# BioPace: Complete Technical & Strategic Dossier

## I. PATENT CLAIMS: US Patent 5103821 A

**What is claimed is:**

1. A method for providing for pacing of a human heart of a patient comprising:
2. a. isolating a plurality of viable sino-atrial node cells from a human heart; and,
3. b. implanting said plurality of viable sino-atrial node cells within said human heart, whereby said implanted viable sino-atrial node cells pace said human heart.
4. A method according to claim 1 wherein said implanting step further comprises implanting said plurality of viable sino-atrial node cells within a ventricle of said human heart.
5. A method according to claim 2 wherein said implanting step further comprises implanting said plurality of viable sino-atrial node cells within the right ventricle of said human heart.
6. A method according to claim 3 wherein said implanting step further comprises implanting said plurality of viable sino-atrial node cells within the apex of said right ventricle of said human heart.
7. A method according to claim 4 wherein said plurality of viable sino-atrial node cells are from said patient.
8. A method according to claim 5 further comprising, after said isolating step and before said implanting step, removing said plurality of viable sino-atrial node cells from said patient.
9. A method according to claim 6 further comprising, after said removing step and before said implanting step, culturing said plurality of viable sino-atrial node cells.
10. A process for providing a biological pacemaker implant for the human heart which comprises the steps of:
11. a. identifying S-A node cells in the right atrium of the heart;
12. b. removing a quantity of said S-A node cells from the wall of the right atrium;
13. c. culturing said quantity of S-A node cells to grow a quantity of said S-A node cell to produce a critical mass of said S-A node cells sufficient to generate a depolarization wave in myocardial tissue; and,
14. d. implanting said critical mass of S-A node cells in the right ventricle of the heart to provide a depolarization wave of sufficient magnitude to stimulate contraction of the myocardial tissue of the ventricles of the heart to initiate and sustain substantially natural heartbeat.
15. A process in accordance with claim 8 in which the quantity of S-A node cells is removed from and implanted in the same heart.
16. A process in accordance with claim 8 in which culturing of said S-A node cells is carried out in-vitro and in a culture medium compatible with culture of myocardial tissue.
17. A process in accordance with claim 8 in which said quantity of S-A node cells is temporarily transplanted in a temporary site of the patient’s body and in which said

culturing takes place at said temporary site for a sufficient period of time to grow said critical mass of S-A node cells after which said critical mass of S-A node cells are removed from said temporary site for implanting in said right ventricle.

18. A process in accordance with claim 8 in which said critical mass of S-A node cells is implanted in the wall of the lower two thirds of the right ventricle.
19. A process in accordance with claim 8 in which said critical mass of S-A node cells is implanted at the apex of the myocardial tissues of the right ventricle of the heart.
20. A process in accordance with claim 8 which further includes the step of destroying the S-A node cells remaining in the right atrium to prevent generation of a depolarization wave out of synchronization with the depolarization wave generated by said implanted mass of S-A node cells.
21. A process in accordance with claim 14 in which said S-A node cells remained in said right atrium are cryogenically destroyed.
22. A process in accordance with claim 14 in which said S-A node cells remaining in said right atrium are destroyed through electrical ablation.
23. A process for providing a biological pacemaker implant for the human heart which comprises the steps of:
24. a. inserting a mapping catheter into the right atrium of the heart;
25. b. mapping the site of the S-A node cells of the right atrium to determine the boundaries of the S-A node site and to identify the location of healthy S-A node cells;
26. c. removing a quantity of said healthy S-A node cells from the site of said S-A node cells in the right atrium;
27. d. culturing said quantity of S-A node cells to grow a quantity of said S-A node cell to produce a critical mass of said S-A node cells sufficient to generate a depolarization wave in myocardial tissue; and,
28. e. implanting said critical mass of S-A node cells in the right ventricle of the heart to provide a depolarization wave of sufficient magnitude to stimulate contraction of the myocardial tissue of the ventricles of the heart to initiate and sustain substantially natural heartbeat.
29. A process in accordance with claim 17 in which the quantity of S-A node cells is removed from and implanted in the same heart.
30. A process in accordance with claim 17 which further includes the step of recording the boundaries of the site of the S-A node cells in the right atrium.
31. A process in accordance with claim 19 which further includes the steps of locating the site of the S-A node cells in said right atrium from said mapping of said sites and destroying the S-A node cells remaining in the right atrium to prevent generation of a depolarization wave in the right atrium.
32. A process in accordance with claim 17 in which said critical mass of S-A node cells is implanted at the apex of the myocardial tissues of the right ventricle of the heart.
33. A process in accordance with claim 17 in which said critical mass of S-A node cells is implanted in the wall of the lower two thirds of the right ventricle of the heart.
34. A process for providing a biological pacemaker implant for the human heart which comprises the steps of:
35. a. identifying S-A node cells int he right atrium of the heart;

