

Comparison of Bio-signal Characteristics between Ventricular Fibrillation Observed in Clinical Experiments and Ventricular Fibrillation in Animal Models

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Abstract

Ventricular fibrillation is one of the most common causes of sudden cardiac arrest in adults. A lot of research has been done on ventricular fibrillation. However, that research draws conclusions from animal studies and they could not induce artificial ventricular fibrillation in human subjects. This paper looks at whether there is a difference between ventricular fibrillations in animal models and in human models, with comparisons of ventricular fibrillation obtained from the two groups. This study compares and analyzes electrocardiography (ECG) wave forms as electrical bio-signals of the two groups, in which the histogram of gradient (HOG) and auto-associative multilayer perceptrons (AAMLN) are applied for feature extraction and pattern analysis, respectively, of the bio-signals. The characteristics of electrical signals in animal ventricular fibrillation and those in human ventricular fibrillation are conclusively similar and it is reasonable to adapt the results obtained from animal research to clinical practices.

Keywords: Ventricular fibrillation, ECG, histogram of gradient, auto-associative multilayer perceptrons (AAMLN)

1. Introduction

Deaths suddenly occurring as a result of unexpected cardiac arrest account for approximately 63% of all deaths due to cardiovascular causes [1]. In death caused by cardiac arrest, which usually occurs suddenly, the early stage is ventricular tachycardia such as the pulseless ventricular tachycardia that rapidly changes to ventricular fibrillation, or primary ventricular fibrillation [2].

In other words, ventricular fibrillation is the most common cause of the sudden cardiac arrest in adults, and a lot of research on this was conducted, in which they attempted to predict the prognosis by analyzing ventricular fibrillation waveform and by finding its features [3]. Amann *et al.*, organized the waveform analysis methods, such as amplitude, frequency, bispectral analysis, amplitude spectrum area, wavelets, nonlinear dynamics, $N(\alpha)$ histograms, and combinations of all these, a study that reviewed the previous research on waveform analysis of ventricular fibrillation. They reported that, up to now, the research has not found noise removal caused by cardiopulmonary resuscitation (CPR) and the appropriate point when successful defibrillation can be predicted. In addition, they reported that the number of subjects in such studies was few and new analytical methods are necessary [4]. Young *et al.* have reported that as a result using amplitude spectral area

using the sum of amplitude within 3-48 Hz in the study that was conducted targeting the cardiac arrest patient outside the hospital, the possibility of defibrillation is high when this value is higher than 13.0 mV-Hz. Moreover they have reported that amplitude spectral area was shown high specificity to judge whether defibrillation is success or not [5]. Amann *et al.*, compared the differences between the average frequency of ventricular fibrillation and $N(\alpha)$ -histogram analysis as the method for predicting whether defibrillation is successful or not during cardiopulmonary resuscitation (CPR), and they reported that, in their study, $N(\alpha)$ -histogram analysis was the better method for predicting whether defibrillation would be successful. However, these studies were the research that tried to find the method predicting the possibility of success of defibrillation from the cardiac arrest patients caused by ventricular fibrillation rather than the research that identifies the characteristics of waveform of ventricular fibrillation. Thus, Callaway *et al.*, have reported that analyzing ventricular fibrillation by using amplitude and frequency was difficult to explain the characteristics of the waveform, and the method using scaling exponent was more suitable for explaining the waveform with physiological characteristics [6]. However, the results of these studies were obtained being based on animal experiments, and the ventricular fibrillation artificially induced from practical patients could not be experimented, and also the question referred to "Is it rational that the results of animal experiments are applied to practical patients?" was arisen.

