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Effect of Pulsed Magnetic Field on Red Blood Cell Aggregation: Mobility

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The disaggregation and displacement of stacked red blood cell (RBC) are known to be dependent on the electric state of hemoglobin and the strength and gradient of external magnetic field. The present study has been investigated the dependence of the change in aggregation and mobility of RBCs on the intensity and time duration of pulsed magnetic field (PMF), in addition to stimulus area. The magnetic field intensities are 0.07, 0.19, and 0.27 T, pulse time of 0.102 ms and pulse repetition rate was 1 Hz. Live blood analysis was used in order to quantitatively estimate the mobility and morphology of RBC exposed to PMF stimulus. The optimal time and intensity of PMF stimulus were 10 minutes and 0.27 T. The difference in the stimulus area did not show much. The continuance of the effect of PMF stimulus was observed to be 2 hours. Also it was verified the movement of the RBCs was accelerated for steady exposure of PMF stimulus. In order to identify a link between disaggregation in rouleau-formed RBCs and PMF stimulus, it is necessary to investigate the correlation between PMF intensity and the stimulus time, the mobility of RBCs, and the number of stacked RBCs.

Keywords : Pulse Magnetic Field, Red Blood Cells, Aggregation, Magnetic Stimulus, Rouleau formation

1. Introduction

Stimulation therapy using pulse and alternating magnetic field has been accomplished with electric and thermal stimulus in the field of physical medicine for a long time. The typical and popular stimulus therapeutic apparatus, electric stimulator, has disadvantage such as hygiene and skin problems due to adhesive contact and current flows only to the skin surface. On the other hand, magnetic field has been attracted because of its excellent permeability to stimulate a deep part of body, as well as non-invasive and non-contact stimulus [1]. For many years, the use of the pulsed electromagnetic field (PMF) was proposed as an alternative noninvasive medical treatment for influencing human physiology, via inducing electric current in deep tissue with the rapidly changing field of the magnetic impulses [2]. After the approval of FDA in 1979, magnetic field stimulus as therapeutic tool has been used widely. Recently, repetitive Transcranial Magnetic Stimulation (r-TMS) has been actively used due to increasing senile dementia and depression [3].

Red blood cells (RBCs) deliver oxygen to the body tissues by means of blood flow through the circulatory system and their flat surface of discoid can be stacked at length to a few tens. The aggregation of RBCs or rouleaux formation is caused by fibrinogen in blood plasma and physically, interaction between the electric field by the Fe^{+3} ion in the center of RBC and the anion dissolved in the blood. It is known as a useful qualitative and empirical index of nonspecific disease activity because the aggregation of RBC reduces blood flow and increases vascular resistance in the human circulation [4]. Shvartsman *et al.* reported that the size of aggregates and their shape change in time due to blood flow variations [5]. Sharygin *et al.* observed migration of RBCs along the magnetic field gradient. The disaggregation and displacement of stacked RBCs are expected to be dependent on the electric state of hemoglobin and the strength and gradient of external magnetic field [6]. Although various therapeutic effects on the magnetic field stimulation have been reported, research on the change of disaggregation and micro-circulatory blood flow in the rouleau-formed RBCs on PMF has been deficient yet.

Complete blood cell count tests have long been used to quantify disease symptom through clinical trials, such as measuring concentration of various proteins including blood cells, with a few ml of blood sample. Live blood analysis (LBA) under microscope is performed by obtaining

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only 1 μl of blood sample directly from the subject, and provides the morphologies of aggregation and deformation as well as the movements of RBCs. Therefore, in this study, LBA was used to confirm changes in the rouleau formation and mobility of RBCs, although it is less systematic, and accurate and stable than the conventional blood tests.

As already mentioned in our previous paper, it seems that the staked RBCs slow the blood flow down and thus it causes serious problems in the oxygen supply of the tissues [7]. Accordingly, it is necessary to systematically study for the aggregation and deformation of RBCs and their movements. In this works, PMF stimulus was tried to check whether the aggregation of RBCs are improved through the blood flow circulation in the body. The change of RBCs movement rate by PMF stimulus was measured and analyzed.

