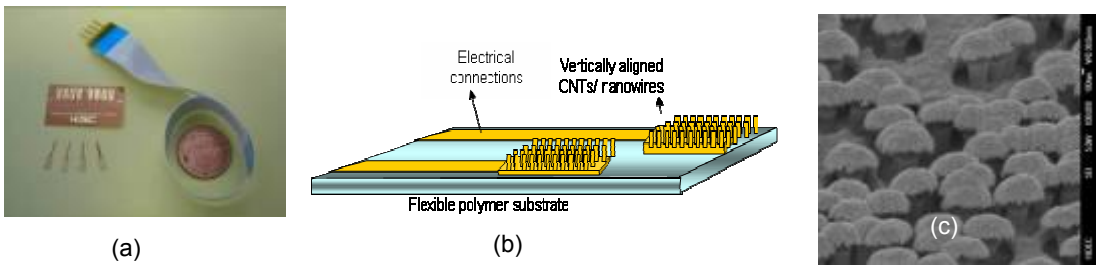
There is no cure for Parkinson’s disease (PD). When the symptoms grow severe, doctors usually prescribe levodopa (L-dopa), which helps replace the brain’s dopamine. L-dopa is a dopamine precursor, a substance that is transformed into dopamine by the brain. The prescription of high dosages of levodopa was the first breakthrough in the treatment of PD. Unfortunately, patients

experienced dehabilitating side effects, including severe nausea and vomiting. Sometimes doctors prescribe other drugs that affect dopamine levels in the brain. In patients who are severely affected, a kind of brain surgery known as pallidotomy has reportedly been effective in reducing symptoms. Pallidotomy is indicated for patients who have developed dyskinetic movements in reaction to their medications. It targets these unwanted movements, the globus pallidus, and uses an electrode to destroy the trouble-causing cells. Another kind of brain surgery, in which healthy dopamine-producing tissue is transplanted into the brain, is also being tested.

Recently, neurosurgeons are looking at alternate method of employing implantable deep brain stimulator-electrodes . These electrodes are implanted in the thalamus or globus pallidus and connected to a pacemaker-like device, which the patient can switch on or off as symptoms dictate. The deep brain stimulator (DBS) uses an implantable eelctrode to deliver continuous high-frequency electrical stimulation to either thalamus, globus pallidus (GPi), or the subthalamic nucleaus (STN), another part of the brain controlling movement. High frequency stimulation of cells in these areas actaully shuts them down, helping to rebalance control messages throughout the movement control centers in the brain. It is also interesting to note that DBS of the globus pallidus is useful in treatment of dyskinesias as well as tremor. DBS of the subthalamic nucleus may have an effect on most of the main motor features of PD including bradykinesia, tremor, and rigidity. DBS requires surgical procedure to place an electrode in the brain connected by a wire to battery source. Electrode placement is performed under local anesthesia. The wire is implanted under the scalp and neck, and the battery is implanted in the chest wall just below the collar bone. A series of stimualtion adjustments are required I nthe weeks following implantation. Most of the time the battery lasts for 3 to 5 years and it is replaced through an incision in the chest. It is usually performed as an outpatient procedure. In USA, FDA has approved bilateral (both-sided) DBS developed by Medtronic [9]. DBS ahs the advantage that instead of destroying the oceractive cells that cause symptoms in PD it temporarily disables them by firing rapid pulses of electricity between four electrodes at the tip of the lead. DBS has three implantable components; lead, extension, neurostimulator.The lead is a thin, insulated coiled wire with four electrodes at the end which is implanted in the brain through a small opening in the skull; the extension is an insulated wire that is passed under the skin of the head, neck and shoulder to connect the lead to the neurostimulator; neurostimulator is a battery-operated device which is implanted under the skin near the collarbone and generates the electrical signals, see Figure 3 of the Medtronic DBS system.

