



Radiation of electromagnetic waves to a finger using Yubi-MR reduces oxidative stress in blood by electron-transfer via negatively charged water formation

Naomasa Yamamoto (1), Yuichi Koike (2), Katsuyuki Kumano (3), Norifumi Yonehara (4)

Dept. of Biochemistry (1), Dept. of Drug Metabolism and Clinical Pharmacokinetics (2), Dept. of Pharmacology (4), School of Pharmaceutical Sciences, Ohu University, 31-1 Misymido, Tomitamachi, Koriyama, Fukushima, 963-8611 Japan. Japan System Planning Co., Ltd. (3), 2-21-12 Sasazuka, Shibuya-ku, Tokyo, 151-0073 Japan.

Introduction

Accumulation of oxidative stress elevates physiological aberrances such as aging, atherosclerosis, hypertension, obesity, myocardial infarction, and stroke. It is desired to reduce the oxidative stress in blood as much as possible. We have developed an apparatus named Yubi-MR (Japan System Planning Co.) to reduce oxidative stress in blood by radiation of electromagnetic waves to “Yubi” meaning a finger in Japanese. Yubi-MR mimicked a NMR-Pipetector which is widely used as a dehydrator of Fe(III) ions by reduction through inducing negatively charged water. In this study, we demonstrated that Yubi-MR reduced dROM after irradiating a finger for 10 min. On clinical trials undertaken with mice, Yubi-MR radiation suppressed their behaviors which resulted in a prolongation of their resting time. Thus, Yubi-MR is the oxidative stress reducer, possibly applicable to clinical therapeutic use for reducing oxidative stress in patients with oxidative-related diseases.

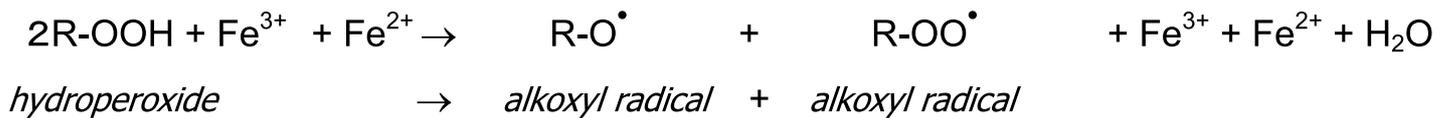
Methods

Blood donors: This experiment has been cleared by the ethics committee, Ohu University according to, and in compliance with the declaration of Helsinki. After 9 healthy volunteers before/after radiation by the Yubi-MR, plasma was collected by centrifugation.

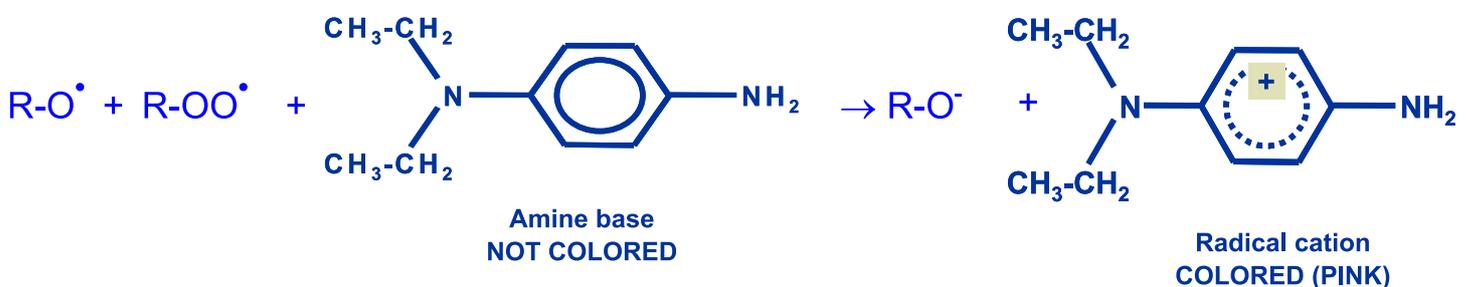
Measurement of dROM and BAP: A reactive oxygen metabolites (d-ROMs) and a biological antioxidant potential (BAP) in the plasma were measured by FRAS4 (Wismerll).

