



**MDXViewer Patient Monitoring System -
Real-time Monitoring of a Patients
Metabolic State**

General

MDX Life Sciences is active in the development of technology that will enable the monitoring of patients in critical care medicine. The upgraded device named MDXViewer (“The device”) is a real time continuous monitor of Tissue Metabolic Score (TMS) based on the simultaneous measurement of four physiological parameters from a tissue of patients in critical condition. The TMS based on changes in the microcirculation and cellular function (mitochondrial NADH) is integrated with the systemic hemodynamic and respiratory vital signs parameters and provide the most advance diagnostic tool to the clinician in critical care medicine. The main application of the MDXViewer at this stage is in monitoring patients in the various operation rooms (ORs) and or in the various intensive care units (ICUs). The device is based on the knowledge accumulated by Prof. Avraham Mayevsky during his academic research activities since 1972 as well as his R&D activities in the medical devices industry for more than 25 years. The device that he developed together with a large team of physicists, engineers of hardware and software experts was tested in patients and was cleared by the FDA. In its present application the device includes a disposable 3-way Foley catheter that was developed and cleared by the FDA as well. The catheter contains optical fibers that enable to measure physiological parameters, from the inner layer of the urethra. The TMS calculated by the device provide real time information on the total body oxygen balance of the patient. The information provided by the device will serve as a warning signal to the development of changes in the oxygen balance in the body (decrease in oxygen availability) that reflects the development of pathological processes in the body of the patient. To the best of our knowledge this information could serve as an indicator to the response of the patient to the treatment given. To the best of the company’s knowledge such a monitoring device is not available in the clinical market to provide, the clinical team, real time information regarding the tissue metabolic state of the patient although this type of information requested by the international scientific and clinical community. The device is aiming to contribute a significant improvement of the treatment quality and the prognosis of the monitored patient. Also, the treatment may reduce the cost of patient hospitalization since the treatment may start earlier in the OR as well as in the ICU.

The treatment given to critical care patients, in the ICU or during complicated operations require continuous real time monitoring of vital signs including cardiovascular and respiratory parameters. This includes arterial blood pressure, heart rate, ECG, respiratory rate, saturation of oxygen in arterial blood and core body temperature. Those parameters are monitored by various sensors and the results are presented on a multiparametric standard monitors located in the ORs and the ICUs. Monitoring of those parameters will enable the clinician to identify, as early as possible, changes in the status of the patients that require change in the treatment given to the patient. Also, the monitoring process should identify the point of saturation using a specific treatment which is the best for the specific patient.

Patients in critical condition, in addition to the specific medical problem that force the team to keep them in the ICU or underwent a specific operation, may develop emergency metabolic state such as sepsis, or a state of shock that will decrease the supply of blood and oxygen to various organs in the body that may end up in a negative oxygen balance and dysfunction of the specific tissue or organ. Early detection of those critical processes and the ability to diagnose them in a reliable way enable to intervene with an early new treatment. This early intervention should increase the efficacy of the treatment and thus may decrease the mortality rate or improve the prognosis of the treated patients. In part of the patients the length of stay in the ICU will be shorter which will decrease the total cost of the hospitalization period. Also, the ability to monitor in a reliable way the perfusion of the tissues with oxygenated blood and evaluate the balance between oxygen demand and supply is critical in optimizing the treatment given in emergency state or metabolic dysfunction. A successful treatment could be evaluated by the

stabilization of the physiological state of the patient after intensive treatment by various drugs, infusion of blood or physiological solution after an operation.

As of today, the monitoring of patients in the ICUs or during surgical procedures is done by multiparametric monitoring devices that are displayed in real time the vital signs and general physiological parameters of the patient. In general, the diagnostic tools of hemodynamic and respiratory functions are global, namely they represent the entire systems of the ill patient. The treatment rationale is that global parameters in the normal range are indirect indicators of the physiological normality metabolism at the tissue and cellular levels. The diagnosis and monitoring tools available today are not measuring directly the metabolism of the patient at the tissue and cellular level namely, in a specific tissue in the periphery of the body. Therefore, those monitors are not able to differentiate between a general problem in the body and a specific dysfunction in one of the systems or organs. For example, monitoring of lactic acid in the blood is performed by taking a blood samples at certain interval of time and testing it in the ICU in a specific instrument. An increase in the level of lactic acid indicates that the lack of oxygen led to anaerobic metabolism, but the source of the increased lactic acid can't be identified. Also, it is not clear whether the increase in lactic acid is due local decrease in oxygen supply or the inability of the cell to use the available oxygen (mitochondrial dysfunction). In addition, the existing metabolic monitoring tools, available in the market, for determination of oxygen balance are invasive instruments that require penetration the body with various catheters in large blood vessels in the patient. In conclusion, the clinical team is missing an efficient and easy to use tool that will enable continuous real time monitoring of the oxygen balance at the microcirculation and cellular compartment of the patient. This type of information is critical in the management of the treatment given to the patient in the ICUs of the ORs. This information is needed as a diagnostic tool as well as indicator for the efficacy of the treatment given to the patient.

The basic idea of using our device in ORs and ICUs is based on a specific mechanism that is activated in the body during a situation of decreased oxygen balance in the body of patients. Under that condition, a unique process will increase the blood flow to the most vital organs in the body- the brain and heart. These 2 organs will continue its normal activity by getting adequate amount of oxygen from the increased blood flow. At the same time the less vital organs such as the skin, muscles, the GI tract and the urogenital system will get decreased blood flow and therefore less oxygen. In these organs mitochondrial function is inhibited due to the lack of oxygen and ATP production will decreased. Due to this blood flow redistribution process the urethral wall (a less vital organ) will be the first one to be affected by the lack of oxygen in the body and therefore could provide and serve as an early warning signal to the change in total body oxygen balance developed under various emergency situations.

The MDX Life Sciences Inc. company was established in order to implement the technology developed into the monitoring setup of patients in critical care medicine. The company will use the previous published technology developed by Prof. Avraham Mayevsky during his academic and industrial experience in the last 25 years. Also, the new device to be built by MDX Life Sciences Inc. will provide a new concept of patient monitoring in critical care medicine. The New device will be based on a new Provisional patent submitted to the US patent office recently. In this device, the Tissue Metabolic Score (TMS) is calculated according to 4 physiological parameters monitored from the urethral wall and will be integrated with the vital signs parameters measured from the patient.

The device developed previously was cleared by the FDA and was tested in a small group of patients under went cardiovascular operations as well as in the cardiovascular ICU. The results of those monitored patients were published few years ago. The company will optimize the size of the device and will developed the revolutionary software that will present the total body oxygen balance formulated in the TMS. The company will continue the R&D of a new model of the device that will monitor the TMS

using the skin of the adult or the newborn patients. This new development may need another application to the FDA, but this issue must be evaluated later on in the R&D process.

