

Atrial Pacing to Treat Sleep Apnea in Heart Failure

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A. Study Purpose and Rationale

Sleep apnea occurs frequently in patients with chronic heart failure (HF). The incidence of sleep apnea among patients with HF is unknown, but available data suggests that a majority of HF patients have some type of sleep apnea. In the largest case series, which studied HF patients whose physicians had referred them to a sleep center, 72% of 450 patients with HF met diagnostic criteria for sleep apnea [PMID: 10508793].ⁱ The second largest series, performed in ambulatory male HF patients regardless of their sleep apnea symptoms or risk factors, found that 51% of 81 patients met polysomnographic diagnostic criteria for sleep apnea [PMID: 9626176].ⁱⁱ These data include patients with either Cheyne-Stokes respiration/central sleep apnea (CSR/CSA) or obstructive sleep apnea (OSA).

CSR/CSA is associated with increased mortality in HF. It is uncertain whether this occurs because CSR/CSA reflects very poor cardiac function or because its presence constitutes a separate and additive harm. However, where multivariate analyses have controlled for potentially confounding risk factors, CSR/CSA remains an independent risk factor for death or cardiac transplantation [PMID: 10086966] [PMID: 10880416].^{iii,iv}

Pathophysiologic evidence suggests that obstructive sleep apnea may also worsen HF symptoms and prognosis via several proposed mechanisms [PMID: 12682029]^v. Apnea-induced hypoxia has been linked to increased sympathetic nervous stimulation of the cardiovascular system, increasing left ventricular afterload while causing cardiac myocyte necrosis and apoptosis, beta-adrenoceptor downregulation and desensitization, arrhythmogenesis, and increased mortality. Other physiologic perturbations, including OSA-induced chronic hypertension and negative intrathoracic pressure, cause increased myocardial oxygen demand in the face of reduced oxygen supply, cardiac output, and coronary perfusion. This sets the stage for recurrent nocturnal ischemia and arrhythmia.

Treating sleep apnea can reverse these pathophysiologic processes in patients with both CSR/CSA and OSA, improving HF symptoms as well as left ventricular structure and function. Several studies have evaluated the effects of continuous positive airway pressure (CPAP) therapy, which demonstrate a marked reduction in the frequency of apneic and hypopneic episodes [PMID: 10209985] [PMID: 9927358] [PMID: 10382693].^{vi,vii,viii} A recently published prospective trial studied 24 patients with both HF and OSA [PMID: 12660387].^{ix} During the one-month study the 12 patients randomized to receive CPAP had statistically significant improvements in mean blood pressure, systolic blood pressure, daytime heart rate, and ejection fraction. Control group patients experienced no improvement in any of those variables. One randomized [PMID: 9826313]^x and one non-randomized [PMID: 1683918]^{xi} study of CPAP in patients who have both HF and OSA found similar results.

CPAP produces similar benefits for HF patients with sleep apnea of a primarily central etiology. Among CSR/CSA patients, randomized trials of 3-months' duration have demonstrated that nightly application of CPAP increases left ventricular ejection fraction, reduces mitral valve regurgitation and nocturnal and daytime sympathetic activity, and improves quality of life [PMID: 7633695] [PMID: 7812579] [PMID: 9283534].^{xii,xiii,xiv} In a randomized trial of 29 patients with both HF and CSR/CSA, those who tolerated CPAP therapy experienced a significant reduction in the combined rate of mortality and cardiac transplantation over a 2.2-year period [PMID: 10880416].^{iv}

Nevertheless, CPAP therapy has several limitations. Short-term compliance with CPAP ranges from 50 to 80 percent, and worsens over long-term intervals [PMID: 9093094].^{xv} Some people find CPAP obtrusive and become frustrated by frequent mask leaks and nasal congestion [PMID: 12181405].^{xvi} These shortcomings have prompted a search for alternative therapies.

A recent study evaluated atrial pacing as a novel therapy for sleep apnea [PMID: 11832528].^{xvii} Subjects were patients who had previously received implantable cardiac pacemakers for symptomatic bradyarrhythmias. Sleep studies were performed, and among those found to have sleep apnea (either OSA or CSR/CSA), the investigators adjusted the subject's pacemaker to raise the pacing rate to 15 beats per minute (bpm) faster than the intrinsic nocturnal heart rate. This pacing reduced the frequency of both central and obstructive apneas by approximately 50% compared to spontaneous rhythm in the same subjects. No other study has investigated the effect of atrial pacing on sleep apnea.