ROMs(U CARR)	ROMs(mg H2O2/dL)	Oxidative stress(severity)
250 – 300	20.08 - 24.00	Normal Range
300 - 320	24.08 - 25.60	Border-line range
321 - 340	25.68 - 27.20	Low level oxidative stress
341 - 400	27.28 - 32.00	Middle level of oxidative stress
401 - 500	32.08 - 40.00	High level of oxidative stress
> 500	> 40.00	Very high level of oxidative stress

Oxidative Stress in Blood



The principle of d-ROMs test



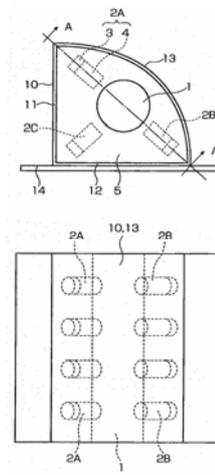


Figure 1 Structure of Yubi-MR

Yubi-MR is a perfectly engineered and designed apparatus with a single well which allows a human finger or thumb to be inserted for exposure to the electric magnet waves. Twelve sections of blackbodies made from ceramics are embedded in the surrounding wall in 3 lines from top to the bottom (See Illustration). There are a couple of the Winger-magnets in array which are placed in front of the blackbodies. The blackbodies will

emit specific electromagnetic waves, and then the waves are sharpened to become a certain length to induce the NMR reaction by passing through the Winger-magnet array. The Yubi-MR does not contain any radioisotopes or harmful materials.

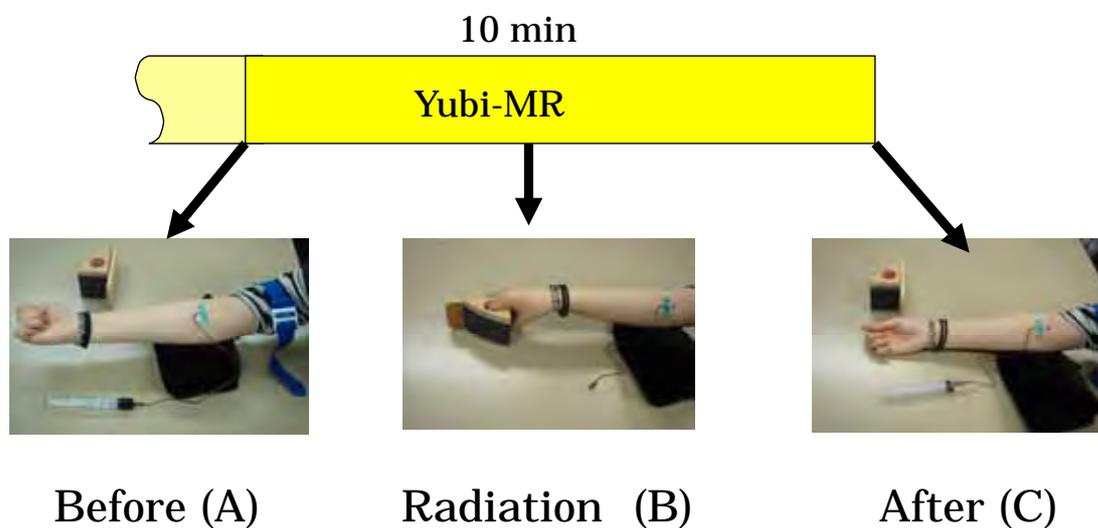


Figure 2 Blood sampling from donor for dROM/BAP analysis

Blood was taken from a donor (A). A finger from the same donor was exposed to the Yubi-MR radiation for 10 minutes without removing the catheter which was used for the purpose of taking the blood sample, and then the radiation was stopped. The blood sample in the catheter (about 1ml) was removed and the collected subsequent 2.5 ml blood.

Monitoring mouse behavior: Four mice were treated with Yubi-MRm for describing time in Table 2. Dummy MRm (Removed blackbody from Yubi-MRm) was used instead of Yubi-MRm as a control. The behavior of a mouse was monitored after exposure to the Yubi-MR radiation (Figure 3 and 4).

