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Development of a Temperature and Heat Flux Measurement System Based on Microcontroller and its Application in Ophthalmology

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The paper describes the design and technical parameters of a medical thermoelectric device developed for diagnosing and monitoring the ophthalmic diseases. The main elements of the device are a specially designed thermoelectric heat flux sensor and a thermocouple temperature sensor connected to a data acquisition unit. The sensor is a thermoelectric micro-module that converts the heat flux into an electric voltage, which is recorded by the measuring channel of the data acquisition unit. The device allows high-precision measurements of both heat flux and temperature from the ocular surface. The paper contains examples of clinical piloting of the device.

Keywords: thermocouple, temperature, heat flux, thermoelectric medical device, heat flux sensor, ophthalmology, ophthalmic disease.

1. Introduction

Heat transfer processes in the human body occur according to the laws of thermodynamics, which studies the fundamental rules of energy conversion and transfer [1]. Biological objects, in particular the human eye, can be regarded as an open thermodynamic system that is not in the state of thermal equilibrium and in which heat transfer always happens. For heat transfer, the existence of a temperature gradient is necessary, which is a prerequisite for the occurrence of a heat flux [2]-[4].

In the human eye, blood circulation in the choroid is the main source of heat. Blood, the temperature of which is almost equal to that of the body, entering the eye forms a thermal gradient that induces the heat transfer from the blood to the tissues of the eye. The more intense the blood circulation, the more heat is transferred to the structures of the eye. Heat, distributed over the eye tissues, passes into the environment through the outer tissues of the eye [5]-[7]. Thus, the temperature gradient present in the eye ensures the existence of heat flux, which can be registered on the ocular surface.

In ophthalmology, there is a problem of early diagnosis of various pathologies characterized by changes in intraocular blood circulation, such as inflammation, choroidal tumors, glaucoma and more. It is obvious that circulatory disorders of the eye should be accompanied by changes in the dynamics of heat transfer [7], [8].

Evaluation of heat transfer processes is based on the measurement of temperature and heat flux. Temperature measurement in medicine is traditionally well provided with instrumentation and metrology [9], [10]. Despite the fact that considerable success has recently been achieved in the development of means for measuring the heat flux and its surface density [11]-[13], devices for direct heat measurement in medicine, in particular in ophthalmology, are absent. This considerably limits our ability to assess the thermal processes that occur in the human eye. To date, scientific knowledge about the nature of heat fluxes in the human eye in different environmental conditions and in various ophthalmic diseases is insufficient. Thus, the

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development of new highly sensitive efficiency of early diagnosis of the ophthalmic pathology.

Therefore, the purpose of this work was to develop and test a thermoelectric medical device for measuring the temperature and heat flux from the ocular surface.

2. DESIGN AND TECHNICAL PARAMETERS OF DEVICE

The phenomenon of thermoelectricity was discovered in 1821 by Thomas Seebeck [14]. Five years later, Antoine Becquerel proposed to use it to measure temperature [14]. Thermoelectricity has always played an important role in science, e.g. it was used by Georg Ohm to discover his famous law [15]. Due to its wide temperature range, low cost and mechanical strength, the thermocouple is the most popular temperature sensor. That is why the thermoelectric method of converting thermal energy into the electrical signal was used in the development of a medical device for measuring the temperature and heat flux for the needs of ophthalmology.

In spite of the large number of temperature sensors [12], [20]-[22] and noninvasive methods of measurements [23], the conventional thermocouple is a very important sensor and much attention is paid to its study. For example, EURAMET issued a roadmap for thermometry [16], which declares the need for further study of a thermocouple. The study is carried out in three directions: (i) study of the existing thermocouples [17]-[19]; (ii) study of new materials which can be used for thermocouples [20]-[22]; (iii) study of novel designs based on the conventional thermocouples [24], [25]. This paper considers the studies in the directions (i) and (iii).

The appearance of the device is shown in Fig.1. The main elements of the device are as follows: a specially designed thermoelectric heat flux sensor and a thermocouple temperature sensor, which are connected to the electronic data acquisition unit [26]. The power source is a battery, which provides autonomous work of the device, allowing us to avoid problems with unstable power supply voltage [27], [28] and common mode noise [29].

Fig.1. The appearance of the thermoelectric device for ophthalmology. 1 - thermoelectric heat flux sensor, 2 - thermocouple sensor, 3 - data acquisition unit.

The block diagram of this device is given in Fig.2. The main functional blocks of the device are as follows: the heat flux measurement channel, the temperature measurement channel, the measurement channel of supply battery voltage, the channel for measuring the ambient temperature, the microcontroller, the battery pack with a charger, and the digital display.

The measurement channel of heat flux is designed to measure the voltage developed by the thermoelectric sensor under the action of heat flux. The resolution of voltage measurement is 1 μV, which allows measuring the heat flux with a high accuracy.