2. Experimental Methods

The PMF stimulator system including the magnetic coil used in this study were shown in Fig. 1. The power source generating magnetic field was fabricated using SCR, in order to adjust discharge time charged in the capacitor. The high-voltage pulse output device consists of the charger withstanding high voltage of 1,500 volts, SCR control software system, and magnetic field generating coil system. The magnetic field coil stimulating the palm and sole was wound to a single layer of 10 turns, coil shape was elliptical and size of 12.0 × 4.5 cm using flat square wire of 1.5 × 3.0 mm. The maximum intensity of the pulse is 0.27 Tesla and it is rapidly decreasing and pulsating pulse. One cycle of the pulse shows the period

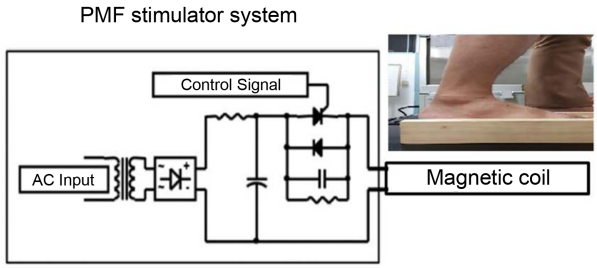

Fig. 1. (Color online) Schematic diagram of our designed PMF stimulator system including the magnetic coil. Mold system was used for prevent shaking hand and foot during PMF stimulation.

of 0.102 ms and frequency of about 10 kHz. Since magnetic field coils flowing high current generate a lot of heat, the coil and the stimulated palm and sole should be sufficiently distanced, and the temperature change should be minimized. Also in order to prevent shaking hand and foot during PMF stimulation, gypsum was used and coil was placed under the foot mold system.

Five normal volunteer subjects (4 males, 1 female, average ages: 23.4 ± 2.3 years) were participated in the current study. The subjects were stabilized for 30 minutes before experiment. And all subjects were clearly informed the purpose and method of the experiment and provided the written agreements.

To observe the morphology of the RBC aggregation and its mobility, the blood was exsanguinated from distal phalanx of the middle fingers of left hand before and after PMF stimulus, respectively. Stimulus was applied to the right palm and sole for 5-20 min. to observe the effects of the stimuli on the circulation in the whole body. The mobility of RBC depending on the intensity of PMF

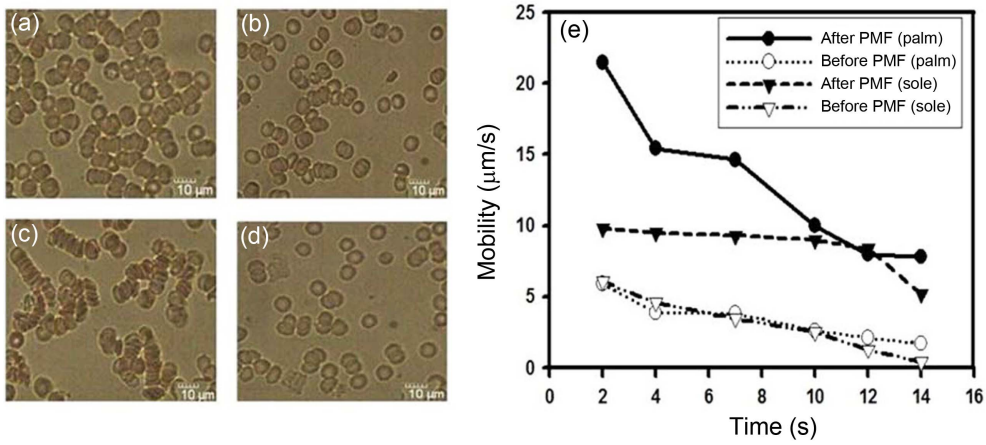

Fig. 2. (Color online) RBCs aggregation under the PMF stimulus with 0.27 T for 10 min, where (a) and (b) are the morphologies of before and after stimulus on the right palm, (c) and (d) are corresponding to the stimulus on the sole of right foot. (e) the mobility as a function of moving time of RBCs in the palm and sole, before and after PMF stimulus.