Table 1 Experimental conditions for Yubi-MRm-radiation

Experiment	Number	No. of Exp.	Accumulation	Radiation
No.1-1	8	11x-81x	1min	10 min
No.1-2	8	91x-103x	15 min	30 min
No.2	8	104x-150x	15 min	30 min
No.3	8	160x-300x	15 min	30 min
No.4-1	8	310x-390x	15 min	30 min
No.4-2	8	400x-430x	15 min	10 min
No.5	8	450x-590x	1 min	10 min
No.6	8	600x-770x	1 min	1 min
No.7	8	800x-890x	1 min	1 min
No.8	8	900x-930x	1 min	1min



Figure 3 Yubi-MRm (Yubi-MR for mouse), a device for mouse

Yubi-MR is fundamentally the same device as the NMR Pipetector technology which has been designed for radiation to a mouse. A NMR Pipetector mounted on a section of pipe (5 cm diameter x 20cm in length) which had both ends of the pipe covered with a metal net. The mouse was released in it for a measuring period of time.



Figure 4 Monitoring for mouse behavior by SuperMex

SuperMex (Muromach Kikai) has eight channel sensors for the detection of IR which comes out from the mice who are moving freely in the cages, and it can convert them to a score as athletic point-values. SuperMex can accumulate the scores by each minute and can record subsequently for 72 hours.

Resting time: Score " "zero" implies that the mouse dose not move during the measuring period by SuperMex. In order to calculate the resting time

in 24 hours, all the zero-scores were summarized, and were expressed as minutes.

Statistic analysis: Paired t-test was used for analysis.

Results

Effect of Yubi-MR radiation on dROM and BAP

Data on dROM and BAP in heparinized plasma from 9 donors were summarized in Table 1. D-ROM value was 249.6 ± 6.7 (mean \pm SE) before the irradiation. After the irradiation with electromagnetic waves for 10 min at 1.0×10^{-3} dB V/m \times 3 intensity, d-ROM significantly dropped to 230.4 ± 14.8 (mean \pm SE) ($p < 0.01$). In contrast, BAP was not changed at all (before/after = 2401.1 ± 37.5 vs 2401.2 ± 37.0 , mean \pm SE). The results of d-ROMs test expressed as concentration unity, CARR U indicate the blood levels of hydroperoxides which directly parallel with the levels of free radicals. Reference value in healthy people are estimated to be

250-300 CARR U (20.08-24.00 mg/dL of H_2O_2). One CARR unit corresponding to 0.08 mg H_2O_2 . The values obtained here were in a normal range, suggested the they are all healthy individuals. Even under the normal condition, Yubi-MR radiation for 10 min could quenches approximately 0.16 mg H_2O_2 in the body.

Table 2. Summary of Data on dROM and BAP from 9 donors

Human	BAP Before	dROM Before	BAP After	dROM After	BAP/dROM Before	BAP/dROM After
No.1	2223	364	2214	323	6.107	6.854
No.2	2224	237	2213	219	9.383	10.105
No.3	2486	222	2448	188	11.198	13.021
No.4	2491	241	2416	231	10.336	10.458
No.5	2537	266	2503	261	9.537	9.590
No.6	2381	201	2451	186	11.845	13.177
No.7	2444	267	2404	224	9.153	10.732
No.8	2377	193	2468	187	12.316	13.197
No.9	2447	256	2494	255	9.558	9.780
Average	2401.111	249.666	2401.222	230.44*	9.937	10.761

