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Articles

Vascular access function assessment by combination of normalized cross-correlation coefficient and duration time

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I. Introduction

In blood purification therapy, vascular access (VA) is established when a surgical anastomosis is performed between an artery and a vein to perform blood removal and blood return in extracorporeal circulation. At the VA, the flow of arterial blood from artery to vein is very powerful, creating non-physiological hemodynamics. The nonphysiological hemodynamics and frequent punctures damage the vascular wall, causing the vascular intima to thicken, triggering stenotic lesions. Monitoring of VA function is defined as evaluating physical findings related to VA to detect VA dysfunction, and shunt murmur auscultation is one method for performing such monitoring. Since auscultation enables quick and easy diagnosis of the shunt murmur before the start of dialysis, and the results can be used for non-invasive assessment of changes in VA function, it is an essential technique for VA management. That said, it has been noted that the results of auscultation depend on the amount of experience of the dialysis staff and subjective assessments, and they, therefore, lack quantification and objectivity. Accordingly, there is a need for clear VA function assessment criteria using the shunt murmur to be established. The most common cause of VA dysfunction is a stenotic lesion, and an important challenge is to determine how to maintain the form and function of VA for as long as possible. In recent years, Vascular Access Intervention Therapy (VAIVT) has been advancing rapidly as a minimally-invasive method with low loss of vascular access, in which the same lesion can be treated repeatedly[1)]. There is, therefore, an even greater need to be able to appropriately assess VA function based on changes in the shunt murmur and determine the best timing for performing VAIVT.

Shunt murmurs are said to occur when a large volume of blood passes quickly through an arterio-

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venous anastomosis and sprays like a jet, causing the vascular wall to vibrate[2]. In our previous clinical studies, we found the frequency band of shunt murmurs to be roughly 20 to 1,000 Hz[3]. When VA function is good, you can hear a shunt murmur called Low Pitch that has a continuous low frequency component as the main component. As VA function declines, this Low Pitch changes to a shunt murmur called High Pitch, with an intermittent high frequency component as the main component[4, 5]. We converted shunt murmur signals obtained during good VA function into wavelets and calculated the normalized cross-correlation coefficient R that represents temporal changes in VA function in the frequency domain and normalized duration time (NDT) representing temporal changes in the time domain. We are proposing a non-invasive method for quantitatively assessing VA function based on temporal changes in R and NDT[6–8]. However, the presence of severe stenosis or occlusion triggers a mechanism to relieve ischemia that involves creating new circulation, called collateral circulation. It may be impossible to assess VA function correctly with R alone in cases where collateral circulation has developed. We therefore created a branched artificial angiostenosis model to simulate collateral circulation and experimentally investigated changes in R and NDT with different stenosis rates in order to determine the effectiveness of this method for VA with collateral circulation.

II. Experimental Methods

10 mm-long acrylic stenosis parts with incrementally increasing stenosis rates were inserted into silicon tubes with an inside diameter of 6 mm and an outside diameter of 8 mm to create straight artificial angiostenosis models with different stenosis rates. To reproduce a simulated shunt murmur under conditions that are more similar to living tissue, the fabricated models were fixed to a special purpose jig, and water was pumped through the jig. Water was pumped through the models with a simplified pulsatile pump. The conditions for pulsatile inflow were a pulse frequency of 60 pulses per minute, duty rate of 50%, maximum inflow port pressure of 140 mmHg, and minimum inflow port pressure of 80 mmHg. The intracircuit flow rate was measured with a measuring cylinder downstream of the stenosis. The pressure at the inflow and outflow port of the stenosis models was measured with a biological information monitor. Simulated shunt murmurs produced during pulsatile circulation were measured with the Bio Sound Analyzer (BSA). For the sensors needed to measure the shunt murmurs, floating type acceleration phonocardiographic sensors (diameter, 20 mm; height, 16 mm; weight, 41 g) were used. The BSA can measure biological sounds on up to three channels at the same time and has a 44.1-kHz sampling frequency and 16-bit resolution. The acceleration sensors were attached to the 10-mm silicon tube downstream of the stenosis to obtain simulated shunt murmur signals just after the stenosis. Since the amplitude of the simulated shunt murmur varied by stenosis rate, changing the signal amplification of the BSA could result in different luminance of the color map images obtained after wavelet conversion. Therefore, the signal amplification was set to the same level even for different stenosis rates when taking measurements. The simulated shunt murmur signals obtained were then converted into wavelets, and time-frequency analysis was performed. Next, a Wavelet Bmp Analyzer (WBA) was used to calculate R and NDT from the results of time-frequency analysis. In these investigations, to quantitatively assess changes in simulated shunt murmurs accompanying changes in stenosis rate, the simulated shunt murmur signals from a model without stenosis (stenosis rate of 0%) were used as the reference data, and the simulated shunt murmur