As described, the main field of activity at this stage of prospectus preparation will include the introduction of the 1st device to daily clinical use in parallel to the R&D process of the 2nd generation of monitoring the skin of patients.

General environment and the influence of external factors on activities in the company

The activities of the company and the demand for its products are dependent of factors that the company can't control. They are connected to the late stage after the end of the R&D and the beginning of sales as follows:

a. Macroeconomic events

The activity of the company will concentrate on the development of medical devices to be used in the diagnostic area of medicine. This area may be affected more significantly by macroeconomic trends as compared to other medical field and will suffer from a slowdown of sales as compared the new drugs or treatment devices.

b. Budget allocated to diagnostic devices

The main budget allocated to the diagnostic medicine sector is coming from the most developed countries such as USA, The European union countries and Japan. Therefore, the company assumes that the amount of money allocated to diagnostic devices in the developed countries will be affected by its economic growth.

c. The effects of developments in the field.

The development of medical research, Medical devices and therapeutic drugs in the field of diagnostic and treating critical acute situations may decrease the size of the monitoring devices.

d. Development and production of competitive devices

The activity of the company is affected by competition in the field of clinical monitoring as well as the development and marketing of products using other technologies that may compete with the device developed by the company.

e. Policy of clearance of device by the regulatory authorities

The activity of the company is affected by the policy of the regulatory authorities that approve the introduction of new devices in the target clinical field. Any delay in the clearance of the devices made by the company will affect the business of the company.

f. Policy of medical centers in the introduction of new devices

During the last few years, changes in the policy of medical centers regarding the buying of new medical devices for patients monitoring were changed and are according to the following criteria:

1. The use of new medical devices may shorten the length of patients stay in the ICUs.
2. The introduction of new devices may improve the ability to detect critical changes developed in the metabolic state of the patient that will improve the treatment given.
3. New medical device may fill the missing tool in the critical care departments.

The financing of the device expenses, including the device itself as well as the disposable parts, is not expected to be refundable to the medical center in a specific way. The encouragement to buy a new device will come from the shortened length of stay in the hospital and the center obtain a total amount of money per day of stay in the ICU regardless to total number of days.

Regarding patients that are monitored during and after surgery, the company believe that the benefit from using the device is expected to come from the improvement of the care given to the patients including the early detection of problems and the optimization of the treatment given. As a result, the outcome from the operation will be improved and the length of stay will be shorter.

g. The reimbursement policies of insurance companies

In the main sector of patients that the company will approach, namely the USA and Europe, there are two types of medical providers (public and private systems). The public system that is operated by governments and public organization, cover a major part of the population while the private medicine is operated by insurance companies. In both systems, the coverage to the insured individuals or families are recognizes expenses. To the best of our knowledge, there is a tendency in those insurance entities to decrease the cost of the services to the population by checking the economic efficacy in using medical devices in daily medical practice. There is a tension between the pressures to decrease the expenses while keeping the high level of medical treatment to the patients. In the reimbursement system used in the USA and partially in Europe, the hospital is compensated according to the medical diagnosis or the type of surgery that is planned to be performed. In this case, any type of saving of expenses (i.e. shorten the length of stay after surgery) will enable the hospital to gain a higher profit and therefore the hospital will have an economic interest to decrease the cost of care but keeping the high quality of treatment and the outcome of the patient. As mentioned before, the expenses of buying a medical device is part of the general cost of the hospitalization in the ICU or the cost of the surgical procedure and is not affected by the medical insurance organizations.

Description of company's activities

The company is aiming to be a leading body in the introduction of new monitoring technology approaches in patients that needs evaluation of tissue metabolism in real time during various surgical procedures or hospitalization in ICUs. To the date of this prospectus, MDX Life Sciences Inc. will concentrate in the implication of a new medical device that will be connected to the human urethra by a Foley catheter that contain bundles of excitation and emission optical fibers. The aim is to monitor in real time the Tissue Metabolic Score (TMS) based on the measurements of 4 physiological parameters from the wall of the urethra. More details will appear later on in the prospectus.

Information on the patient monitoring market and activities.

The sector of patient monitoring market is part of the world market of medical devices and diagnostic that cover at least 150 billion US \$ yearly expense. Out of it, the sales of monitoring devices in hospitals per year are 3 Billion US \$ (with a 3.6% yearly growth).

World Hospital Multiparameter Patient Monitoring Equipment Market 1995-2005; Frost & Sullivan, #5935-56, November 2000.

Patient monitoring in the various ICU units and in the operation rooms as well as during the post-operative period, are based on technology that was developed during the last 3-4 decades. Since the management of patients in those units is dependent on the ability to monitor the status of the patient in real time, there is a significant value in the development of new technologies for patient monitoring. As of today, in the ORs and ICUs, the monitored parameters are representing the activities of the

cardiovascular and respiratory systems. The most common monitored parameters are Arterial blood pressure, heart rate, ECG, respiratory rate, blood gases, hemoglobin saturation and body temperature. In more specific units there are few more parameters that are monitored. In neurosurgical ICU, the intracranial pressure (ICP) and Electrical activity (EEG) are monitored from the brain itself. In addition, blood samples are tested, from time to time, for changes in lactic acid or bicarbonate that are related to the oxygen availability in the patient. The main missing monitored parameters are those that provide in real time the oxygen balance at the tissue microcirculation and the cellular level. This type of monitors may provide early warning signal for the change in total body oxygen balance. The MDXViewer made by MDX Life Sciences Inc. is aiming to fill the missing gap in patient monitoring devices.

It is possible to classify the multiparametric monitoring devices according to the end users. In general, the most sophisticated devices are used in ICUs and ORs while the less complex devices are used in other hospital departments. The most sophisticated monitors are built in a modular way the enable to add more small units that will measure more parameters. The cost of those monitors is above \$ 20,000 per unit.

US Multiparameter Patient Monitoring Markets; Frost & Sullivan, #F336-56, September 2005

The device that MDX Life Sciences is aiming to sell is a complimentary product to the multiparametric sophisticated monitors to be use in the ICUs and the ORs. The company believes that the ability of the new device to diagnose in real time the metabolic crisis develops in a patient will provide a powerful tool in patient monitoring hospitalized in the ORs, ICUs as well as during post-operative stage. The monitoring of a high-risk patient (due to it medical state or the complexity of the procedure) may started before the operation, during the surgical procedure and end up in the post-operative ICU stay. The MDXViewer will be connected to the monitored tissue by a 3-way Foley catheter that in addition to urine collection contain optical fibers the enable the evaluation of the Tissue Metabolic Score in real time based on the measurements of 4 physiological parameters from the wall of the urethra. The catheter will stay in the body of the patient as long as urine collection is needed.