Although this evidence establishes atrial pacing as a promising intervention for sleep apnea, several characteristics of this study limit its clinical relevance. It included only 15 subjects, and none of them had symptoms of HF. All subjects had once suffered from bradyarrhythmia severe enough to warrant placement of a pacemaker. The subjects received atrial pacing during one night only, and the study presented no follow-up data on the study subjects. The investigators also failed to offer a coherent pathophysiologic rationale for its treatment effect. Further investigation is required to establish the mechanism and efficacy of atrial pacing in the therapy of sleep apnea, especially among patients with HF who may not have bradyarrhythmia.

This evidence suggests that atrial pacing may provide valuable therapy for HF patients. However, according to our literature search, no published report has evaluated the effects of atrial pacing on patients with sleep apnea and heart failure. Additionally, no study has evaluated the effects of atrial pacing on sleep apnea for longer than one night, and no study has elucidated the pathophysiologic mechanism by which atrial pacing ameliorates sleep apnea. Therefore, this study proposes to test the following hypotheses for subjects with stable, symptomatic HF who already have a permanent cardiac pacemaker or cardioverter-defibrillator:

Atrial pacing for one month will decrease the frequency of apneas and hypopneas during sleep.

Atrial pacing for one month will reduce symptoms and severity of heart failure.

B. Study Design and Statistical Analysis

a. Study Design

i. Baseline Evaluation

At the start of the study, all subjects will complete the Minnesota Living with Heart Failure Questionnaire [PMID: 10128563]^{xviii} and the Weaver Functional Outcomes of Sleep questionnaire [PMID: 9415942].^{xix} Subjects will receive blood tests for serum sodium, b-type natriuretic peptide, norepinephrine, and angiotensin II. All subjects will receive a six-minute walk test and a transthoracic echocardiogram. Subjects will then receive overnight polysomnography. A maximum of ten subjects with an apnea-hypopnea index less than ten will be included in the study as an internal control group, however, further subjects will be excluded from the study. In addition, subjects with a mean nocturnal heart rate >90 bpm in absence of pauses or periods of bradycardia will be excluded from the study.

During the morning following the baseline polysomnography study, investigators will randomize subjects on a 1:1 basis into two groups. Investigators will reprogram the pacemakers of group 1 subjects to receive atrial pacing (DDD pacing at 15 bpm above mean nocturnal heart rate). Group 2 subjects will receive backup pacing (DDD pacing at 40 beats per minute). Ventricular depolarization sequence will not change between the two arms; for instance, the mode in both pacing modes will be DDD with an identical effective AV delay. Thus, ventricular depolarization will be either the result of intrinsic conduction, ventricular pacing or biventricular pacing, but will not differ between treatment arms; only the atrial rate will differ. Subjects with biventricular devices will continue to receive biventricular pacing during all aspects of the study.

ii. One Month Assessment

Subjects will return to complete the Minnesota Living with Heart Failure Questionnaire and the Weaver Functional Outcomes of Sleep questionnaire. They will complete a questionnaire concerning health events that occurred during the study period (e.g. hospitalizations, surgeries, etc.) and a repeat six-minute walk test, echocardiogram, and blood test. Subjects will then receive overnight polysomnography.

iii. Crossover

On the morning following the one month polysomnography study, investigators will institute backup pacing in group 1 and atrial pacing in group 2. Subjects will then leave the sleep laboratory.

iv. Two Month Assessment

Subjects will return to complete the same questionnaires and tests that they completed on day thirty. They will then receive overnight polysomnography.

v. Completion

Investigators will reprogram patients' pacemaker settings to return to their pre-study specifications. Based upon patient symptom scores and unblinding of the sleep study results, patients and their referring physicians will have the option of continuing long-term atrial pacing if it was found beneficial.

b. Statistical Analysis**i. Outcomes**

This study will compare the performance of the intervention and control groups based on several outcome measurements. Although the study aims primarily to improve quality of life in patients with HF and sleep apnea, this study will also measure several secondary outcomes in an attempt to elucidate the physiologic mechanisms involved in a possible treatment effect. These outcomes include the change in each subject of the following variables:

