Higher Tachycardia Prevalence in a Smoker's Pacemaker

Rational

Pacemakers, for many, is an essential implantable machine that helps keep one alive. It ensures that an individual's heart is beating consistently through small segmented electrical pulses while simultaneously helping in any abnormal heart rhythms that may occur ¹. Single chamber, dual chamber, and biventricular pacemakers are the 3 types of pacemakers used in modern day to correct irregular heart rhythms. Tachycardia is a common type of irregular heart rhythm that is referred to an irregular/abnormal fast paced heart rhythm, that range over 100 beats per minute (bpm) where a normal heartbeat ranges from 60-80 bpm. The types of tachycardia, such as atrial flutter, ventricular tachycardia, and ventricular fibrillation are classified by the part of the heart it originates from. Tachycardias can cause dizziness, light headedness, and shortness of breath and if untreated, can lead to heart failure, stroke, and/or sudden cardiac arrest or death ¹. With tachycardia being one of the most common heart arrhythmias present in all types of individuals, and the number of smokers and pacemaker patients steadily increasing due to population growth and Coronavirus Disease 2019 (COVID-19) ^{2,3}, respectively, it is important to ensure that pacemakers are being kept up-to-date with modern lifestyles and health pandemics. The proposed research project will investigate if a smoker's pacemaker will display more signs of tachycardia than a pacemaker of a non-smoker through two analysis: (i) determining if the pacemaker's functionality for correcting atrial flutter, ventricular tachycardia, and ventricular fibrillation is affected because of smoking and (ii) determining if smoking increases one's heart rate that has a dual-chamber pacemaker.

Hypothesis

Smokers with a pacemaker will show more signs of tachycardia than non-smokers with a pacemaker.

Objectives and Specific Aims

The long-term objective of this research project is to identify that pacemakers can adapt accordingly with global pandemics, currently COVID-19, and mitigate common heart arrythmias that are steadily becoming more prominent in individuals around the world, like tachycardia. With no cure for COVID-19, as of yet, and the number for tachycardia, smokers, and implanted pacemaker individuals steadily increasing, this research proposal will help gain a better insight in determining if the current pacemakers are able to adapt with the fast changing lifestyle in today's society. **The immediate objective of the current proposal** is to study the affects smoking has on a pacemaker and if tachycardia is more noticeable in a smoker's pacemaker than in a non-smoker's pacemaker. The two **specific aims** of this proposal are as follows:

- 1) Determining if a pacemaker's functionality for correcting atrial flutter, ventricular tachycardia, and ventricular fibrillation is affected because of smoking
- 2) Determining if smoking increases one's heart rate and pulse generator in a dual-chamber pacemaker.

Recent Progress/Background in Research Activities Related to the Proposal

a) Nicotine Implications on Cardiovascular Disease

Previous studies by the *applicant and previously supervised HQP* investigated that nicotine in cigarettes and e-cigarettes contribute to acute cardiovascular diseases (CVD) such as fatal tachycardia and fibrillation ⁴. In their study, animals were used to discover that the threshold for the heart chambers become weaker causing the heart to pump uncontrollably, at times, leading to a higher chance of irregular heart rhythms to occur. Studies also showed an acceleration of plaque forming in the vessels, blood flow in coronary blood vessels are limited, and medication for angina pain in the heart is disrupted ¹². Even after knowing the adverse effects smoking has on someone's body, people continue to do so as a study indicate a 7% and 9% increase in male and female smokers, respectively, due to population growth – according to

the Institute for Health Metrics and Evaluation (HIME) ^{2,3,8,13,14}. They concluded that although electronic cigarettes decreased the risk of CVD than that of smoking, signs of irregular heart rhythms, like tachycardia, remain. It was found that smoking contributes a huge factor to CVDs and that smokers are seven times more likely to receive a jolt from heart devices ^{5,6}.

b) Heart Diseases and Irregular Heart Rhythms on Permanent Pacemaker Patients

Prior studies by the *applicant and previously supervised HQP* investigate and explain the prevalence of heart failures in a group of patients with permanent pacemaker implantation. The pacemaker's purpose is to signal the heart to pump blood to the body. These pumps are called contractions that are controlled by steady periodic electrical impulses. However, when these electrical impulses start to desynchronize and pump unpredictably, arrhythmias in the heart commence. Arrhythmias is referred to a heart that has irregular heart beats which include beating too fast, slow, or displaying irregular pumping patterns. A total of three hundred and seven patients with identified permanent pacemakers were asked to various activities and exercises to identify heart risks failure. It was found that 83 of those 307 patients displayed signs of heart failure and that it was more present in patients that had a single chamber pacemaker as opposed to a dual chamber pacemaker⁷. It heavily discusses about various heart conditions and tests different factors that contribute to heart diseases and irregular heart rhythms in pacemakers but does not identify a relationship between smoking and pacemakers.

