

Verification of the effect of hot springs on arteriosclerosis based on the mathematical model of arteriosclerosis onset II : in case of weak radioactive springs

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Introduction

- The mathematical model of arteriosclerosis onset by Kagami (2021) mathematically shows that improvement of blood cholesterol levels can be a factor in suppressing the progression of arteriosclerosis [1].

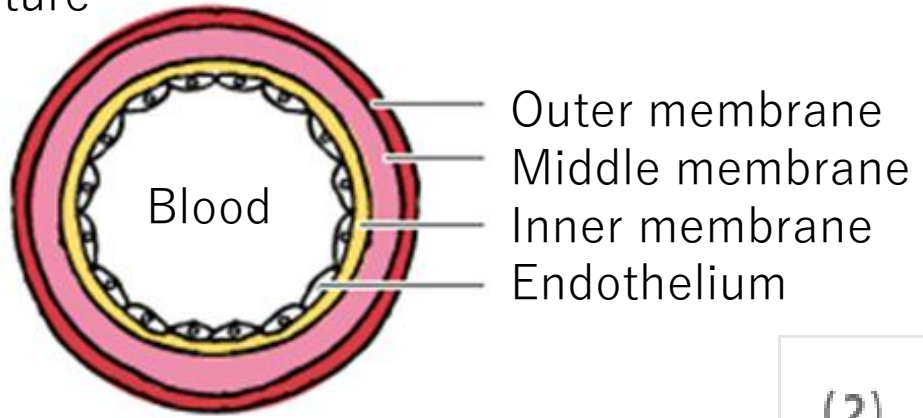
[1] H. Kagami, "The Modified Mathematical Model of Arteriosclerosis onset: Adding the Effect of Repairing Flaws of the Intima," (The conference proceedings of) The 12th International Symposium on ADVANCED TOPICS IN ELECTRICAL ENGINEERING (IEEE Xplore), DOI: 10.1109/ATEE52255.2021.9425180, 2021.