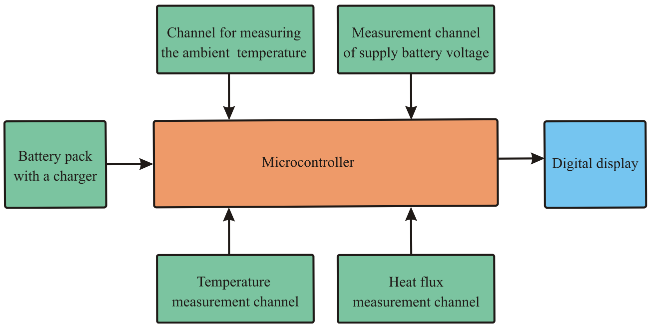


Fig.2. The block diagram of the thermoelectric device.

The temperature measurement channel is designed for processing the signal from the thermocouple sensor. The type L thermocouple is used. It was specially made with minimal geometrical dimensions.

The voltage measurement channel of the battery power supply allows monitoring the charge of the battery and predicting the duration of its continuous operation.

The channel for measuring the ambient temperature is intended for measuring the signal from the calibrated platinum resistance thermometer. This thermometer measures the ambient temperature at the terminals to which the reference junctions of the type L thermocouple are connected. Thus, the thermometer signal is used to compensate the reference junction temperature of the type L thermocouple. The resolution of ambient temperature measurements is 0.001 K.

The microcontroller is used to control measuring channels, normalization and conversion of the measured signals to physical quantities. The microcontroller can be programmed using the keys on the front panel of the device, which are used to select either heat flux or temperature measuring mode and the measurement ranges.

A battery power supply with a charger is designed for galvanic isolation of the device and the biological object under study to prevent possible electric shock and improve the noise immunity of measurements where the thermocouple is used [29]. The galvanic isolation of the device from the power grid ensures a safe and efficient use of the device in ophthalmic praxis as well as considerably improves the measurement accuracy due to suppression of common-mode noise.

Table 1. shows the technical parameters of the device, which are important for its practical application, particularly

in ophthalmology. The main technical advantage of the device is its ability to measure both the heat flux and temperature. The maximum heat flux density value that can be measured is 50 mW/cm^2. In this case, the measurement uncertainty does not exceed 5 % [30]-[32]. The measured temperature value should be within the range of 273 to 323 K. The resolution of temperature measurement is 0.01 K. The power source of the device is a rechargeable battery with a voltage of 4.5 V, the time of continuous operation of which reaches 12 hours. The device's small dimensions and weight make it convenient to use. Safety of using the device due to its galvanic isolation from the power grid and the ability of real time monitoring of the thermal and temperature state of the surface of the human eye are its important features.

Table 1. Technical parameters of thermoelectric device.

Parameter	**Value**
Maximum heat flux density	50 mW/cm^2
Uncertainty of heat flux density measurement	5 %
Temperature measurement range	273÷323 K
Temperature measurement resolution	0.01 K
Ambient temperature measurement range	273÷323 K
Ambient temperature measurement resolution	0.001 K
Battery supply voltage	3.7÷4.5 V
Time of continuous operation from a fully charged battery	12 h
Overall dimensions of the thermoelectric heat flux sensor	Ø3×0.7 mm
Overall dimensions of the data acquisition unit	180×140×90 mm
Weight	0.6 kg

3. DESIGN OF THE THERMOELECTRIC HEAT FLUX SENSOR

For this medical device, a special miniature thermoelectric heat flux sensor was developed and manufactured at the Institute of Thermoelectricity of the National Academy of Sciences and Ministry of Education and Science of Ukraine [33]-[35]. The appearance of the sensor is given in Fig.3. The main component of the sensor is a thermoelectric micro-module with the dimensions of (2×2×0.5) mm. The module comprises 100 pieces of n- and p-type crystals with the dimensions of (0.17×0.17×0.4) mm made of high-performance thermoelectric Bi_2Te_3-based materials. The Seebeck coefficient of such materials is about 200 µV/K at 300 K. The micro-module is placed between two insulating Al_2O_3 plates with the diameter of 3 mm and the thickness of 0.1 mm and is sealed with a special sealant. The diameter and height of the manufactured thermoelectric heat flux sensor are 3 mm and 0.7 mm, respectively. The sensor diameter was chosen with respect to the medical requirements [36] of ophthalmological devices. The electrical resistance of this thermoelectric sensor is 14 Ω.

The developed heat flux sensor is not conventional, therefore it has to be calibrated prior to use.

The calibration of the sensor is carried out using a specially designed apparatus to determine the volt-watt sensitivity [37], which uses the blackbody radiator as the heat flux source. The schematic of the apparatus is given in Fig.4.