In order to resolve these questions, another analyzing method of waveform was required, and it was considered that the method should be able to conduct the inter-comparative analysis for the characteristics of waveform as electrical bio-signal. There are many methods that provide an electrocardiogram (ECG) as a bio-signal corresponding to these purposes. But it was judged that using histogram of gradient (HOG) and auto-associative multilayer perceptrons (AAMLP) was appropriate to identify whether a bio-signal is homogeneous by comparing the characteristics of two or more signals and identifying their patterns. In this study using this method, ventricular fibrillation was analyzed as a bio-signal on the assumption that there may be differences in the characteristics of ventricular fibrillation electrical signals artificially generated in animal experiments and ventricular fibrillation naturally found in human patients, and the characteristics were classified. Consequently, the differences between ventricular fibrillation generated in animal experiments and ventricular fibrillation found in human patients were compared. This study investigates whether the method of using results of previous research on ventricular fibrillation based on animal experiments for treatment of ventricular fibrillation in clinical patients is reasonable.

This paper is organized as follows; Section 2 describes the materials and methods of this work and Section 3 describes the experiments. The discussions and conclusions will be followed in Section 4 and Section 5, respectively.

2. Materials and Methods

In this study, the ECGs of ventricular fibrillation obtained in the experiments targeting dogs among the artificially generated in the animal experiments were determined as the model for animal experiment regardless to period. And the ECGs in the case that ventricular fibrillation was observed among cardiac arrest patients coming to Emergency Medical Station were determined as the human clinical model. As well, the ECGs of ventricular fibrillation were obtained from the database in a web site [7] that is open to the public, which was appointed as the human representative model. These models were compared in this study.

In the ECGs of ventricular fibrillation used in this study, as shown in Table 1, the number of subjects used for the model of animal experiments was 5, and ventricular fibrillation ECG that could be acquired were 119 cases. Among them, learning data was 61 cases and test data was 58 cases, respectively. The number of objects in the human clinical

model was 8, and ventricular fibrillation ECG that could be acquired were 8 cases, and among them, both learning data and test data were 4 cases. And ventricular fibrillation ECG obtained from the human representative models were 6 cases, in which both learning data were 3 cases. Each ECG used in this study was sampled at 100 Hz for a total of 1281 sampling data. Learning data was used to train AAMLPL, and test data was used to apply AAMLPL [8, 9].

The dogs considered as the animal experimental model were all healthy individual, and their ventricular fibrillation was induced through coronary artery ligation. The ECGs of three persons among eight human clinical models could not be acquired as the adequate ECG in the study owing to technical problems. As well, one person's ECG was excluded from the objects in this study since the person who is a survivor did not agree on this study. Thus the person's ECG was excluded from the objects of this study. Thus, the human clinical models were three men and one woman as shown in Table 2, and their age was within the range from 68 to 82 and the mean age was 77. The human clinical models having the history of cardiovascular disease were three persons, and among them, the human clinical models having diabetes and its complications were two persons. And there was one person whose special history of disease was not possible to listen. They had a temporary recovery of self-circulating but they all died, and the causes of cardiac arrest were estimated on the basis of their death certificates.

Table 1. Contents of Ventricular Fibrillation ECG used in this Study

	No. of subjects	Obtained VF ECG (cases)	Learning Data ¹ (cases)	Test Data ² (cases)
Animal Experimental Model	5	119	61	58
Human Clinical Model	4	8	4	4
Human Representative Model	3	6	3	3

¹ No. of ECG data that allow the prerequisite learning of AAMLPL

² No. of ECG data drawing the results by applying to the prerequisite trained AAMLPL

Table 2. Characteristics of Human Clinical Model

No.	Gender	Age	History	Estimated cause of Cardiac Arrest
HCM01	Male	79	Hypertension, diabetes kidney failure	Acute myocardial infection
HCM02	Female	79	Atrial fibrillation, Diabetes	Acute myocardial infection
HCM04	Male	82	Cardiac insufficiency, Angina	Cardiac insufficiency
HCM06	Male	68	Do not disclosed	Acute myocardial infection

The comparative method in this study was the method that the characteristics of ECG signals were extracted by using the HOG that represents a histogram of the temporal changing pattern of electrical signal, and the extracted HOG was compared and analyzed by the AAMLPL. And the similarity was compared by Euclidean distance between input

pattern and output pattern of AAMLPLP. In other words, the temporal characteristics of ECG signals can be interpreted by gradient information, where gradient means the derivative value of amplitudes of sampled signals. Such all gradient information for ECG signal within certain time is obtained, and the changing pattern of the ECG signal within the certain time can be expressed as one histogram, and the histogram obtained by such a method is an HOG. Figure 1 shows the proposed ECG signal pattern analysis process using the HOG and AAMLPLP.

