Study on effects of thoron and thermal treatment for aging-related diseases in humans

Y. Aoyama¹, T. Kataoka¹, Sh. Nakagawa², A. Sakoda¹, Y. Ishimori³, F. Mitsunobu⁴, K. Yamaoka*¹

¹Graduate School of Health Sciences, Okayama University, 2-chome, Shikata-cho 5-1, kita-ku, Okayama-shi, Okayama, 700-8558, Japan
²The Sakakibara Heart Institute of Okayama, 2-1-10 Marunouchi, Kita-ku, Okayama-shi, Okayama, 700-0823, Japan
³Ningyo-toge Environmental Engineering Center, Japan Atomic Energy Agency, 1550 Kagamino-cho, Tomata-gun, Okayama, 708-0698, Japan
⁴Misasa Medical Center, Okayama University Hospital, 827 Yamada, Misasa-cho, Tohaku-gun, Totori 682-0192, Japan

*Corresponding author:
Dr. K. Yamaoka,
Okayama University, 2-chome, Shikata-cho 5-1, Kita-ku, Okayama-shi, Okayama, 700-8558, Japan.
Fax: +81 86 235 6852
E-mail: yamaoka@md.okayama-u.ac.jp

Background: The aim of this study was to analyze the effects of thoron and thermal treatment for aging-related diseases in humans. Materials and Methods: All subjects inhaled thoron with a high concentration (about 4900 Bq/m³) for 2 weeks. Blood pressures were measured and blood samples were collected after each treatment 1, 2 and 3 weeks after the first treatment. Results: The α-atrial natriuretic peptide level of the rheumatoid arthritis group was increased and the blood pressure was significantly decreased. Superoxide dismutase activity of rheumatoid arthritis group was significantly increased by treatment. In addition, thoron and thermal treatment significantly enhanced the concanavalin A-induced mitogen response and increased the level of CD4-positive cells; it decreased the level of CD8-positive cells. The results suggest that thoron and thermal treatment activates antioxidative function. Furthermore, these findings suggest that thoron and thermal treatment prevents diabetic ketoacidosis and contributes to the prevention of aging-related diseases. Conclusion: Thoron and thermal treatment may be part of the mechanism for the alleviation of diabetes mellitus and rheumatoid arthritis. Iran. J. Radiat. Res., 2012; 9(4): 221-229

Keywords: Thoron and thermal treatment, health effect, diabetes mellitus, rheumatoid arthritis, antioxidant function.

INTRODUCTION

Radon (²²²Rn) is a radioactive gaseous element that mainly emits α-rays. The half-life of thoron (²²⁰Rn, 55.6 sec), which is an isotope of radon, is shorter than that of radon (3.824 days), and the α-particle energy of thoron (6.288 MeV) is larger than that of radon (5.490 MeV).

Therapy using radon gas, which is volatilized from radon-enriched water and induces a small amount of active oxygen in the body, is performed for various diseases. A large number of patients are treated in countries with a tradition of spa therapy (i.e. Japan (¹,²), central Europe (³) and Russia (⁴)), but the mechanism of radon effects is almost unknown. Despite reports of a potentially increased risk of lung cancer development induced by radon inhalation (⁵, ⁶), radon treatment facilities have been established in many countries (³). If radon is inhaled, the lungs will be subjected to the actions of free radicals created by radiation and may suffer inflammation. Although radon inhalation has been thought to be hazardous in general, radon hot-springs have been reported to have therapeutic effects on senile brain disorders and hypertension (⁷). Radon inhalation promotes the effects of tissue perfusion agents such as adrenaline in plasma; that is, the level of plasma adrenaline is increased by radon inhalation (⁸, ⁹).

We previously reported that radon effects, such as antioxidative function, are
twice as effective as thermal effects (10). This suggests that antioxidative function was more enhanced by radon therapy than by thermal therapy. Furthermore, we have reported that thoron and thermal treatment was effective for the prevention of peroxidation reaction in hypertension (11). So far, no epidemiologic data exist on the hazardous effects of radon (12).