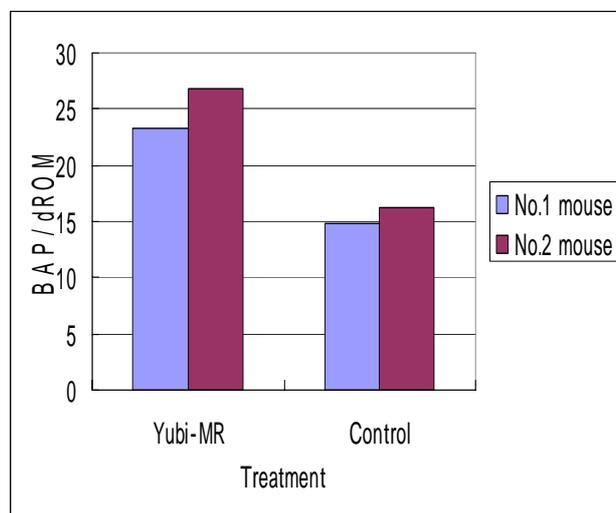
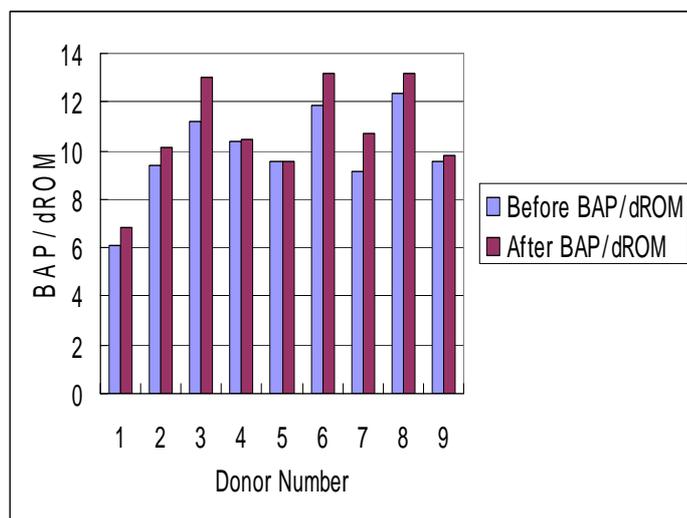


Figure 5 Suppression of oxidative stress by Yubi-MR radiation.

Effect of Yubi-MR on BAP/dROM was observed. Ratio of BAP/dROM was significantly increased after Yubi-MR treatment to humans (left) and the mouse (right).

Effect of Yubi-MRm on mouse behavior: Normal mice (n=64) were

grouped into two groups with Yubi-MR treatment and a dummy device treatment (control). Behavior of the mice were assessed by SuperMex and expressed as point/min. Yubi-MR significantly slowed down the behavior of the movements of the mice ($p < 0.05$) (Table 3).

Table 3 Effect of Yubi-MRm on mouse behavior

Yubi-MRm (Point/min)	Dummy device (Point/min)
48.7 ± 8.3	52.7 ± 7.7
Mean ± SD	Mean ± SD

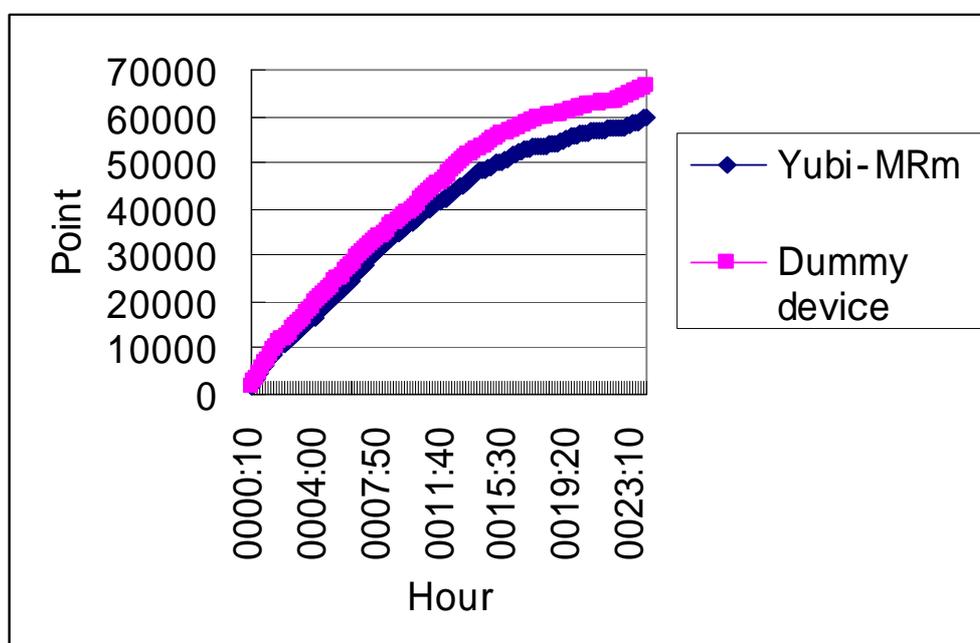


Figure 6 Yubi-MRm treatment suppresses mouse behavior

Movement of the mouse (points) were integrated from start to 23 hours. Yubi-MR (blue line vs control pink line) potentially suppressed the behavior of the mouse.