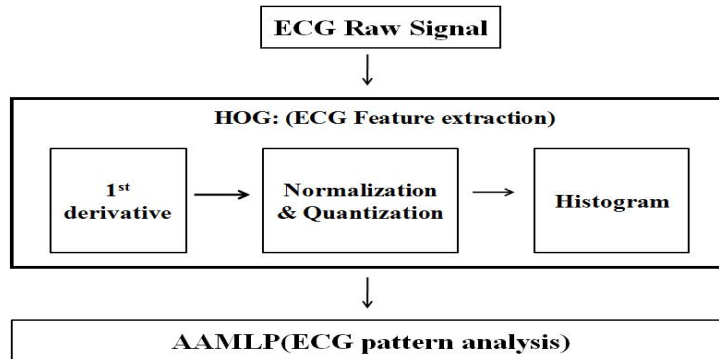


Figure 1. ECG Signal Pattern Analysis Process

The ECG signals that they are same kinds will have the similar characteristics, which causes HOGs extracted from the ECG signals are similar. And the ECG signals that are different kinds have different HOG characteristics. Temporal changing pattern information of different kinds of signals can be expressed as different HOGs because the ECG signals that have different type and characteristics will have different changing pattern according to time. In other words, the statistical characteristics of temporal changing patterns of ECG signals are properly expressed as a histogram of gradient.

Each HOG of each ECG signal is obtained by a following procedure.

(1) The 1st derivative of input raw ECG signals is calculated by

$$g(t) = \text{raw_signal}(t + \Delta t) - \text{raw_signal}(t), \text{ where } \Delta t \text{ is a sampling time} \quad (1)$$

Next, an HOG is obtained through consecutively applying a normalization process of $g(t)$, and a quantization process for adjusting the number of levels, where the formula used here are as follows:

(2) Normalization of the 1st derivative of input signals is obtained by

$$\bar{g}(t) = \frac{g(t)}{\max\{|g(t)|\} \text{ for } \forall t}, \text{ where } |g(t)| \text{ is an absolute value of } g(t) \quad (2)$$

(3) Quantization of normalized 1st derivative signals, $\bar{g}(t)$, is calculated by

$$q(t) = \left(\frac{\max_{\bar{g}} - \bar{g}(t)}{\max_{\bar{g}} - \min_{\bar{g}}} \times 100 \right) \bmod N \quad (3)$$

where $\max_{\bar{g}}$ and $\min_{\bar{g}}$ are maximum and minimum values for all $g(t)$, respectively. And N is the number of quantization levels for generating a histogram.

(4) A histogram of gradient is finally computed using $q(t)$ by

$$\text{HOG}(i) = \# \text{ of } q(t), \text{ where } q(t) = i, 0 \leq i \leq N - 1 \quad (4)$$

Each HOG extracted from each ECG signal is utilized as a training data of AAMLN that has the strong characteristics for partially exposed problem as a pattern analysis model [8, 9]. ECG signals have much within-class variability. Such an ECG detection problem might be one of the partially exposed environments problems which are well known problems where training data from one class is very little or non-existent [8, 9]. Thus, AAMLN is appropriate for the analysis of several ventricular fibrillation ECGs. AAMLN has been used successfully in many such partially exposed problems. In the proposed model, we use an AAMLN with 4-layers which are a mapping layer, a bottleneck layer, a de-mapping layer, and an output layer as shown in Figure 2.

