Jackie R. See, M.D., F.A.C.C.

CARDIOVASCULAR DISEASES AND INTERNAL MEDICINE
Email: jrseemd@aol.com

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SUMMARY

EXECUTIVE SUMMARY OF UNITED STATES PATENT NO. 8,313,477 BY SEE ET AL NAMED DEVICE AND METHODS FOR MONITORING THE ADMINISTRATION OF A STEM CELL TRANSPLANT

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The reason for this executive summary is that this patent was written, accepted, and issued by United States Patent Office by a research physician trained at Harvard in imaging, physics, and characteristics in conjunction with two California Institute of Technology theoretical and practical physicists including laser radar imaging and detection. Thus the scientific and technical portion of this patent will be simplified hopefully for review by those not skilled in these arts. The importance of this device is that it can measure whether or not a stem cell is alive or not, what the derivation of the stem cell is from, the number of the stem cells delivered directly to the tissue is intended for, whether or not the tissue is intended to be delivered to, has damaged any specific type by means of a fiber optic wire placed through the lumen which means the hole in the catheter which means a tube. This fiber optic wire is preceded by a 14000 of an inch diameter flexible wire followed by the catheter to the site either in the brain, the spinal cord, the liver, the heart, the spleen, the kidneys, the legs, the aorta, or any other portion of the arterial and venous system of the body. This wire is then removed and the fiber optic wire called the linear member and particle detection device in the patent. Importance of this fiber optic laser or light, blood casting to the cells to be delivered through the tissue as then previously probed by the laser wire is that the laser reflection from the tissue or the cells being delivered down the catheter to the area of damaged tissue has a unique signature related to wavelength and reflection angle based on the laser or light wavelength to be reflected back in the fiber optic catheter and displayed on a screen outside the catheter that is introduced into the vein artery of behind the operator for computer processing to determine the state of the cells, the number of the cells, the viability of the cells, and whether they have clumped together, whether there are any other particular matter that should not be injected into the

site. In addition, the cells can be imaged with the same fiber optic wire in the culture plate or in the actual media containing the stem cells and the growth factors to get a signature of the size of these cells based on the laser radar reflection capacity.

Since there are 22 known different sites for stem cells it is important and critical to know that the proper stem cells are being delivered to the patient and that they did not contain other types of cells which may be harmful or not viable. Therefore, they would not be effective. In addition, the area presumed to be damaged will be imaged directly by the laser radar wire once the catheter is placed in place for the targeted organ anywhere in the body. As the cells are delivered and one can measure the laser light reflection reflected back onto the computer on the imaging screen to determine that they are still alive that they are going into the proper tissue and the characterization of the tissue as they enter into the damaged tissue. There is no other way to do this particularly for cells that are bound for the brain, the spinal cord, the heart, the retina of the eye, the kidneys, or other vital organs or even the skin or ischemic areas of the legs due to atherosclerosis and so forth. This is important for safety as well as therapeutic reasons.

It will be necessary before human delivery of stem cells that have either been cultured from a primary source or transferred from the patient themselves from any number of sites known in the art to contain stem cells by looking at the laser radar characteristic of these cells and the viability or not before they are injected after they are injected and into the place that they are going to. There is no other way to do this other than through imaging device. It cannot be done by taking biopsies of the area and looking under microscope or with a chemical analyzer to determine these characteristics. Therefore, there are over 35000 PubMed publications on stem cell biology and over 5000 are clinical trials underway that are registered regarding the use of stem cells for therapeutic purposes and it will be necessary to use this technology to determine whether the cellular therapy and the contents therein that are being placed in the body for therapeutic or healing purposes is measured properly in a full proof manner that is reproducible which is described in this patent.

I will use for description of page by page analysis of this patent. The patent as published at www.uspto.gov. Let us start with page I.

PAGE I
This gives the title, the authors, the related documents in reference sited.

PAGE II
It shows a continuation of other patents and related publications and the date of the provisional application and number which was filed March 5, 2011.

The remainder of the page contains the six claims which talked about the specific of the catheter, the detecting system which is the fiber optic wire, and the sizing and size distribution, administration, and the monitoring of the different types of cells and how one determines them to have a Tumorigenicity or not, immunogenicity or not, cell surface marker profile, proliferation potential, plasticity engraftment potential, therapeutic potential, or combination throughout.

The claim #6, sub claim talks about counting exactly the number of cells that are being delivered through the administered site and the phenotype of the cells, phenotype meaning whether they are from a mesenchymal, a neurological, a neuronal, a central nervous system, a retinal, a heart, a kidney, a kidney glomerular cell, a skin cell, an arterial cell, or other derivatives thereof.

On page 3 at the top shows the remainder up to #10 of the defendant claims describing the light scattering detection device which is the laser radar fiber optic wire and that the wave length of the light or laser is specifically mentioned.

