INTRODUCTION

Rationale

In a normal heart, the resting heart rate is approximately 60 to 80 beats per minute. The ventricles of the heart contract rhythmically. Blood is pumped efficiently to the body, and blood pressure throughout the body is maintained. During ventricular fibrillation (VF), uncoordinated contraction of the ventricular muscle occurs. Blood is not efficiently pumped to the body, and blood pressure drops. Symptoms of VF include chest pain and shortness of breath. VF can result in sudden cardiac death, which affects more than 250,000 people in the United States each year [1].

Electrical activation of the heart appears to be a critical aspect of VF. Electrical activation of the normal heart follows a distinct pattern. Each heart beat begins at the sinoatrial (SA) node, then the electrical activation of the heart beat spreads across the atria to the atrioventricular (AV) node. From the AV node, the electrical activation travels to the Bundle of His, then to the left and right bundle branches and finally spreads across the ventricles. However, during VF, electrical activation of the heart appears to be disorganized or at least much less organized. Electrical activations do not begin only at the SA node but occur throughout the ventricles. Research indicates that VF may be due to many, disorganized reentrant waves of activation, two independent wandering reentrant waves or a single wandering reentrant wavefront [2].

Unipolar electrograms (UEGs) were used to analyze electrical activations during VF in this study. A UEG is a recording of the electrical activity of the heart made from the surface of the heart. One electrode, which detects cardiac electrical activity, is placed on the heart surface. Another reference electrode is also used. The reference electrode is either not placed on the heart or a Wilson's Central Terminal can be used. As an activation wavefront approaches an electrode, the UEG displays a positive deflection. A negative deflection is recorded as the activation wavefront departs from the electrode [3]. The time of the largest negative deflection of the UEG signal is considered to be the time at which activation occurred in the tissue adjacent to the recording electrode [3-5].

For a normal sinus rhythm, determining the activation sites from UEGs is generally straightforward. However, during VF, identifying activations in UEGs is more difficult. UEGs recorded during VF often display several deflections over short time intervals or double deflections. The multiple deflections may represent colliding wavefronts of electrical activation [5]. UEGs detect activity not only from tissue adjacent to the electrode but also electrotonic activity, which is electrical activity from distant tissue [3]. Therefore, due to the complexity of VF, it is difficult to determine whether the UEG signal is displaying a local activation or distant activity. To further complicate the identification of local activations, the UEG signals recorded during VF may have low amplitudes [3].

More accurate methods for determining the location and timing of the electrical activations during VF would provide several benefits. Cardiac mapping of VF and the understanding of the underlying mechanisms of VF could be improved. Additional information about VF could lead to advances in the treatment of the disorder. For example, more sophisticated implantable cardioverter defibrillators (ICDs) with more accurate methods for detecting the onset of VF could be designed and constructed. The defibrillation techniques, which ICDs use, could also be refined so that perhaps lower voltage shocks applied to specific areas of the heart could be used rather than higher voltage shocks applied to the entire heart. The development of technologically superior ICDs could potentially result in an improved quality of life, as well as, a prolongation of life for patients, who are treated with the devices.

Literature Review

Previous studies have shown that different methods can be used to identify sites of electrical activation during VF. Witkowski, Kavanagh, and their colleagues developed the Transmembrane Current Method (TCM) for differentiating between local activations and distant activity. TCM is used to estimate a value proportional to the transmembrane current [6]. Blanchard and her coworkers showed that the Rule-Based Method (RBM) in combination with TCM can be useful for determining the locations of electrical activations during VF. RBM employs maximum negative voltage derivatives with rules for

necessary time separations between the derivatives to determine sites of electrical activation [7].

Pieper and Pacifico have demonstrated that a third method, the Current Source Density (CSD) method, can identify electrical activations during normal sinus rhythm. CSD is a scalar quantity that represents the magnitude of the current source or sink [8]. Prior work has not investigated specifically the use of CSD as a method for the determination of electrical activation during VF. However, Geselowitz and his colleagues have shown that the surface Laplacian, which mathematically differs from the CSD by only a constant, is able to differentiate local and distant activity during VF [9]. (For a mathematical comparison of CSD and the surface Laplacian, see Appendix A.) This study uses combinations of the RBM, TCM, and CSD methods in order to identify more accurately the sites of electrical activation in the UEGs recorded during VF.