In recent years, several attempts have been made to clarify the mechanism of radon effects (1, 2, 8), but there have been only a few studies on thoron effects in humans. As most diseases for which radon or thoron therapy and thermal therapy are applied are related to activate oxygen, it is important to clarify the radioactive effects of radon or thoron and thermal therapy under hot-spring conditions. Therefore, in this study, we examined the biochemical effects of thoron and thermal treatment of diabetes mellitus (DM) and rheumatoid arthritis (RA). We investigated several biochemical parameters, such as antioxidant-, diabetes mellitus- and rheumatoid arthritis-associated substances, which are causes of aging-related diseases, to clarify the mechanism of diseases for which thoron hot-spring therapy is used as a treatment, most of which are called activated oxygen-related diseases.

**MATERIALS AND METHODS**

**Subjects**

The subjects were 76 individuals (31 males and 45 females; mean age 62.7, range 31-83; Japanese) who were divided into 3 groups: normal, DM and RA. The normal group included 25 individuals (12 males and 13 females; mean age 55.1, range 31-78), the DM group 25 individuals (15 males and 10 females; mean age 66.4, range 44-83), and the RA group 26 individuals (4 males and 22 females; mean age 66.4, range 40-78). Informed consent was obtained from all subjects. The study protocol was approved by the ethics committee of Iwate Health Service Association (Iwate, Japan), and was executed by the Medical Association in Iwate Prefecture and Hanamaki city.

**Thoron and thermal treatment**

All subjects attended a Hanamaki spa (Iwate, Japan) with a high concentration of thoron. The room temperature was 39 °C, humidity 90 %, water 40 °C, and the air concentration in the thoron hot-spring was about 4900 Bq/m³. All subjects stayed in the bathroom for 30 minutes a day under the following conditions. Furthermore, they bathed for more than five days a week and continued for 2 weeks.

**Assays**

Blood pressures (BP) and height and weight were measured before each thoron and thermal treatment and blood samples were collected after each treatment (before meal) 1, 2 and 3 weeks after the first treatment; BP was also measured and blood samples collected before the first treatment (at body temperature and thoron level background) to used as the control. Body mass index (BMI) is calculated by the following equation:

\[ \text{BMI} = \frac{\text{body weight (kg)}}{\text{height (m)}^2} \]

We entrusted the biochemical assays of the blood samples to the clinical analysis service. Briefly, each biochemical indicator was measured: SOD activity was measured by the nitroblue tetrazolium (NBT) method. High-density lipoprotein-cholesterol (HDL-cho) was measured by the direct method. The free fatty acid (FFA), creatinine (Cr), blood urea nitrogen (BUN), uric acid (UA), 1, 5-anhydro-D-glucitol (1, 5 AG), glycoalbumin (GA) and ketone bodies were measured enzymatically. Glucose was measured by the hexokinase UV method. Hemoglobin A1c (HbA1c) was analyzed by the latex agglutination-turbidimetric immunoassay (LA). Immunoreactive insulin (IRI) was analyzed by the radioimmunoassay (RIA). Total protein (TP) was measured by the biuret method. α-atrial natriuretic peptide (α-hANP) was analyzed by the chemiluminescent enzyme immunoassay (CLEIA). Concanavalin A (Con A) was measured by
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the DNA quantitative method using a nucleic acid/fluorescent probe. CD4 and CD8 were measured by the monoclonal antibody assay.

**Statistical analysis**

Data are presented as the mean ± standard error of mean (SEM). Statistical significance of differences was determined using Student’ t-test for comparison between two groups or two-way repeated measures analysis of variance (ANOVA).

**RESULTS**

*Temporal changes in BMI of normal and each patient after thoron and thermal treatment*

Before treatment (before the first treatment), the BMI in all groups was 22.4-24.4 (figure 1). In weeks 1, 2, and 3, the BMI in the RA group was significantly decreased compared to before the first treatment by thoron and thermal treatment.

*Temporal changes in BP of normal and each patient after thoron and thermal treatment*

Without treatment, the diastolic BP in DM and RA groups were significantly lower than in the normal group (figure 2). The systolic BP in each group was decreased by thoron and thermal treatment compared to non-treatment. In week 2 after the first treatment, in particular, the diastolic BP was significantly decreased in the RA group.