**(a)** **(b)** **(c)** **(d)**

Figure 3 a) Medtronic DBS unit, b) the lead, c) the extension and d) the neurotransmitter




(a) (b)

Figure 4. Photograph of the nanowire integrated implantable neural probe;(b) vertically aligned functionalized nanowires dopamine sensor; (c) SEM picture of the functionalized nanowires for dopamine sensor

The drawbacks to this current technology includes the following: 1) the hard wiring is known to disconnect and/or fracture during patient wear; 2) a battery replacement requires invasive surgery and involves the risks attending to surgery including infections, failure, and damage to surrounding

tissue; 3) the battery life is limited, and therefore it is impractical to have the device operating at all times. Moreover, the tremor motion of the specific part of the body is not sensed and controlled by DBS.

What is needed and also attractive is to design and develop a wireless microsystem with sensors communicating to the implantable lead which in turn controls the frequency of electrical signal transmitted to the electrodes of the lead. In this paper, we address such a system in which the sensors wirelessly transmit detection of such tremors directly to a thalamic deep brain stimulation unit. The unit is powered not through an implantable battery source, but through a battery source that may be worn by the patient in the form of a wrist watch or other externally mounted source. The system presented consists of 1) Polymer MEMS based lead with organic thin film transistor, 2) accelerometer and gyro sensor for monitoring tremor motion and 3) wireless control unit to monitor ad control the tremor motion.

Deep brain stimulation using implantable probes is now accepted as a therapeutic technique for the treatment of PD. However, present probe design has very high impedance as well as smaller electrode areas. Developing nanotechnology for neural applications will be ideal for implantable electrodes to reduce the impedance and to increase the effective areas so that it can effectively transfer the signals to the brain. As shown in figure 4(a), we have developed a neural probe with an array of vertically aligned nanowire at the tip of the probes [7]. This will effectively enhance the electrical conductivity as well as reduce the cell-electrode impedance. These nanoelectrodes will open more signal pathways inside the brain that can deliver control signals at the cellular level. In addition, the increased surface area of the nanodevices is utilized to control the surface impedance, which plays a critical role in today's DBS electrodes. The attractive feature of the nanowire neural implant is that, it can probe many neurons simultaneously in a given network, which is almost impossible using present methods. Similarly we have developed dopamine sensors [8] using vertically aligned nanowire as shown in figure 4(b) and (c).

Initial observations in patients with tremor treated with deep brain stimulation (DBS) of the thalamus suggested that application of high-frequency stimulation (HFS) had a lesion-like effect. New clinical information from patients treated with DBS of the subthalamic nucleus (STN) and globus pallidus internus (GPi) suggested a more complex mechanism of action. Recent experiments in the rat have shown that HFS of the STN was accompanied by increased release of glutamate and dopamine in the substantia nigra and striatum, respectively. Observations made in the GPi of parkinsonian patients during surgery suggest that stimulation may excite GABA release in axons from afferent connections. Therefore, although depolarization block may remain a major mechanism of action, generation of action potentials and release of neurotransmitters may also be involved in the therapeutic effects of DBS in Parkinson's disease.

There is a large amount of evidence from experimental and clinical data that stimulation frequency represents a key factor with respect to clinical effect of DBS. Interestingly, high-frequency stimulation mimics the functional effects of ablation in various brain structures. The main hypotheses for the mechanism of high-frequency stimulation are: (1) depolarization blocking of neuronal transmission through inactivation of voltage dependent ion-channels, (2) jamming of information by imposing an efferent stimulation-driven high-frequency pattern, (3) synaptic inhibition by stimulation of inhibitory afferents to the target nucleus, (4) synaptic failure by stimulation-induced neurotransmitter depletion. As the hyperactivity of the STN is considered a functional hallmark of PD and as there is experimental evidence for STN-mediated glutamatergic excitotoxicity on neurons of the substantia nigra pars compacta (SNc), STN-DBS might reduce glutamatergic drive, leading to neuroprotection. Further studies will be needed to elucidate if STN-DBS indeed provides a slow-down of disease progression.

