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MULTIFACETED EVALUATION OF ARTERIAL FUNCTION THROUGH TRANSMURAL PRESSURE MANIPULATION

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INTRODUCTION

Healthiness of the arteries can be evaluated with their mechanical properties and functions of the cells comprising the vessel wall. Major cell types found in blood vessel wall include endothelial cells (ECs) in the lumen and smooth muscle cells (SMCs) in the wall. Function of ECs has been assessed with flow-mediated dilation (FMD) [1]. In standard FMD protocol, the brachial artery is occluded first for 5 min, and then reperfused to measure its dilation [2]. The dilation is caused by NO secreted by the ECs in response to abrupt increase in wall shear stress at the brachial artery, and the amount of dilation, i.e., the amount of NO secretion is believed to reflect endothelial cell function. However, the dilation is inhibited not only by the reduction of NO production in the ECs but also by the decrease in the vasomotor activity of the SMCs. To evaluate smooth muscle activity, vasodilation assay with nitroglycerin has been used. Nitroglycerin is a powerful vasodilator compared to shear stress increase and this assay might not be able to detect subtle changes in smooth muscle contractility as FMD assay does for the ECs. Thus, a method for the evaluation of vasomotor activity of the SMCs needs to be developed.

Clinically, mechanical properties of the artery have been evaluated with mechanical parameters such as stiffness and compliance obtained in a physiological pressure range. It is well known that these parameters are highly pressure-dependent and a method to obtain artery stiffness in a wide pressure range has been awaited.

In this study, we have developed a new method to evaluate vasomotor activity of the SMCs and to obtain pressure-diameter relationship of the artery in a wide pressure range by changing its transmural pressure [3].

METHODS

Principle of transmural pressure manipulation is shown in Figure 1. A rigid airtight chamber equipped with a US probe (Figure 2) was attached to the upper arm to manipulate transmural pressure of the brachial artery by changing the pressure in the chamber. Pressure-diameter relationship of the artery was obtained by measuring its diameter change with the US probe during transmural pressure manipulation. Endothelial function was measured with a standard FMD protocol. Smooth muscle function was evaluated by its myogenic response, i.e., spontaneous contraction of the artery following its stepwise passive dilation caused by the stepwise application of negative pressure to the chamber. We call this response a pressure-mediated contraction (PMC).

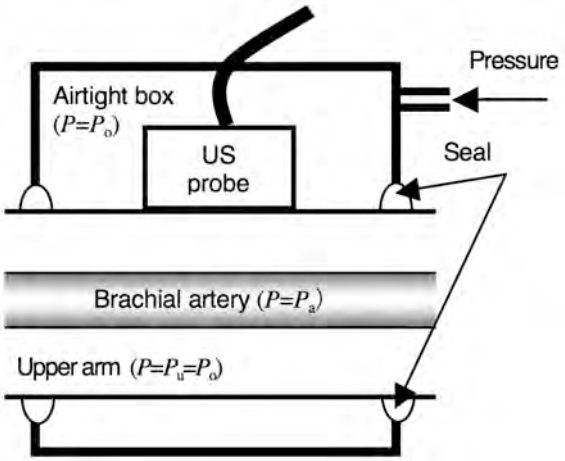

Figure 1: Schematic diagram of the transmural pressure manipulation method.

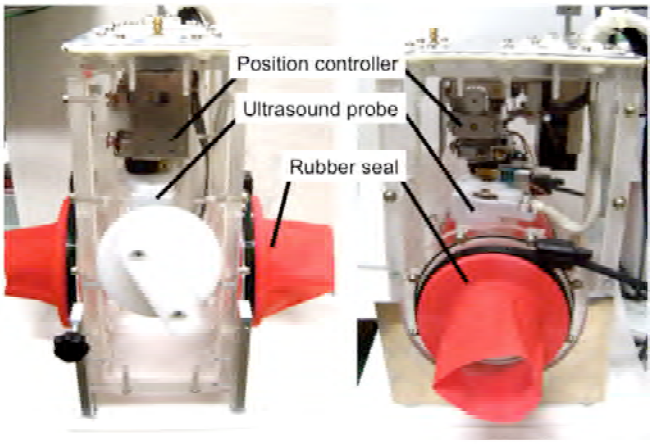

Figure 2: The airtight chamber with a US probe.

RESULTS AND DISCUSSION

Figure 3 shows an example of pressure-diameter relationship obtained in the left brachial artery of a 22-y-old male. Non-linear relationship typical to the arteries was obtained. Typical change in brachial artery diameter during FMD and PMC measurements are shown in Figure 4. In FMD measurement (upper panel), the artery diameter began

to increase after the release of the forearm cuff occlusion and reached a plateau in 30-40 s. A parameter %FMD was obtained as %FMD = $(D_2 - D_1)/D_1$ x 100 (%), where D_1 is the baseline diameter of the artery before occlusion and D_2 is the peak diameter after reperfusion. In the PMC measurement (lower panel), the diameter increased stepwise in response to negative pressure loading (-50 mmHg) and then decreased sharply to the diameter slightly larger than that before negative pressure loading. A parameter %PMC was calculated as %PMC = $(D_3 - D_4)/D_3$ x 100 (%), where D3 is the peak diameter and D4 the diameter just before unloading.

