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복부 대동맥류 진단을 위한 심층신경망 기반 질환 심각도 회귀

Deep Neural Network based Disease Severity Regression for Diagnosis of Abdominal Aortic Aneurysm

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서울대학교 대학원

기계공학부

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이 논문을 공학석사 학위논문으로 제출함

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Abstract

Deep Neural Network based Disease Severity Regression for Diagnosis of Abdominal Aortic Aneurysm

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Disease in the medical field correspond to fault from an engineering point of view. In diagnosing machine failure, prognostics and health management (PHM) are essential. PHM chases the degradation of the health of the target system and produces information on health status. In this paper, the target system is selected as human. The target disease of human being the target system is selected as abdominal aortic aneurysm (AAA). Two of the main issues related to aneurysm are the lack of diagnostic indicators and lack of disease data. Aneurysm is not diagnosed using diagnostic indices, but is discovered using imaging techniques such as computed tomography (CT) or magnetic resonance imaging (MRI). However, these techniques are expensive and time consuming. In addition, because it is difficult to diagnose this disease in advance, it is not easy to secure disease data.

Against these issues, this study proposes a disease diagnosis and severity regression technique that combines deep learning. There are three research thrusts here: 1) generating normal and disease data through simulation model, 2) regression of disease severity, 3) reflecting individual diversity when generating data. In the first thrust, data is generated using a simulation model. One of the simulation models

for diagnosing human disease is a transmission line model (TLM). A transmission line model modified from the model proposed in other previous papers [1] is used. In order to obtain blood pressure through the model, the input impedance needs to be calculated, which was calculated using a recursive algorithm. In the second thrust, disease incidence is monitored through severity regression. Deep neural network (DNN) is used as a tool to perform regression. In the third thrust, biometric parameter values are given as distributions. In consideration of the characteristics of each parameter, an appropriate distribution is assigned to each. The structure of this algorithm is formed of four tasks: simulation model modification, data generation, DNN design, and solving severity regression problem. It is confirmed that the blood pressure waveform data generated through literature research is valid and that the regression is well performed through the mean squared error (MSE) loss value.

Keywords: Cardiovascular Disease
Abdominal Aortic Aneurysm
Severity Regression
Blood Pressure Waveform Data
Deep Neural Network

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Nomenclatures

PHM	Prognostics and health management
TLM	Transmission line model
AA	Aortic aneurysm
AAA	Abdominal aortic aneurysm
BP	Blood pressure
BF	Blood flow
DNN	Deep neural network
ICT	Information and communication technology
OECD	Organization for economic cooperation and development
GDP	Gross domestic product
CNN	Convolution neural network
ReLU	Rectified linear unit
MSE	Mean squared error
CT	Computed tomography
MRI	Magnetic resonance imaging

Chapter 1. Introduction

1.1 Motivation

Healthcare is the set of services provided by a country of an organization for the treatment of the physically and the mentally ill [2]. In the past, a healthcare was a symptom based intuitive medical. However, in today, a healthcare is a pattern and evidence based medical. Also, healthcare is changing to an algorithm based precision medical.

Table 1-1 Changing the way of healthcare [3]

Past	Present	Future
Symptom-based	Pattern-based	Algorithm-based
Intuitive medical	Evidence-based medical	Precision medical

Big data is a collection of data elements. The main four characteristics of big data are: sheer volume, complexity, diversity, and timeless. The advent big data has had an impact on the healthcare sector. It is introduced in image processing, signal analysis and genetics, and is of great help in care delivery and disease exploration. In other words, healthcare is providing personalized and optimized treatment for individuals.

In addition to the introduction of big data, a healthcare service is customized by integrating ICT (Information and communication technology) and individual health record. Also, it is possible that real time monitoring and management of individual

health status without time and place restrictions. According to OECD statistics, a health expenditure is growing.

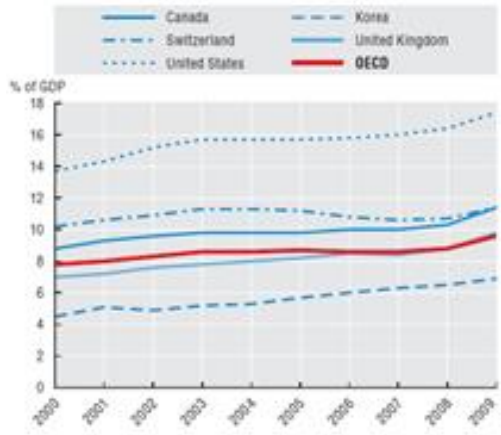


Figure 1-1 Total health expenditure as a share of GDP [4]

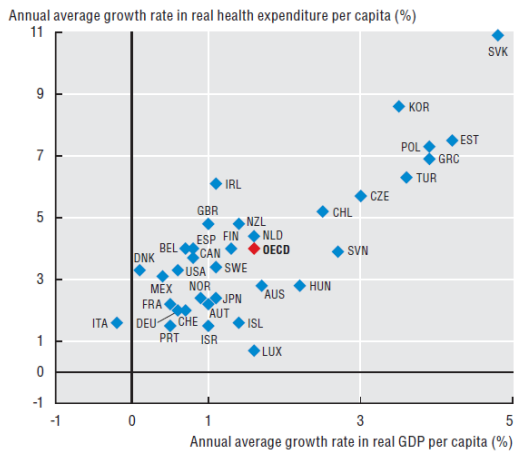


Figure 1-2 Annual average growth in real per capita expenditure on health and GDP [4]

The existing medical based treatment consists of event data and doctor's opinion. Prognostics and health management (PHM) of human sees disease in terms of combining monitoring data and physical knowledge. In other words, the main difference between human PHM and healthcare is the convergence with physics knowledge. For example, in physiology, retinal arterial analysis can be performed by fusion of blood flow and fluid mechanics. In pathology, the integration of cell medicated immunity and thermodynamics can execute blood cell analysis. In orthopedics, an osteology analysis can be carried out by the convergence of human gait motion, dynamics, and robotics. In sum, more accurate diagnosis and prediction of human health becomes possible through human PHM. It can also describe how the result is reasoned by algorithm.

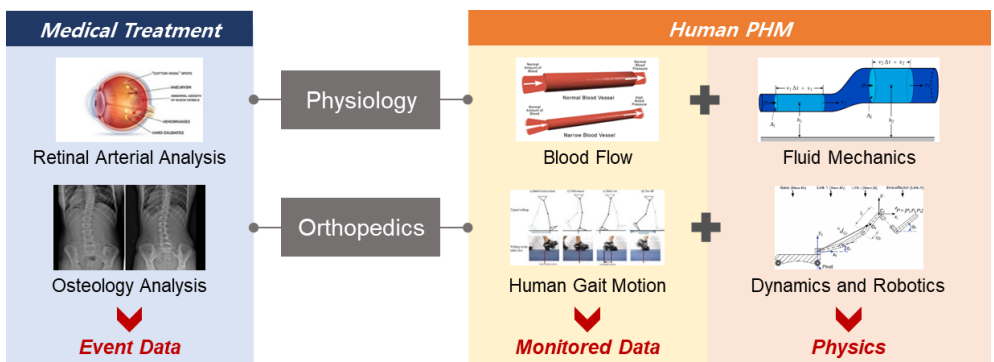


Figure 1-3 Difference between healthcare and human PHM

1.2 Research Thrust

The objective of this research is development of fault diagnosis method combining deep learning. There are three major problems in performing human PHM. First problem is insufficiency of data. The anonymous data is acquired from various people and the dataset is sparse. So, the regression accuracy is low. Cardiovascular disease can be diagnosed by analyzing the correlation between the proximal and the peripheral blood pressure waveform. However, the proximal blood pressure waveform cannot be measured on a routine basis, so the amount of data for developing a diagnostic model is insufficient. Second problem is dispersion of disease severity. Blood pressure waveform data corresponding to various disease severity cannot be obtained realistically, and only distributed disease severity data can be obtained. Third problem is a lack of individuality. Due to the small amount of data secured, it is difficult to consider individual deviations. Also, the blood pressure waveform data has a large variation according to individual such as gender, race, and body composition. So, the population norm based disease diagnosis method has limitations in accuracy. Thus, the research objective is to develop applicable and practicable deep learning base fault diagnosis techniques.

Research Thrust 1: Generating Normal and Disease Data through Simulation Model

Research Thrust 1 proposes a simulation model that generates normal and disease state data. First, assume a single arterial segment is a thin-walled cylindrical tube. That way, we can calculate blood pressure and blood flow in a single artery. Then, Transmission line model is modified by setting various disease severity.