The mathematical model of arteriosclerosis onset and its fruits

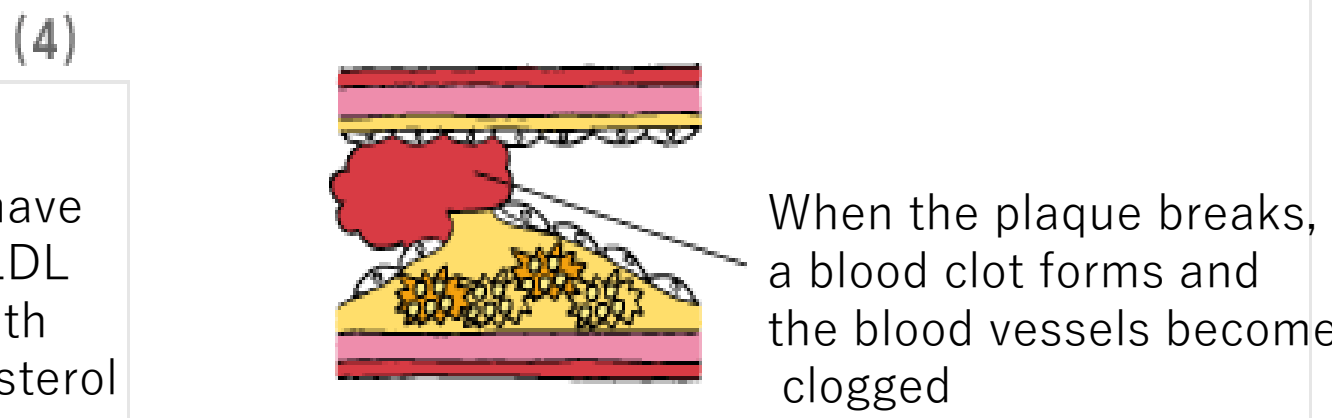
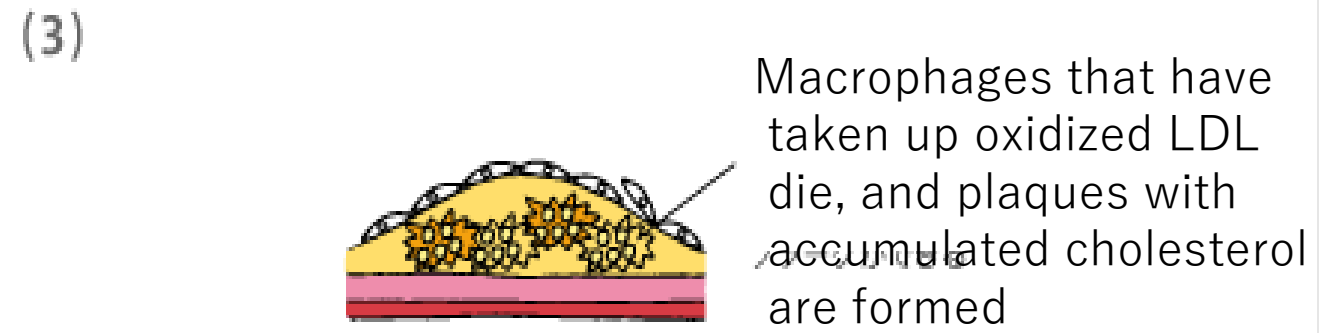
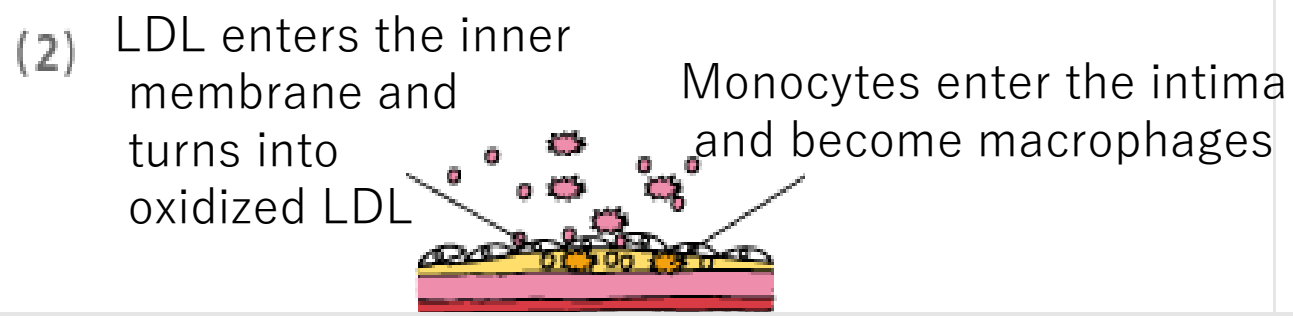
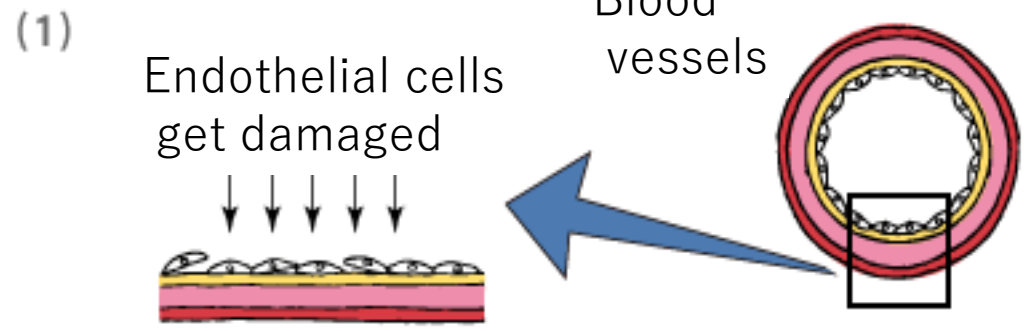
- In the beginning, the process of developing arteriosclerosis is outlined.
- First, when blood vessels are loaded on by high blood pressure etc. and the endothelial cells of blood vessels are damaged, LDL (bad cholesterol) in the blood enters the inner lining and is oxidized to oxidized LDL.
- To process oxidized LDL, monocytes enter the intima and turn into macrophages. Macrophages take up oxidized LDL and die, but at this time, the fat contained in LDL accumulates in blood vessels as plaque and the intima becomes thicker and thicker.
- As a result, the volume per unit length of the blood vessel becomes smaller and the blood flow deteriorates.