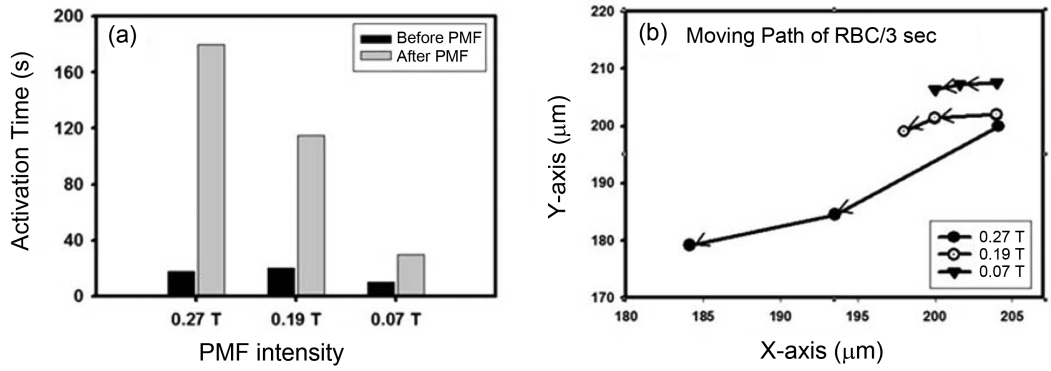

Fig. 3. Effect of PMF intensity with 0.27, 0.19, and 0.07 T on the dynamic motion of RBCs aggregation. (a) the activated time taken to stop the motion of RBCs and (b) schematic diagram for the dynamic motion of RBCs after PMF stimulus in the palm.

stimulus, duration of stimulus as well as different region were observed by analyzing RBC movement recorded using video camera attached to the microscope.

3. Results and Discussion

Figure 2 shows the RBCs aggregation under the PMF stimulus with 0.27 T for 10 min, where (a) and (b) are the morphologies of before and after stimulus on the right palm, and (c) and (d) are corresponding to the stimulus on the sole of right foot. It was confirmed through video that ten to fifteen or more RBCs in the blood collected before PMF stimulus were coagulated, and there were a little movement in the RBCs rouleaux. Agglomerated RBCs after PMF stimulus were changed into independent RBCs and the individual RBCs were actively actuated. The pulsed magnetic field clearly shows the effect of improving the aggregation of RBCs. Figure 2(e) shows the mobility as a function of moving time of RBCs to observe the effects of the stimulus on the blood circulation in the whole body. As expected, the mobility of RBCs after PMF stimulus is much faster than before PMF stimulus, and it lasts for a few minutes, in the cases of both stimuli to the palm and sole. But, the mobility in the sole-stimulus is slower by 50%, compared to that of palm-stimulus. This is probably due to some distance between the location of stimulus and blood collection. However, it could be found that the PMF stimulus on any part of the body affects the blood circulatory system because there is more movement of RBCs, compared to non-stimulus in the sole of right foot.

Figure 3 shows the effect of PMF intensity with 0.27, 0.19, and 0.07 T on the dynamic motion of RBCs aggregation. Figure 3(a) shows the activated time taken to stop the motion of RBCs on the slide glass. Figure 3(b) is trajectory for the dynamic motion of RBCs after PMF stimulus in the palm. The points tell the position of RBC under microscope in the interval of 3 sec. Although the intensity decreases down to 0.07 T, the mobility of stacked-RBC could be measurable as well as the improvement of rouleaux formation. But moving paths for 3 s are much longer in the high intensity, compared to the low intensity,

Table 1. Moving paths of RBCs during 3 sec vs. PMF intensity, based on Fig. 3(b).

PMF Intensity	Moving Paths of RBCs during 3 sec (μm)	
	1st	2nd
0.27T	19.14	10.91
0.19T	4.01	3.78
0.07T	2.83	1.92

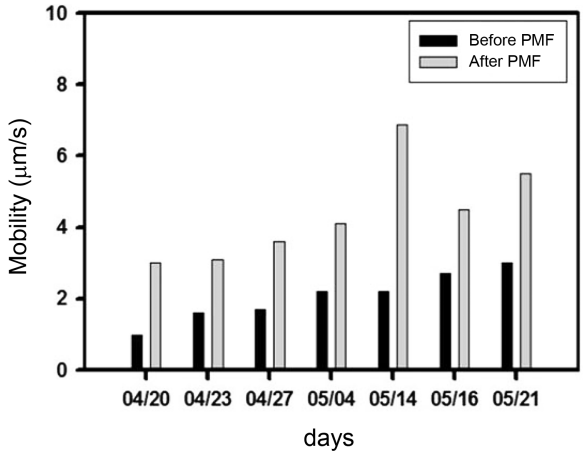

Fig. 4. Continuous effect of PMF stimulus for one month through the mobility of RBCs. PMF stimulus applied in the palm day by day for one month and blood samples were collected every 2-3 days to examine the mobility of RBCs before and after PMF stimulus. RBCs movement was found to be gradually faster than that of the first day even before PMF stimulus.