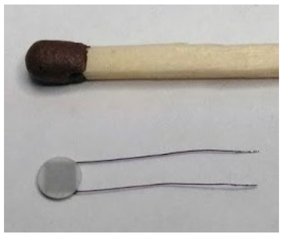


Fig.3. The thermoelectric heat flux sensor.

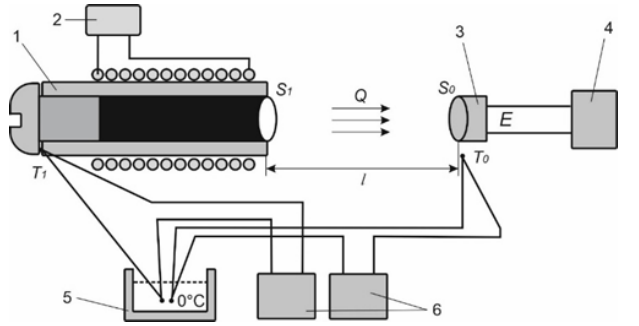


Fig.4. The schematic of the apparatus for measuring the volt-watt sensitivity of the thermoelectric sensor: 1 - blackbody, 2 - power supply unit of the blackbody heater, 3 - thermoelectric heat flux sensor, 4 - millivoltmeter, 5 - zero-thermostat of the thermocouple, 6 - temperature meters.

The volt-watt sensitivity of the thermoelectric sensor is determined by the formula

$$\nu = \frac{E}{Q}, \tag{1}$$

where E is thermoEMF developed by the sensor, Q is the heat flux radiated by the black body and absorbed by the receiving pad of the thermoelectric sensor. Q is determined as follows:

$$Q = \frac{\varepsilon_1 \varepsilon_2 \sigma \left(T_1^4 - T_0^4\right) S_1 S_0}{\pi l^2}, \tag{2}$$

where σ is the Stefan-Boltzmann constant, $\varepsilon_1 = 1$ for black body radiator, $\varepsilon_2 = 0.82$ for the receiving pad of the sensor, T_1 is the temperature of the blackbody package, T_0 is the temperature of the receiving pad, S_1 is the area of radiating hole of the blackbody, S_0 is the area of the receiving pad, l is the distance between the hole and the receiving pad.

As a result of the calibration of the thermoelectric sensor, the conversion factor $K = 1/\nu S_0$ of the developed thermoEMF of the sensor to the physical quantity in units of heat flux density is determined. The value of this conversion factor for this particular sensor is $K = 4.163$ mW/mV·cm^2.

4. Practical implementation of the device in ophthalmology, and results of its clinical piloting

4.1. Subjects and methods

The clinical fragment of the work is an open piloting study. The study was approved by the Bioethical Committee of the State institution "The Filatov Institute of Eye Diseases and Tissue Therapy of the National Academy of Medical Sciences of Ukraine". All subjects signed informed consent.

The study included 32 healthy people (64 eyes) and 10 (10 eyes) patients with dry age-related macular degeneration (AMD) who voluntarily agreed to the study. The age of the examined healthy persons ranged from 18 to 86 years, patients with AMD – from 69 to 85 years.

All healthy subjects were divided into three groups depending on their age. The first group included 11 people (22 eyes) aged from 18 to 30 years, the second group – 10 people (20 eyes) aged from 31 to 60 years, the third group – 11 people (22 eyes) aged from 61 to 86 years.

In all cases, the following studies of both eyes were performed: thermometry of the outer surface of the cornea, measurement of the heat flux density of the eye, infrared thermography, and the measurement of the thickness of the choroid.

The developed thermoelectric device was used to measure the heat flux density and the temperature of the outer ocular surface. Infrared thermography system (FLIR® Systems, Inc., USA; spectral range, 8-14 µm; accuracy, 0.1 K; resolution, 160×12 pixels) was used to measure ocular surface temperature. Measurements of the thickness of the choroid were carried out by the method of optical coherence tomography (SOCT Copernicus OPTOPOL Technology S.A., Zawiercie, Poland).

To perform temperature measurements of ocular surface, the thermocouple sensor of the device is placed in a special standard medical probe for measuring the eye temperature. To measure heat flux density, the thermoelectric sensor is attached to a contact prism and a tripod, which are adapted to the conventional Goldman tonometer used to measure intraocular pressure [36]. The contact prism and the tripod are universal and can be attached to a slit lamp biomicroscope (Fig.5.). The contact surfaces of the heat flux sensor and the temperature probe were made atraumatic and could be disinfected.