Overview of the formation mechanism of arteriosclerosis

Blood vessel structure



(<https://www.astellas.com/jp/ja/diseases/moreinformation-01/atheros-02>)



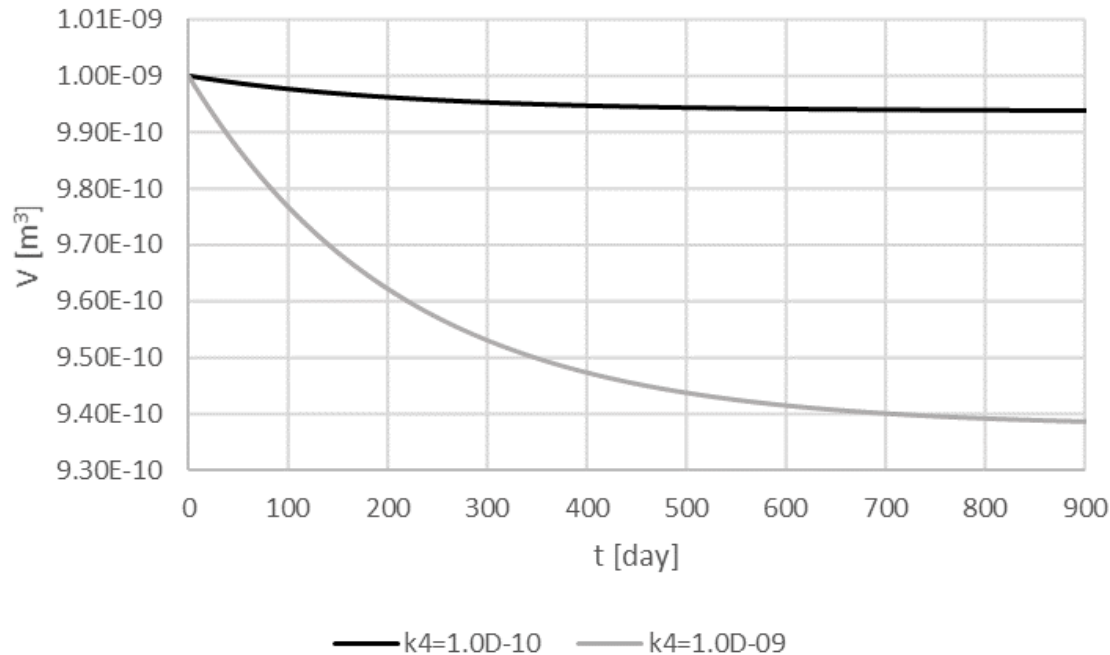
The mathematical model of arteriosclerosis onset

- Kagami (2019) mathematically modeled the above process and then improved it to derive the following equation as the time evolution equation for the blood vessel volume of arteriosclerosis-developed parts.

$$\frac{d^2V}{dt^2} + \frac{r}{V} \frac{dV}{dt} - \frac{r}{V} p_i k_1 k_2 u (k_3 + k_4 p_k) u_0 e^{-k_5 t} = 0$$

- Where V is the volume of the blood vessel in the arteriosclerosis-causing part, r is the flow rate of the blood, p_i is the concentration of monocytes in the incoming blood, p_k is the cholesterol concentration in blood, u is the number of flaws per unit area of the intima, u_0 represents u when $t=0$ and k_1, k_2, k_3, k_4 or k_5 is a coefficient, respectively.