36. b. removing a quantity of said S-A node cells from the wall of the heart;
37. c. implanting a pacemaker electrode in the right ventricle of the heart;
38. d. periodically inducing a depolarization wave in the myocardial tissue of the right ventricle through said electrode to promote a regular heartbeat function in the heart;
39. e. culturing said quantity of S-A node cells to grow a quantity of said S-A node cell to produce a critical mass of said S-A node cells sufficient to generate a depolarization wave in myocardial tissue;
40. f. implanting said critical mass of S-A node cells in the right ventricle of the heart to provide a depolarization wave of sufficient magnitude to stimulate contraction of the myocardial tissue of the ventricles of the heart to initiate and sustain substantially natural heartbeat of the heart; and,
41. g. removing said pacemaker electrode from the right ventricle of the heart.
42. A process in accordance with claim 23 in which the quantity of S-A node cells is removed from and implanted in the same heart.
43. A process in accordance with claim 23 in which culturing of said S-A node cells is carried out in-vitro and in a culture medium compatible with culture of myocardial tissue.
44. A process in accordance with claim 23 in which said quantity of S-A node cells is temporarily transplanted in a temporary site of the patient's body and in which said culturing takes place at said temporary site for a sufficient period of time to grow said critical mass of S-A node cells after which said critical mass of S-A node cells are removed from said temporary site for implanting in said right ventricle.
45. A process in accordance with claim 23 in which said critical mass of S-A node cells is implanted in the wall of the lower two thirds of the right ventricle.
46. A process in accordance with claim 23 in which said critical mass of S-A node cells is implanted at the apex of the myocardial tissues of the right ventricle of the heart.
47. A process in accordance with claim 23 which further includes the step of destroying the S-A node cells remaining in the right atrium to prevent generation of a depolarization wave out of synchronization with the depolarization wave generated by said implanted mass of S-A node cells.
48. A process in accordance with claim 29 in which said S-A node cells remaining in said right atrium are cryogenically destroyed.
49. A process in accordance with claim 29 in which said S-A node cells remaining in said right atrium are destroyed through electrical ablation.

# II. SCIENTIFIC DESCRIPTION & BACKGROUND

### BACKGROUND OF THE INVENTION

A major cause of death and poor health in significant segments of the population in the United States and in many other areas of the world involve disease and insufficient function of the heart. The vitality of all tissues in the body depends upon a continual flow of blood at an adequate rate to permit efficient and satisfactory function of the organs. The heart typical pumps

75 gallons of blood per hour when the body is at rest and is required to function at even higher rates during moderate or heavy levels of exertion and activity.

Interruption or interference with the continuous and efficient function of the heart can occur for a variety of reasons. The arteries of the heart may become diseased and obstructed with the result that the heart will either develop insufficient blood flow or blood flow will become terminated. Arteriosclerosis is a leading killer, especially in men. Diseased coronary arteries provide restricted circulation, and the heart fails to contract as forcefully as necessary.

The conduction system of the heart is a group of structures that determine heart rate in response to influences from the nervous system and chemical information from other organs. The system provides stimulating impulses to all parts of the myocardium in a coordinated fashion. Proper coordination ensures the heart act as an effective fluid pump. The conduction system depends upon a regular generation of a depolarization wave of adequate magnitude. This wave must be generated at a specific location and frequency responsive to the needs of the body.

The depolarization wave is a result of unique characteristics of myocardial tissue. It occurs as cell tissue is stimulated, and the stimulus is transmitted to the next cell. This selective permeability at the cell membrane is essential for nutrients, waste, and electrical function.

# III. SCIENTIFIC MEDIA: "Could the Biological Pacemaker Replace the Mechanical Version?"

*By Brian Buntz | July 17, 2014*

The pacemaker of the future could be biological, according to scientists at Cedars-Sinai Heart Institute. Researchers have developed a method of converting cardiac muscle cells into pacemaker cells. In a trial described in *Science Translational Medicine*, researchers explained how they reestablished normal heart rates in pigs with heart block.

The scientists injected a gene known as **Tbx18** that triggers the growth of pacemaker cells during fetal development. Using a virus as a vector, they coaxed a small area of the heart to form a new sinoatrial node. This development led to a new functional biological pacemaker.

**Key Benefits:**

- Catheter-based delivery instead of open-heart surgery.
- Potential to treat infants with congenital heart block while still in the womb.
- Solving side effects like infections and lead breaks stemming from traditional hardware.

# IV. BIOPACE EXECUTIVE SUMMARY & STRATEGY

**Elevator Pitch:** The first heart pacemaker made entirely of your own living cells. No batteries. No steel cans. No steel leads. Set to obsolete the multi-billion dollar steel lead pacemaker industry.

- **Problem:** Steel can pacemakers are costly and suffer risks of battery depletion, toxic reactions, infections, and lead breaks.
- **Solution:** BioPace builds a pacemaker from your own cells that will last forever and is far less costly. Works exactly how natural pacemakers work.
- **Stage of Development:** Completed dog study. Preparing for historic landmark first-in-man case.
- **Management Team:** Howard Leonhardt (CEO), Wendell King (COO), Dr. Eric Duckers (CSO), Dr. Sergio Pinski (CMO).
- **Forecasted Sales:** * Year 1: $300M
    - Year 3: $2B
    - Year 5: $5B
- **Target Exit:** $2 billion acquisition (Targeting Medtronic, St. Jude, Abbott Labs, etc.) in 2018.