In the ICUs, the device is needed for patients that are hospitalized due to injury or previous illness as well as in patient during the post-operative period. Each patient, in the ICU, have a Foley catheter for urine collection as long as he is in a critical condition and needs intensive follow-up due to physiological instability state. It is necessary to monitor such patients in real time and the Foley catheter that is needed for urine collection will be used also for his metabolic monitoring. The published medical research and clinical papers indicate that direct monitoring of the metabolic state of the patient is needed as a tool to detect metabolic instability as a supportive clinical decision making in those critical situations that need improvement in patient care and treatment.

Sepsis Handbook, National initiative in sepsis education; Society of Critical Care Medicine, 2004.

To the best of our knowledge, at this point in time, the ICUs as well as the ORs are not equipped with medical devices that enable multiparametric monitoring of the microcirculation and cellular functions (Mitochondrial NADH) in real time. There are devices that provide information on one parameter such as tissue blood flow or hemoglobin oxygenation and therefore such devices are not used in many hospitals in the ORs or in the ICUs.

The USA market

According to public available information, the average cost of hospitalization in the American ICU is around \$5,000 per day. The number of beds in the 7.500 ICU units in the US is around 90,000 and are serving 5.9 million hospitalizations every year that cost a total of 67.5 billion US \$ representing 23% of the total hospital expense in the US. In addition, 35 million surgical procedures are performed yearly out of which 40% are caring out in the hospitals ORs. According to our evaluation, 10-15% of the surgical

procedure is in the high-risk category and may need intensive monitoring. The demand for the multiparametric monitoring in the US, ICUs was 20,900 in 2003 with a yearly increase of 1.4%. The average cost of a multiparametric monitoring device was around 21,000. To the best of our knowledge, the leading companies in the multiparametric monitoring devices in the US are:

Dräger Medical, Spacelabs, GE Healthcare, Philips Medical Systems, Mennen Medical, Mindray, Ivy Biomedical, Welch Allyn, Nihon Kohden, Datascope, Alaris

The introduction of the device to the US market may need approval of the regulatory authorities.

The European market

In western Europe there are 12,500 hospitals including 2.5 million beds out of which 10% are ICUs beds (250,000). There are 10 million hospitalizations every year and the surgical procedures in the 5 large European countries were 25.7 million in 2005.

European Mid-range Patient Monitors Markets; Frost & Sullivan B697-56, January 2006.

In 2005, 13,500 multiparametric monitors were sold in Europe with an average price of \$25,000 per monitor.

World Hospital Multiparameter Patient Monitoring Equipment Market 1995-2005, Frost & Sullivan; #5935-56, November 2000.

The leading companies of the multiparametric monitoring devices in Europe are:

Philips Medical, Datascope, Dräger Medical, GE Healthcare Systems, Fukuda Denshi, Spacelabs, Welch Allyn, Nihon Kohden, Schiller, Criticare

The introduction of new monitoring devices requires approval of the regulatory authorities.

Limitations, regulation and standardization procedures

The activities of the company are exposed to the international regulatory rules including the CE Mark in Europe and FDA in the USA as well as ISO standard of quality assurance of the products.

Critical success factors in company's activity.

In the activity of the company there are a number of factors that will affect the activities and the status of the company.

- a. Completion of the upgraded device that includes the presentation of the TMS.
- b. Clinical testing of the device in a large number of patients (400-500).
- c. Obtaining the CE Mark and FDA clearance for the upgraded device.
- d. Starting the distribution of the upgraded device to leading hospital in the US and Europe.
- e. Development of additional products based on the same concept of patient monitoring. This will enable the company to penetrate to new market such as monitoring of newborns in neonatal ICU.

Entrance and exit barriers in the present market sector

There are few entrance barriers that will affect the ability of potential competitors to penetrate the activity area of the company.

a. The device developed by the company is based on original technology that was developed under the leadership of Prof. Avraham Mayevsky during his past industrial activities. The new technology is based on a new patent that protect us from competitors to enter this area of medical devices to be used in ORs and ICUs.

b. Another barrier is the Huge amount of knowledge (Clinical, Technological and regulatory) accumulated during the past 25 years by Prof. Avraham Mayevsky and his team. More than \$7 million were invested during these past activities. The current project is very complex in terms of scientific and engineering background in addition to the clinical experience in patient monitoring. As far as the company is aware, there are no competitors in this field of multiparametric monitoring of the microcirculation and mitochondrial function in real time.

c. The device to be presented by the company was presented in its previous versions to the clinical and scientific teams that are dealing with patient monitoring in real time. Therefore, other possible potential competitors will have to publicize the new ideas and device to the clinical society and obtain its recognition.

d. An important barrier is the clearance of a new device by the regulatory authorities such as the FDA. This will be very hard in the approval of a device that measure mitochondrial NADH in patients tissues.

The structure of competition and dynamic changes.

The area of patients monitoring in the ICUs and ORs is characterized in general by an intense competition between the various companies that are selling monitoring devices. This competition is important regarding the efficacy of the device used as well as the price of the hardware units and the attached disposable parts. A new device that will be minimally invasive or noninvasive will have an advantage in the market penetration process. To the best of our knowledge, the companies that are selling the multiparametric monitoring devices of vital signs are not presenting the new generation of tissue metabolic monitors based on measurements of more than 2-3 parameters.

The company product

General description

The MDXViewer is the first revolutionary product developed by MDX Life Sciences Inc. This medical device is expected to enable continuous real time evaluation of a new concept named Tissue Metabolic Score (TMS) in patients hospitalized in ORs, ICUs and other critical care patients. The determination of the TMS is based on the monitoring of 4 physiological and metabolic parameters at the tissue level in combination with vital systemic signs measured from the cardiovascular and respiratory systems.