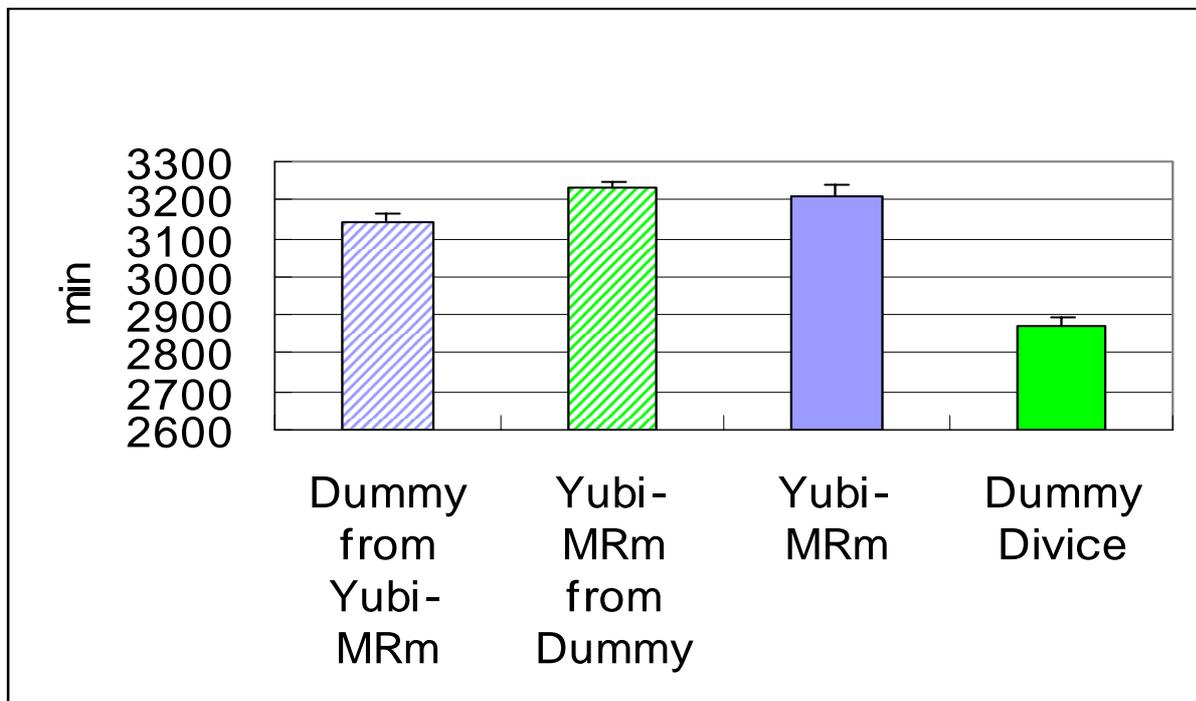


Figure 7 Reduction of the resting time by cancellation of the Yubi-MR radiation.

The Yubi-MRm significantly increased the resting time compared to the

dummy device (solid column). The mice (n=4) were subsequently treated with opposite device (hatched column).

Discussion

Radiation with Pipetector/Yubi-MR to water increases negative-charged water that can provide free-electrons enough to reduce Fe(III) ions to Fe(II) ions. Yubi-MR might function in a similar way in the blood, resulting in reduction of oxidative stress (dROM). In our preliminary survey about effect of Yubi-MR on human sleep, Yubi-MR induces being sleepy, suggested that the reduction of blood causes suppression of behavior. We hypothesized that Yubi-MR influences animal behavior such as resting time. We demonstrated that Yubi-MR(m) radiation prolonged the resting time of the mice, however, the mechanism of the prolongation of the resting time is still unclear. The accumulation of oxidative stress in the blood induces sleep (xx). However, the removal of oxidative stress may help to sleep easily. The relation

between oxidative stress and sleep is therefore clarified.

Conclusion

Yubi-MR is the first oxidative stress-reducer, possibly applicable to clinical therapy for patients with oxidative stress-related diseases.