Research Thrust 2: Regression of Disease Severity

Research Thrust 2 is disease severity regression. When generating simulation data, label the severity. Labels are randomly assigned to train data and sequentially assigned to test data. Then, a deep neural network is designed. In this study, a DNN with 3 hidden layers was designed.

Research Thrust 3: Reflecting Individual Diversity When Generating Data

Research Thrust 3 is to simulate the data of various individuals. First, parameters that have an important influence on personal characteristics are selected. This can be done by comparing the effects of arterial compliance, length, internal radius, and wall thickness on the aortic input impedance. Then, a distribution that fits each parameter characteristic is assigned.

1.3 Dissertation Layout

This dissertation This dissertation is organized as follows. Chapter 2 reviews the background of this research, such as target disease, simulation model, and regression tool. Chapter 3 presents a methodology that how to modify the simulation model and implement aneurysm. Chapter 4 presents the blood pressure waveform obtained through the simulation model. In this chapter, we verify whether the blood pressure waveform data makes sense, and compare the results for each aneurysm type. Chapter 5 presents the results of regression using the data obtained in Chapter 4. Finally, Chapter 6 summarizes the dissertation with its contributions and suggests future researches.

Chapter 2. Background

This chapter introduces the core concepts of this dissertation. Chapter 2.1 describes the target disease, abdominal aortic aneurysm. The sub-chapters describe the mechanisms of disease, diagnosis, and treatment. Chapter 2.2 explains the concept of a simulation model that generates data and its operation algorithm. Chapter 2.2.1 describes the concept of transmission line model (TLM), and chapter 2.2.2 describes the recursive algorithm. Chapter 2.2.3 describes the artery tree that is the framework of the TLM. Chapter 2.3 is composed of an overview of DNN and description of the basic structure.

2.1 Abdominal Aortic Aneurysm (AAA)

In this study, the target disease is abdominal aortic aneurysm (AAA). Aortic aneurysm is a condition in which a part of the aorta has increased by more than 1.5 times its normal diameter. The size of the aortic aneurysm determines the potential for rupture of blood vessels. When the blood vessel wall stress is larger than the wall strength, the aneurysm is ruptured. In general, if the size of an aneurysm is 5cm of more, it is classified as a severe disease state. Also, treatment is recommended when the size of an aneurysm exceeds 5.5cm. It is called abdominal aortic aneurysm when the aneurysm is occurred in the abdominal aorta. Among aortic aneurysm rupture, AAA has the largest annual mortality rate. The dangers of this target disease is that it is asymptomatic. Some aorta aneurysms have pain during palpation, but at that time a likelihood of rupture is high. Also, AAA cause complication such as thrombosis and embolism.

2.1.1 Hypothesis for the Development of AAA and Rupture

The mechanisms by which AAA occurs are diverse. There are four typical hypotheses: 1) proteolytic degradation of aortic wall connective tissue, 2) inflammation and immune responses, 3) biomechanical wall stress, and 4) molecular genetics. These mechanisms act in combination rather than independently, creating AAA. Patients with AAA have a disability in the formation of elastin and collagen. When the aorta wall is weakened by various causes, the aorta expands into a saccular or fusiform. As the diameter of the artery increases, the pressure acting on the aorta wall increases by Laplace's law, and the aorta gradually expands. AAA fails to withstand pressure when they reach a certain limit and finally ruptures. The rupture of aneurysm can be seen as a failure from a mechanical point of view. When the arterial wall stress becomes greater than the wall strength, aneurysm ruptures. Normal abdominal aorta diameter size is 2.0cm. If the diameter is more than 2cm and less than 3cm, it is classified as mild aortic aneurysm (AA). If the diameter is more than 3cm and less than 5cm, it is classified as moderate AA. If the diameter begins to exceed 5cm, it is classified as a serious condition from then on [5]. There is a correlation between blood vessel diameter and rupture rate. When the diameter is 5cm or more, the rupture rate is 3 to 15%, but when the diameter is more than 8cm, the rupture rate rises rapidly from 30 to 50%.

2.1.2 Diagnosis and Treatment

Despite many previous studies, there are still no indicators for diagnosing AAA. The magnitude of wall stress, which is most widely used as a diagnostic index, does not necessarily coincide with the onset of symptoms of AAAs. Hardman index is model that predicts survival after intervention for ruptured AAAs [6]. Therefore, this index

cannot be used until the AAA has ruptured. Augmentation index is used as a marker of wave reflections and arterial stiffness [7]. Increased augmentation index means that arterial stiffness evaluates in patients with AAA. This index is derived from central aortic pressure waveform analysis. Although this index is related to AAA, it cannot be an index that can diagnose the disease. Peak wall rupture index (PWRI) is used to predict AAA volume growth. A wall rupture risk index is defined by locally dividing the von Mises wall stress to an estimate of wall strength [8]. Among these indices, the highest wall risk index is a peak wall rupture index. Biomechanical variables, such as aneurysm diameter, peak wall stress, peak wall shear stress, wall strain, wall stiffness, are useful for assessing the risk of AAA rupture, but are difficulty to use clinically due to lack of standardization. Thus, there are no indicators that can be diagnosed before AAA ruptures.

Existing diagnostic methods for AAA includes ultrasonography, computed tomography (CT) and magnetic resonance imaging (MRI). Ultrasonography is useful for examining organ form and vascular blood flow. CT is suitable for long-term examinations with large movements. MRI is recommended for soft tissue examination. However, these methods are not only for AAA diagnosis. In most cases, AAA is discovered while using these diagnostic methods to test for other diseases.

There are two typical treatments for AAA. The first is to remove the aneurysm and replace it with artificial blood vessels. However, the disadvantages of this method are that the abdomen needs to be opened for surgery, the length of hospital stay is long, and complications may occur during surgery. The second treatment is to insert a stent graft into the blood vessel. But, this method is not applicable to all patients, and whether or not it is applicable depends on the bending angle and

diameter condition of the aorta.

2.2 Data Generation Model

2.2.1 Transmission Line Model (TLM)

In this research, data generation simulation model is a transmission line model. This model is developed in a prior work [9]. The model is multi-branch model and each transmission line represents an arterial segment. Each vessel segment can be viewed as a thin-walled cylindrical tube. Making these assumptions allows you to calculate blood pressure and blood flow in a single artery. It is based electrical network model and recursive algorithm. The blood flow waveform can be gained by calculating the input impedance. Blood pressure and flow are linked by input impedance at any point of the arterial system. The relation of reflection coefficient, impedance, propagation constants defines the blood pressure and flow formula. The blood pressure (BP) waveform equation and the blood flow (BF) waveform equation are as follows:

$$P_{outlet} = P_{inlet}(1 + \Gamma)/\left(e^{\gamma l} + \Gamma e^{-\gamma l}\right) \tag{2.1}$$

$$F_{outlet} = F_{inlet}(1 - \Gamma)/\left(e^{\gamma l} - \Gamma e^{-\gamma l}\right) \tag{2.1}$$

where P_{outlet} and P_{inlet} are blood pressure waves at the outlet and the inlet of the artery, F_{outlet} and F_{inlet} are blood flow waves at the outlet and inlet of the artery, Γ is the reflection coefficient, γ is the propagation constant, l is the arterial length. The blood relationship of blood pressure and blood flow is as follows:

$$P_{inlet} = F_{inlet}Z_{input} = F_{inlet}Z_C\frac{\left(e^{\gamma l} + \Gamma e^{-\gamma l}\right)}{\left(e^{\gamma l} - \Gamma e^{-\gamma l}\right)} \tag{2.3}$$

where Z_{input} and Z_C are the input impedance and characterstic impedance of the artery. If the input of the arterial system is a flow or pressure source, the flows and pressures at any point of the arterial system can be calculated, respectively. By obtaining the flow or pressure of a point, we can see the flow or pressure at the other nearest point.

2.2.2 Recursive Algorithm

A recursive algorithm is an algorithmic technique that calls itself. If the small decomposed problem is the same as the original problem, it can be solved by applying the algorithm. The input impedance calculation problem can be easily solved through a recursive algorithm. In this model, the input impedance is calculated in the backward way. Impedance from the distal vessel segment to the ascending aorta is sequentially worked out.

2.2.3 Arterial Tree

An arterial tree based on Noordergraaf's 55 arterial segments model is used [9]. There are no coronary arteries in this artery tree. The rough diagram of the arterial segments model is shown in Figure 2-1.