Page 3 then goes on in the description to talk about the field of the invention which one can read easily from the pattern which talks about this device, the method for monitoring the administration of stem cell transplant and in the background it mentions that the only other technology available is magnetic resonance imaging which looks at paramagnetic imaging of agents that are usually iron oxide which are toxic to the cells themselves and very poor target-to-background ratios are noted. Therefore, the placement of the cells in human organ or tissue also does not tell whether the cells are alive or not because nonviable are dead cells which still have the iron oxide in them as the current magnetic imaging factor, therefore this is the only way that the viability number and residents within the organ itself such as the brain which cannot be biopsied and would not reveal whether the cells are alive or not at the time there is biopsy done.

On page 4, the pattern then talks about the real time monitoring of the stem cell transplant in which the light scattering detection device which is the laser radar fiber optic wire going through the lumen of the catheter that is in place to the targeted area over a guidewire which has been removed and replaced by the laser light.

The second paragraph of page 4 talks about a kit in which the catheter, the laser, radar, wire, the light scattering detection device, and the computer are all included in a kit. Also, the definitions on page 4 declines themselves as a non-differentiated cell which has ability to both self-renew and undergo differentiation to form a more specialized cell. It also talks about the term differentiation, differentiation potential, spasticity, and the explanation of the higher the number of specialized stem cell that a stem cell assume the greater its differentiation potential will be and greater its therapeutic potential will be. The term proliferation is talking about the ability of one of the 22 known different types of stem cells and origin and have the ability to grow and divide under suitable conditions and these culture conditions are making a viable cells, etc., can be measured using the same fiber optic system before the cells are put into location. The definitions go on to talk about observable characteristics or traits of an organism and the current type in the organs genes which can be checked by putting the laser radar fiber optic probe into the cell before they are placed through the catheter into the deceased or nonfunctioning, or damaged tissue.

Page 5 talks about pharmaceutically acceptable carrier which are known culture media and phosphate buffered saline and other acceptable carrier is known in the art of stem cell culture. We defined that the particle are of particular matter whether it is in gasses, liquid, solid, gel or combination thereof and nanosomes, vesicles, microspheres or other polymer materials or other support media which can be distinguished easily by the laser radar signature from a stem cell of any type by this laser radar fiber optic computer system. We go on to do certifying body space terminal end which means the end of the catheter where the winder is. The guidewire is removed and laser fiber optic wire is placed for reflection of laser radar characteristic beamed at the origin outside of the body and then reflected back on to the screen after being processed by the computer looking at wavelength angle of refraction and angle of penetration of the cells which distinguish them from a particular matter. A catheter is defined as well as targeted delivery site.

On page 6, we talked about catheter space and the linear member which is the particle detection device and how this goes down the catheter and to the tissue where the stem cells will be placed through the catheter. Their characteristics is measured as noted in the next paragraph talking about light or spectrographic techniques or radiate energy visible, infrared, ultraviolet frequencies and laser light is one non-limiting example of light as the term used herein.

Page 6 goes on to talk about the stem cell transplant characteristics which are the number of stem cells, size distribution of the stem cells, and stem cell phenotype and whether or not there are other particles, i.e., solid or debris or other particular matter as described above. Regarding to describe monitor monitoring and monitors

that are used to determine the stem cell phenotype size distribution, quantity of self concentration and combination thereof. We go on to describe a tumor as a neoplasm or a solid lesion formed by abnormal growth of cell which can be benign, pre-malignant, or malignant which can be tested by the laser radar fiber optic wire through the end of the catheter and end of the tissue before pulling that back into the catheter as the cells flow by and they are being delivered into the tissue of interest and imaged thereby reflecting the particular laser light scattering characteristics of the stem cells as they flow into the tissue.

Page 7 talks about the computer processor for determining the characteristics of the administration of the stem cell transplant. The rest of the page talks about the particle detection device and the linear member in paragraph 3 is the fiber optic laser radar wire and that is described. The particle detection device can measure electromagnetic energy by a light scattering mechanical energy such as Brownian motion and acoustic energy such as Doppler devices and combination thereof and this is spelled out.

Page 8, we described the light sources and the optical sensors and the different scattering angles later picked up from different cells that are either viable, i.e., alive or nonviable, i.e., dead or debris and it should be noted that different stem cells from different origins have different laser radar scattering and angle deflections as noted prior to placing another tissue and this can be matched to see if live cells indeed are being given or not or the proper cells defined by what one thinks one is giving is in fact that which is given.

On page 8 as well the different light sources and the wave lengths of either light or lasers particularly 420 nanometer lasers which are safe for human tissue and have been used for many years that wave length for detecting different parts of the body including the retina without damaging the retina of the eye.

The bottom of the page 8 talks about disclosures of other types of light scattering detection devices which are listed in the references cited.

On page 9, we talked about the fiber optic wires themselves and how the detection device, the lasers, the fiber optic wire, the wave length, and ultrasound which is laser radar in origin very much like a jet plane which is used in advance of the plane to determine a mountain while the plane is going over mark initiates to in speed. Therefore, we are doing something different but that is an example what one can do with laser radar sourcing. In addition, we talked about laser energy source or pump laser, how it is activated in the electromagnetic energy conduction through the fiber optics in the Mather Medical algorithms and determine conversion factors obtained by computer

programs known in the art and described. We also talked about the different types of counters that use laser reflection that are used in clinical laboratories that we can combine with this device.