Comparison of time development of V at large and small k_4



k_4 dependence on time development of V
(in case of $k_5 = 5.4 \times 10^{-8}$ [1/s])

$$\frac{d^2V}{dt^2} + \frac{r}{V} \frac{dV}{dt} - \frac{r}{V} p_k k_1 k_2 u (k_3 + k_4 p_k) u_0 e^{-k_5 t} = 0$$

V : Volume of blood vessels in areas where arteriosclerosis develops

p_k : Cholesterol concentration in the blood

- This is a graph of the dependence of k_4 on the time evolution of V , and it can be seen that the smaller k_4 is, the smaller the decrease in V is, that is, the volume of the blood vessel in the area where arteriosclerosis develops does not become smaller, and the onset of arteriosclerosis is suppressed.
- From the numerical simulation results of the equation, it is found that the smaller p_k , that is, the lower the cholesterol concentration in the blood, the not smaller the volume of blood vessels where arteriosclerosis develops, that is, the stronger the development of arteriosclerosis is suppressed.

Effect of radiation on cholesterol

- On the other hand, although radioactive springs are said to be effective against arteriosclerosis, no scientific verification has been done yet.
- In past research results, Nakagawa et al. (2008) found that radon inhalation in mice decreased the amount of lipid peroxides produced by the oxidation of cholesterol in various organs over time. This result suggests that radioactive springs containing radon may reduce blood cholesterol levels in humans.

Verification experiment at Yuno Onsen (Japan)

- Based on this speculation, an experiment to verify whether the blood cholesterol level decreased after bathing at Yuno Onsen (Yamaguchi Prefecture, Japan), which is a weakly radioactive alkaline simple sulfur spring, in 2021.
- As a result, it was clarified that a statistically significant reduction in blood cholesterol levels after bathing was observed even after bathing only once.
- As a result, based on the above mathematical model, it was indirectly verified that Yuno Onsen has an efficacy on arteriosclerosis.

Suggestions from the efficacy of Yuno Onsen

- On the other hand, Yuno Onsen has three characteristics: (1) radioactive spring, (2) alkaline, (3) sulfur spring.
- It is not yet known which of these three characteristics contributed to the post-bathing reduction in blood cholesterol levels described above.