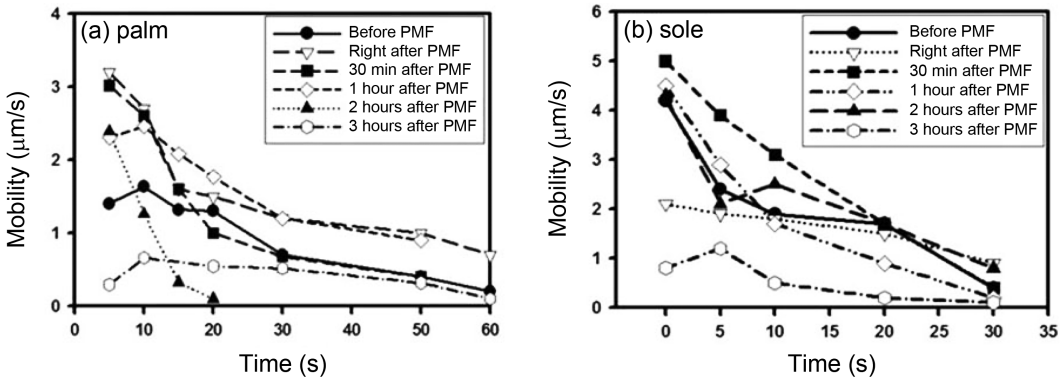

Fig. 5. The mobility as a function of movement time of RBCs after PMF stimulus of 0.27 T for 10 min. in the (a) palm and (b) sole.

from 2.83 to 15.03 μm by 6 times increased. Table 1 shows calculated moving paths of RBCs during 3 sec on the PMF intensities, based on Fig. 3(b). We need to investigate the least intensity of PMF for sufficently deaggregation and the movement of stacked RBCs in case of developing PMF stimulation for the therapeutic use. In order to see the improvement of rouleaux formation and blood circulation under PMF stimulus, we need to observe consistently the mobility of RBCs after exposure to the magnetic field every day.

Figure 4 shows the mobilities of RBCs aggegation under PMF stimulus with 0.27 T during 1 month in the palm. The subject was exposed every day to the PMF stimulus of 10 min for a month, but blood sampling was performed once every 2 or 3 days, and the mobility was calculated corresponding to those days. It was found that not only the mobility was significantly increased after PMF stimulus but also the mobility before PMF stimulus was gradually improved with increasing stimulus days. Therefore, we have confidence that the steady PMF stimulus every day might improve the blood flow in vascular system due to accelerating the movement of RBCs as the collapse of rouleau formed RBCs.

Figure 5(a) and (b) show the mobility as a function of movement time of RBCs after PMF stimulus of 0.27T for 10 min. in the palm and sole, respectively. In order to observe how long the effects of magnetic fields last, the mobility of RBCs was observed before and right after PMF stimulus, and after 30 min., 1 hour, 2 hours, and 3 hours, separately. Up to 2 hours after PMF stimulus, the movements of RBCs are still active and the mobilities are faster than those before PMF stimulus in the both of palm and sole. For clinical use, we need to investigate the continuance time for the effects of magnetic field on the different intensities of PMF.

4. Conclusion

Our present study has proposed that PMF stimulus with 0.27 T on the right palm and sole increase RBC's mobility as well as the disaggregation of rouleau-formed RBCs. Also optimum stimulus time of 10 min. might induces the disaggregation of stacked RBCs and fast movements of RBCs, but longer stimulation cause the re-aggregation because of stress, and reduce its mobility. In addition, PMF stimulus affects blood circulatory system even though it is locally applying to other area from exsanguinating area. Also the effectiveness of PMF stimulus was testified and proved its continuance time up to be 2 hours, regardless of stimulus location. However, the exact physiological role of disaggregation and mobility of RBCs in the blood circulatory system has not been clearly elucidated yet. In order to verify and expand our findings, the real-time velocity measurement closely related to the venous flow resistance need to be done with diverse intensities, exposure time, frequency, and pulse shape of PMF.

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