c) Effects of COVID-19 on Cardiac Arrhythmias

This study conducted by the *applicant and previously supervised HQP* have established that COVID-19 has promoted cardiac arrhythmias. This article mentions that COVID-19 causes the pacemaker to work harder in keeping heart rhythms steady and that changing pacemaker batteries is an urgent procedure ⁸. This paper also talks about COVID-19 resulting in many pacemaker dependent and non-pacemaker dependent individuals to display signs of tachycardia. It illustrates that COVID-19 is increasing the amount of people experiencing tachycardia through ECG, continuous ECG monitoring, and Transthoracic echocardiograph ^{2,14}. Due to this increase, a rise in pacemakers have also increased over the last 2 decades. In 1993, the number of pacemakers that were implanted was approximately 121,300 but by 2009, a 56% increase was seen where the number of implanted pacemakers went to 188,700 ^{3,15}. This statistic is for the United States *alone*.

d) Preliminary Results

From previous studies, it addresses the effects smoking has in promoting heart diseases, CVD, due to cardiac dysfunction in permanent pacemaker patients and the effects health pandemics, like COVID-19, has on increasing the number of individuals with tachycardia and heart diseases. These studies demonstrate a strong correlation between **smoking and heart diseases** and **tachycardia and heart diseases**. This proposal will help bridge the gap between these studies to help gain a better understanding of whether *tachycardia is induced by smoking* and *if tachycardia is more present in smoker's or non-smokers' pacemaker*. With the COVID-19 pandemic tachycardia cases and smokers and pacemaker implantations rising, it is important to ensure that pacemakers can adapt to fast lifestyle changing events.

Methods and Research Project

Project 1: Determining if a pacemaker's functionality for correcting atrial flutter, ventricular tachycardia, and ventricular fibrillation is affected because of smoking. The primary objective of this research project is to determine if tachycardia is present, at all, in a smoker's pacemaker. Since the pacemaker device is known to control heart beats and remove irregular heart rhythms, this test will help identify if the pacemaker can mitigate/control different types of tachycardia. To achieve this objective, the following will be investigated: (i) determining the pacemaker's atrial rate for atrial fibrillation, (ii) determining the pacemaker's ventricular rate for ventricular tachycardia, and (iii) conducting blood tests and ECGs for ventricular fibrillation in smokers and non-smokers. This research will be conducted on humans who have an implanted pacemaker and will be divided in two groups – smokers and non-smokers.

Dividing these two groups will help in distinguishing patterns and correlations between the groups and data. The smokers will have to be regular smokers, smokes 4-5 cigarettes/day, for at least a year and half or more as studies show that it takes approximately one year for smokers to develop lung damage and possible heart problems ^{13,14,16}. The subjects will range from the age of 18 and 65 and should have no previous signs of stroke or heart related issues as this can cause outliers resulting in effecting the accuracy and efficacy of the collected data. The cut-off at age 65 will be used to ensure that tachycardia is not caused due to age related factors. In addition, the subjects will be screened for COVID-19 as this will possibly skew the results that are found. Although studies show that COVID-19 causes individuals to have tachycardia, this proposal is focusing more on the effects smoking has on an individual's pacemaker. Thus, COVID-19 individuals will be omitted for the scope of this experiment. An ECG will be used in this experiment as it can record/display normal and abnormal pacemaker functions and heart rhythms ^{16,20}. (i) Pacemaker's Atrial Rate for Atrial Fibrillation in Smokers and Non-Smokers: These experiments will help determine if the atrial rate increases, decreases, or remains unchanged in a smoker's and nonsmoker's pacemaker. In atrial fibrillation, the heart does not pump blood efficiently to the body as the blood vessels in the atria quiver causing the heart to beat irregularly. Measuring the atrial rate before and after smoking in pacemakers will help determine if the blood flow changes in the heart as even a small change or irregularity can be deemed as detrimental. The subjects will be connected to a 12-lead electrocardiogram (ECG), using surface electrodes, where they will be monitored for a total of 15 minutes in the seated position ^{7,16}. This allows enough data to be collected from the initial connection of the electrodes to the subject till the end of the 15 minutes. This gives the subject's heart enough time to go to a resting state, if not already, and gives the subject time get comfortable and avoid moving. It is worth noting that a common issue that arise is that the subject might try to unconsciously regulate his/her breathing when noticing the ECG. For this reason, 2 out of the 15 minutes is allocated for the subject to become comfortable with their surrounding and be less mindful of staged breathing. This will be done for both groups, smokers and non-smokers. Atrial fibrillation is noticeable when the action potential is rapidly firing in the pulmonary vein or atrium ¹⁷. Due to the rapid uncontrolled beating, approximately 400 to 600 bpm, the amplitude in the ECG will be low due to the fast action potentials and rapid atrial rate. The P wave in an ECG indicates the depolarization of the left and right atria however, the P waves will not be visible, on an ECG strip, because of the low amplitudes. Thus, the P-P intervals, which indicate the duration of the atrial cycle, for the last 12 minutes will be measured electronically ensuring that accurate recordings will be observed ¹⁶. Once all the data is recorded, if the smoker's pacemaker does not show any signs of increased or decreased atrial rate, this indicates that the pacemaker can control one form of tachycardia – atrial fibrillation to be specific.