On page 10, we talked about other uses of the particle detection device which shows a light scatter detection device with any number of wires, i.e., as we find out fiber optic wires which are bundled together and bound by a sheath. The diameter of same would be less than the inside diameter of the hole of the catheter, i.e., the lumen. In this instance, we use a 14000th wire in a 20000th to 30000th of an inch diameter lumen. We can go to as large as one inch in diameter of the lumen down to 12000th of an inch in diameter of the hole or the end of the catheter to deliver. We deliver the cells of any length to any part of the body. At the bottom of page 10, we discussed the intention of using and determination of the size of the cells, this can also be determined to shown the differentiation potential which is inversely correlated with stem cell size, that his higher degrees of differentiation and self renewing potential are correlated with small cell size. The example we give is for a human hematopoietic stem cell which means human stem cells that may be rather white blood cells which are usually less than 10 microns they have certain cell marker profiles that show that there were primitive than larger cells which are between 10 and 14 microns that being the macrophages of both cell types being derived from the same tissue. Therefore, using this laser radar detector wire in a catheter system as well as the computer algorithm and reflection of the laser radar back to the fiber optic from either the culture plate, the tissues removed from the patient themselves are continuing the stem cells or cultures cells prior to doing and after delivery into the area of interest. Also on page 10, in the last paragraph we talked about size being related to viability or what if the cells are still alive, one should deliver them into the catheter and then to the patient organ or damage tissue from whatever cause. If the cells are disrupted and not ground or they are smaller and alive cells that you image prior to putting them in the catheter then they are viable cells, and by this monitoring device, we can determine that.

On page 11, we talked about how by using this device and the imaging technology described we avoid the administration of clumping of stem cell transplantation well pass other debris such as clumps, platelets, or other unwanted cells and we can monitor by a feedback loop that is explained in the third paragraph on page 11 so that we know exactly what quantity and number of cells have been delivered as our predetermined based upon prior research experience in thousands of cases over the last 50 years by Europeans and now Americans and other places in the world. At the bottom of page 11, we again talked about and explained the phenotype which is relative purity of the stem cell type, population of the 22 known types of stem cells.

On page 12, we discussed how the device can lend itself to identification of tumor and/or immunogenic cells before they have been either delivered to the body or by probing the tissue outside the end of the catheter placed near the target tissue and measuring the laser radar scattering technology which distinguishes between the packed type cells noted in tumor cells versus normal tissue which are known throughout the body of medical work through histology and pathology study. This is discussed and is written in non-scientific language and easily understandable. The size of the fiber optic wire versus the size of the stem cells and the laser emitting diodes as well as the optic wire and the use of those. We at the bottom of the page talked exactly about the type of the catheter, the laser emitting diode, the optical sensors, and how when the cells flow by them in the catheter, how the imaging characteristics are carried out.

The page 13 talks about the light scattered detection device again detecting specific stem cell phenotypes meaning as different stem cells that are one of the 22 different types that they have not changed in culture or from the time of collection to the time of delivery into the tissue down through our catheter pass the optical sensors in the laser radar fiber optic communicator to a computer processor by reflection and the rest of this page talks about a hostile environment and which is determined by the different types of abnormalities which we cover almost all types of different abnormalities of tissue that are present in various disorders, dysfunctions, or diseases, and the measurement of same by the laser radar probe being used prior to delivering results to the patient. At the bottom of the page, we give prior disclosure of the guide wires is to place the catheter and the catheters prior to removal of the guide wire from the catheter and the placement of our patented laser radar fiber optic wire of 14000th of an inch in diameter.

On page 14, we discussed the use of 64 slice and about CT scans to use mapping systems for the planned movement of the guide wire and the catheter and the placement exactly where one wants to place the catheter prior to removal of the guide wire and placement of the fiber optic wire into the tissue for imaging to determine its characteristics as well as the pulling back of the wire into the catheter while injecting the cells down the catheter into the area of abnormal tissue to be treated by the cells themselves to make sure they are compatible, and page 15 of 15 on the patent office site mentioned at the beginning of this review is the final page.

Therefore in summary, this patent determines the cell type, the number of cells, whether they are alive or not, whether they are into the tissue, the abnormality of the tissue that is being predetermined either by testing by biopsy with different staining and spectrographic analyses or enzyme analyses, jean analyses, or other analyses to determine the defect of the tissue to be treated by the stem cells

and the accompanying embodiment of the either tissue or culture media that the cells are derived from of the 22 different types. This ensures that the patient is receiving viable cells, that they are proper cell type for the proper defined dysfunction of the tissue to be treated as well as after they are delivered to put in a laser radar fiber optic wire into the tissue to look at the effects of the stem cells as they are in place in the diseased tissue wherever they are delivered in the body to determine if they remain viable during the initial entry particular into a hostile environment as the majority of cell attrition will be in the first few minutes of delivery as determined by extensive experimental data over the last 50 to 75 years of stem cell biology.