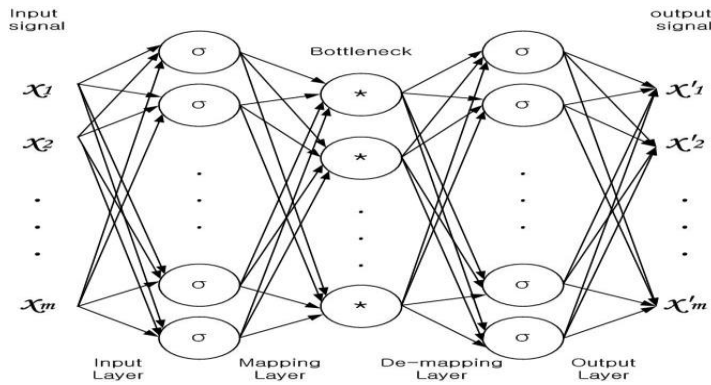


Figure 2. Four Layers Structure of AAMLN

Dimension reduction is achieved by projecting the vectors in a subspace captured by the set of weights in the bottleneck layer through the mapping layer. Dimension expansion is achieved by mapping the lower dimensional vectors onto a hyper-surface captured by the set of weights in the output layer through the de-mapping layer. An auto-associative neural network is basically a neural network whose input and target vectors are the same. The training process of an AAMLN is the same with multi-layer perceptron (MLP). In a course of test phase, the correlation of inputs and outputs of AAMLN is used for comparing similarity between an input vector and a corresponding output vector. In the proposed model, the HOG of ECG signals is utilized as both the input data and the output data for AAMLN. Let F denotes an auto-associative mapping function, and x_i and x'_i indicate the i^{th} input node value and output node value, respectively. Then the function F is usually trained to minimize the following mean square error computed by

$$E = \sum_{i=1}^n \| x_i - x'_i \|^2 = \sum_{i=1}^n \| x_i - F(x_i) \|^2 \quad (5)$$

where n denotes the number of output nodes.

After performing of successful learning, every HOG of input ECG signal is used for an input of AAMLN, and a similarity value of the input vector and the corresponding output vector of AAMLN is measured. Eq. (5) is also used as the similarity measure between input and output of AAMLN. If E in Eq. (5) is small, the similarity is high, which means that the input can be regarded as a similar pattern of a trained class pattern. Or, the input is regarded as an untrained class signal. Thus, using the similarity value of input and output of AAMLN, it will perform the role of the pattern analyzer.

3. Experimental Results

In order to extract the features of a ventricular fibrillation ECG signal from animal experimental models, human clinical models, and human representative models, each ventricular fibrillation ECG signal went transformation into primary derivatives,

normalization, and quantization, and the results were finally represented in an HOG descriptor, which is trained by AAMLPL. Figure 3 shows normalized signals of the first derivatives of raw ECG signals, where the horizontal axis and the vertical axis represent quantization level and normalized amplitude value, respectively. HOG of raw ECG signals are shown in Figure 4, where quantization level N in Eq. (3) is 35 with each HOG represented by a 35-dimension vector. In Figure 4, the horizontal axis and the vertical axis represent a quantization level and a frequency value, respectively. HOG was utilized as input data for AAMLPL after being normalized, which are shown in Figure 5. In Figure 5, the horizontal axis and the vertical axis represent quantization level and normalized frequency value, respectively.