(ii) <u>Pacemaker's Ventricular Rate for Ventricular Tachycardia in Smokers and Non-Smokers:</u> In this experiment, the objective will determine if there is a change in the ventricular rate between a smoker's and non-smoker pacemaker. This helps identify if ventricular tachycardia will be more visible in a smoker's or non-smoker's pacemaker. To do this, the 12-lead ECG will be used where the QRS complex will be observed. The R-R interval can be used to measure the ventricular rate also, however, due to possible significant varying in the R-R interval dependent on their breathing, the heart rate becomes difficult to measure. Thus, the frequency of the QRS complex in the 10th minute will be counted and multiplied by 6 to identify the beats per minute in the subject. If the pulse for any of the subjects is lowering/fading, then the subject is showing signs of ventricular fibrillation. An echocardiogram will also be used to gain a graphical representation of the chambers and valves in the heart because of the high-frequency sound waves being emitted ²¹. From the echocardiogram, the hearts functions will be assessed along with potentially determining possible types of heart diseases like valves, pericardial, myocardial diseases which can be useful for future studies. Echocardiogram is identified as one of the safe methods

for identifying pacemaker defects and/or irregular heart rhythms that may occur ^{21,25}. Once the data is recorded for both the smoker's and non-smokers, the ventricle rate values will be compared to identify if smoker's or non-smokers with a pacemaker have more chances of displaying ventricular tachycardia.

(iii) Blood Tests and ECGs for ventricular fibrillation in Pacemakers for Smokers and Non-Smokers: In this experiment, the objective is to use an ECG and blood tests to determine if the subjects display any signs of ventricular fibrillation. The subject will be connected to a 12-lead ECG for 15 minutes where an ECG strip will be produced. From the ECG strip, risks of ventricular fibrillation can be identified if any of the following occur: 1) uncontrolled/chaotic changes in amplitude, 2) no visible P waves, QRS complexes, or T waves, 3) the subject's rate ranges from 150 bpm to 500 bpm, and 4) the amplitude decreases with respect to duration ²². A blood test for both groups will be conducted to find electrolyte imbalances, irregular blood pressure, and ischemia as these are common factors that contribute to ventricular fibrillation. A study showed that chronic smoking causes electrolyte imbalances in one's body ²³. They mention that the reason these imbalances occur is due to the disruption of homeostasis which is responsible for ensuring the internal state of the body regardless of outside factors. Some internal states include internal body temperature, pH level, and ratios of water and minerals. Blood tests will also help identify the blood pressure of the subject which will be useful when comparing the blood pressure of a smoker and a non-smoker. Theoretically, smoking causes the blood vessels to constrict forcing the heart to pump more forcefully to supply blood to the body; except, in this case, we will be checking if the blood pressure rises for smokers with an implanted pacemaker. There have been studies conducted in the past illustrating that smoking does cause blood pressure to rise in one's heart ²⁴ – without a pacemaker, however from this research project it will become evident if blood pressure rises when a person has a pacemaker. If signs of blood pressure rising in pacemaker subjects are visible, then tachycardia is induced by smoking as this proves that the blood vessels are shrinking in diameter, making it harder for the blood to flow with ease. This results in the heart to pump faster and harder to ensure that all the body parts and organs are receiving adequate blood to perform their desired function. Due to this increase in heart from pumping, this makes irregular heart rhythms and increased heart rate more prominent.

Project 2: Determining if smoking increases one's heart rate and pulse generator in a pacemaker.