1. Primary Outcome

- Apnea-hypopnea index

2. Secondary Outcomes

- Minnesota Living with Heart Failure Questionnaire score
- Left ventricular ejection fraction
- Distance walked in 6-minute walk test
- Left ventricular end-diastolic and end-systolic dimensions
- Severity of mitral valve regurgitation
- Serum sodium concentration
- Serum norepinephrine concentration
- Serum B-type natriuretic peptide concentration
- Serum angiotensin II concentration
- Weaver Functional Outcomes of Sleep questionnaire score
- Total sleep time

To detect a change of 10 on the apnea-hypopnea index with a standard deviation of 18, the study must include 37 patients in order to have a power of 90% with a P value < 0.05 by paired t-test. Regression analyses will be performed to attempt to isolate the effect of treatment on each independent variable. All analyses will be two-tailed, intention-to-treat analyses.

ii. Blinding

This study will be performed in a double-blind manner—only the physician who performs the pacemaker programming will be privy to the pacemaker settings, and this physician will not be involved in any outcome assessments. Physicians performing and interpreting echocardiograms and sleep studies will not be informed of the pacing mode and will be blinded to ECG data or heart rate trends. Whether in the atrial pacing or backup pacing group, all subjects will receive pacemaker interrogation at the same time points during the study. During the study investigators will not inform subjects whether they are receiving atrial pacing or not. Investigators will make all reasonable attempts to minimize contact between subjects and study personnel who adjust patient pacemakers to reduce the subjects' ability to intuit their pacing status through nonverbal cues from the pacemaker adjusters.

In the event that the subject's physician requests information concerning the subject's pacing status for the purpose of providing patient care, investigators will reveal the subject's pacing status to the physician. Investigators will discontinue pacing at physician request, and will note the relevant details of the event in published reports of the study.

Investigators who interpret the sleep monitoring data and echocardiograms will have the information presented to them in a manner that does not include identifying information about the subject or the date of the study.

C. Study Procedure

a. Atrial Pacing

Two periods of pacing therapy will be provided: atrial pacing and back-up pacing. All subjects will spend one month in each of these pacemaker settings in randomized order.

During the atrial pacing period of the study, investigators will program the pacemaker to provide atrial stimulation in DDD mode at a rate 15 bpm faster than the subject's mean nocturnal heart rate (as determined during the baseline polysomnography study). Subjects with a mean nocturnal heart rate above 90 bpm will be excluded from this study, so no subject will receive atrial pacing in excess of 105 bpm. During the "back-up pacing" period of the study, the pacing mode will be DDD at 40 ppm. During both periods, the pacing mode will be DDD and ventricular activation sequence will be either intrinsic conduction, paced (in cases of AV block) or biventricularly paced (in patients with biventricular pacemakers). The ventricular activation sequence will be identical during both atrial pacing and backup pacing periods of the study.

b. Sleep Monitoring

Subjects will undergo overnight polysomnography during the study at three times during the study: at baseline, during the one-month assessment, and during the two-month assessment. Monitoring will include electroencephalography, electromyography of the chin and legs, electro-oculography, oronasal air-flow tracing, recording of the movement of the chest wall and abdomen, finger oximetry, and electrocardiography. Because of the double-blinding, physicians interpreting sleep studies will not be allowed to view electrocardiography during analysis of the sleep study. Measurements will include the apnea-hypopnea index and total sleep time.

c. Six-Minute Walk Test

Investigators will measure the distance that a subject can walk along a flat surface for six minutes as a validated surrogate measurement for the severity of a subject's HF [PMID: 8697828] [PMID: 12091180].^{xx,xxi} Technicians will escort and encourage subjects with the standardized statements, "You are doing well" or "Keep up the good work," but will not use other phrases. Technicians will instruct patients to walk at their own pace but to cover as much ground as possible in 6 min. Technicians will receive training in proper technique for performing the test, including the American Thoracic Society's guidelines for patient safety during the test [PMID: 12091180].^{xxi}

d. Echocardiography

Subjects will receive two standard transthoracic echocardiograms during the study, at baseline and one at one-month follow-up. Measurements will include left ventricular ejection fraction, left ventricular end-diastolic and end-systolic dimensions and severity of mitral valve regurgitation.

e. Phlebotomy

Phlebotomists will collect 20mL blood samples by standard venipuncture technique three times during the study; at baseline, at the one month assessment and at the two month assessment. Blood samples will be handled according to laboratory specified procedures and will be sent for serum chemistry profile, norepinephrine concentration, angiotensin II concentration, and B-type natriuretic peptide concentration.