signals obtained from models with incrementally increasing stenosis rates were used as comparison data. R was then calculated from the image results of wavelet conversion of the reference data and comparison data. The WBA can approximate the measured simulated shunt murmur signals with a cubic spline function and calculate the time required for the amplitude to attenuate from the peak amplitude of the fitted curve to an arbitrary threshold. For this investigation, the time required to attenuate from the peak amplitude to 10% of the amplitude was determined, and this value was used to calculate NDT. Next, a T-shaped connector was attached to a point upstream of the stenosis on straight artificial angiostenosis models with different stenosis rates to create a branch in the circulation route, and a silicon tube with an inside diameter of 4 mm was attached to the T-shaped connector to reproduce collateral circulation. A branched artificial angiostenosis model that simulates collateral circulation is shown in ***Fig.1***. In the experiments with models that had collateral circulation, a clamp was attached downstream of the stenosis part with a stenosis rate of 90%, and the flow rate was adjusted so as to drop by half on the stenosis side when the stenosis rate was 90%. These branched artificial angiostenosis models were used to perform the same experiments that were performed with the straight artificial angiostenosis models.

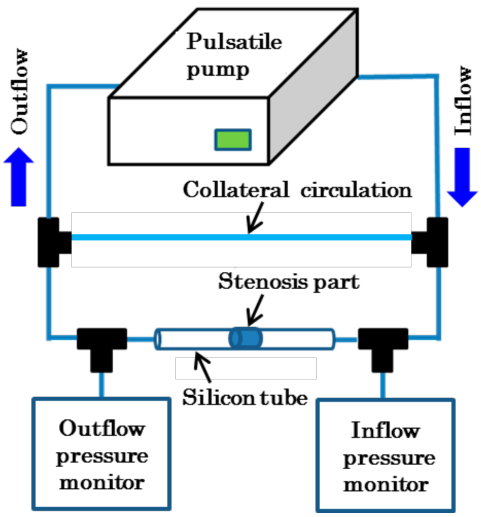
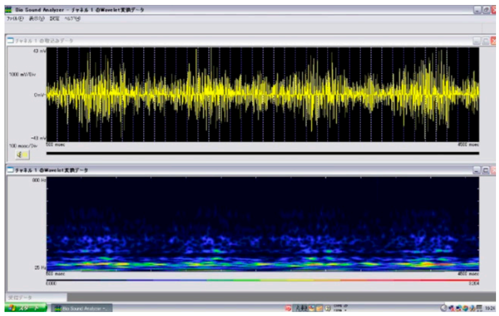


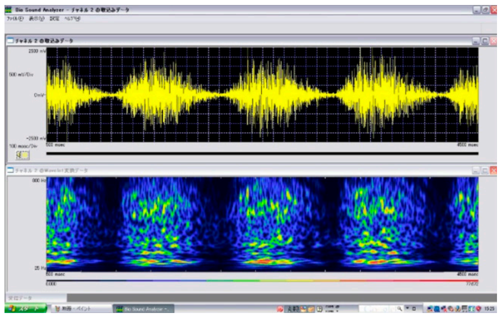
Fig.1 Branched artificial angiostenosis model

III. Experimental Results

R and NDT were calculated for the simulated shunt murmur measured downstream of the stenosis in the straight artificial angiostenosis models with incrementally increasing stenosis rates. The amplitudes of the measured simulated shunt murmur signals were similar to those of the shunt murmur signals from patients undergoing maintenance hemodialysis. This shows the simulated shunt murmur signals measured from straight artificial angiostenosis models with stenosis rates of 20% and 80% and the results of wavelet conversion (***Fig.2***). For both analytical results, the upper part shows the simulated shunt murmur signal (vertical axis, signal amplitude [mV]; horizontal