*Temporal changes in antioxidative function-associated substances*

SOD activities in the normal group (in week 2) and DM group (in weeks 1 and 2) were significantly decreased compared to each non-treatment by thoron and thermal treatment (figure 3); however, SOD activity in the RA group (in weeks 1 and 3) was significantly increased compared to non-treatment.
**Temporal changes in lipid-associated substances in normal and DM groups**

The HDL-cho in the DM group was increased slightly by thoron and thermal treatment (figure 4). The FFA levels in the normal group (in weeks 2 and 3) and DM group were decreased by treatment compared to non-treatment. In week 2, in particular, it was significantly decreased compared to the normal group.

![Figure 4](image-url) Temporal changes in lipid-associated substances of normal and patients with DM after thoron and thermal treatment. Each value is the mean ± SEM. The number of subjects in each experiment was 6-25. Statistical significance: *p < 0.05 vs. each control (non-treatment) value.

**Temporal changes in renal function-associated substances in normal and DM groups**

Without treatment, BUN in the DM group was significantly higher than in the normal group (figure 5); however, BUN in the DM group (in week 3) was slightly decreased by thoron and thermal treatment compared to non-treatment and there was no significant difference compared to non-treatment in the normal group. There were no significant differences in other renal function-associated substances.

![Figure 5](image-url) Temporal changes in renal function-associated substances of normal and patients with DM after thoron and thermal treatment. Each value is the mean ± SEM. The number of subjects in each experiment was 7-25. Statistical significance: *p < 0.05, **p < 0.01, vs. control (non-treatment) value of normal.

**Temporal changes in DM-associated substances of normal and DM groups**

Without treatment, glucose, HbA1c, IRI and GA in the DM group were significantly higher and 1, 5AG in the DM group was significantly lower than in the normal group (figure 6). In week 1, IRI in the normal group was significantly decreased by thoron and thermal treatment compared to non-treatment. The IRI in the DM group was decreased compared to non-treatment, and there was no significant difference compared to non-treatment in the normal group. In week 3, the GA in the normal group was significantly increased compared to non-treatment, but this was a reference value.
Without treatment, the ketone bodies in the DM group were higher than in the normal group, but there was no significant difference (figure 7). Further, the ketone bodies in the normal group (in week 2) and DM group were decreased by treatment. In week 2, TP in the normal group was significantly decreased by treatment compared to non-treatment (figure 8).

**Temporal changes in RA-associated substances in normal and RA groups**

Without treatment, α-hANP in the RA group was significantly higher than in the normal group (figure 9). The α-hANP in the normal group (in weeks 1, 2 and 3) was significantly increased by thoron and thermal treatment. The α-hANP level in the RA group was also increased by treatment.

**Temporal changes in immune-associated substances in normal and RA groups**

Con A in the normal group (in week 1) and RA group (in week 2) was significantly increased by thoron and thermal treatment compared to each non-treatment (figure 10-A). In weeks 1 and 2, CD4-positive cells in the RA group were significantly increased, and CD8-positive cells were significantly decreased by treatment compared to non-treatment (figure 10-B).
Low-dose irradiation induces various stimulating effects on living organs, especially the activation of a biological defense system such as antioxidative (13-17) and immune functions (18, 19). For example, low-dose X- or γ-irradiation activated antioxidative functions in some organs and inhibited oxidative injury (20-25). In addition, recent reports suggested that the exposure dose to activate antioxidative functions with X- or γ-irradiation is much lower than with radon inhalation (26). As discussed previously, it is highly possible that low-dose X-irradiation activates defense systems in the
living body and therefore contributes to pre-
venting or reducing reactive oxygen species 
(ROS)-related injuries, which are thought to 
involve peroxidation.

It has been reported that the activity of 
SOD, which is a scavenger of superoxide 
radicals, is increased in cultured cells (28) in 
various organs of rats (29), rabbits (30) and 
mice (31) by exposure to radon; however, 
there have been only a few studies on 
thoron effects in humans. Thoron is slightly 
different from radon. The half-life of thoron 
(55.6 seconds), which is an isotope of radon, 
is shorter than that of radon (3.824 days), 
and the $\alpha$-particle energy of thoron (6.288 
MeV) is larger than that of radon (5.490 
MeV).