D. Study Drugs

This study protocol intends patients to receive their current medical care from their regular doctors; the study does not include administration of specific medicines and does not intend to affect the administration of drugs to the patients.

E. Medical Devices

This study will use a permanent pacemaker or cardioverter-defibrillator previously implanted in the patient to treat previously present clinical conditions. This pacemaker must have an atrial lead. No patient will receive new implantation of a pacemaker or other device for the purpose of participating in this study.

F. Study Questionnaires

Patients will complete the Minnesota Living with Heart Failure Questionnaire [PMID: 10128563]^{xxii} to assess HF symptoms and the Weaver Functional Outcomes of Sleep questionnaire.

G. Study Subjects

This study will recruit patients who receive care at the New York-Presbyterian Hospital. Candidates must have a clinical diagnosis of left ventricular heart failure of at least six-months' duration on the basis of a history of HF as defined by at least one prior episode of symptomatic HF, characterized by dyspnea at rest or on exertion. Candidates must be in New York Heart Association functional class II or III at the time of enrollment. Study candidates will receive an echocardiogram, which must show a left ventricular ejection fraction of 40% or less. Candidates must have a previously implanted pacemaker or defibrillator capable of atrial pacing but not have a severe bradyarrhythmia. Severe bradyarrhythmia will be excluded by absence of paced atrial rhythm while the bradycardia parameters of the implanted device are set to DDD mode at a rate of 40 bpm. Since AV conduction will be programmed not to differ for a given individual between the active atrial pacing and backup atrial pacing groups, presence of AV block will be permitted.

Exclusion criteria include a previously established clinical diagnosis of OSA or CSA, current continuous or bi-level positive airway pressure (CPAP or biPAP) therapy; inotrope dependence; mean heart rate > 100 bpm (determined from pacemaker interrogation); atrial fibrillation or flutter, excessive ectopy or other severe arrhythmia; history of unstable angina, myocardial infarction, or unstable heart failure, or thoracic surgery within four weeks of enrollment; history of cardiac transplantation; history of any surgery within seven days, acute pulmonary edema; severe congenital heart disease; severe or decompensated pulmonary diseases; decompensated renal and liver disorders; kyphoscoliosis; untreated hypothyroidism; and use of morphine derivatives, benzodiazepines, or theophylline. This study will exclude patients under eighteen years old, and will exclude pregnant patients.

H. Recruitment of Subjects

Residents, clinical fellows, and attending physicians will identify potential subjects among their patients. It is anticipated that the majority of the patients will be recruited from the heart failure clinic and the arrhythmia device clinic at Columbia University Medical Center - New York Presbyterian Hospital. Investigators will request permission from the candidate's attending physician prior to any discussion of the study with the candidate. Subjects will receive no financial incentive to participate, but will receive reimbursement for reasonable costs of transportation to and from the studies.

I. Confidentiality of Study Data

The data obtained from this study will track each subject by a unique, confidential numeric identification code; investigators will remove all other patient identifying information from all records maintained for the purposes of this study. Access to the key to the numeric identification code will be permitted only under exceptional circumstances, and only to personnel who require patient identifying information.

The study involves the collection of information contained in a subject's medical record. Study investigators and their designees will have access to pertinent medical records to gather pertinent information for the study on a strictly need-to-know basis.

J. Potential Conflict of Interest

None.

K. Location of Study

Columbia University Medical Center.

L. Potential Risks

This study performs six interventions on the subject: atrial pacing, questionnaires, the six-minute walk test, phlebotomy, standard transthoracic echocardiography, and sleep monitoring. Echocardiography and monitoring during sleep pose effectively no risks for the subject. Previous series analyzing the six-minute walk test in 45 subjects uncovered no adverse effects during the test, including among subjects with advanced (New York Heart Association stage IV) heart failure.^{xx} Phlebotomy poses minimal risk.

We performed a literature search to examine the safety of atrial pacing. The MEDLINE search term "Cardiac pacing, artificial" from 1966 to June, 2003 in the subcategory "Adverse Effects" yielded 212 entries on human subjects that had text containing the words "atrium" or "atrial." All entries were reviewed, as were references from studies with safety data relevant to this investigation. Several studies have provided baseline atrial pacing to a rate equal to or lower than 100 bpm (the rates used in this study), and none of these reported any adverse effects in any subjects. One study analyzed safety data of atrial pacing to rates higher than 100 bpm in subjects with coronary artery disease, and this study found that all adverse effects (e.g. arterial hypotension) disappeared within two minutes of the termination of atrial pacing [PMID: 9174289].^{xxiii} All subjects in this study also received atrial pacing at 100 bpm, and no adverse effects were observed at that rate.