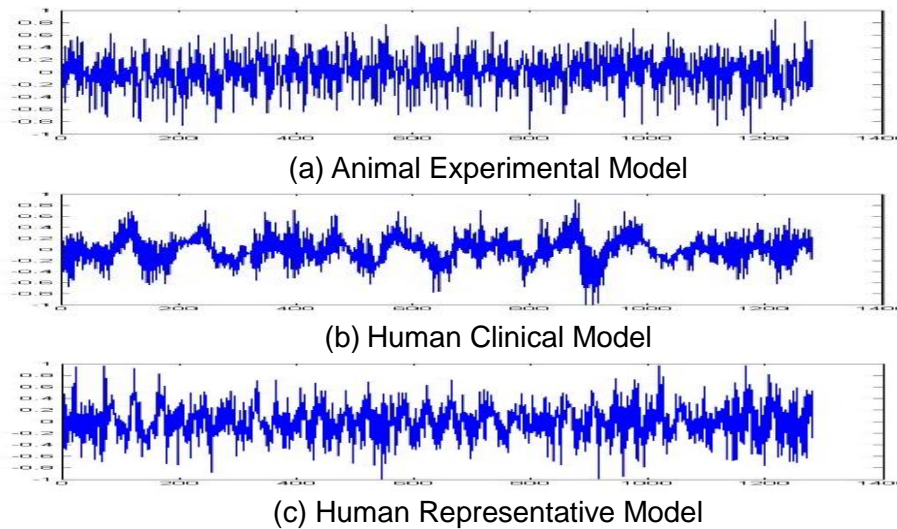


Figure 3. Normalized Signals of the 1st Derivatives of Raw ECG Signals

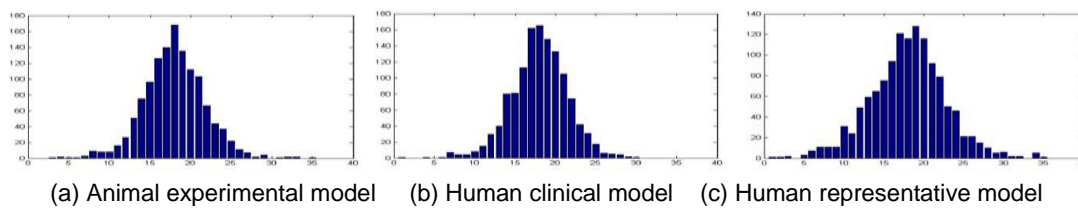


Figure 4. HOG of Raw ECG Signals

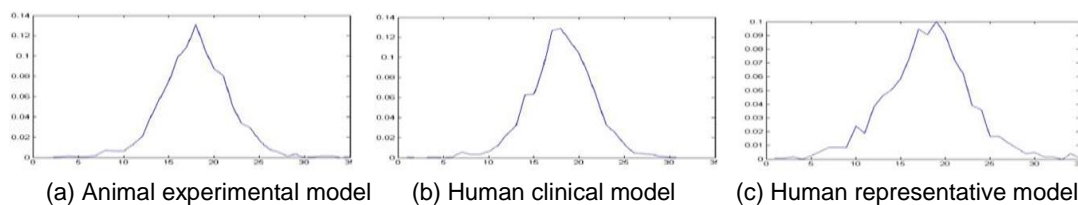


Figure 5. Normalized HOG for Training AAMLPL

Experiment 1.

Features of the signals were extracted by using data from dogs in animal experimental models. After learning them via AAMLPL, the data from animal experimental models, human clinical models and human representative models were tested using AAMLPL. In the results on similarity of the input and output values of AAMLPL, the average of the similarity values and the dispersion values were 0.00662 and 0.003538, respectively from

the animal models, 0.009561 and 0.00423, respectively, from the human clinical models, and 0.012566 and 0.006598, respectively, from the human representative models, as shown in Table 3. Therefore, data from animal experimental models, human clinical models and human representative models showed similar data characteristics.

Experiment 2.

The method of Experiment 2 is the same as Experiment 1. Features of the signals were extracted by using data from human clinical models. After learning them via AAMLPLP, the data from animal experimental models, human clinical models and human representative models were tested using AAMLPLP. In the results on similarity of the input and output values of AAMLPLP, the average of the similarity values and the dispersion values were 0.011551 and 0.001624, respectively, from the animal models, 0.011379 and 0.002238, respectively, from the human clinical models, and 0.014698 and 0.002012, respectively, from the human representative model, as shown in Table 3. Therefore, data of the animal experimental model, human clinical model and human representative model showed similar data characteristics.

Experiment 3.