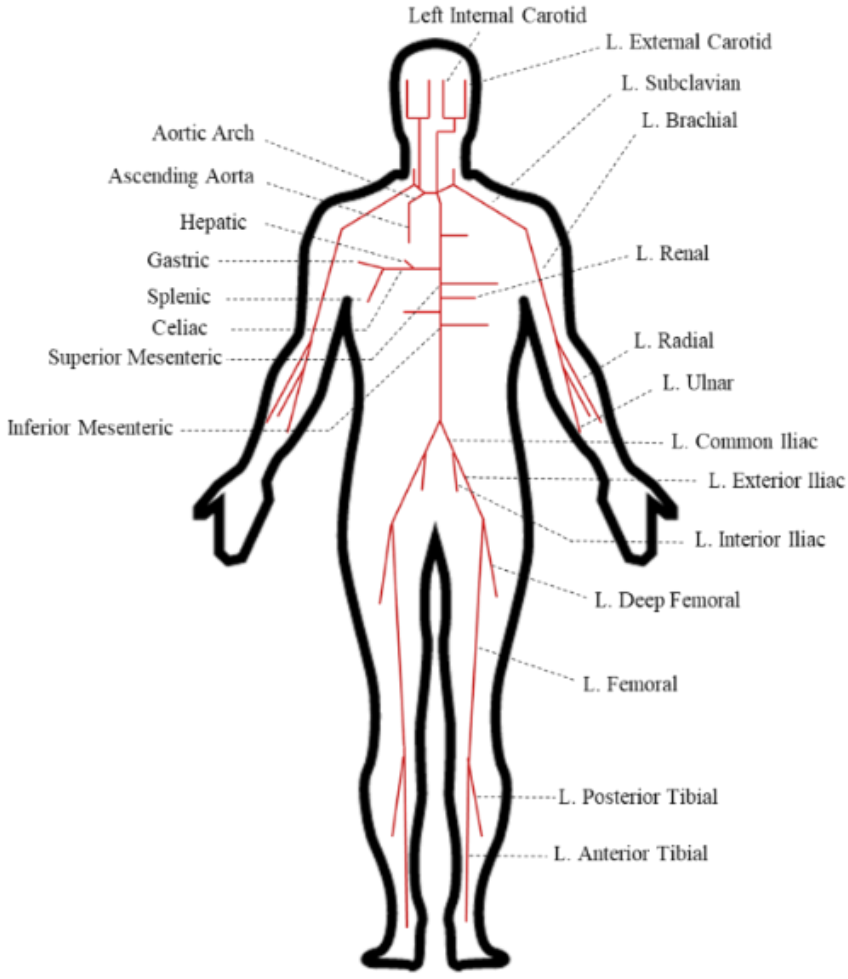


Figure 2-1 Arterial tree

Table 2-1 Number and name of 55 segments of arterial tree [9]

Segment number	Arterial segment name	Segment number	Arterial segment name
1	Ascending aorta	29	Abdominal aorta III
2	Aortic arch I	30	Left renal
3	Brachiocephalic	31	Abdominal aorta IV
4	Right subclavian I	32	Inferior mesenteric
5	Right carotid	33	Abdominal aorta V
6	Right vertebral	34	Right common iliac
7	Right subclavian II	35	Right external iliac
8	Right radius	36	Right internal iliac
9	Right ulna I	37	Right deep femoral
10	Aortic arch II	38	Right femoral
11	Left carotid	39	Right external carotid
12	Thoracic aorta I	40	Left internal carotid
13	Thoracic aorta II	41	Right posterior tibial
14	Intercostals	42	Right anterior tibial
15	Left subclavian I	43	Right interosseous
16	Left vertebral	44	Right ulnar II
17	Left subclavian II	45	Left ulnar II
18	Left ulnar I	46	Left interosseous
19	Left radius	47	Right internal carotid
20	Celiac I	48	Left external carotid
21	Celiac II	49	Left common iliac
22	Hepatic	50	Left external iliac
23	Splenic	51	Left internal iliac
24	Gastric	52	Left deep femoral
25	Abdominal aorta I	53	Left femoral
26	Superior mesenteric	54	Left posterior tibial
27	Abdominal aorta II	55	Left anterior tibial
28	Right renal		

2.3 Deep Neural Network (DNN)

2.3.1 Overview of DNN

Deep learning is a set of machine learning algorithms. Deep neural network (DNN) is one of the deep learning algorithms. The objective of DNN is approximating any function. DNN improves the learning result of the artificial neural network by increasing the number of hidden layers. The more the number of hidden layers increases, the better the approximation can be. The depth of the model is related to the number of nodes. DNN is commonly used to solve regression and classification problems. In the medical field, convolution neural network (CNN) techniques using image data are often used. Since this study uses blood pressure waveform data, a simple DNN was used instead of a complex CNN.

2.3.2 General Structure of a DNN

This chapter describes the basic structure of DNN. The linear layer computes the output from the input using a linear function, and stores weight and bias in tensor. In deep learning, the gradient is calculated by putting input data into the model and updating the model is repeated. When putting data into the model, it is divided into batch units and entered. Training data divided into batches may have different distributions. Normalizing these distributions by adjusting the mean and variance is called batch normalization. Batch normalization is placed before the activation function. The activation function converts an input into an output and plays a role of expressing nonlinearity by stacking layers in the network. The loss function computes a value that estimates how far the output is from the correct answer. In the regression problem, the mean squared error is used as the loss function. The optimizer is a rule to update weights.

2.4 Summary and Discussion

An aneurysm is a balloon-like swelling of the artery and can occur at any point in the artery. It usually occurs most often in the aorta. The basis for aneurysm is variable, and it ruptures after dilation. There are currently no indicators for diagnosing AAA. Most of the cases found are when using the imaging technique. Treatment consists of replacing blood vessels with artificial blood vessels or inserting stent graft into blood vessels.

The simulation model implements the artery tree as TLM, and calculates the input impedance through a recursive algorithm. Each transmission line can be viewed as a thin-walled cylindrical arterial tube. Blood pressure and blood flow are related by input impedance and can be calculated at any point in the artery.

A DNN is one of deep learning algorithms and has several hidden layers of artificial neural networks. This algorithm is generally used when solving classification or regression problems. The typical organization of a DNN includes the following contents: 1) linear layer, 2) batch normalization, 3) activation function, 4) loss function, and 5) optimizer.

Chapter 3. Methodology

This chapter explains how to conduct research using the concepts induced in Chapter 2. Chapter 3.1 explains how the TLM was modified to implement the AAA. Chapter 3.2 describes how different types of aneurysms are implemented. Chapter 3.3 explains how the structure of the DNN that performs disease severity regression is constructed.

3.1 Alteration of Transmission Line Model

Original transmission line model [9] is a model that well reflects the general characteristics of hemodynamics. Some modifications to the model can implement a disease in which the diameter of the arteries becomes narrower, such as peripheral occlusive artery disease [1]. In this study, the model was modified to indicate a disease that expands rather than narrows blood vessels.

3.1.1 Materialization of AAA

When aneurysm occurs, blood vessel swells, the wall thickness becomes thinner, and the radius increases. Sins the aneurysm swelling is not uniform, the thickness of the aneurysm is not consistent. In this study, by simplifying the problem, it is assumed that the thickness of the swollen arterial wall is not decreased and is consistent. The aneurysm radius is increased according to the severity of the disease. The radius of the aneurysm is set to be 2.5cm when the disease is the most severe.

3.1.2 Data Description

The aneurysm was applied to the abdominal aorta. The total length of the abdominal aorta is 8cm. The blood pressure measurement point was in the right deep femoral.

In fact, since there are cases where pressure is measured in the thighs, the thighs were selected as the measurement point. The reason why the measurement point was selected as one is because the blood pressure waveform in the left and right thighs is the same. The maximum aortic aneurysm diameter was 5cm, because a significant proportion of patients with an AAA rupture develop a rupture at aneurysm diameter of less than 5cm [5]. When aneurysm has a maximum diameter, the label of severity is given as 1. In the normal state, the label is 0. In addition, individual diversity was realized by giving the values of the variables representing the characteristics of blood vessels as a distribution. A normal distribution is assigned to modeling parameters such as body height, artery radius, and wall thickness. A lognormal distribution was assigned to physical parameters such as Young's modulus, arterial viscosity, resistance, and compliance. The literature confirms that the blood vessel diameter and blood flow velocity histogram follow a normal distribution [10], and that a lognormal distribution is used for the coefficient of an organism [11]. 480,000 train data and 196,830 test data were generated.