To clarify the health effects of thoron and 
thermal treatment, we examined the BMI 
after thoron and thermal treatment. Obesity 
is a condition resulting from excess body fat, 
and is associated with several disease risk 
factors. High BMI is a risk for lifestyle 
diseases (32), and BMI is used as an indicator 
of health and obesity. The definition of 
obesity by the Japan Society for the Study of 
Obesity is BMI $\geq 25$, and the normal value is 
22 (27). Warm-water bathing enhances the 
blood circulation and increases energy 
consumption (33). In addition, radon 
inhalation enhances tissue perfusion (6). In 
this study, the BMI in the RA group was 
significantly decreased by thoron and 
thermal treatment. This might be because of 
the enhancement of metabolism by thoron 
and thermal effect.

Next, to clarify the clinical effects of 
thoron and thermal treatment on DM or RA, 
the SOD activity was examined: that is, we 
examined whether thoron and thermal 
treatment could improve the reduced enzy-
matic antioxidant activities in the study. 
Our results showed that SOD activity in 
normal and DM groups was significantly 
decreased in week 2 after the first treat-
ment, but not after 3 weeks in the normal 
and DM groups. On the other hand, it was 
significantly increased by treatment in the 
RA group. These findings suggest that clini-
cal effects were observed even after SOD 
activities decreased to the initial level. The 
same effect was observed in our previous 
study and the reports suggest that the de-
crease of SOD activities was a symptom 
similar to slight “yuatari”, that is the effect 
of taking a hot bath for too long (34).

Ketone bodies are the generic name for 
acetoacetic acid, 3-hydroxybutyric acid, and 
acetone, and are the imperfect resolution 
product of fatty acid and amino acid. In-
creased release of unesterified fatty acids 
from adipose tissue into the blood is 
especially common in Type 2 diabetes (35). 
Ketone bodies are produced as byproducts 
when these fats are broken down for energy, 
and the risk of ketoacidosis is very high in 
Type 2 diabetic patients. We previously re-
ported that thoron inhalation decreased FFA 
and total ketone bodies in diabetes, suggest-
ing that thoron inhalation prevents diabetic 
ketoacidosis (11). In this study, thoron and 
thermal treatment significantly decreased 
FFA in normal group. In addition, total ke-
tone bodies decreased by about 20% in both 
group, but this difference was not 
significant. These findings may indicate 
that thoron inhalation has role in reducing 
FFA and total ketone bodies.

Controlled clinical trials on the effects of 
rodon therapy for the treatment of RA are 
rare. Falkenbach et al. found that five trials 
meeting the inclusion criteria, three with a 
double-blind study design, showed beneficial 
effects of radon therapy as compared to 
inventions without radon inhalation; that 
is, interventions including radon showed 
significantly better pain reduction than 
those without radon (36). In this study, the $\alpha$
-HANP in normal and RA groups increased 
and BP decreased, suggesting relaxation of 
the vascular smooth muscle. This finding 
indicates what may be part of the 
mechanism of increased tissue perfusion, 
namely, the decreased BP brought about by 
rodon inhalation. These findings were 
consistent with the inhibitory action of
α-hANP. Furthermore, thoron and thermal treatment enhanced a ConA-induce mitogen response and increased the level of CD4-positive cells (CD4: antigen, which is a marker of helper T cells) and decreased the level of CD8-positive cells (CD8: antigen, which is a common marker of killer T cells and suppresser T cells). These findings suggest that thoron and thermal treatment contributes to the prevention of aging-related disease, which is related to immune suppression, by enhancement of the immunity function.

These findings suggest that thoron and thermal treatment contributes to alleviation of the symptoms of aging-related diseases, such as activation of the biological defense mechanism, or promoting physiologic changes such as tissue perfusion.

In this study, we did not elucidate the detailed mechanism of the effects of thoron and thermal treatment. In the future, detailed clarification of the mechanisms of these phenomena is required to understand the effects of thoron and thermal treatment on the functions of the living body, including adaptive responses.

ACKNOWLEDGMENTS

The authors are indebted to Dr. Akira Yoshida and his staff (Iwate Health Service Association, Japan) for assays and bathing guidance for the subjects.

REFERENCES