The method of Experiment 3 is also the same as Experiment 1 and 2. Features of the signals were extracted by using data from human representative models. After learning them via AAMLPLP, the data from animal experimental models, human clinical models and human representative models were tested using AAMLPLP. In the results on similarity of the input and output values of AAMLPLP, the average of the similarity values and the dispersion values were 0.012488 and 0.002989, respectively, from the animal experimental models, 0.014693 and 0.004074, respectively, from the human clinical models, and 0.018054 and 0.005737, respectively, from the human representative models, as shown in Table 3. Therefore, data of the animal experimental model, human clinical model and human representative model showed similar data characteristics.

In order to verify the reliability of the experimental method in this study, HOG of the ECG signal from normal human applied as an input data of AAMLPLP trained using the animal experimental models, in which the average of the similarity values between the input and output values of AAMLPLP was 0.510014. This experimental result showed relatively very low similarity when compared with the similarity results obtained in Experiment 1. Therefore, we can conclude that three models considered in this study have similar characteristics since similarities of three models as shown in Table 3 are much smaller values than 0.510014.

Table 3. Results of Similarity by Three Models using AAMLPLP

Learning Data	Test Data	Average of Similarity	Dispersion of Similarity
Animal Experimental Model	Animal Experimental Model	0.006620	0.003538
	Human Clinical Model	0.009561	0.004230
	Human Representative Model	0.012566	0.006598
Human Clinical Model	Animal Experimental Model	0.011551	0.001624
	Human Clinical Model	0.011379	0.002238

	Human Representative Model	0.014698	0.002012
Human Representative Model	Animal Experimental Model	0.012488	0.002989
	Human Clinical Model	0.014693	0.004074
	Human Representative Model	0.018054	0.005737

4. Discussions

One of the objective methods that the status of patient's heart can be identified with relatively simple and easy is an electrocardiogram, which is also considered as a quick method in the clinical field. The ECG has its own regular pattern, and because these consistent patterns can see as the nature of the signal, it can become the features that can distinguish to the signal of other types.

Ventricular fibrillation is the most common cause of the sudden cardiac arrest in adults. In addition, because it is known that the most effective treatment of ventricular fibrillation is the defibrillation, the fast recognition of the ventricular fibrillation can be the basic treatment reducing the death caused by suddenly occurred cardiac arrest [10]. Therefore, the efforts that attempt to analyze the rhythm of ventricular fibrillation have been done by a lot of research. It was known that any rule in ventricular fibrillation exists through the analysis of ECG representing ventricular fibrillation, and the analysis methods for them have been studied [11, 12]. Now the clinicians are applying the indicators of treatment that have been made based on these studies to the actual patients, and on the other hand, while progressing the studies that analyze the waveform of ventricular fibrillation, various methods have been proposed.

There are amplitude measurement, frequency measurement, bispectral analysis, amplitude spectrum analysis, wavelets analysis, nonlinear dynamics, and $N(\alpha)$ histograms, etc., in the methods that analyze the ventricular fibrillation signal of ECG [3]. However, because these methods are difficult to represent the characteristics of the electrical signal of ventricular fibrillation, it was limited that carried the comparative analysis of the difference between ventricular fibrillation in an animal experimental model and a human clinical model.

And, Wang *et al.*, have reported that in the study that compared the ventricular fibrillation induced by AC current connected in the endocardium and the ventricular fibrillation induced through the coronary artery ligation of a pig, in the case of latter, more numbers of the relapses of ventricular extra systole and ventricular fibrillation were appeared after that the self-circulation is recovered. And also they have reported that there were not the difference between both experimental groups in the myocardial dysfunction, the neurological recovery and the survival of 72 hours after cardiovascular pulmonary resuscitation (CPR) [13]. It was considered that any signal characteristics in ventricular fibrillation exists through these research, but we sought other method because it was difficult to seek it by the analysis methods used until now.