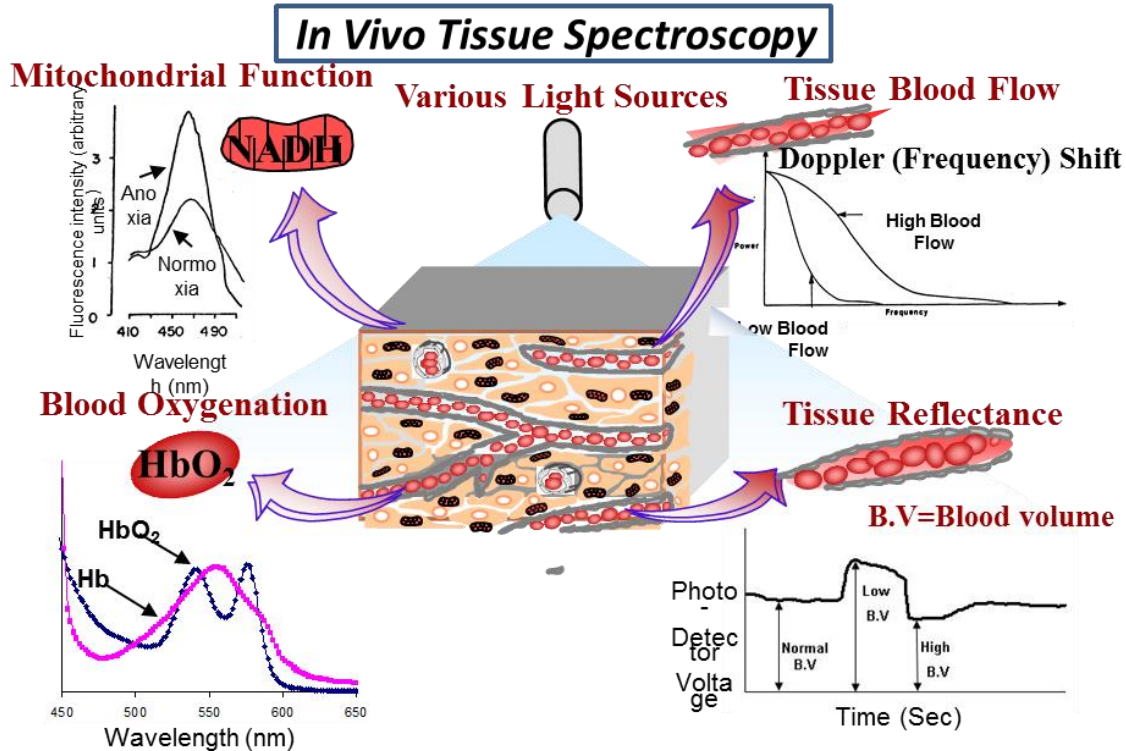


Figure 1: The four parameters to be measured by the three devices to be developed during the two years of activity.

The four parameters monitored (Figure 1) at the tissue microcirculation and cellular compartment are as follows:

a. **Mitochondrial function level**

The mitochondrion (mitochondria – plural) is the intracellular organelle the produce energy and serves as a “power station” of the cell. Each cell in the human body contain few tens to few hundred mitochondria that convert the energy stored in the digested foodstuff into high energy molecule named ATP (Adenosine Tri Phosphate). In the absent of Oxygen, the mitochondria stop producing the ATP the cellular functions are disturbed due to the lack of energy.

The MDXViewer evaluate the mitochondrial function by continuous measurement of the NADH redox state or level. The NADH- Nicotinamide Adenine Dinucleotide is a coenzyme produced from vitamin B2 (Niacin) exists in all living cells and its level is regulated by the activity of the respiratory chain in the mitochondria. The level of NADH is dependent on the availability of oxygen as well as the utilization of ATP by the cell. The NADH level is inversely correlated to the level of oxygen in the intracellular space. When the oxygen level is optimal, the redox state of the NADH is in the normoxic range and the ATP level is optimal for cellular functions. When oxygen level in the cell is limited (i.e. Hypoxia) the NADH is accumulated in the mitochondria and the production of ATP will decrease.

b. **Microcirculatory blood flow (TBF)**

The oxygenated blood leaving the heart via the large arteries, is reaching the very small arterioles and capillaries where the oxygen is diffuse toward the cells and finally consumed by the mitochondria.

This microcirculatory system provides the food and oxygen to the cells and removed the carbon dioxide (CO₂) to the lung and external air. The TBF is regulated by the consumption of oxygen by the cells, the higher the utilization, the higher the TBF. Normal TBF and intactness of its regulation mechanisms is a necessary step to enable normal mitochondrial function. The measurement of the TBF is based on the shift in the wavelength of the emitted laser light from the flowing red blood cells in the microcirculation (Doppler Shift). When TBF will decrease to a very low-level production of ATP will stop.

c. Microcirculatory hemoglobin saturation (HbO₂)

In the flowing blood from the lungs toward the heart, the hemoglobin in the red blood cells is almost 100% saturated with oxygen. The oxygen is bound to the hemoglobin when the blood is flowing in the capillaries of the lungs and is released in the capillaries of the various tissues in the body. Under certain conditions, the TBF is normal but the HbO₂ is not saturated to the maximal level. Therefore, oxygen supply to the cells will be below the normal range and the monitoring of HbO₂ is important to the clinician. The microcirculatory HbO₂ level reflects the balance between the supply and demand of oxygen in the capillaries.

d. Tissue backscattered light (reflectance).

This parameter reflects, indirectly, the blood volume in the monitored tissue at the NADH excitation wavelength (i.e. 375nm). In addition, this parameter is used in the calculation equation when calculating the corrected NADH fluorescence.

The TMS, calculated in real time using the 4 monitored parameters, is affected by changes in the vital signs measured routinely in each patient. The main vital sign parameters are: heart rate, systemic blood pressure, respiratory rate, systemic hemoglobin saturation and body core temperature. The combination between the tissue metabolic score (TMS) and the systemic vital sign parameters is the way to optimize the treatment given to the patients in critical care medicine.

The human body is made of systems (cardiovascular and respiratory) and organs (liver, kidneys) that are in charge of its normal function. The organs and systems are dependent on continuous supply of metabolic energy produced in each cell of the body by the degradation of food stuff when oxygen is consumed. This metabolic activity needs continuous supply of blood containing energy source (i.e. sugar) and oxygen as well as normal function of the mitochondria. In critical care patients exposed to negative oxygen balance in the body, due to the lack of oxygen in the blood, decreased microcirculatory blood flow or disturbances in mitochondrial or cellular functions the monitoring of TMS is critical to the clinician in order to optimize the treatment given.

According to the published medical studies, disturbances in mitochondrial function could be the critical factor in the development of tissue metabolic dysfunction

(Fink, M.P. Cytopathic hypoxia Mitochondrial dysfunction as mechanism contributing to organ dysfunction in sepsis. Crit. Care Clin, 17:219-237, 2001

Continuous evaluation of mitochondrial function, in real time, by the measurement of NADH redox state could provide continuous metabolic information with a very short response time. According to the knowledge accumulated in the company, a device that monitors NADH redox state in vivo and in real time was not cleared by the FDA or introduced to daily clinical use. Therefore, the monitoring of NADH as part of the TMS may turn to be a breakthrough technology in patients monitoring.

In addition, the use of TMS in combination with systemic vital signs may help to identify the development of sepsis in critical care patients. Sepsis is a central problem of metabolic crisis that may end up in multi system failure of the human body. Sepsis may develop in patients as a result of infection or a wound that lead to general body inflammation reaction. Various events developed during sepsis may lead

to dysfunction of various organs in the body due to the decrease in oxygen supply and in many cases will end up in septic shock. Due to the negative oxygen balance developed, cellular respiration is inhibited and ATP production by the mitochondria is diminished – Cytopathic hypoxia.