M. Potential Benefits

This study will offer a free and comprehensive evaluation for sleep-disordered breathing in a patient population that is at extremely high risk for sleep apnea. This is important because sleep apnea breathing is underdiagnosed in the HF population in routine clinical practice. Moreover, there is emerging evidence that recognition and treatment of sleep-disordered breathing in HF may result in substantial improvements in HF severity and quality of life.

This study will also evaluate whether a simple pacemaker setting adjustment can help patients who already have the device implanted. Garrigue et. al. [PMID: 8697828]^{xvii} administered an intervention similar to the intervention proposed in this study, and found that 13 out of 15 subjects had fewer episodes of apnea while receiving atrial pacing than they did at baseline. Because studies of other therapies that reduce sleep apnea caused significant improvements in subjects' overall quality of life and HF symptoms [PMID: 12660387],^{vii,viii,ix,x,xii} we anticipate that subjects in the atrial pacing group will experience similar benefits. Patients and their referring physicians will be informed of the results of their polysomnography tests and the value of atrial pacing at the conclusion of the study.

N. Alternatives

At the initial interview, investigators will inform candidates about other options for treatment of sleep apnea, including diagnosis through polysomnographic methods and potential treatment with CPAP. Investigators will also inform candidates that they may enroll in the study and, at the conclusion of the

study and at no cost to them or their insurance carriers, be provided detailed information as to whether they have a diagnosis of sleep apnea, whether atrial pacing was beneficial in its treatment, and be referred for standard therapies for sleep apnea such as CPAP.

Candidates will be informed that they may withdraw from the study at any time. Investigators will inform them that they will reprogram a subject's pacemaker to its baseline setting at any point that a subject wishes to discontinue atrial pacing.

Candidates will have no obligation to enter the study. Investigators will inform candidates that they have the option to continue to receive the medical care that their current medical team provides. A candidate's decision to enter or avoid the study will have no effect on the care rendered to him or her except as described above in Section 2, Study Design.

O. Compensation to Subjects

This study will pay reasonable transportation and parking costs for all subjects for all study-related hospital visits. Subjects will receive no other compensation.

P. Costs to Subjects

None.

Q. Minors as Research Subjects

No minors will be research subjects in this study.

R. Radiation or Radioactive Substances

No radiation or radioactive substances will be employed in this study.

APPENDIX 1: SCIENTIFIC ABSTRACT

BACKGROUND. Sleep apnea frequently occurs in patients with heart failure (HF), and it is associated with worse outcomes. Continuous positive airway pressure (CPAP) can abolish sleep apnea and improve clinical outcomes in HF, but it is poorly tolerated, prompting a search for other therapies. A preliminary 3-night study suggested that atrial pacing can improve sleep apnea, but it included no patients with HF and no follow-up data.

METHODS. This protocol will enroll 40 subjects with HF who have previously received permanent pacemakers or implantable cardioverter-defibrillators capable of atrial pacing, but do not have severe bradyarrhythmias nor standard indications for a pacemaker; It is anticipated that most of these patients will have either dual chamber ICDs, biventricular ICDs or biventricular pacemakers. At baseline subjects will receive six-minute walk tests, echocardiography, blood tests, and questionnaires to assess severity of heart failure and sleep apnea symptoms. In a randomized, double-blind manner all subjects will spend one month in either dual-chamber pacing mode with atrial pacing (pacing mode DDD at 15 bpm faster than their mean nocturnal sinus rate) or in spontaneous rhythm (pacing mode DDD at 40 ppm). Ventricular depolarization will not change between the two arms; for instance, the mode will be DDD with an AV delay that either results in either intrinsic conduction, ventricular pacing or biventricular pacing (subjects with biventricular devices will continue to receive biventricular pacing during all aspects of the study). Subjects will then begin the crossover month of the study, in which the subjects who received atrial pacing will then receive spontaneous rhythm, and vice versa. At the end of the each of the two months, subjects will receive repeat six-minute walk tests, echocardiography, blood tests, questionnaires, and polysomnography.