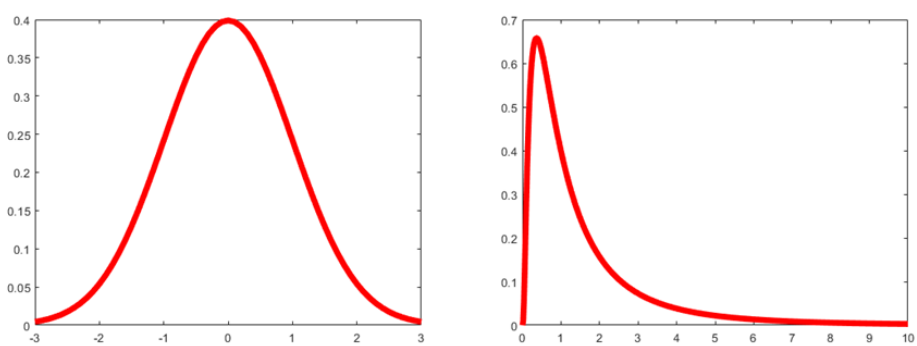
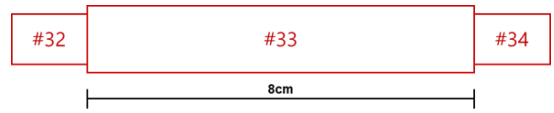


Figure 3-1 Statistical distributions

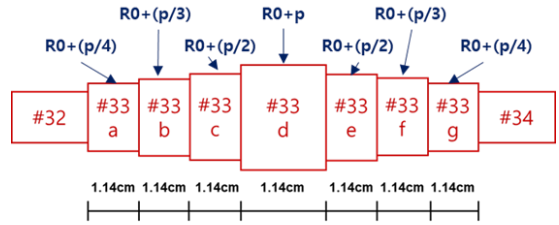
(a): Normal distribution, (b): Lognormal distribution

3.2 Materialization of Four Types of Aneurysms

Aneurysm has a shape that gradually swells like a balloon. Therefore, in order to specifically simulate an aneurysm in this simulation model, it is necessary to differentiate the arterial segment. In other words, it simulates a sphere by gradually changing the diameter of a finely divided artery segment. In this study, four types of aneurysms were implemented. The reason for implementing various types of aneurysms is that the shape of aneurysm is very diverse. Type 1 is an aneurysm by inflating the entire abdominal aorta. That is, the radius of the blood vessel of 8cm expanded uniformly. In type 2, the abdominal aorta was divided into 7 segments and the radius of each piece was different. Each segment is $\frac{8}{7} = 1.14$cm long. Let the initial radius be R0, and the radius increment according to the severity is p. The radius of the 7 segments is sequentially $R0 + (\frac{p}{4})$, $R0 + (\frac{p}{3})$, $R0 + (\frac{p}{2})$, R0, $R0 + (\frac{p}{2})$, $R0 + (\frac{p}{3})$, $R0 + (\frac{p}{4})$. In type 3, the abdominal aorta was divided into 7 sections and the radius and length of each segment were different. The method of increasing the radius is the same as for Type 2. The length of each segment is given symmetrically around the center segment. Specifically, the length of each segment was sequentially given as 0.5cm, 1cm, 1cm, 3cm, 1cm, 1cm, and 0.5cm. Finally, type 4 is similar to type 3, but the length of each segment is given asymmetrically. The length of each segment was sequentially given as 1cm, 2cm, 1cm, 2cm, 0.5cm, 1cm, and 0.5cm.



(a)



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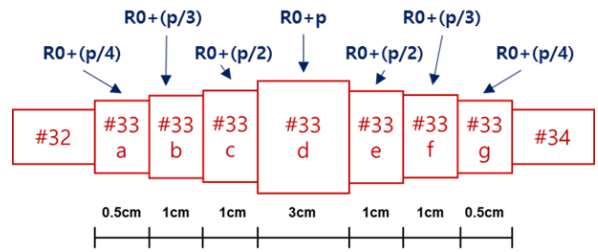
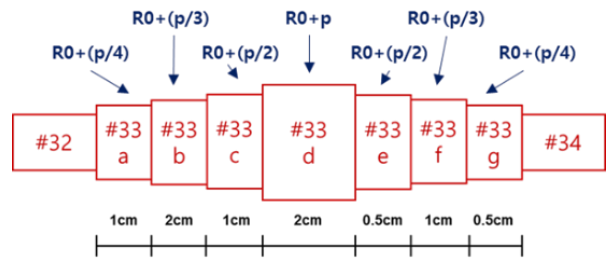


(c)



(d)

Figure 3-2 Types of aneurysms

(a): Type 1, (b): Type 2, (c): Type 3, (d): Type 4

3.3 Architecture of DNN

In this study, PyTorch was used as a machine learning library. The most basic DNN structure was used. We used three hidden layer with 300 nodes each. The input of the model is blood pressure waveform at the measurement point and the output is a severity of disease. The dimension of input is 66 and the dimension of output is 1. Input and output have a linear function relationship. Data is learned in mini-batch units. The batch size is 2,000. ReLU was used as an activation function. Also, we used the mean squared error loss, which is the loss used in the regression problem. The optimizer is Adam optimizer with initial learning rate of 1×10^{-5}.

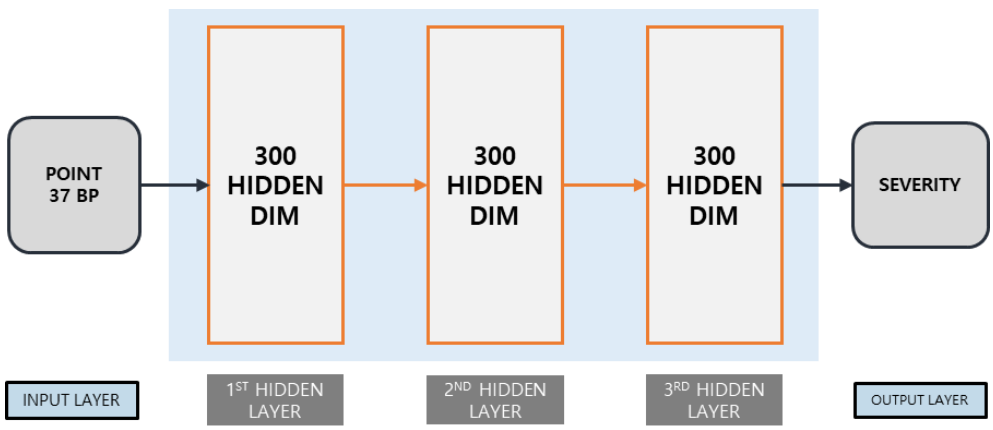


Figure 3-3 DNN architecture

3.4 Summary and Discussion

A model with an AAA was implemented by modifying the TLM that implements hemodynamics well. When the artery swells, the radius increases and the wall thickness of the vessel is designed to be constant. The site of the aneurysm is the

abdominal aorta. The blood pressure measurement point is the deep femoral on the right. The maximum diameter of the AAA was set to 5cm. Distributions appropriate for each characteristic were assigned to important variables related to blood vessels.

Considering that the shape of the aortic aneurysm is not standardized, a total of four types of aortic aneurysms were implemented. Type 1 is a dilation of the entire AAA. In Type 2, the abdominal aorta is divided equally into 7 pieces, and then the degree of expansion is different. In Type 3, the AAA was divided into 7 pieces of different length, and the degree of dilation was different. Type 4 is similar to Type 3, but the length of the AAA is different.

DNN was designed in the PyTorch language. It was configured to have three hidden layers. The input of DNN is the blood pressure waveform and the output is the severity. The flow chart of the methodology of this study is as follows.

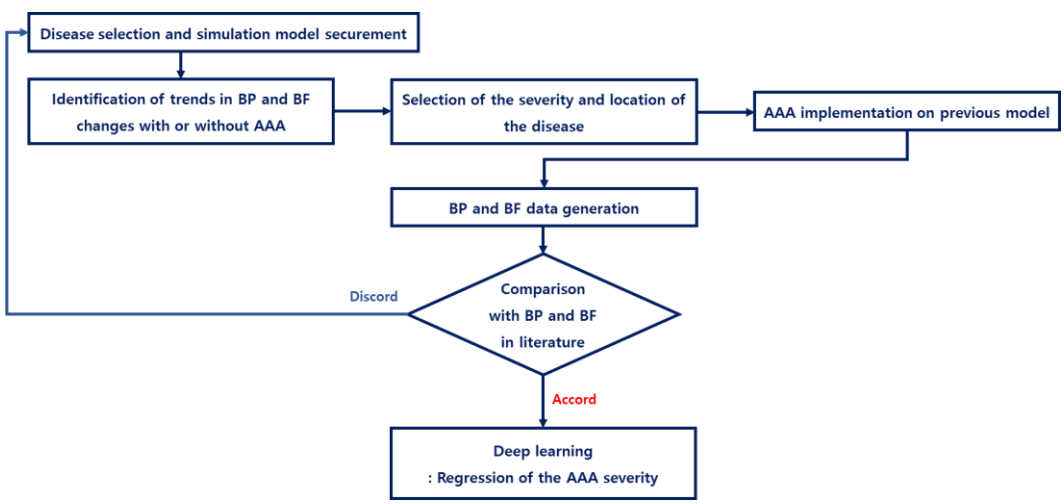


Figure 3-4 Flow chart of the methodology

Chapter 4. Data Generation Results

In this chapter, the blood pressure waveform graph obtained through the modified TLM is presented. First, blood pressure waveform graphs by types and disease severity are shown. Next, the validity of the acquired blood pressure waveform data is verified by comparing it with data in the literature.