As a result, it is judged that the HOG feature extraction technique and the pattern similarity verification method using AAMLN used as the method that compares and analyzes the electrical signal, are suitable for the purpose of this study as the method that can compare and analyze considering ventricular fibrillation as an electrical signal. As the results of such analysis, it was analyzed that the data of the ventricular fibrillation ECG of animal experimental model, human clinical model and human representative model represents similar characteristics, each other. On the other hand, as the results that enter a

person's normal ECG signal to AAMLP learning with the ventricular fibrillation ECG signal, the output of AAMLP showed the result that the similarity with its input is very low. This shows that the electrical signal of ventricular fibrillation ECG has the different characteristics than the electrical signal of normal ECG, and it can be said to represent the reliability of the comparison analysis method used in this study.

It is considered that the characteristics of the ventricular fibrillation ECG signal in animal experimental models, human clinical models and human representative models are similar. Accordingly, HOG and AAMLP were appropriately chosen for feature extraction and pattern analysis in this study, and also their performance are superior.

This study is significant in the aspect that the characteristics extraction of the electrical signal using HOG, and the similarity judgment method are new method different from the method that have been used in the waveform analysis of ventricular fibrillation until now. This method is commonly used in the engineering community as the method that compares and analyzes the electrical signal occurred in the external environment of the human, but it has a meaning that attempted to compare and analyze the ECGs of animals and human by applying to the ECG occurred in vivo which is the internal environment of animals and humans.

In the previous study of Wang et al., the fact that ventricular fibrillation in pigs can have the different characteristics according to the induced factors, may be inferred. However, in this study, the ventricular fibrillation of the animal experimental models were induced by the ligation of the coronary arteries of a dog, and the reason of ventricular fibrillation in human clinical models and human representative models could not be clearly found, but they were occurred owing to the different reason than those of the animal experimental models. As the results of the experiments in this study, the ventricular fibrillation ECGs of animal and human are judged to similar in the characteristics of electrical signal occurred in vivo, therefore, it is predicted that both ventricular fibrillation in vivo are similar in the aspect of the characteristics of the electrical signal, regardless of the cause.

The point that induces ventricular fibrillation with only coronary artery ligation among both the coronary artery ligation and the revulsion of ventricular fibrillation using an electric shock that used in other studies of animal experimental models, and the point that was not acquired the ventricular fibrillation ECG occurred by various reasons in human clinical models can be appointed to the limitation of this study in the aspect of the diversity of inductive factors of ventricular fibrillation.

In addition, in this study, all ECGs obtained from the animal models, human clinical models and human representative models were those that were obtained from Lead II. Because ventricular fibrillation can be occurred via a complex electrical circuit in the heart, it is difficult to conclude that the ECG obtained from a single Lead is the characteristics of the whole heart. Therefore, in order to compensate for these shortcomings, it is considered that building up the database that the ventricular fibrillation ECG due to various causes over a long period of time is obtained from various Lead will be needed.

In future, it is considered that a broad comparative analysis should be made by securing a large amount of ventricular fibrillation ECG induced by the experiments and various methods for various animal species, and at the same time, by securing the person's ventricular fibrillation shown in the cardiac arrest caused by various reasons.

Moreover, it is considered that this study can be more and more developed through the comparative studies with several methods that have been reported to be valuable to predict the effect of defibrillation in the studies until now with the comparative analysis method used in this study.

5. Conclusion

Characteristics of ventricular fibrillation ECG signals were compared in order to analyze the similarity between ventricular fibrillation in a human model and that of an

animal model, in which characteristics of each ECG signal were represented by HOG of the ECG signal, and then AAMLPLP was applied to analyze similarities or differences in characteristics. Through cross-validated experiments, it can be judged that the characteristics of ventricular fibrillation ECG signals in the animal experimental models, human clinical models, and human representative models are similar.

The characteristics of ECG signals in animal ventricular fibrillation and those in human ventricular fibrillation are conclusively similar and it is reasonable to adapt the results obtained from animal research to clinical practices.

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The authors would like to cordially devote this paper to the late Prof. Seong Ho Kim.

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