Primary outcome measures will be changes in apnea-hypopnea index, heart failure questionnaire forms, six-minute walk test, and left ventricular (LV) ejection fraction. Secondary outcome measures will include LV end diastolic and LV end-systolic diameter, mitral regurgitation severity, Weaver Functional Outcomes of Sleep questionnaire score, total sleep time as well as serum concentrations of sodium, norepinephrine, B-type natriuretic peptide (BNP) and angiotensin II.

ANTICIPATED FINDINGS AND SIGNIFICANCE: In this two-month crossover study, we anticipate that atrial pacing will reduce the apnea-hypopnea index as compared with baseline. In addition, we anticipate that atrial pacing for one month will improve the symptoms and severity of congestive heart failure in our population, as measured by six-minute walk test, symptom assessment on the Minnesota Living with Heart Failure questionnaire, ejection fraction, LV dimensions, severity of mitral regurgitation, and serum markers of heart failure severity. The comprehensive polysomnography protocol, echocardiogram protocol, symptom assessment based upon validated questionnaires, functional assessments with six-minute walk tests and serological evaluation will provide not only information regarding the presence or an absence of benefit to atrial pacing in sleep apnea and/or heart failure but also will provide detailed physiologic data suggesting the mechanism of any such benefits.

This study will provide a comprehensive evaluation of the role of atrial pacing in improving the sleep disordered breathing in congestive heart failure. The implications are widespread, including (1) a potential new indication for atrial based pacing in patients with sleep apnea – if this study is positive a randomized trial of implantation of new atrial pacing devices in patients with sleep apnea may be justified, (2) evaluation of the effects of atrial based pacing in heart failure and whether these effects may be mediated by improvement of sleep-disordered breathing or by other mechanisms, (3) new support for the use of dual chamber ICDs in place of single chamber ICDs at the time of implantation in patients with heart failure who meet indications for an ICD but do not have standard indications for atrial pacing, and (4) new guidelines for the programming of biventricular pacing devices to enforce atrial pacing – raising the question of whether the benefits of biventricular pacing have been underestimated in large clinical trials through the use of pacing modes such as VDD where only atrial tracking but not atrial pacing occur.

APPENDIX 2: LAY ABSTRACT

Heart failure affects five to six million North Americans, causing substantial suffering and death [PMID: 11834347].^{xxiv} A large proportion of people with heart failure also have sleep apnea, a condition where people repeatedly stop breathing during sleep, often for periods longer than one minute at a time. Sleep apnea harms people with heart failure, exacerbating symptoms and possibly hastening death.

The definitive treatment for sleep apnea is continuous positive airway pressure (CPAP), which involves a mask worn on the face during sleep. CPAP effectively prevents sleep apnea, and may even improve cardiac function in people with both sleep apnea and heart failure. However, many people do not tolerate it, prompting a search for other, less obtrusive therapies.

Researchers recently proposed a therapy for sleep apnea for people who already have pacemakers. In this therapy, called atrial pacing, a clinician reprograms the pacemaker to make the heart beat slightly faster during sleep. Only one study has evaluated the effect of atrial pacing in sleep apnea. In this study 13 out of 15 subjects who spent two nights in a sleep laboratory breathed significantly better while sleeping during a night when they received atrial pacing than during a night when they slept with the pacemaker essentially shut off. This study included no subjects with symptoms of heart failure. This study also failed to provide a clear rationale for why atrial pacing would affect sleep apnea.

We propose to administer atrial pacing to heart failure patients for one month. At the start of the study subjects will undergo several tests to assess their baseline level of heart disease and sleep quality. Investigators will administer questionnaires to assess symptoms of heart failure and sleep apnea, and investigators will measure how far subjects can walk in six minutes. Subjects will give a blood sample and receive an echocardiogram, then spend one night in the sleep laboratory. The subjects will be randomly assigned to two different pacemaker settings, one which allows more of a patient's own heart rhythm and one that provides a greater degree of pacing the heart. Subjects will go home for one month and then return for repeat sleep evaluations and cardiac function assessments. After this assessment the subject will be crossed over to the other pacing group and sent home with their pacemaker in the other setting. At the end of the month, subjects will return for a final sleep evaluation and cardiac function assessment.

Following this assessment, their pacemakers will be set to their initial parameters and the study will be concluded. Investigators will then analyze this data to detect differences between subjects during their months with and without atrial pacing. Investigators will provide information to patients and their referring physicians regarding whether they have a diagnosis of sleep apnea and whether atrial pacing improved either their sleep physiology or cardiac function. At this point patients can be referred for other treatments for sleep apnea if appropriate.

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