Since large amounts of data often must be analyzed and stored when examining cardiac signals, the use of computers to automate the signal processing is highly desirable. Artificial neural networks (ANNs) are one computational tool that is being applied to problems in cardiovascular medicine. ANNs are modeled after biological neural networks. Implemented as computer programs, ANNs consist of multiple, interconnected neurons arranged in different layers. Although substantially simpler than biological neural networks, the goal of ANNs is to build computer systems that have

learning, generalized processing, and adaptive capabilities resembling those seen in biological neural networks. ANNs can learn to recognize certain inputs and to generate a particular output for a given input.

For the analysis of cardiac signals, ANNs offer advantages over conventional methods. ANNs are reliable for pattern identification and classification. The networks can detect patterns and make distinctions between different patterns that may not be apparent to human analysis [10]. ANNs perform well for the analysis of signals, such as cardiac arrhythmia signals, that are complex and may contain high levels of noise. With the many, interconnected neurons, ANNs are massively parallel and thus are suitable for real-time applications [11].

The uses of ANNs to solve problems in different areas of cardiovascular medicine have begun to be investigated. These areas include electrocardiography, coronary artery disease, cardiovascular drug administration, and cardiac image analysis [10]. The literature review for this study will focus on those applications of ANNs that involve electrocardiography. An electrocardiograph (ECG) is a recording of the electrical activity of the heart made from electrodes placed on the body surface, unlike a UEG recording that is made from the heart surface.

Studies have shown that ANNs, trained with ECG recordings, can identify myocardial infarction [12-14]. Myocardial infarction is a region of necrotic tissue that results from an insufficient supply of arterial blood, in the

cardiac muscle. More accurate and efficient diagnosis of patients with acute myocardial infarction could help decrease the number of patient deaths. Baxt trained an ANN to identify patients with acute myocardial infarction, and the ability of the ANN to diagnose acute myocardial infarction was found to be superior to that of emergency room physicians [12]. Heden *et al.* used an ANN to recognize acute myocardial infarction in the 12-lead ECG. The results of the study showed that the ANN performed better than conventional rule-based computer systems and an experienced cardiologist [13]. It has also been demonstrated that ANNs can be trained to detect acute myocardial infarction in patients that were considered difficult to diagnose [14].

Several studies have investigated the use of ANNs to recognize and classify cardiac arrhythmias. Ham and Han trained an adaptive ANN using fuzzy set theory to distinguish between normal and abnormal premature ventricular contraction (PVC) beats [11]. PVCs can occur with coronary thrombosis, and the chances of fibrillation can be increased. More recently, Barro, Fernandez-Delgado, and their colleagues used an ANN for the morphological classification of heartbeats detected in multi-channel ECGs [15]. The recognition of abnormal heartbeats is important for the identification of ventricular arrhythmias. Clayton and coworkers demonstrated that ANNs are capable of distinguishing between VF signals and artifacts similar to VF [16].

ANNs have also been trained to accurately identify ventricular

tachycardia (VT). Dassen and colleagues showed an ANN was able to correctly classify VT for 95 percent of the test examples [17]. VT is a cardiac arrhythmia that occurs when the ventricles beat at an abnormally high rate and independently of the atria. Since VT can degrade into VF, the ability to automatically detect the arrhythmia is crucial for ICD devices. A chip with an ANN for the morphological analysis of heart rhythms has also been developed for ICDs. ICDs using the ANN chip in combination with conventional heart rate timing classification methods were able to detect VT more accurately than ICDs using heart rate timing classification techniques only [18].

Approach

The use of ANNs for distinguishing between local activations and distant activity during VF has not been explored. In this study, the performances of two ANNs for identifying local activations during VF are evaluated. The ANNs were trained to identify local activations from digitized UEGs of VF that were recorded from four pigs. The UEGs were preprocessed using RBM, TCM, and CSD to generate training and test examples for the ANNs. Simple feedforward ANNs, that were trained with the backpropagation of errors method, were used [19, 20]. A new ANN training method, referred to as staged training and designed to improve the ability of an ANN to identify the activations, was also examined.