(Fink, M.P. Cytopathic hypoxia mitochondrial dysfunction as mechanism contributing to organ dysfunction in sepsis. Crit. Care Clin, 17:219-237, 2001)

The number of new patients suffer from Sepsis are 20 million every year and about 30% of them are dying after hospitalization on the ICUs. Early detection of Sepsis development by better monitoring of patients may save a Hugh amount of money and will decrease the mortality rate especially in the older population of patients.

Principles of MDXViewer design and operation

The MDXViewer system (Figure 2) includes all necessary sub-units for tissue spectroscopic measurements. The system comprises a probe, a bedside unit, a panel computer and power supply. All these subunits can optionally be mounted on a cart

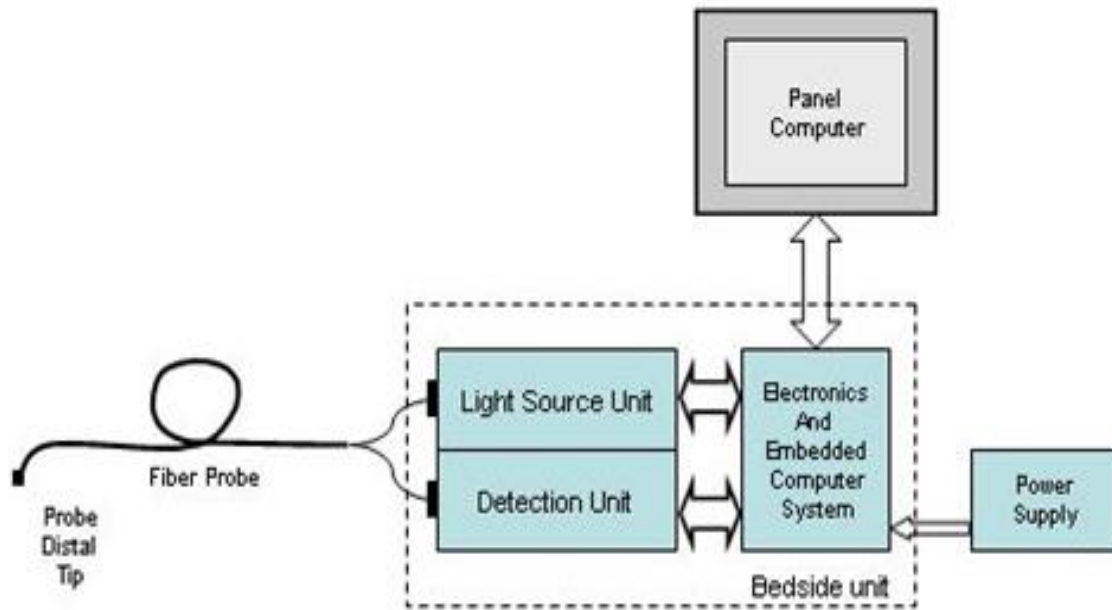
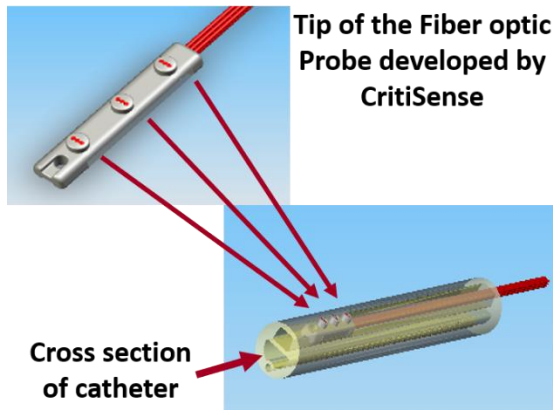


Figure 2: The MDXView system subunits - The Light Source Unit (LSU) emits multiple wavelength light into a fiber optic probe that delivers the light to the tissue and collects the returning light. The Detection unit converts light signals into electrical signals. The electronics and embedded computer system that controls the light source and detection unit functions and performs data acquisition and preliminary data processing.

The MDXViewer is connected to the monitored tissue by different types of fiber optic probes to be constructed by the company. In patients monitored in the operation rooms (ORs) or in the intensive care units (ICUs), the TMS will be calculated in the urethral wall by monitoring the 4 tissue parameters using a 3-way Foley catheter inserted into the bladder for urine collection.

The “smart” Foley Catheter

The fiberoptic sensor for measuring Urethral wall vitality, is embedded in a disposable 3-way Foley catheter.



The 3-Way Foley catheter in the human bladder

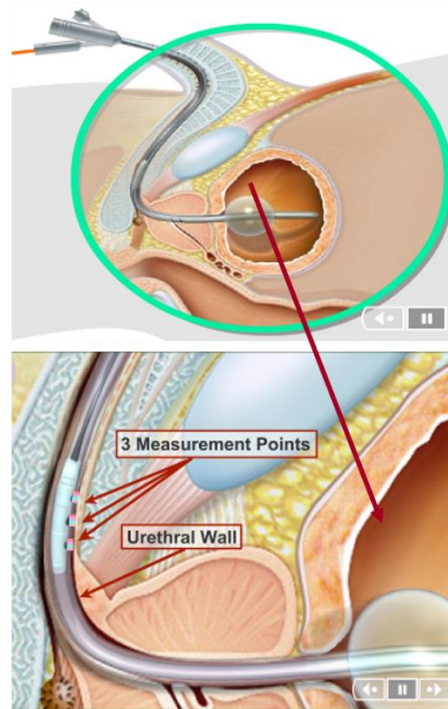


Figure 3: The Smart Foley Catheter

The insertion of a Foley catheter is a standard procedure in most patients in the ORs and ICUs and considered as a minimally invasive procedure. The 3-way Foley catheter (Figure 3) includes one channel that enables the collection of urine into the urine bag. A 2nd channel enables the inflation of a balloon that fixes the tip of the catheter inside the bladder. In addition to the standard 2 channels, a third channel contains optical fibers that at a certain point in the urethra are bended in 90 degrees and are glued and polished in the wall of the catheter. Part of those fibers is transmitting light from the MDXViewer to the inner layer of the urethra and another part of the fibers are collecting the reflected light from the urethra toward the detection unit of the monitoring device. The MDXViewer contains a special design light source unit (Figure 4) that provides light at different wavelength (colors) that will illuminate the urethral wall.