The objective of this project is to (i) determine if heart rate increases when smoking in pacemakers and (ii) determining that the pulse generator increases in pacemakers for smoking subjects. Since pacemakers are responsible for sending coordinated electrical impulses to the heart to signal a contraction this project essentially evaluates the performance of the pacemaker and its efficiency for regulating irregular heart rhythms. If the pacemaker performs as intended, there should be a consistent pulse being generated that can be seen on the ECG monitor and no visible patters of irregular heart rhythms/arrythmias should be observed.

(i) <u>Measuring Heart Rate in Smoking Subjects with Pacemakers:</u> The smoker and non-smoker subjects will be connected to the 12-lead ECG where their heart rate will increase. The results that should be seen is that the smoker's heart rate is higher than the non-smoker's heart rate. The reason for this is because studies show that major arteries tend to build plaque and blood vessels are constricted making it harder for the blood to flow in a smoker's body. This causes the heart to pump faster resulting in an increase in one's heart rate and blood pressure since the body demands more blood. As mentioned in Project 1, the QRS complexes, for 10 seconds, will be counted and multiplied by 6 to get the users heart rate for 60 seconds. R-R intervals are also another form of measuring heart rate however, when discussing irregular heart rhythms, it can be hard to distinguish where the R-R intervals are on the ECG strip. Thus, the QRS complex will be the best method for measuring heart rate in this project. Once the ECGs are recorded, the QRS complexes should be counted in either the 10th to 12th minute, simply because the first few minutes

will most likely have forced/conscious breathing and unwanted movement as explained earlier. If the heart rate that is measured is over 100 bpm, then the subject is experiencing tachycardia. In both groups, tachycardia should not be seen because pacemakers are known for controlling irregular heart rhythms and heartbeat. If tachycardia is seen in any group, this indicates that the pacemakers are not properly fulfilling its purpose and needs to be modified to enable it to.

(ii) Monitoring Pulse Generator Signals in Pacemakers for Smoking Subjects: The pulse generator in pacemakers will be used to ensure that correct contractions of the heart are functioning and that the pulse generator is not affected from smoking lifestyles. The battery life of the pulse generator is approximately two to three times per year with a life expectancy of 10 years ²⁶. The regular check ups are necessary to make sure that the battery is not corroding or causing an unwanted infection over time. Since it is a lithium battery that is encased in titanium, chemicals like lithium leakage can damage or destroy heart tissues and induce severe arrhythmias ²⁷. By conducting this project, we will be able to distinguish if any part of the heart is beating faster than the other. In other words, we will be able to observe if the right atrium is beating faster or slower than the right ventricle or the contrary. This can be seen on the 12-lead ECG where the P wave represents the depolarization of the atriums and indicates that the atrium is contracting. At the QRS complex, it indicates the contraction of the ventricles where depolarization of the ventricles occurs. By measuring the frequency of the P wave with the frequency of the QRS complex, it can be determined if the atrium is contracting quicker than the ventricle and vice versa. For instance, if the P wave, that denotes articular contraction, appears more often than the QRS complex in an ECG strip, then the contractions are not synchronized causing the atrium to contract quicker than the ventricle. The same can be said for the ventricle if the QRS complexes appear more frequently than the P wave.

Timeline/Milestone

A total of 300 subjects will be gathered – 150 smokers and 150 non-smokers with a pacemaker. After receiving the consent of the participants, a screening process will be conducted to ensure the subjects do not have any previous heart conditions and verify that they are all using a pacemaker. The intended ECG and blood tests should take approximately an hour per person in total to conduct. It is worth noting that with COVID-19 affecting operating hours for blood work labs, time delay should be expected. The scheduling for the subjects may vary depending on the subject's availability but the aim is to gather the data in a span of 4 weeks. Once the data is collected, the data will be recorded and analyzed to find trends and patterns which can take up to 2 months.

Anticipated Significance of the Research

The proposed research project is expected to make significant contributions in the pacemaker industry as it will help identify if pacemakers currently can be adaptive based on one's lifestyle in mitigating irregular heart rhythms. A person's lifestyle is drastically changing, and pacemakers should too, especially when irregular heart rhythms and arrythmias, like tachycardia, is so common in today's time. Similarly, pacemakers should also adapt to global pandemics that have been seen to increase arrythmias, specifically tachycardia. This research project will help identify if smoking in pacemaker users affects their heart rhythm which can promote other studies to investigate other factors that could result in the pacemaker not to function properly. Furthermore, this research could help reduce the number of people, with pacemakers, that suffer from tachycardia and reduce the number of deaths caused stroke and cardiac arrests. An echocardiogram will also be conducted which other studies can use and analyze to gain better understanding of their topic. Ultimately, this will result in the pacemaker to become more efficient, adaptive, and suitable for all types of users as time progresses.

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