(a) stenosis rate : 20%



(b) stenosis rate : 80%

Fig.2 Simulated shunt murmur signals and results of wavelet conversion
(Straight artificial angiostenosis model)

axis, time [ms]), and the lower part shows the results of wavelet conversion of the simulated shunt murmur signals from the upper part (vertical axis, frequency [Hz]; horizontal axis, time [ms]). A color map for the image results of wavelet conversion on the lower part represents the size of the amplitude spectrum for each frequency component increasing from blue to red. It also shows changes in R and NDT_{10} with differences in stenosis rate of the straight artificial angiostenosis models (***Fig.3***). In the straight artificial angiostenosis model, the murmur obtained with a low stenosis rate was similar to a continuous Low Pitch with a low frequency component as the main component, but the process of the murmur turning into one that is similar to a High Pitch with a high frequency component as the main component as the stenosis rate increased could be reproduced. It also shows the results of measurements of the intracircuit flow rate and intracircuit pressure during measurement of the simulated shunt murmur for each stenosis rate (***Fig.4***). Of particular note is that a stenosis rate of more than 50% caused a decrease in the intracircuit flow rate accompanied by a drop in amplitude in the simulated shunt murmur signals. Moreover, a continuous murmur from the start to the end of the pulse corresponding to the systolic phase in the heartbeat was measured when the stenosis rate was smaller. In contrast, as the stenosis rate increased, the intracircuit flow rate decreased, and the duration of the continuous murmur shortened. With these changes, R and NDT tended to decrease as the stenosis rate increased.

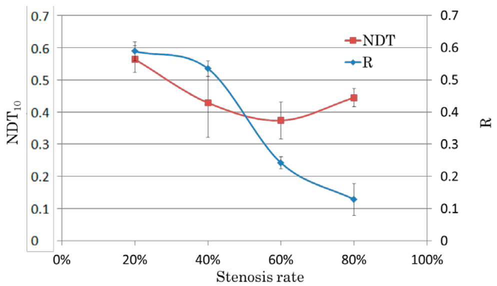


Fig.3 Changes in R and NDT10 for each stenosis rate
(Straight artificial angiostenosis model)

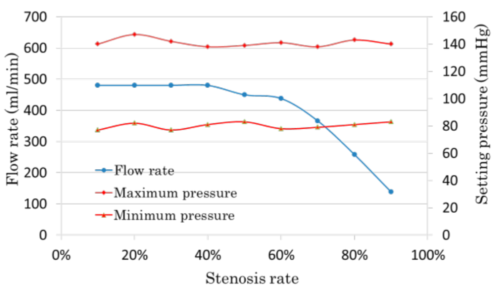
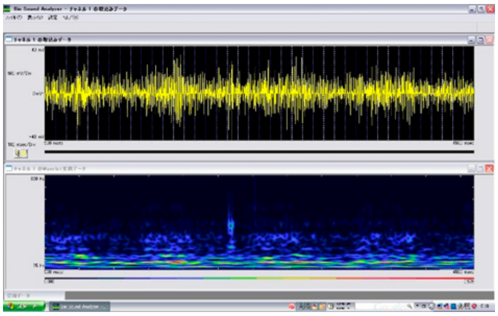
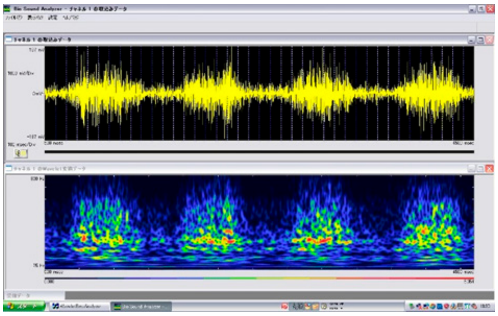


Fig.4 Intracircuit flow rate and intracircuit pressure for each stenosis rate
(Straight artificial angiostenosis model)

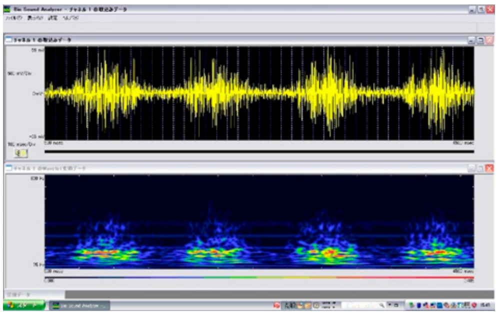
The simulated shunt murmur signals measured