4.1 Blood Pressure Waveform Data

The characteristics of the blood pressure waveform when having type 1 aneurysm are as follows: 1) the waveform becomes wavy as the disease becomes more severe, and 2) the value of the peak point increases. In the case of type 2, 3, and 4 aneurysm, the characteristic of showing the blood pressure waveform was the same as that of type 1. That is, in common for all types, it can be seen that the BP waveform becomes convoluted as the disease severity level increases. When comparing the blood pressure waveforms for each type of aneurysm when the disease is the most severe, there is a difference in peak value, but there is no clear trend.

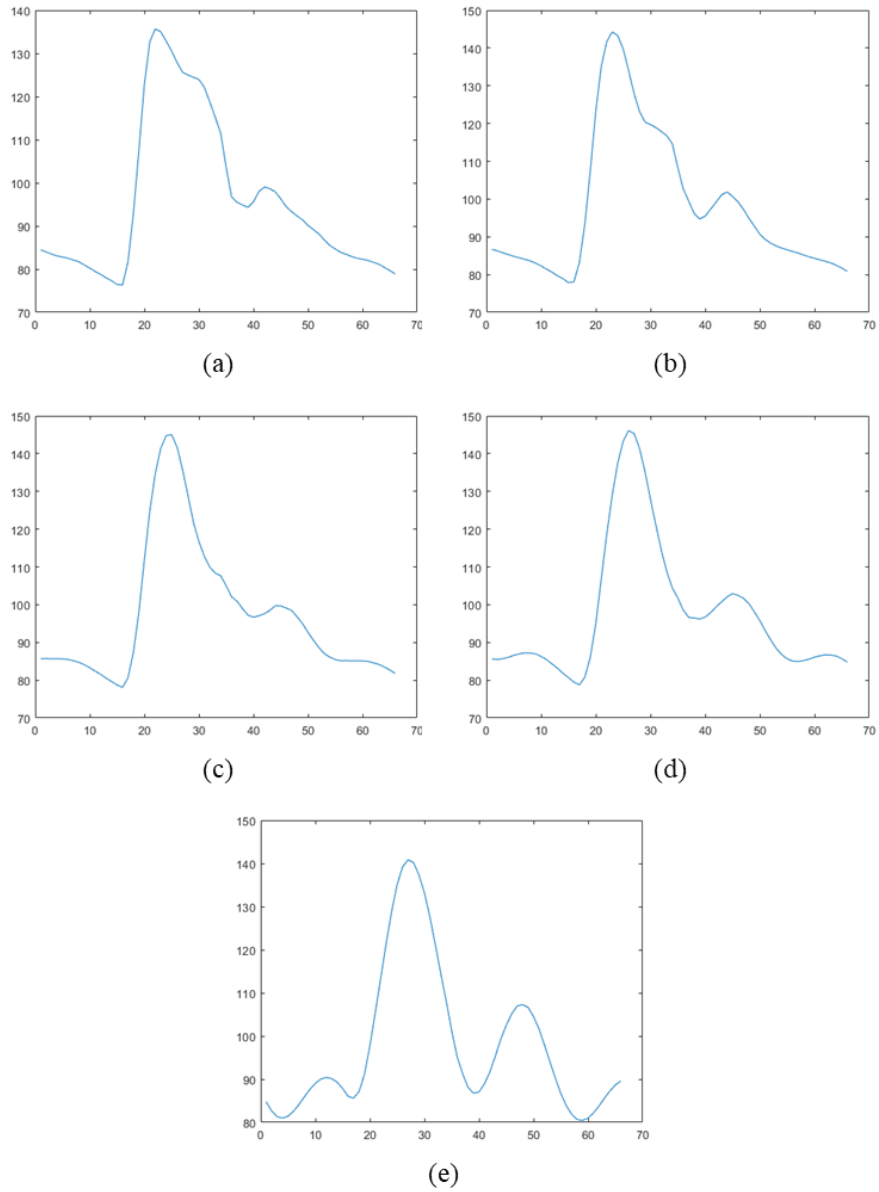


Figure 4-1 BP waveforms of Type 1

(a): Severity level 0, (b): Severity level 0.3, (c): Severity level 0.5,

(d): Severity level 0.7, (e): Severity level 1

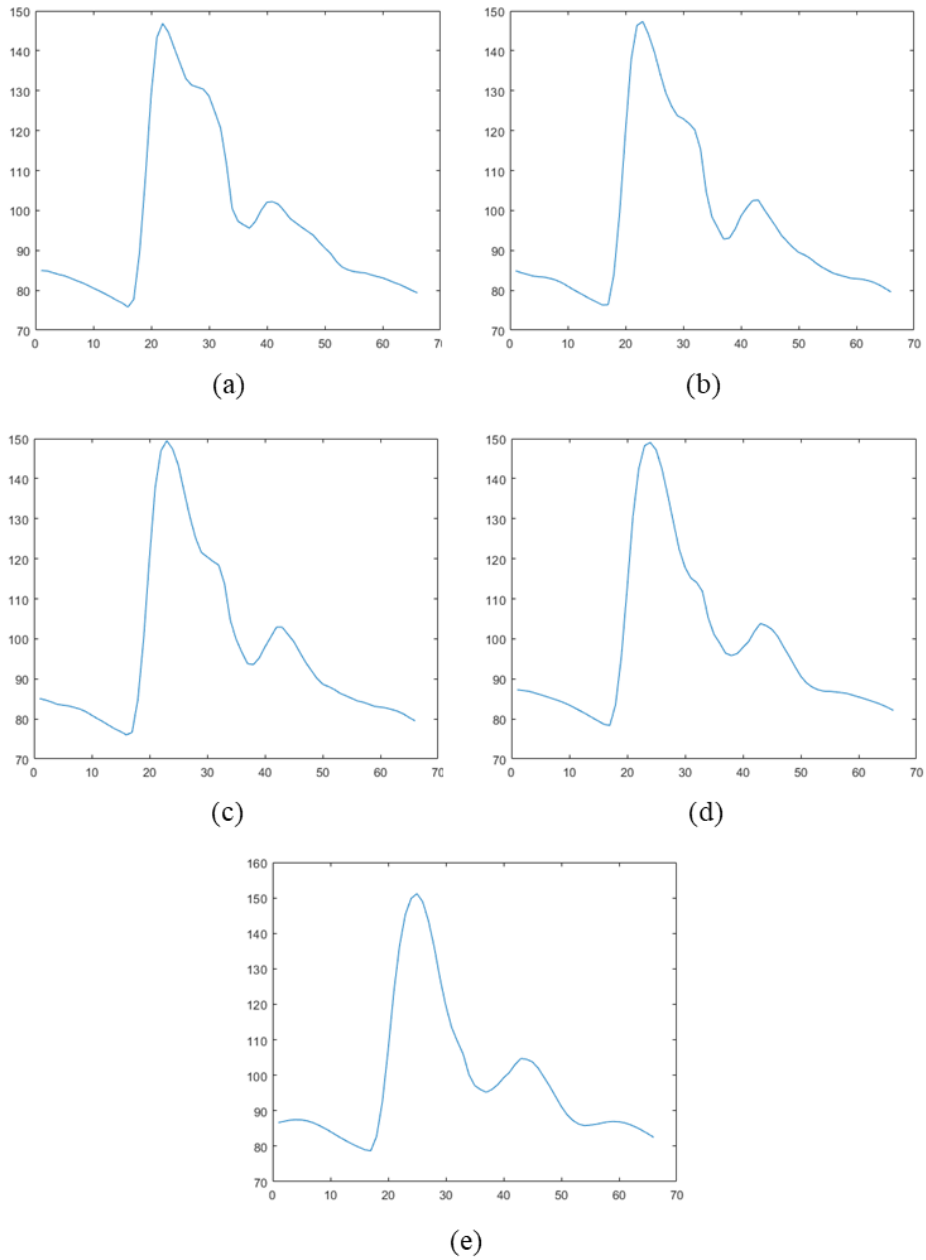


Figure 4-2 BP waveforms of Type 2