**Heath monitoring and drug delivery with Point-of-Care (POC) sensors and wireless devices:**

Minimal invasive determinations of various physiological parameters are more and more demanding for medical applications. Nanowire sensing probes have potential applications not only in electronics and optoelectroncs industry, but have tremendous potential in evaluating minute changes in cellular level, particularly for designing various sensing and diagnosis tools. Many techniques have been evolved in nanotechnology using one dimensional nanostructure to aid the analytical tools for chemical and biosensing, disease diagnosis and treatment. Some of the nanotech based devices which are being developed are listed below. The details will be given at the presentation:

a) Electroencephalogram (EEG) is a widely used and effective technique to monitor conditions of the brain. The brain generates uniform potential charges, which can be picked up with electrodes either from the scalp or directly from the cerebral cortex. EEG involves placing small, non-invasive electrodes (usually 16-26 in number) on the surface of patient's scalp which pick up these very low voltage potentials (1-100 microvolt). These voltages are appropriately amplified, filtered and either recorded using an ink-fed plotter or digitized and sent to a computer through wired lines for monitoring by a doctor or automatic analysis of the waveform. This is similar to Electrocardiogram (ECG) except that the physiological mechanisms that produce the ECG waveform are largely known, whereas the synchronizing mechanisms that generate different EEG waveforms are less known. Epilepsy is characterized by synchronous electric discharges of large groups of neurons resulting in a noticeable change in EEG waveform. Wireless EEG, EOG and EMG hat sensor using carbon nanotube and nanowire (instead of the traditional gold cup with silver

chloride and wired configuration). This sensor network system is also being used for epilepsy patients and patients with movement disorder. The same wireless system is also applicable for cardiovascular diseases recording electrical activity of the heart that shows abnormal rhythms (arrhythmias or dysrythmias) and detects the heart muscle damage.

b) Remote Patient Monitoring (RPM) is an emerging area of telemedicine which includes devices and technology that enable doctors and health care providers to remotely diagnose, treat and advise patients. Such RPM systems cater to mainly two classes of the public: senior citizens requiring constant monitoring and care while going about their regular routine; and providing a continuous monitoring solution for chronically ill patients requiring round-the-clock monitoring in their homes itself Wireless Smart vest integrated with GPS, internet of cellular network for physiological monitoring including EKG, respiration recording, temperature, etc,

c) Organic polymer based sensor: (which replaces the conventional bulky Doppler sonography) for measurement of blood flow, viscosity, oxygen, etc., to cerebral cortex

d) Gait is a semi-automatic motor task, which is sensitive to ON-OFF (due to medication effects) changes of PD. During the OFF state, a patient tends to walk slowly with short shuffling steps, reduced arm swing, stooped posture. During the ON state, the same patient may walk nearly normal without 'dancing' steps. Hence, an ambulatory gait measurement system is very important for the real-time monitoring of patients. Sensors in the shoe, ankle foot, etc., are used for gait analysis and movement disorders.

e) Lab-on-chip with functionalized nanostructures for diabetes and cardiovascular diseases: Coronary artery narrowing (called stenosis) is the main cause of the coronary artery diseases (CAD). This is because the stenosis in blood vessels can reduce the flow of blood to heart, making the heart no longer functional. Every year, near 500,000 new heart failure cases are reported, with 5,000,000 Americans suffering from heart failure. Carotid neurovascular diseases causing strokes is the third leading cause of death, and the first for adult disability. Every year, about 700,000 Americans experience a stroke, and 160,000 of these people die.

f) Nanotherapeutic and drug delivery systems

g) Implantable devices for monitoring and control of neurodegenerative diseases such as epilepsy and Parkinson's disease

**Other clinical research efforts**: The research efforts in clinical side focus on the areas of cardiology, neurosurgery, oncology, infectious diseases, diabetes and metabolism, and drug delivery. The goal would be to provide innovative solutions using nanotechnology to medical concerns in these areas. Current nanotechnology research is already proving to have a significant impact on medical device development and enhancement. Some examples of authors group are described below that would benefit greatly from the nano-medicine initiative.

Cardiology - research is being conducted on implantable nanosensors that would provide vital information on Myocardium Ischemia (by simple injection of passive wireless nanosensors in the myocardium tissue) in the detection and prevention of heart disease. These sensors would enable doctors to monitor a patient's heart and provide indications of

irregular heart conditions that could lead to the prevention of a major heart attack or heart failure.