(a) stenosis rate : 20%



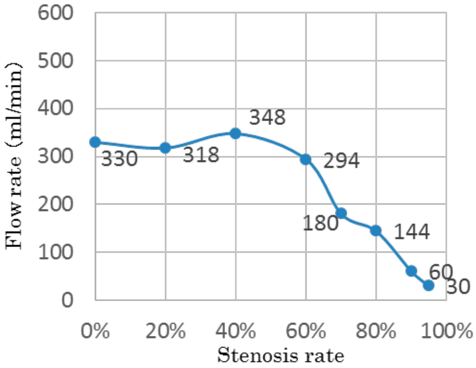
(b) stenosis rate : 80%



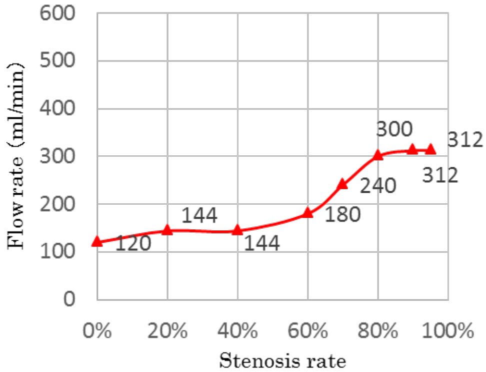
(c) stenosis rate : 95%

Fig.5 Simulated shunt murmur signals and results of wavelet conversion
(Branched artificial angiostenosis model)

from branched artificial angiostenosis models simulating collateral circulation with stenosis rates of 20%, 80%, and 95% and the results of wavelet conversion are shown in ***Fig.5***. The results of flow rate measurement on the stenosis side for the stenosis rate and in the collateral circulation are shown in ***Fig.6***. First, the results of wavelet conversion of the simulated shunt murmur with 20% and 80% stenosis rates, respectively, showed similar changes in frequency components and duration as the straight artificial angiostenosis models. In the analytical results from a stenosis rate of 95%, only low frequency components that were similar to cases with no stenosis were seen as shown in ***Fig.7***, and the results were impossible to distinguish from a case with a low stenosis rate from comparison of the frequency components alone.



(a) stenosis side



(b) Collateral circulation side

Fig.6 Flow rate on stenosis side and collateral circulation side for each stenosis rate
(Branched artificial angiostenosis model)

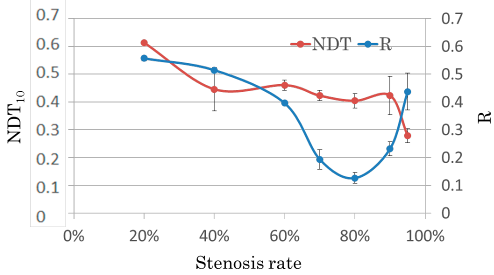


Fig.7 Changes in R and NDT10 for each stenosis rate
(Branched artificial angiostenosis model)

Up until a stenosis rate of about 90%, the flow rate on the stenosis side was maintained to a certain degree, suggesting that R tended to decrease relatively uniformly. When the stenosis rate increased to 95%, however, R reversed and began increasing. Nevertheless, the duration dropped dramatically at a stenosis rate of 95%, indicating that NDT dropped continuously and uniformly when severe stenosis, as would be seen immediately before VA occlusion, was simulated.

IV. Discussion

The simulated shunt murmur signals in the straight artificial angiostenosis models with incrementally increasing stenosis rates showed that it was possible to reproduce a state that was similar to body tissue by fixing the model to a special purpose jig and pumping water through the jig. In the analytical results from straight artificial angiostenosis models with incrementally increasing stenosis rates, both R and NDT were low with stenosis rates from 20% to 80%. R, which is a parameter quantifying the changes in shunt murmur in the frequency domain, was calculated as reference data for simulated shunt murmur data without stenosis (stenosis rate of 0%). In the simulated shunt murmur without stenosis (stenosis rate of 0%), only low frequency components are detected. In contrast, among the frequency components of the comparison data, the low frequency component gradually diminishes and disappears as the stenosis rate increases, and moderate to high frequency components appear. These changes are likely the results of vibration of the vascular wall caused by turbulence components arising downstream of the stenosis as the stenosis rate increases. The image results of wavelet conversion of the reference data and comparison data begin to diverge as the stenosis rate increases, resulting in a drop in R. For NDT, which is a parameter quantifying changes in shunt murmur in the time domain, as the stenosis rate increases, water only flows during the time phase with a high enough pressure for it to pass through the stenosis site. Accordingly, the vascular wall vibrates only during the phase in which water flows, and the water flow breaks during the phase that corresponds to the diastolic phase of the heartbeat, creating a short duration. This may be the reason why NDT decreases similarly to R at this point.

In the experimental results in artificial angiostenosis models with collateral circulation, R tended to decrease as the stenosis rate increased up to a stenosis rate of 90%, but it then reversed and began to increase when the stenosis rate was 95%, simulating the state just before occlusion. Meanwhile, NDT continued to decrease even when the stenosis rate increased. Analysis of the results of wavelet conversion of the simulated shunt murmur heard when the stenosis rate ranged from 20% to 80% showed similar R and NDT trends as the experimental results observed in the straight artificial angiostenosis models. When the stenosis rate was 95%, the amplitude of the simulated shunt murmur was markedly lower than the amplitude when the stenosis rate was low, and the frequency components were mainly comprised of the low frequency component similar to the Low Pitch heard when there is no stenosis. When the water flows through the stenosis site, it will only flow during the phase corresponding to the systolic phase of the heartbeat during which there is sufficient pressure for the water to pass. As a result, when there is a severe stenosis, for example with a stenosis rate of 95%, the volume of water flowing through the stenosis site drops drastically, the duration decreases markedly, and NDT drops.