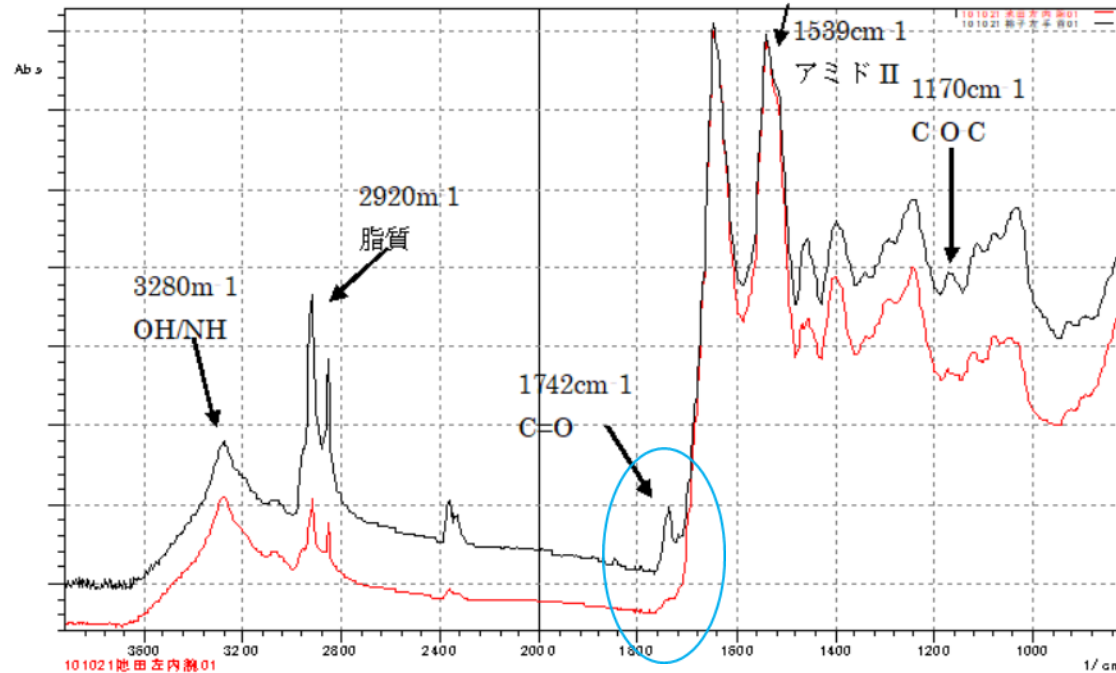
Purpose of this study

- Therefore, in this study, similar measurements were carried out at Yobizuru Onsen (Yamaguchi Prefecture, Japan), which is classified as a simple weakly radioactive cold mineral spring and has only the characteristics of (1) radioactive spring among the above three characteristics.
- Then it is verified whether the characteristics of the radioactive spring cause a decrease in blood cholesterol levels after bathing.

Principle of measurement of blood cholesterol level

- Cholesterol levels were measured using CLE-80, a minimally invasive cutaneous cholesterol ester level measuring device from Photoscience Co., Ltd.
- Measurement of the concentration of cholesterol ester levels in the skin with this device provides an estimate of the total cholesterol concentration in the blood.
- The measurement principle is to irradiate the skin with light in the mid-infrared region and determine the cholesterol ester level of the skin from the absorption spectrum intensity.

Infrared absorption spectrum



(Provided by Photoscience Co., Ltd)

- The valley portion (1724 [cm^{-1}]) next to the cholesterol ester peak in the absorption spectrum is called the "ester valley", and the peak portion (1742 [cm^{-1}]) is called the "ester peak".
- Changes in these values were used to determine the increase or decrease in blood total cholesterol concentration.

Validity of this measurement method

- On the other hand, the cholesterol ester level to the total cholesterol level is approximately constant at about 70%.
- And according to Photoscience Co., Ltd., the correlation coefficient between blood total cholesterol level and skin cholesterol ester level is as high as 0.997.
- From these facts, it can be considered that the cholesterol ester level obtained by this measurement method almost accurately reflects the total blood cholesterol level.

Method for measuring cholesterol levels after bathing

- Among the customers who visited Yobizuru Onsen during the 11 business days from February 4 to March 4, 2023, 200 people who gave their consent were measured for cholesterol ester levels in the skin after one bath.
- Excluding missing data, the number of data obtained by age group is 15 people in 10's to 30's, 44 people in 40's to 50's and 140 people in 60's and older.
- Of these, excluding the data of 4 people whose sweat was detected in the measurement after bathing, finally 195 people's data in 10's to 30's: 15 people, 40's to 50's: 44 people and over 60's: 136 people were analyzed.

Results: All ages

- It was investigated whether the values of "estelle valley" or "estelle peak" was increased or decreased after bathing in the hot springs for the valid data of 195 people and the results shown in Table I were obtained.
- Concerning this result, from the chi-square value of "ester valley" or "ester mountain" is 9.48 or 23.0, respectively and $\chi^2_{0.01} = 6.64$ statistically significant increase of the cholesterol level after bathing is confirmed (significance level: 0.01).

TABLE I

CHANGES IN CHOLESTEROL ESTER LEVELS AFTER BATHING IN HOT SPRINGS (ALL AGES)

	"estelle valley"	"estelle peak"
descent	76	64
rise	119	131
descent rate	0.390	0.328
rise rate	0.610	0.672

Results: By age (in 10's to 30's)

(In the following, the same investigation results by age group are shown.)

- It was investigated whether the values of "estelle valley" or "estelle peak" was increased or decreased after bathing in the hot springs for the data of people in 10's to 30's and the results shown in Table II were obtained.
- Concerning this result, from the chi-square value of "ester valley" or "ester mountain" is 0.600 or 0.0667, respectively and $\chi_{0.05}^2 = 3.81$ statistically significant variation of the cholesterol level after bathing is not confirmed (significance level: 0.05).