The light source unit comprises 3 different types of LEDs at 3 wavelengths and a single laser diode. The excitation wavelengths of the LEDs and the laser are:

- UV LED – 375nm
- Blue LED – 470nm
- Green LED – 530nm
- NIR laser – 785nm

The light from all LEDs and laser diode is mixed into the excitation channels and guided to body tissue by a flexible optical fiber. The light interacts with the tissue and subsequently emits from the tissue volume. The light emitted from the tissue contains several components:

- NADH fluorescent emission at 450nm
- Total backscattered light at 375 nm
- Doppler shifted laser light at 785 nm *
- Total backscattered light at 470 nm **
- Total backscattered light at 530 nm **

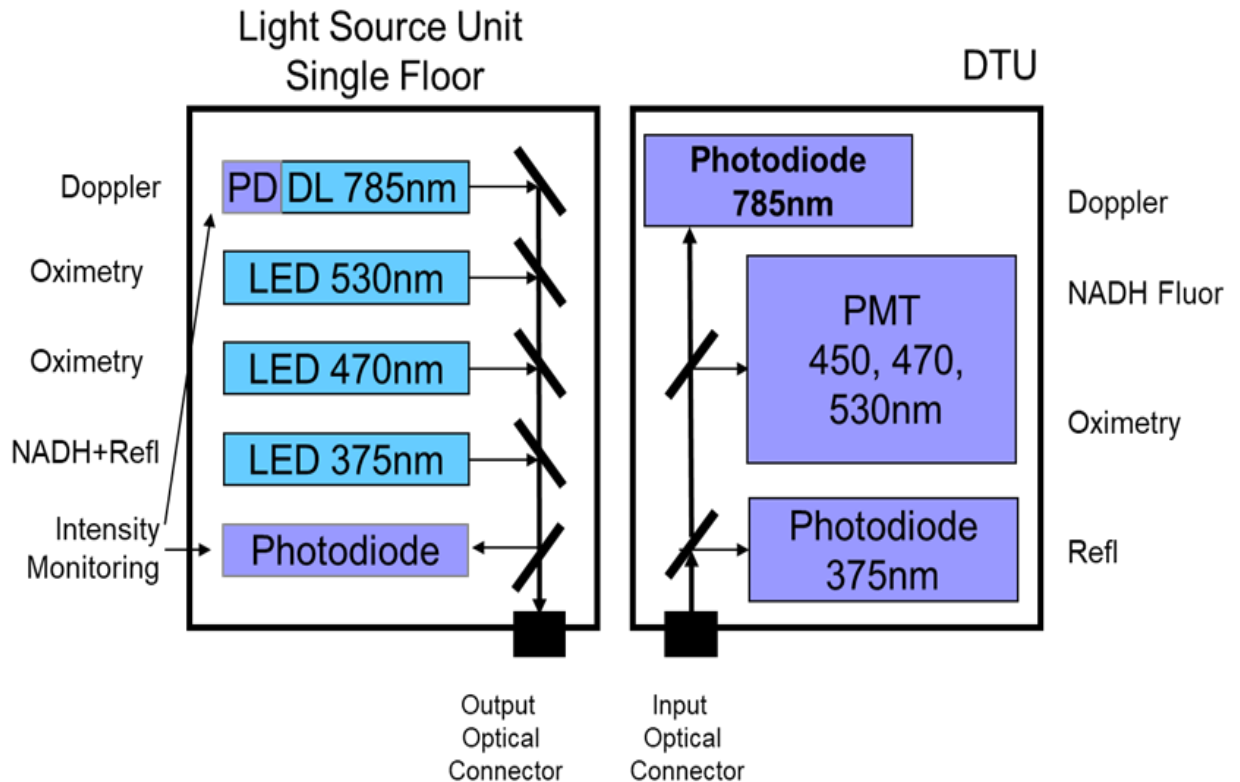


Figure 4: The light source unit

The light source unit (Figure 4) of the MDXViewer comprises a 785nm CW laser diode which serves for laser Doppler measurement, a UV LED (375nm) for NADH fluorescence excitation and for total backscatter (or reflection) measurement, a Blue LED (470nm) and a Green LED (530nm) for hemoglobin saturation measurement. In order to enable a very high measurement dynamic range of fluorescence and reflection parameters the light source unit is designed to enable a very wide range of the excitation intensities.

The near IR laser diode at 785nm, for laser Doppler measurements, operates in Continuous Wave (CW) operation mode. Its output intensity is dramatically attenuated by the internal fiber optic attenuator-isolator (not shown on the figure). The output intensity of 785nm light at the measurement point is always below 150 μ W which is well below the safety limit.

The UV LEDs, Blue LEDs and Green LEDs operate in chopping mode. This enables usage of synchronous detection techniques in order to detect the NADH fluorescence and total backscatter light. Additionally, the chopping operation mode enables one to perform NADH measurements with very low excitation intensities well below the limits specified by the laser safety standards.

The Detection Unit (DTU)

All six collection fibers of the fiber optic probe are assembled into a single male SC optical connector. The light from the probe passes through the panel connector into a single thick optical fiber that delivers the light to the DTU. At the DTU entrance the collimation lens collimates the fiber output light. The collimated light is split according to the different wavelengths into the respective photo detectors by means of dichroic beam splitters. The first dichroic beam splitter reflects the total backscatter signal at 375nm towards the photodiode detector. The higher wavelengths pass through the first beam splitter towards the second dichroic beam splitter. The second dichroic beam splitter reflects the NADH fluorescence signal at 450nm and total backscatter signals at 470nm and 530nm towards the photomultiplier detector. Due to the chopping operation of the LEDs the photomultiplier detector detects each one of the above-mentioned signals at different time, i.e., time sharing operation detection mode. The second dichroic filter enables the laser Doppler signal at 785nm to pass through it towards the photodiode detector. All acquired signals are digitized into the DSP processor by high resolution 16bit A/D.

The DSP processor

The DSP processor is responsible for whole system control, initial data processing and calculation of Doppler parameter. The DSP is built around Tern Inc. 586-Engine-P controller board with AMD SC520 CPU. After initial data processing the calculated values are transmitted to the panel computer for final data processing display through RS-232 serial interface.

Power Supply

The MDXViewer device utilizes medical grade main power supply for all electronic circuits including the panel computer.

The MDXViewer in clinical application

The device as seen in detail in Figure 5 will be used mainly in the ICUs and ORs as seen in Figure 6.