It has already been reported that, if there is a severe stenosis in the blood vessel shunt of a patient undergoing maintenance hemodialysis, collateral circulation will develop, and most of the VA blood will flow through this collateral circulation, resulting in an excessive decrease in the blood flow through the stenosis site. As this change occurs, looking at the changes in the frequency domain shows that the shunt murmur also changes to one similar to the Low Pitch that is heard when there is no stenosis. Because of this, especially in VA in which collateral circulation has developed, assessing VA function with only R that shows frequency changes in shunt murmurs may result in mistakenly judging VA function to be good despite the presence of a severe stenosis. NDT, which is being proposed, however, continues to drop as the stenosis rate increases until just before occlusion, and it may therefore be possible to use NDT together with R to detect the process of stenosis progression with high sensitivity as numerical changes, even in cases with collateral circulation.

In recent years, with ultrasonography, which is recommended as one way to screen VA function and form, it has become possible to measure not only the brachial artery flow rate, but also the Resistive Index (RI) and stenosis rate. RI is a parameter that reflects the peripheral blood vessel resistance obtained from pulse-Doppler waveforms. It is calculated with the formula (peak systolic velocity - end diastolic velocity) / peak systolic velocity, and it increases when stenosis forms in a blood vessel, because the peripheral blood vessel resistance increases. A brachial artery flow rate of 500 mL/min and RI of 0.6 are roughly correlated, so it has been reported that setting these as the cutoff values can be a guide when considering treatment for poor blood removal or PTA[9, 10]. When there is no stenosis, the blood flow velocity waveform pattern seen on pulse-Doppler is a steep increase in peak systolic velocity at the start of the systolic phase and a gentle decrease as the pulse moves to the diastolic phase. In contrast, if there is a stenosis rate of about 50%, the velocity drops rapidly from the peak systolic velocity, and a notch appears, after which the velocity drops greatly in the diastolic phase. When the stenosis rate becomes 50% or more, the blood flow velocity drops steeply from the peak systolic velocity, becoming extremely sharp, then a counterflow consistent with the notch appears, and the velocity gradually moves to the diastolic phase and hits zero for a moment. In our measurements with a low stenosis rate, the signal amplitude of the simulated shunt murmur continued from the systolic phase to the diastolic phase and then decreased gradually. As the stenosis rate increased, the peak signal amplitude dropped, the signal amplitude was observed only during the phase corresponding to the systolic phase, and the signal changed to an intermittent and steep signal. In our investigations, it was determined experimentally that these types of changes in shunt murmur signal amplitude are very similar to the changes in pulse-Doppler waveform during RI calculation. Therefore, if the relationship between NDT and RI calculated from temporal changes in shunt murmur signal amplitude is clarified, it may be possible to measure and analyze shunt murmurs quickly before starting dialysis to obtain an NDT similar to RI to be used as an indicator for estimating angiostenosis.

V. Conclusion

The acoustic properties of shunt murmurs vary by not only blood vessel inner diameter and blood flow rate, but also by various unique patient variables, such as hardness of the blood vessel, damage in the vascular wall from punctures, and nonphysiological hemodynamics caused by the VA. Nevertheless, information obtained from shunt murmurs reflects VA function appropriately and can be extremely useful. It is therefore recommended as a routine method for physical assessment despite the fact that there is no standard objective method for its evaluation. Nonetheless, there have been no reports of studies testing methods to estimate stenosis rates from changes in shunt murmurs and quantify the decreases in VA function. By creating simple VA models with incrementally increasing stenosis rates and experimentally investigating the acoustic properties of the shunt murmur, as in the present study, it is possible to clearly determine the occurrence and progression of stenotic lesions from changes in the R and NDT values that were proposed. In particular, if a correlation is obtained between NDT and RI, it may be possible to use NDT to estimate the stenosis rate even in VA with collateral circulation that cannot be assessed with R alone. This suggests that experimentally creating various shapes of VA models and eliminating unique patient parameters to investigate the acoustic properties of shunt murmurs corresponding to changes in stenosis rates, as in the present study, may aid in the establishment of objective assessment criteria.

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