(a): Severity level 0, (b): Severity level 0.3, (c): Severity level 0.5,

(d) Severity level 0.7, (e): Severity level 1

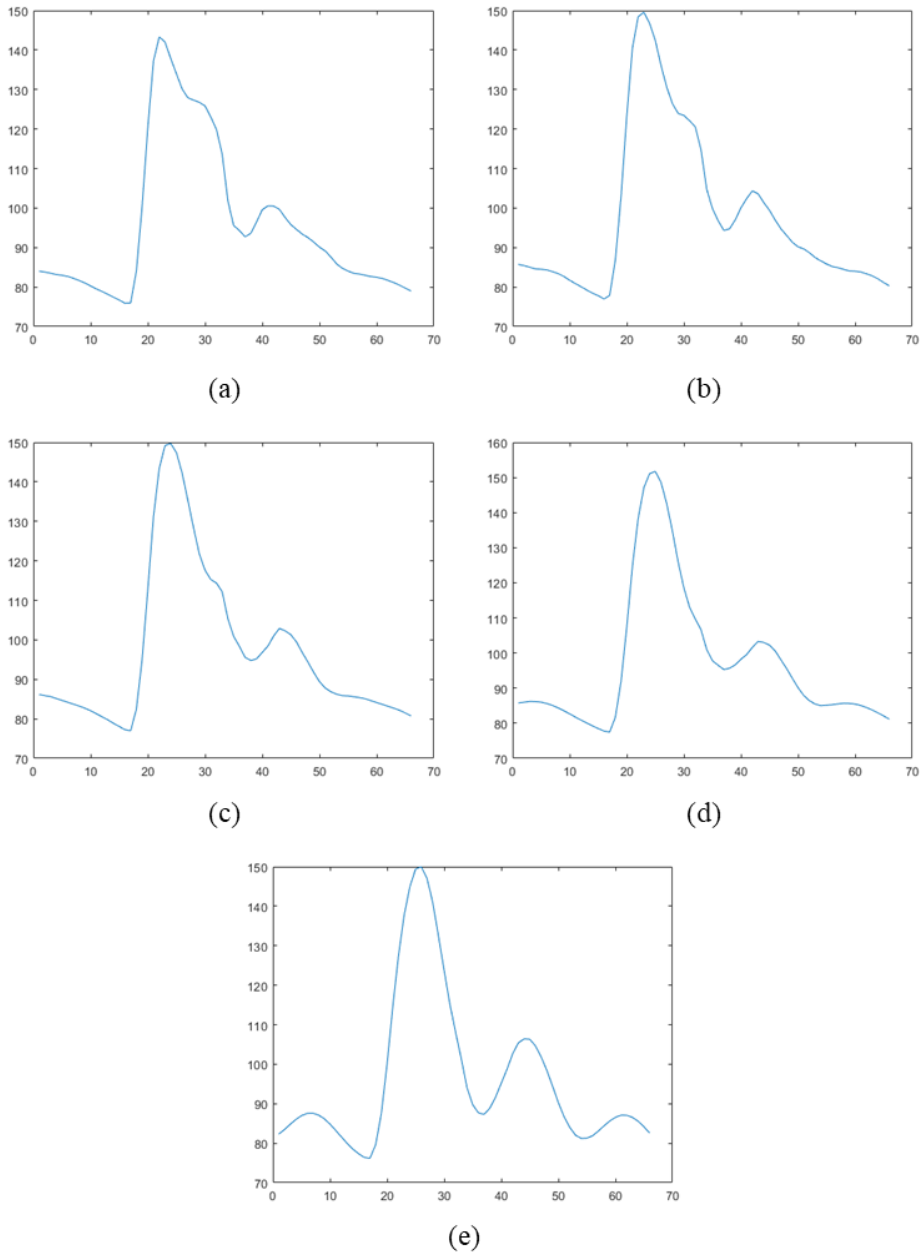


Figure 4-3 BP waveforms of Type 3

(a): Severity level 0, (b): Severity level 0.3, (c): Severity level 0.5,

(d): Severity level 0.7, (e): Severity level 1

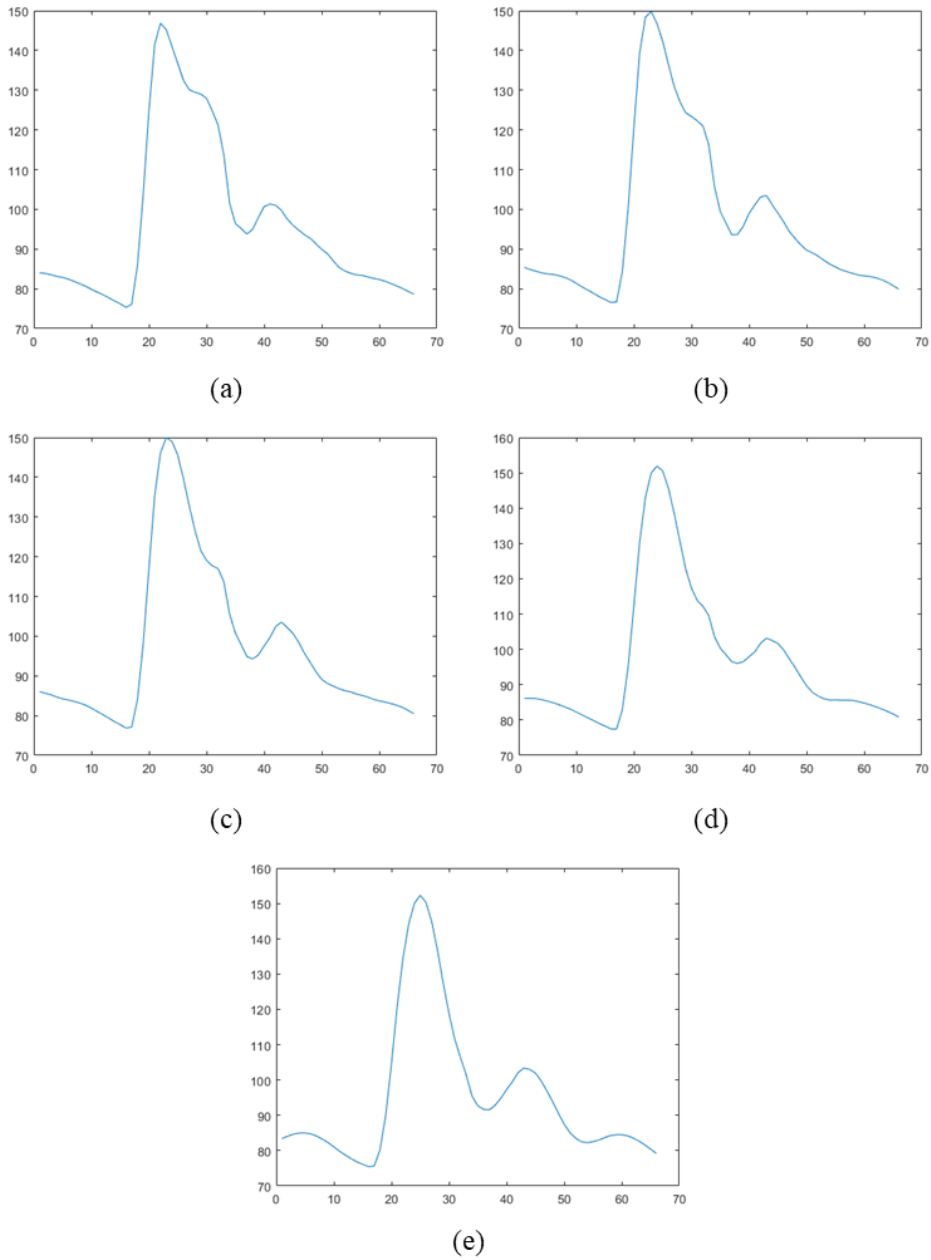


Figure 4-4 BP waveforms of Type 4

(a): Severity level 0, (b): Severity level 0.3, (c): Severity level 0.5,

(d): Severity level 0.7, (e): Severity level 1

4.2 Validation of Blood Pressure Waveform Data

We conducted a literature survey to ensure that these simulated data follow trends in real-world data. In this chapter, the validity of blood pressure waveform data is verified by comparison with the literature data. The disease in the literature examined was also a disease with an abdominal aortic aneurysm [12]. In the literature, it was confirmed that the blood pressure waveform became convoluted from normal to disease state.

