IRB Proposal

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Title of Project: Anodal Stimulation in Pediatric Patients with Permanent Epicardial Pacemakers

1. STUDY PURPOSE AND RATIONALE:

Permanent bipolar pacing systems typically consist of two closely spaced electrodes, the cathode (negatively charged) and the anode (positively charged). These electrodes can be part of the same implanted lead, as with a permanently implanted right ventricle (RV) tip and RV ring electrode, or as two separate leads, as in some permanent epicardial electrode systems. This is in contrast to unipolar systems in which there is only a single tip electrode operating as the cathode and the pulse generator itself operating as the anode. In bipolar systems, both the cathode and the anode are in contact with the myocardium. However, intrinsically, capture of the ventricle or ventricles typically occurs at the cathode. Capture of the anode does not regularly occur, as the anode may have a larger surface area and a higher stimulation threshold (Mehra, 1979). However, the phenomenon of anodal stimulation or capture is not uncommon (Tamborero, 2006).

Anodal stimulation has been of particular concern in biventricular pacing systems. It has been described in systems that utilize a unipolar left ventricle (LV) electrode and bipolar RV-distal electrode to RV-proximal electrode. In these types of systems, the LV cathode can cause stimulation of the RV-proximal anode (Van Gelder, 2001). This is more common with high pacing outputs (Bulava, 2004). One study showed that anodal stimulation was an under-recognized phenomenon in adult patients undergoing cardiac resynchronization therapy (Dendy, 2011). Cardiac resynchronization therapy depends on the ability to pace the RV and LV separately with the capacity to adjust the interval between the two ventricles. Anodal stimulation may result in simultaneous pacing of the RV and LV without interventricular delay. Thus, anodal stimulation has also been hypothesized as a possible cause of clinical non-response to cardiac resynchronization therapy, as the hemodynamic benefits of resynchronization or programmed interventricular timing delay are lost (Van Gelder, 2005; Shama'a, 2011; Dendy, 2011). However, some have argued that anodal stimulation may actually have beneficial effects in what is known as "triple site pacing" (pacing from the LV, RV-tip cathode, and RV-ring anode simultaneously). They contend that this may result in a narrower QRS and improved resynchronization by tissue doppler (Bulava, 2004).

In pediatric patients with permanent bipolar epicardial pacemakers, biventricular pacing is often not possible. Anodal stimulation may allow synchronous biventricular pacing to become feasible in this type of pacemaker system. Anodal stimulation would allow the clinician to pace both of the ventricles with one ventricular bipolar lead, should the individual cathode and anode be spaced far enough apart. It has been hypothesized that anodal stimulation may be more common in pediatrics patients (Constans, 2008). However, more fundamentally, the prevalence and factors associated with the presence of anodal stimulation have not yet been described in pediatric patients with permanent epicardial pacemaker systems.

Our aims are to:

1. Describe the prevalence of anodal stimulation in pediatric patients with permanent bipolar ventricular epicardial pacemakers.

2. Determine the patient and device characteristics associated with the presence/absence of anodal stimulation.
3. Describe any hemodynamic changes or side effects associated with increased pacing outputs and the presence anodal stimulation.
4. Determine the overall feasibility of synchronized biventricular pacing via intentional anodal stimulation in pediatric patients with permanent bipolar ventricular epicardial pacemakers.

2. STUDY DESIGN AND STATISTICAL PROCEDURES:
We will perform a retrospective analysis of all pediatric patients 0-21 years of age with permanent bipolar ventricular epicardial pacemakers followed at the electrophysiology department of the Morgan Stanley Children's Hospital of New York. These patients will be identified via internal departmental databases. We will also obtain patient characteristics (including demographics, underlying cardiac pathology, underlying cardiac anatomy, device indication, cardiac surgical history, implantation history), device characteristics (including device types, lead types, duration of implant, pacing output, lead position, electrode distance on chest x-ray), and presence/absence of anodal stimulation via analysis of electrocardiographic changes associated with changes in pacing output as part of routine pacemaker interrogation. After data collection, all data will be described using means and standard deviation, or median with IQR/range for skewed data. Comparisons of continuous variables between groups will be made using Student's T-test or Mann-Whitney U as appropriate. Categorical data will be compared using Chi-Squared analysis or Fisher's exact test, if needed.

3. STUDY PROCEDURES:
The study will be a retrospective chart review. Patients will be identified via internal departmental databases. Chart review will be performed on all patients. The data described above will be gathered from the electronic medical record and placed into a spreadsheet with identifying data removed. A separate password protected file will correlate the patient identifiers to the unique study ID numbers used in the spreadsheet. The collected data will then be analyzed using the statistical measures outlined in the previous section.

4. STUDY DRUGS OR DEVICES: Not applicable.

5. STUDY INSTRUMENTS (QUESTIONNAIRES): Not applicable.

6. STUDY SUBJECTS: All patients 0-21 years of age with permanent ventricular epicardial pacemakers seen in the pediatric electrophysiology department of the Morgan Stanley Children's Hospital of New York from July 2016 to July 2017.

7. RECRUITMENT: Not applicable.

8. INFORMED CONSENT PROCESS: As this is a review of existing data only and involves patients who have been followed at this institution, we believe this study qualifies as exempt from the requirement for informed consent.

9. CONFIDENTIALITY OF STUDY DATA: Patient confidentiality will be maintained as all data will be coded and given a unique study ID number. All study materials will be stored electronically, encrypted and password protected on a networked encrypted computer accessible only to study investigators. The linking code will be saved on a computer to which only the study investigators and the administrator will have access.

10. PRIVACY PROTECTIONS: Patient privacy will be maintained, as all data will be coded. All identifying information will be secured as described above.

11. POTENTIAL RISKS: As this is a retrospective chart review, there is no clinical risk to the patient. The only conceivable risk is compromise of confidentiality of patient data, which will be minimized as described above.

12. DATA AND SAFETY MONITORING: Not applicable.

13. POTENTIAL BENEFITS: As a retrospective chart review, there are no immediate benefits to the patients in this study. The information gained from this study may have an impact on the management of patients with permanent bipolar ventricular epicardial pacemakers and patients undergoing placement of these devices, as this may be a feasible method for synchronized biventricular pacing via intentional anodal stimulation.

14. ALTERNATIVES: Not applicable.

15. RESEARCH AT EXTERNAL SITES: Not applicable.

16. COLUMBIA AS LEAD INSTUTITION: Not applicable.

SOURCES:

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