

## Research on Functional Recovery by the Plasma Inhalation into Lungs and Heart Disease Model Rats

肺・心疾患モデルラットへのプラズマ吸入による機能回復に関する研究

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We carried out an experiment about the functional recovery of a cardiopulmonary disease such as myocardial infarction or pulmonary hypertension (PH) by “the plasma inhalation” using atmospheric pressure plasma forming various by-products such as not only an ion class and the ion radical class but also the nitrogen oxides from the aspect of lungs disease treatment with “the nitric oxide (NO) inhalation therapy” or wound treatment by “NO-therapy” in the nitrogen oxide which plays an important role in the activation of the cells and tissue. In this study, we test the plasma inhalation to the model rats which induced PH by using monocrotaline (MCT) which causes PH symptom when it is a type of pyrrolizidine alkaloids and administered to mice or rats and examine the possibility of improving or treating of disease in the cardiovascular system including lungs and a heart.

### 1. Introduction

Plasma is used in various fields not only for industrial applications, but also for medical treatments. Especially, argon plasma can be applied for hemostatic approach, tissue coagulation, and for sterilization treatment. These methods are studied enthusiastically and are put to a practical use. In recent years, plasma medical care to promote the reproduction of tissue has been attracting people's attention by sending plasma the affected part of an injury irradiate plasma directly in treatment such as an injury or diabetic necrosis led by Europe and America. Above all, because it is reported that the plasma inhalation evokes vasodilatation in the pulmonary blood vessel of pigs, it is expected that it may have a healing effect against pulmonary hypertension (PH) or myocardial infarction<sup>[1]</sup>. Particularly, PH had been considered to be an intractable illness until now, but in recently there was the thing which a cause of PH could elucidate, and relaxation treatment by medicine and NO inhalation came to be performed<sup>[2]</sup>. Because these evoke also vasodilatation, it is necessary to examine if the plasma inhalation therapy can be applied as a new approach.

### 2. Material and Methods

#### 2.1 Animals

The total of 12 male Wistar rats at the age of 4weeks (Japan SLC, Hamamatsu, Japan) were used. The rats were administered with monocrotaline (MCT) (60 mg/kg) (Wako Pure Chemical Industries, Ltd., Osaka, Japan) intraperitoneally was categorized as the MCT group (n=6). Ones administered physiologic saline (5 ml/kg) intraperitoneally were called the control group (n=6)<sup>[3]</sup>.

#### 2.2 Measurements

On the 14<sup>th</sup> day of the experiment, percutaneous oxygen saturation (SpO<sub>2</sub>) which examined the change of cardiorespiratory function due to PH and the chest radiograph by the geometric change of the heart and the lungs with PH by an X-ray computed tomography (CT) scanner for experimental animals (Latheta LCT-200, Hitachi Aloka Medical, Ltd., Tokyo, Japan) was evaluated. The test was recorded for 150 seconds, and average was calculated. The normal level of SpO<sub>2</sub> is approximately more than 93%. We analyzed the heart volume with the image photographed in CT and calculated the average. The heart volume is affected by the arbitrary shape that forms three-dimensional image with outlines. We performed the pulmonary artery (PA) catheterization known as the most useful diagnosis method for PH. We inserted PA catheter (polyethylene catheter, Nippon Becton Dickinson Co. Ltd., Tokyo, Japan) from right external jugular

vein and to pulmonary artery [4]. Pentobarbital sodium was used as an anesthetic for these three measurements above. Furthermore, visual observation and measurement of average body weight was performed to examine the physical change characteristics once a day.

### 3. Results

Rats exposed to MCT had less increase in average body weight than Control rats at day 14. On the other hand, SpO<sub>2</sub> measured in each group showed no differences (Table. I). As for the average of each group at day 14, Control group was 88.57% and MCT group is 81.81%. In addition, when CT images were photographed, the number of MCT rats was five and when SpO<sub>2</sub> was recorded, the number of rats in the MCT group was two. Also, cyanosis was confirmed in several rats in the MCT group throughout visual observation as shown in Fig.1. Lower limbs and a tail changed the color to purple shown as an image in Fig.1 (a).

Table I . Measurement body weight and SpO<sub>2</sub>

	Control	MCT
body weight (g)	138.7 ± 10.0	87.4 ± 7.2*
SpO <sub>2</sub> (%)	81.8 ± 3.5	88.6 ± 3.6

Data represented as average ± SD. \*p < 0.01 vs control (n=6 per group).

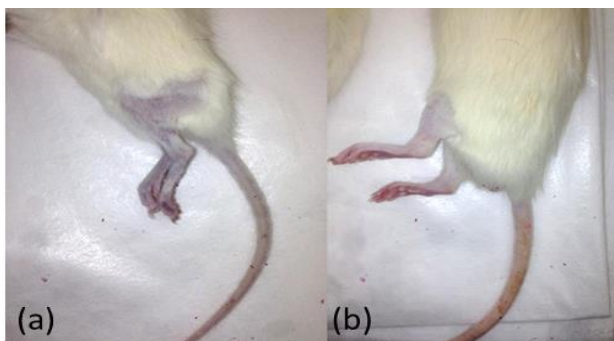


Fig. 1. Visual observation

The clear image shows cyanosis in (a) MCT rats and (b) Control rats.

The blue plots are an arbitrary shape of the heart but we could not confirm any differences from this result in Fig.2. In addition, because contrast medium was not used, the lungs and the blood vessel did not appear and the heart outline didn't become clear.

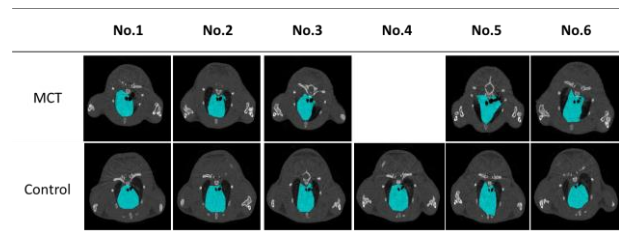


Fig. 2. CT images of the chest  
No.4 MCT rat died during the measurement. The image is flipped horizontally.

Table II . The analysis result of the heart volume

	MCT	Control
heart volume (cm <sup>3</sup> )	0.824 ± 0.12 <sup>#</sup>	1.201 ± 0.11

Data represented as average ± SD. <sup>#</sup>p > 0.05 vs Control.

### 4. Discussion

By the measurement of the body weight, significant difference exists between the MCT rats and the Control rats. It is still unknown whether it is influenced by MCT or not, but possibility of PH is suspected as the source. In addition, it is notable to think of cyanotic onset as a useful information. In the CT images, it is necessary to contrast the lungs and the blood vessels to scan the hypertrophy of the right ventricle. The number of samples is also considered as a problem since there were only two rats used in the measurement of SpO<sub>2</sub>. Anesthetic could be a cause of death since it has almost no difference between an effective quantity and a fatal dose. In this study, PA catheterization was tried, but it did not work well. It was possible to insert a catheter from right external jugular vein, but we were not able to measure blood pressure. Now, we are planning to make a new introducer and a catheter to insert into a thin blood vessel.

### 5. Conclusions

We choose the MCT-induced PH model for its technical simplicity and reproducibility. It may be difficult to say that sufficient data were provided, but the effectiveness of MCT was confirmed.

### References

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