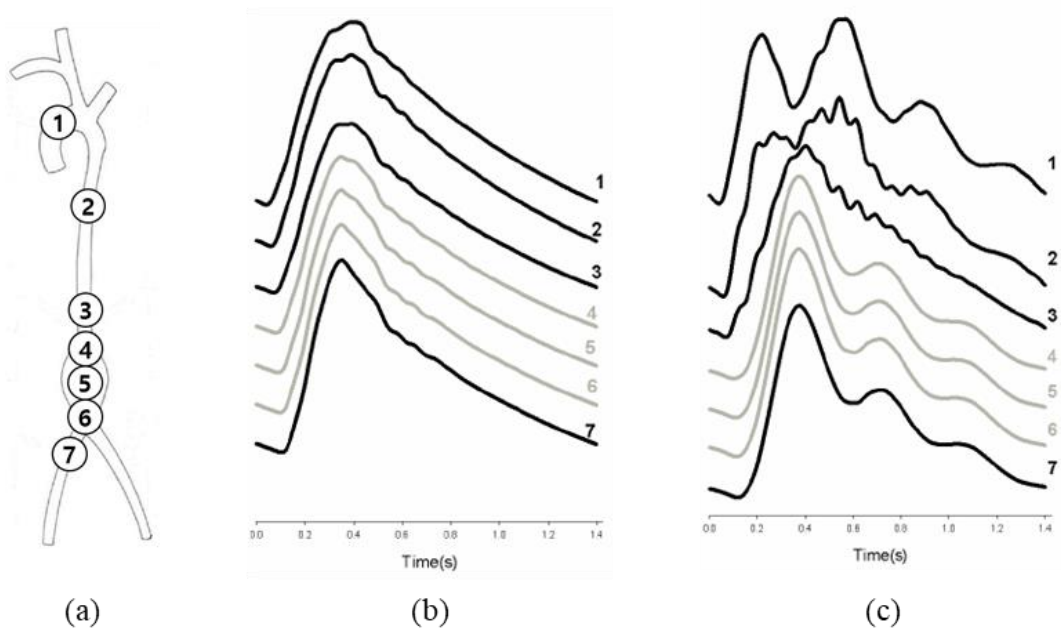


Figure 4-5 BP waveforms from the literature in the presence of an AAA [12]

(a): Abdominal aorta, (b): BP waveform in normal state,

(c): BP waveform in disease state

4.3 Summary and Discussion

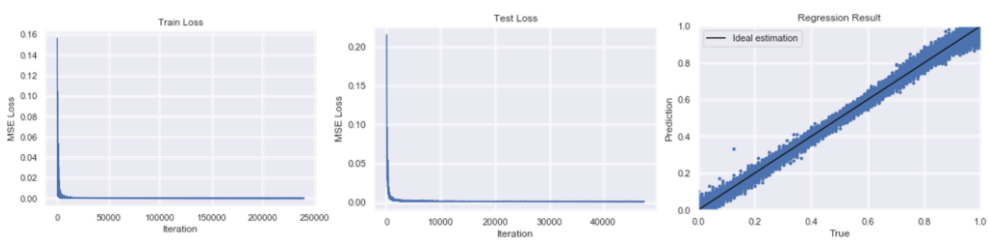
After implementing four types of aneurysm in TLM, blood pressure waveform data was acquired. A common characteristic found in four types of aneurysm models was that the more serious the disease became, the more convoluted the waveform. Furthermore, as the disease became more serious, the peak value of the waveform increased. When comparing results between types, special differences were difficult to find. A literature survey was conducted to verify that the acquired simulation data were significant. As a result, it was confirmed that the blood pressure waveform generated in this research model was similar to the trend. The following limitations exist in this verification: 1) Difficulty finding literature showing blood pressure waveforms in AAAs, and 2) verification was not possible through actual medical blood pressure waveform data.

Chapter 5. Regression Results

In this chapter, disease severity regression is performed using the blood pressure waveform data presented in Chapter 4. The tool to solve the regression problem is the DNN presented in chapter 3.3. To show the performance of the regression model, the train MSE loss and the test MSE loss were calculated. Finally, we present a regression result graph.

5.1 Loss and Regression Plots

From the results of performing DNN, it was confirmed that the train loss and test loss converged to zero in all aneurysm type. In addition, regression was well performed for all aneurysm types. The ideal regression result graph is in the form of $y = x$, and the closer the point is to this line, the better the regression performance. The case with the smallest train MSE loss was 0.0000317 in type 1. The smallest test MSE loss was found to be 0.0001498 in type 2. Since the smallest train loss and test loss are found in different types, it is difficult to say that the regression performance is the best for any type.



(a) (b) (c)

Figure 5-1 Regression result of Type 1

(a): Train MSE loss, (b): Test MSE loss, (c) Regression result graph

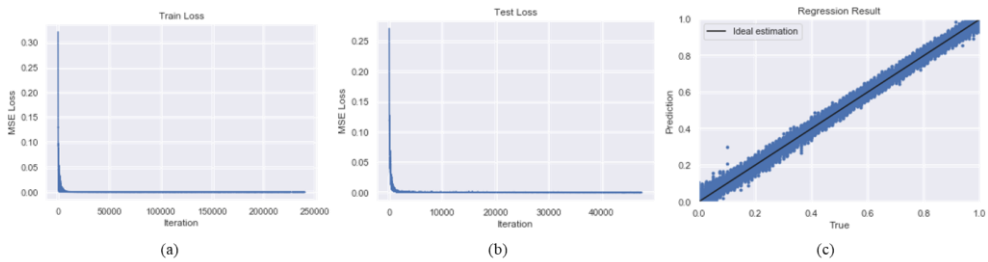


Figure 5-2 Regression result of Type 2

(a): Train MSE loss, (b) Test MSE loss, (c): Regression result graph

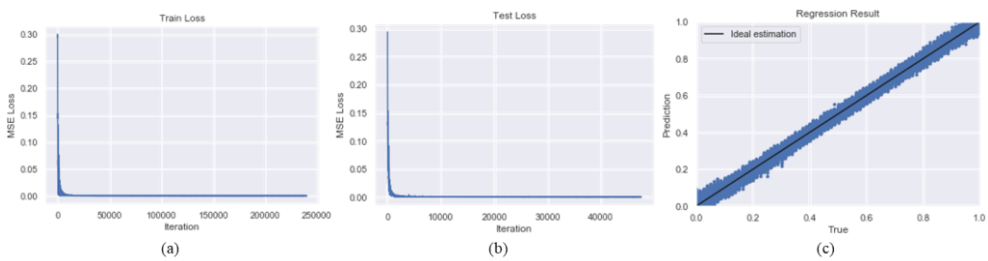


Figure 5-3 Regression result of Type 3

(a): Train MSE loss, (b) Test MSE loss, (c): Regression result graph

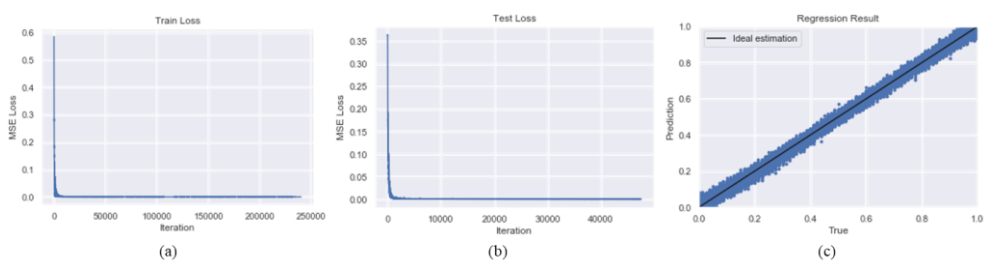


Figure 5-4 Regression result of Type 4

(a): Train MSE loss, (b) Test MSE loss, (c) Regression result graph

Table 5-1 MSE loss values

	Type 1	Type 2	Type 3	Type 4
Train MSE loss	0.317×10^{-4}	1.361×10^{-4}	0.362×10^{-4}	1.941×10^{-4}
Test MSE loss	2.842×10^{-4}	1.498×10^{-4}	2.643×10^{-4}	1.969×10^{-4}

5.2 Limitations

In this study, MSE loss was used as an index to suggest the performance of the regression model. Typically, regression performance is evaluated by how much the loss decreases. However, it is difficult to figure out what it means medically to suggest such a loss. In the literature that solved the disease-related regression problem, we investigated which indicators were presented, but no appropriate indicators were found. Therefore, the lack of an indicator that can suggest the performance of the regression model from a medical point of view is a limitation. No papers were found that regressed disease severity, and most of them were classified as the presence or absence of diseases.

5.3 Summary and Discussion

As a result of regression of disease severity through DNN, both train MSE loss and test MSE loss converged to zero. Also, as it appears close to ideal estimation, it can be confirmed that the regression performs well. When looking at the loss values, there is little difference from each other, so it is difficult to determine which type is better for performing regression. Finally, the diversity of individuals was reflected in the simulation data generation process. It is necessary to supplement that loss, which is used as an index to identify the performance of the regression model, is difficult to have any special meaning from a medical point of view.