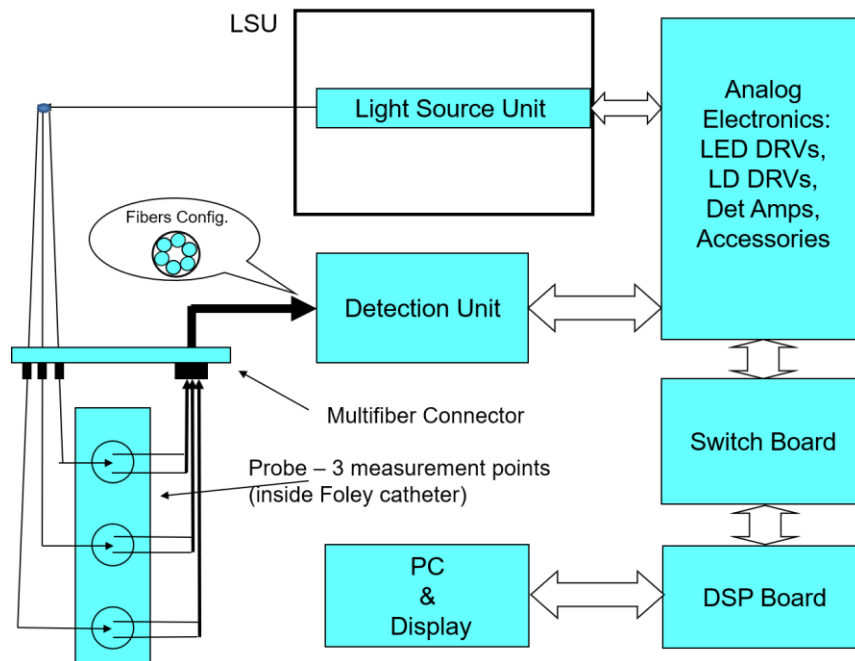


Figure 5: Light Source Unit



Figure 6: The MDXView in the ICU(left) and in the OR (right)

Follow-up and diagnostics

The catheter is connected to the device continuously and the monitoring could be performed for 8 hours every 24 hours. This issue will be treated very soon by adapting the UV light intensities to fit the safety allowance. Afterward the length of monitoring will not be limited in time. The data to be accumulated by the device will be calculated to provide the TMS that will be integrated with the vital signs measurements collected in real time by the standard multiparametric monitoring device located in each ICU and OR. As of today, the information provided by the device is not calibrated in absolute units and therefore will be evaluated in the same patient along the time axis as compared to the initial values collected at the beginning of the monitoring of each patient. This approach will enable the detection of deterioration or improvement in the metabolic state of the patient in real time. In the future the company will improve the technology used in the device and the results will be calibrated in an optimal way.

The status of the MDXViewer

The company will construct the upgraded model of the MDXViewer that will present on the display the 4 monitored parameters and the calculated TMS. The initial group of the devices will be tested in pre-clinical and clinical situations that may be needed for the next application to the FDA for clearance.

The hardware of the device will be made in the company's laboratories after buying the needed critical components from recognized suppliers. The software that will run the device is developing in company by a software expert. The estimated cost of the hardware unit at this stage is around \$25,000 due to the small quantities of the production. The company assumes that the large-scale production cost will be in the range of \$ 2,000-3,000.

The single use disposable catheter will be constructing in the company in the fiber optic laboratory based on production of various parts by subcontractors. The company will collaborate with strategic manufacturer to develop a special 3-way Foley catheter that will fit the specific needs. The packaging and the sterilization will be done by subcontractors.

At this point in time the company is not planning to manufacture the final commercial unit in large quantities.

The evaluation of the production cost of the device and its disposable probe is very sensitive to many factors and difficulties that may show up during the final R&D process. This includes the time requested to overcome various factors, the requested preclinical and clinical testing, the regulatory processes and publications in the appropriate meeting and printed clinical papers. Our evaluations may not be come to optimal solutions and parts or most of our expectations will not come through.

Customer and potential new customers for the device

As of today, the company doesn't have any list of customers for the device. The potential customers are hospitals, and other medical organizations that run ORs and ICUs. As of today, in many developed countries, there is medical insurance system that reimburses the patients for medical treatment and hospitalization costs in ICUs. Since the reimbursement rate is fixed according to the procedure given, there is a tendency in the medical team to minimize the cost of treatment and the length of stay in the ICUs. Buying of new medical devices is dependent also on the efficacy of the device in the treatment given as well as the economic value of the new device in treatment the patient. It's very hard to evaluate the demand for our new device in the ICUs and ORs. At this point in time, the company did not perform and contacts with potential medical institutes or run a marketing search for our device.

Marketing and distribution

At the current time of preparing the prospectus, the company didn't start the mass production of the device or the catheters and therefore the marketing of it never started.

The company will start the activities that will increase the exposure of the new concept of the Tissue Metabolic Score (TMS), based on the 4 monitored parameters, to the clinical potential users in various scientific meetings and exhibitions in the field of ICUs. Also, the accumulated results from the preclinical and clinical studies will be published in well recognized international scientific and clinical publications.

At this point in time, the company doesn't have any marketing agreements with appropriate companies and all the marketing effort will be made by the team in the company. In the near future, the company will negotiate with appropriate distributors including a strategic partner that will take over the world distribution task. This type of activities may need additional significant funding.

Competition

Technological competitors

The MDXViewer developed by the company is a multiparametric spectroscopic based monitoring system that provides real time changes in the Tissue Metabolic Score (TMS) based on 4 monitored physiological parameters. The measurements are performed by a minimally invasive technology that is connected to the inner wall of the urethra in patients hospitalized in the ICUs and ORs. The TMS provide the clinician with highly valuable information regarding the oxygen balance the entire body of the patient. To the best of the company knowledge and according to the published information, there are few technologies that may be partial competitors to our approach of monitoring as follows:

a. Continuous measurement of hemoglobin saturation by pulse oximetry (%HbO₂). This optical technique provides information on hemoglobin saturation of the large arterial blood vessels (in a finger) but not in the microcirculation was the main diffusion of oxygen from the blood to the cells occurs. Is information is related to the ability of the respiratory and the cardiovascular system to oxygenate the hemoglobin but can't provide information regarding the tissue level oxygen supply. Also, the pulse oximetry is possible when there is a pulse in the flowing blood in the artery but in few cases this pulse disappears, and the monitoring is disturbed.

b. Measurement of oxygen supply to a specific tissue evaluated by various technique such as laser Doppler flowmeter or measuring the tissue pO₂ using oxygen electrode. The disadvantage of those techniques is that the measured parameters are indirectly related to consumption of oxygen but are not representing the consumption of oxygen by the mitochondria.

The described potential competing technologies are providing only a single parameter as compared to the multiparametric nature of the MDXViewer.

To the best of our knowledge, the device developed by MDX Life Sciences Inc. is a very unique in terms of the number of monitored parameters (4) as well as the ability to measure mitochondrial function in a direct approach. The TMS is based on the monitoring of mitochondrial NADH and it's the only device that has a clearance from the FDA. Also, the company is not aware of any device that provides 4 different parameters simultaneously from the urethral wall by using a minimally invasive Foley catheter.

Competitive companies

Various companies had developed products based on the technology described in the previous chapter. Among these companies we identified Hutchinson Technology Inc., Vasamed Inc., Edwards Life Sciences and Microvision Medical. The disadvantage of those products is that all of them are measuring a single parameter and mainly the oxygenation level of hemoglobin. This approach is very limited in the diagnosis of a patient in the ORs or in the ICUs and therefore they are not accepted as a standard of care in many hospitals around the world.