An example of time course changes of FMD and PMC responses measured simultaneously in a 27-y-old male is shown in Figure 4. Even measured in the same person, %FMD varied widely in 4 days. Roughly speaking, PMC and FMD responses showed reverse changes to each other, indicating that increase in SMC contractility may stimulate PMC response and suppress FMD response. It is interesting to note that %PMC was highest in Day 4 when he attended a meeting relating to job hunting. Taken together, PMC may change depending on the mental condition of subject, causing change in FMD.

CONCLUSIONS

Multifaceted evaluation of artery function through transmural pressure manipulation would be useful for precise evaluation of the progression of atherosclerosis.

ACKNOWLEDGEMENTS

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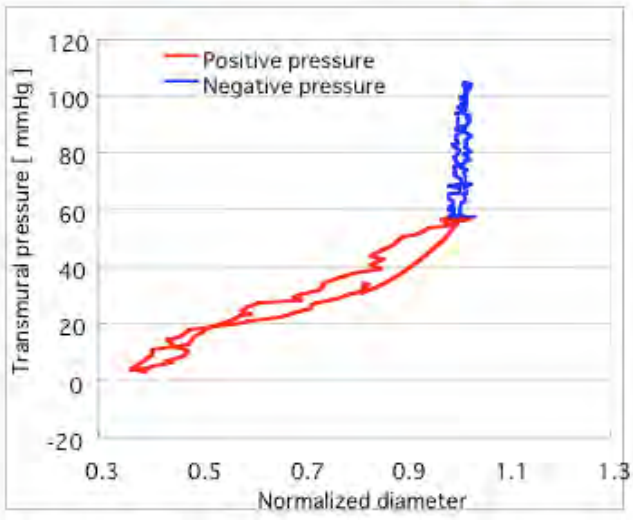

Figure 3: Typical pressure-diameter curve of the right brachial artery of a 22-y-old male.

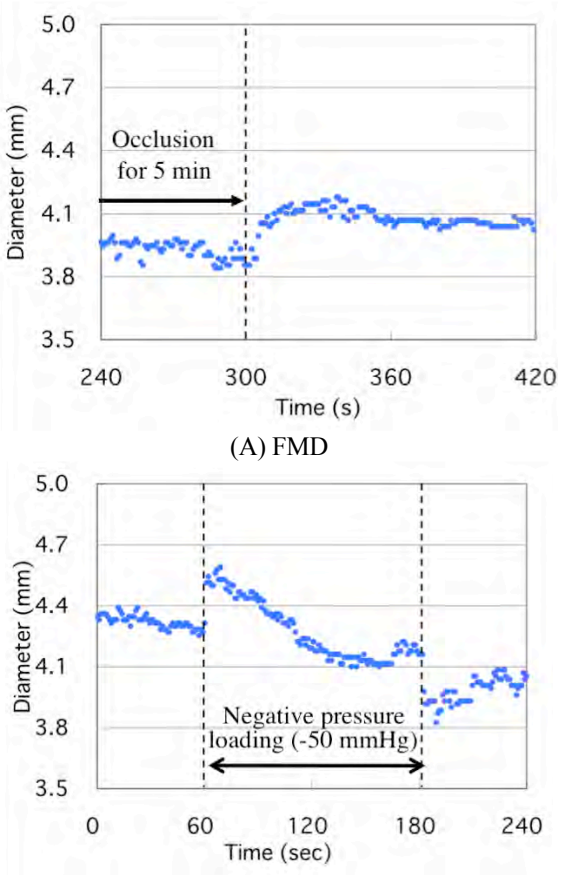

Figure 4: Typical example of FMD (A) and PMC (B) responses.

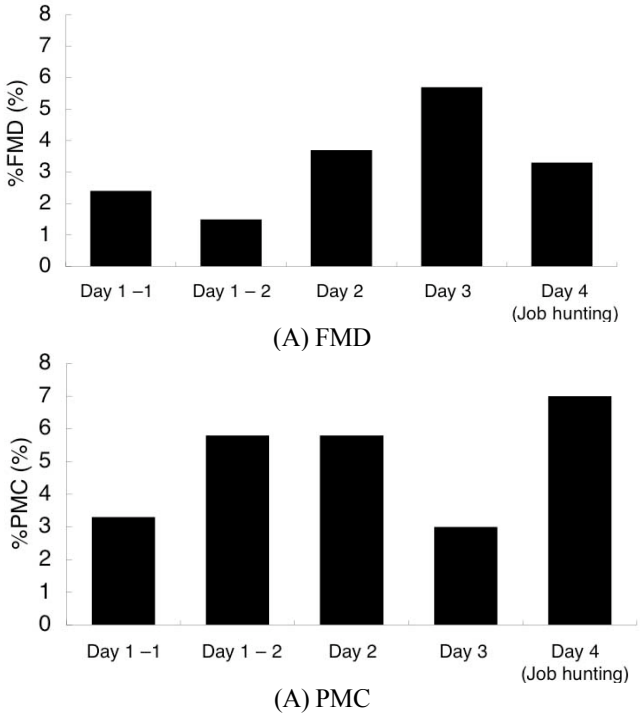

Figure 5: Time course changes of FMD (A) and PMC (B) responses of a 27-y-old male.