Chapter 6. Conclusions

6.1 Summary and Contributions

In this dissertation, normal and disease data were created to compensate for the lack of data. In addition, disease severity regression was performed to determine the severity of the disease progression stage. Also, the diversity of individuals was reflected in the simulation data generation process. Contributions accordingly are as follows.

Contribution 1: Realization of desired disease by modifying simulation models with different target disease

First contribution according to this is that the target disease, abdominal aortic aneurysm, was implemented by modifying the existing simulation model. The possibility of implementing other cardiovascular diseases was confirmed if appropriate modifications were made to the model that implemented hemodynamics well. In addition, other diseases such as thoracic aortic aneurysm can be implemented by changing the disease location of the currently implemented aneurysm model.

Contribution 2: Generation of blood pressure waveforms with trends similar to literature

The second contribution is that it produced BP waveform data with a trend similar to that of the literature. This indicates that the model well reflects the hemodynamics in the presence of the disease. In addition, the diversity of individuals was considered

when generating BP waveform data.

Contribution 3: Disease severity regression using DNN

The third contribution is disease severity regression using DNN. This shows that deep learning can perform the role of diagnosing diseases and identifying the severity. It is also noteworthy that anatomical knowledge such as CT or MRI is required and time-consuming examination methods are not used. It is a great advantage when considering that it is possible to diagnose a disease and use a regression algorithm with only a simple procedure of measuring blood pressure.

6.2 Suggestions for Future Research

Considering the points to be supplemented in this study, there are the following directions for future research that can be suggested.

Issue 1: Preparation of medical indicators to suggest the performance of regression algorithm

Although the problem related to the disease was solved by using mechanical engineering knowledge, efforts to present its performance as a medically understandable indicator are needed. No suitable indicators were found through literature research. In addition to using the existing indicators, it is necessary to consider how to present the regression performance.

Issue 2: Implementation of a larger sized abdominal aortic aneurysm

The maximum diameter of aneurysm implemented in this study was 5cm. In real

world, larger-sized aortic aneurysms also exist. Assuming that it is actually commercialized, it is necessary to implement an AAA having a larger diameter and a complex geometry. It is essential to check whether the blood pressure waveform data acquired after implementing aneurysm is valid.

Issue 3: Simulation model verification using actual patient's blood pressure waveform data

In this study, the validity of the simulation data was verified through the tendency of BP waveform data in literature research. The more powerful verification method is to verify the data of the model by acquiring the data of real patients with AAA. Before commercializing this algorithm, verification through actual data will be essential.

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Abstract (Korean)

복부 대동맥류 진단을 위한 심층신경망 기반 질환 심각도 회귀

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임 주 현

의학 분야에서의 질병은 공학적인 관점에서 보면 결함에 해당한다. 기계 고장을 진단할 때는 예측 및 상태 관리 (prognostics & health management; 이하 PHM)가 필수적이다. PHM은 대상 시스템의 상태 저하를 추적하고 상태에 대한 정보를 생성한다. 본 연구에서는 대상 시스템을 인간으로 선정하였다. 대상 시스템의 대상 질병은 복부 대동맥류로 선정하였다. 동맥류와 관련된 중요한 이슈 중 두 가지는 진단 지표의 부재와 질환 데이터의 부족이다. 동맥류는 진단 지표를 사용하여 진단되지 않고 컴퓨터 단층 촬영(computed tomography; 이하 CT) 또는 자기 공명 영상(magnetic resonance imaging; 이하 MRI)과 같은 영상 촬영 기법을 사용하여 진단된다. 또한 이 질환은 사전에 진단하기 어렵기 때문에 질환 데이터의 확보가 쉽지 않다.

이러한 이슈들에 대한 하나의 솔루션으로써 본 연구는 심층 학습을 결합한 질환 진단 및 심각도 회귀 기법을 제안한다. 세 가지 연구 요지는 다음과 같다. 1) 시뮬레이션 모델을 통해 정상 및 질환 데이터 생성, 2) 질환 심각도 회귀 분석, 3) 데이터 생성 시 개인의 다양성

반영. 데이터는 시뮬레이션 모델을 사용하여 생성된다. 인간의 질환을 진단하기 위한 시뮬레이션 모델 중 하나로 전송 선로 모델(transmission line model; 이하 TLM)이 있다. 본 연구에서는 관련 논문에서 제안된 모델을 수정한 전송 선로 모델을 사용한다. 모델을 통해 혈압 파형 데이터를 얻기 위해서는 재귀 알고리즘을 사용하여 입력 임피던스를 계산해야 한다. 질환 발생률은 질환 심각도 회귀를 통해 모니터링 된다. 이때 심층 신경망을 회귀 분석을 수행하는 도구로써 사용할 수 있다. 생체 관련 매개 변수 값을 분포로 제공하면 개인의 다양성을 반영할 수 있다. 본 연구에서는 각 변수의 특성을 고려하여 적절한 분포를 부여하였다. 본 연구의 구조는 시뮬레이션 모델 수정, 데이터 생성, 심층 신경망 설계 및 심각도 회귀 문제 해결이라는 네 가지 작업으로 구성된다. 문헌 조사를 통하여 본 연구에서 생성된 혈압 파형 데이터의 유효성을 검증하였고, 평균 제곱 오차 (mean squared error; 이하 MSE) 손실 값을 구해 회귀 분석을 잘 수행되었음을 확인하였다.

주제어: 심혈관 질환(cardiovascular disease)
복부 대동맥류(abdominal aortic aneurysm)
심각도 회귀(severity regression)
혈압 파형 데이터(blood pressure waveform data)
심층 신경망(deep neural network)

학 번: 2018-25189

감사의 글

오지 않을 것만 같던 순간도 오는군요. 매일 같은 장소, 같은 풍경을 보면서도 시간이 흘러갔다는 것을 새삼 깨닫습니다. 대학원 생활은 제 인생에서 가장 임팩트가 컸습니다. 또래 무리에 섞여서 초중고 졸업하고 남들 다 가는 대학까지 갔지만 대학원이라는 선택부터는 뭔가 색다르게 느껴졌습니다. 지금까지 왔던 인생경로에서 새로운 샛길을 뽑아낸 것 같았습니다. 단순히 기계공학 연구원이 되고 싶다는 꿈을 위해 선택한 것이었지만 정확히 대학원이 어떤 것인지 잘 몰랐던 저에게 대학원은 매운 맛이었습니다. 학생과 사회인의 중간 어딘가에 위치한 신분이 당황스러웠습니다. 더딘 속도로 배우면서 기대에 못 미치는 성과를 낼 때마다 자괴감이 들었고, 시도는 많이 했지만 실패한 결과를 가져갈 때마다 슬펐습니다. 원하는 결과치에 도달하지 못할 때마다 나는 왜 성장하지 않는지, 이제는 성장할 시간이 아니라 이미 성장체로 왔었어야 하는 건지 혼란스러웠습니다. 못하는 자신이 부끄럽고 동료들에게 미안해서 위축된 채로 한동안 지냈었습니다. 그 힘든 시기에 힘이 되어준 준민오빠, 현배오빠께 정말 감사드립니다. 솔직히 두 분께서 안 계셨으면 여기까지 못 왔을 것 같습니다. 깊은 수렁에서 저를 천천히 꺼내주신 한진오 교수님께도 깊이 감사드립니다. 처음으로 제대로 해보는 과제에서 길을 찾지 못할 때마다 정성껏 도와주신 근수오빠, 수지오빠께 감사드립니다. 피폐해져 있을 때 인간다운 생활을 할 수 있도록 도와주신 윤한오빠께 감사드립니다. 부족한 부사수를 힘들게 이끌어주신 사수 김수호 오빠께도 감사드립니다. 연구하면서, 과제하면서 도움 많이 주신 인찬오빠께도 감사드립니다. 연구실에

들어올 수 있게 해주신 윤병동 교수님께 감사드립니다. 여기 있을 수 있어서 행복합니다. 연구실 선배님들, 후배님들께도 모두 감사드립니다. 그리고 날 때부터 함께한 엄마, 아빠, 오빠께도 감사드립니다. 자주 만나지는 못하지만 만날 때마다 관심 가져주시는 친척분들께도 감사드립니다. 제주도에 있어서 자주 볼 수는 없지만 고등학교의 행복한 기억을 갖고 살아갈 수 있게 해주는 은지에게도 감사합니다. 그리고 마지막으로 처음부터 지금까지 그리고 앞으로도 함께할 자신에게 고맙고 수고했다고 말하고 싶습니다. 앞으로 어떤 인생을 살게 될지 알 순 없지만 절망하고 좌절하더라도 꼭 포기는 하지 않도록 노력하려고 합니다. 감사합니다.

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