- Neurosurgery - ongoing research is being conducted on implantable nanoprobes that enable recovery or motor control for patients with Parkinson's disease and epilepsy. Breakthrough research continues on nanosensors that enable the study of brainwaves for patients with sleep apnea and chronic headaches.
- Oncology – novel nanotechnology based functionalized materials with appropriate antibody and antigen to detect, locate, and treat cancer. These methods would be less invasive and less destructive to the surrounding tissues in the body. They would also provide immediate treatment for diagnosed patients. Research is also being conducted to determine key elements that would indicate the likelihood of developing cancer or detecting it at its earliest stage before further progression.
- Infectious diseases (HIV/Aids, Flu Variants, Malaria, etc) – detection and prevention of infectious diseases through advanced sensing technology enabled by new developments in nanotechnology.

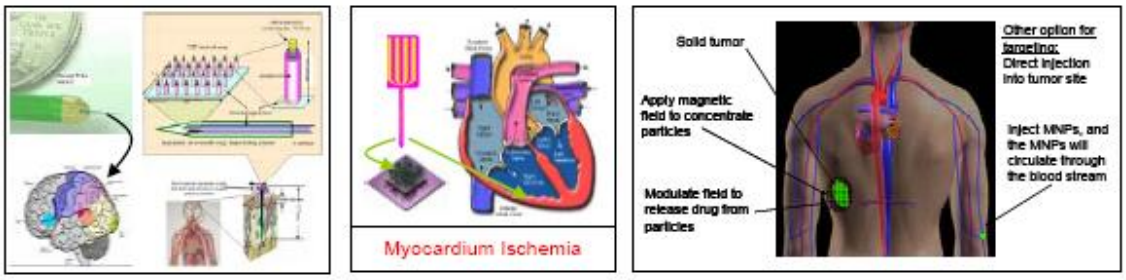



Figure 5. Schematic diagram of the nanowire integrated implantable neural probe;(b) vertically aligned functionalized nanowire probe for the heart disease detection.(c) Schematic representation of the nanomagnetic drug delivery system.

## Conclusions

The application of nanotechnology in cardiovascular disease as well as neurological disorders in disease detection and monitoring and health monitoring and drug delivery is presented in this paper. The nanowire integrated devices designed and fabricated are ideal for monitoring and control of cardiovascular diseases and neurological disorders. The sensors developed include implantable and biocompatible devices, light weight wearable devices in wrist-watches, hats, shoes and clothes. The nanotherapeutics devices include nanobased drug delivery system. Many of these sensors are integrated with the wireless systems for the remote physiological monitoring. The author's research team has also developed a wireless neural probe using nanowires and nanotubes for monitoring and control of Parkinson's disease. Light weight and compact EEG, EOG and EMG monitoring system in a hat developed is capable of monitoring real time epileptic patients and patients with neurological and movement disorders using the Internet and cellular network. Physicians could be able to monitor these signals in real-time using portable computers or cell phones and will give early warning signal if these signals cross a pre-determined threshold level.

## References


1. I.Brigger, C. Dubernet amd P. Couvreur, Advanced Drug Delivery Reviews, 54:631-651, 2002
2. D. A. LaVan, T. McGuire and R. Langer, Nature Biotechnology, 21(10):1184-1191, 2003
3. S. Eastman, W. Ruan, M. Doctolero, R.Nuttall, G.De Feo, J.Park, J.S.Chu, P.Cooke, J.W.Gray, S.Li, F.Chen, Nano Letters, v 6, n 5, 2006, p 1059-1064
4. J. Wang, P. Vernier, Y.Sun, M.Gundersen, L.Marcu; Proceedings of SPIE, v 5703, Plasmonics in Biology and Medicine II, 2005, p 127-134
5. A.Van Der Steen, C.L.De Korte, J.A.Schaar, F.Mastik, R.A Baldewsing, P.W. Serruys, 2nd IEEE International Symposium on Biomedical Imaging: Macro to Nano, v 1, 2004, p 49-52
6. M. Delvauz, S. Demoustier-Champagne, A. Walcarius, *Electroanal.* vol.16, pp.190-198, 2004.
7. J.K. Abraham, J. Xie, V.K.Varadan, Proceedings of SPIE- Smart Electronics, MEMS, BioMEMS and Nanotechnology, vol 5763, 2005, p 133-138.
8. P.T. Hankins, H Yoon, and V. K. Varadan, to be published in SPIE 2007
9. www.medtronics.com