Research and Development

Previous R&D activities

The technology and knowhow that the company has is based on the R&D activities made by Prof. Avraham Mayevsky since 1972 in his academic and industrial occupations. During the years, the 2 companies that were established were able to raise more than \$7million and the 3 developed products that were cleared by the FDA in 2000, 2006 and 2007. During the years, the technology was tested in patients in clinical studies after pre-clinical testing in animal models.

Status of the developed devices.

The 2 Israeli companies that were active in the development of the specific medical devices are not registered any more. Prof. Avraham Mayevsky who was the chief scientist of those companies has all the information needed for the continuation of the future activities by MDX Life Sciences Inc.

Preclinical and clinical studies

The products developed previously by Prof. Avraham Mayevsky and his 2 companies were requested to perform preclinical and clinical studies during the various R&D stages in order to obtain the FDA clearance.

a. The preclinical studies included in vitro laboratory studies, that tested the properties of the product and its efficacy, and in vivo experiments that tested the efficacy of the device in the physiological environment. Also, bio compatibility studies were performed.

b. The last model of the device was tested in animal models that were mimicking the conditions of lack of oxygen in the human brain or in other organs in the body. The stability of the device was tested by monitoring an animal model for number of hours.

c. The clinical studies were done in well-recognized medical centers under the supervision of a senior researcher that serve as the principle investigator of the clinical project. In early stages a pilot study

using a small number of patients was done in order to check the feasibility of the proposed protocol. The proposed protocol must obtain the approval of the Helsinki committee of each medical center where the device was tested.

d. Performance of clinical studies in patients is under the control of the regulatory authorities in each country. In Israel, for example, the Ministry of health is part of the regulatory authorities and a representative will be part of the Helsinki committee. One of the accepted standard that we used in the past was the Good Clinical Practice (GCP) that is part of the regulatory systems used in the US, Europe and Japan. This code includes the instruction for the planning, performance and documentation as well as reporting to the medical authorities. The GCP covers also the protection of the patients taking part in a clinical study regarding their rights.

e. The company will employ an expert in quality assurance, regulation as well as running the clinical studies as requested by the Helsinki committee. This person will obtain the requirements for a clinical study and will be in charge of preparing the applications to the various medical centers, definition of the criteria for the performance of the study as well as accumulating the various results related to the clinical study.

Research and development program

According to new results and concept developed by Prof. Avraham Mayevsky, a new patent application was written recently, and it will be submitted as a new provisional patent by MDX Life Sciences Inc.

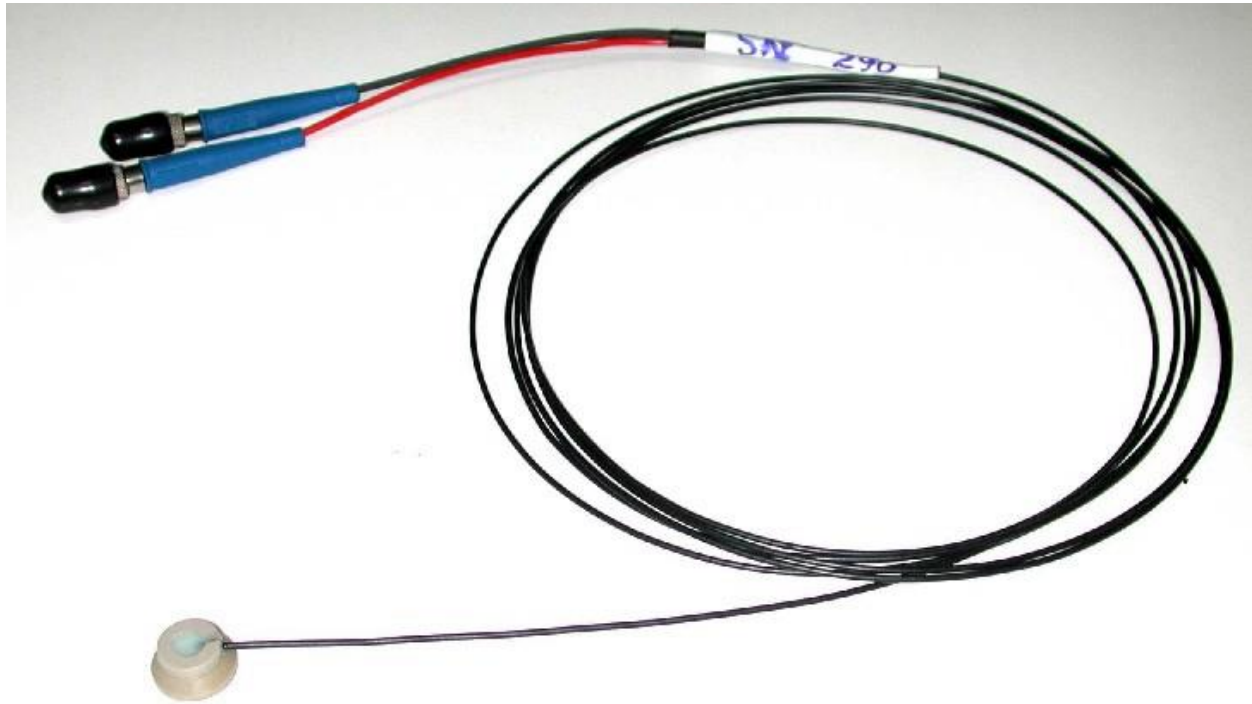


Figure 7: Newborn forehead skin probe

The company estimates that the next upgraded model of the MDXViewer will be ready for clinical testing within 9-12 months after the next round of funding. This device will be submitted to the FDA if needed and also to obtain the CE Mark. In parallel to the mentioned activity the company will run a R&D

project in developing a device that will enable the monitoring of the skin of newborn and adult patients and calculation of the TMS. A probe to be used in newborn babies in the neonate ICU is presented in Figure 7.

High-level Summary of Project Tasks and Deliverables

Development Plan

R&D, Regulatory and Marketing pathway

Activities	Month 1-3	Month 4-6	Month 7-9	Month 10-12	Month 13-15	Month 16-18	Month 19-21	Month 22-24
Engineering		MDXViewer-1 MDXViewer-2	MDXViewer-3					
Software				MDXViewer-2/3 (4+)				
Production				MDXViewer-2	MDXViewer-3			
R & D				MDXViewer-2/3 (4+)				
Clinical		MDXViewer-1				MDXViewer-2	MDXViewer-3	
Regulatory					MDXViewer-2		MDXViewer-2	
Marketing/PR					MDXViewer-2/3 (4+)			

MDXViewer-1 - Urethra
 MDXViewer-2 - Urethra II
 MDXViewer-3 - Skin
 MDXViewer-4+ - Future Projects (Big Data, Wearable, CTE)

Estimated project cost

Total Project Cost	\$ 10 million
---------------------------	----------------------