TABLE II
CHANGES IN CHOLESTEROL ESTER LEVELS AFTER BATHING IN HOT SPRINGS (IN 10'S TO 30'S)

	"estelle valley"	"estelle peak"
descent	9	8
rise	6	7
descent rate	0.600	0.533
rise rate	0.400	0.467

Results: By age (in 40's to 50's)

- It was investigated whether the values of "estelle valley" or "estelle peak" was increased or decreased after bathing in the hot springs for the data of people in 40's to 50's and the results shown in Table III were obtained.
- Concerning this result, from the chi-square value of "ester valley" or "ester mountain" is 2.27 or 3.27, respectively and $\chi_{0.05}^2 = 3.81$ statistically significant variation of the cholesterol level after bathing is not confirmed (significance level: 0.05).

TABLE III
CHANGES IN CHOLESTEROL ESTER LEVELS AFTER BATHING IN HOT SPRINGS (IN 40'S TO 50'S)

	"estelle valley"	"estelle peak"
descent	17	16
rise	27	28
descent rate	0.386	0.364
rise rate	0.614	0.636

Results: By age (in 60's and older)

- It was investigated whether the values of "estelle valley" or "estelle peak" was increased or decreased after bathing in the hot springs for the data of people in 60's and older and the results shown in Table IV were obtained.
- Concerning this result, from the chi-square value of "ester valley" or "ester mountain" is 9.53 or 23.1, respectively and $\chi^2_{0.01} = 6.64$ statistically significant variation of the cholesterol level after bathing is not confirmed (significance level: 0.01).

TABLE IV
CHANGES IN CHOLESTEROL ESTER LEVELS AFTER BATHING IN HOT SPRINGS (IN 60'S AND OLDER)

	"estelle valley"	"estelle peak"
descent	50	40
rise	86	96
descent rate	0.368	0.294
rise rate	0.632	0.706

Results

- From the above, all the data of 195 people showed a statistically significant increase in cholesterol level after bathing.
- By age group, though for the data of people in 50's and under, statistically significant changes in cholesterol level after bathing were not confirmed partly due to the lack of data, for the data of people in 60's and older, a statistically significant increase in cholesterol level after bathing were confirmed.
- This was the opposite result of the above-mentioned experiment at Yuno Onsen conducted in 2021.

Discussion-1

- The results of the experiment at Yuno Onsen conducted in 2021 are shown below.
- It was investigated whether the values of "estelle valley" or "estelle peak" was increased or decreased after bathing in the hot springs for the valid data of 208 people and the results shown in Table V were obtained.
- Concerning this result, from the chi-square value of "ester valley" or "ester mountain" is 81.3 or 81.3, respectively and $\chi_{0.01}^2 = 6.64$ statistically significant decrease of the cholesterol level after bathing is confirmed (significance level: 0.01).

TABLE V

CHANGES IN CHOLESTEROL ESTER LEVELS AFTER BATHING IN HOT SPRINGS (ALL AGES (YUNO ONSEN))

	"estelle valley"	"estelle peak"
descent	169	169
rise	39	39
descent rate	0.813	0.813
rise rate	0.188	0.188

Discussion-2

- In addition, for all age groups, the results that statistically significant decrease of cholesterol levels after bathing were obtained.
- These results indicate that among the above three characteristics that may reduce cholesterol levels after bathing, radioactive springs are eliminated as candidates and alkaline and sulfur springs remain as candidates.
- In the future, a survey with only one characteristic of alkaline or sulfur springs should be conducted and the characteristics that may reduce cholesterol levels before and after bathing should be narrowed down.

Conclusion

- In order to narrow down the characteristics of hot springs that have efficacies on arteriosclerosis, changes in skin cholesterol levels after bathing at the Yobizuru Onsen, which is classified as a simple weakly radioactive cold mineral spring, were measured.
- As a result, a statistically significant increase in skin cholesterol levels after bathing was confirmed.
- As a result, based on the results from the mathematical model of arteriosclerosis onset, it was indirectly shown that the nature of a radioactive spring may not have an efficacy on arteriosclerosis.
- In the future, in order to clarify which of the two characteristics (alkaline, sulfur spring) has the efficacy on arteriosclerosis, it is necessary to investigate hot springs that have only one characteristic, alkaline or sulfur spring.

Acknowledgment

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Thank you for your attention.