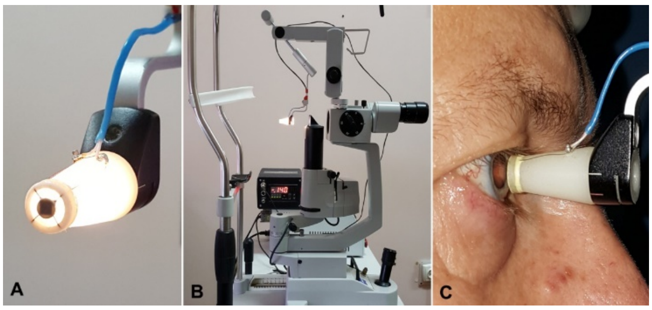


Fig.5. The thermoelectric heat flux sensor adapted to the contact prism of the Goldman tonometer a) and docked with a slit lamp biomicroscope b). The position of the contact prism with the heat flux sensor during the study c).

Before the study, all participants adapted to room temperature for 15 minutes. Epibulbar anesthesia was applied in the form of a single instillation of 0.5 % solution of proxymetacaine hydrochloride (Alcaine, Alcon-Couvreur, Puurs, Belgium). The registration of the temperature and density of the heat flux was carried out 15 minutes after the application of the drops. During the study, the subject was in a sitting position. The sensor of the thermoelectric device during the study in all cases was in contact with the central zone of the cornea. At least three measurements for each eye were performed in real time.

At the next stage of the study, all participants underwent pupil dilation by a single instillation of 1 % tropicamide solution (Mydriacyl, Alcon-Couvreur, Puurs, Belgium). 30 minutes after the application of the drops, the temperature and heat flux density were recorded again in compliance with the measurement protocol.

The study was conducted in a room with stable environmental parameters. The temperature and humidity were monitored. Conditions with a minimum air velocity were maintained.

4.2. Statistical analysis

Data are presented as mean and standard deviation (SD). A two-tailed Student test was used for group comparisons. Statistical significance was set at $p < 0.05$. Pearson correlation was used to assess the independent correlation between the temperature of the ocular surface and heat flux density from the eye; between the thickness of the choroid and the heat flux density/temperature of the cornea; between the age and the heat flux density of the eye's outer surface. Statistical analysis was performed using the Statistica 10.0 (StatSoft, Tulsa, OK, USA) software.

4.3. Results of thermoelectric device clinical piloting and discussion

The ambient temperature during the study averaged 21.3 ± 0.8 °C. The mean values of temperature, heat flux as well as corresponding standard deviations were calculated. It was shown that the cornea surface temperature of healthy individuals varied between 33 °C and 36 °C with the mean of 34.6 ± 0.7 °C. The heat flux density of the human eye varies between 4.9 mW/cm^2 and 11.7 mW/cm^2 with the mean of 7.7 ± 1.3 mW/cm^2. A positive linear correlation between the cornea temperature and the heat flux density was revealed (correlation coefficient $r = 0.3$, significance level $p = 0.006$).

It was also revealed that healthy individuals have symmetry of temperature and heat flux density of the right and left eye (Table 2.).

The results of our observations indicate that healthy individuals with paired eyes have symmetry of the heat flux density measured on the ocular surface. One should also note the symmetry of the temperature of the outer surface of the cornea of the right and left eye of healthy people, which is consistent with previous studies [6].

At the next stage of the work, the effect of the pupil width on the temperature and heat flux density of the outer ocular surface of healthy persons was studied. The data obtained are presented in Table 3.

Table 2. Temperature and heat flux density of the right and left eye.

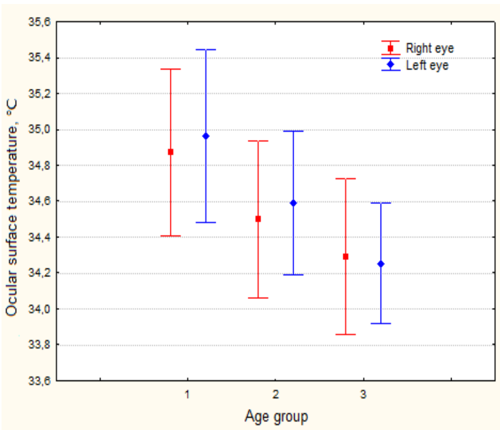
Parameter	Right eye	Left eye	Significance level
Temperature [°C]	34.5 ± 0.7	34.6 ± 0.6	0.78
Heat flux density [mW/cm^2]	7.7 ± 1.3	7.7 ± 1.4	0.9

Note: the table shows mean value and standard deviation (M ± SD).

Table 3. The ocular surface temperature and the heat flux density before and after dilation.

Parameter	Before dilation	After dilation	Significance level
Temperature [°C]	34.6 ± 0.7	34.8 ± 0.5	0.07
Heat flux density [mW/cm^2]	7.7 ± 1.3	8.9 ± 1.1	0.000

Note: the table shows mean value and standard deviation (M ± SD).



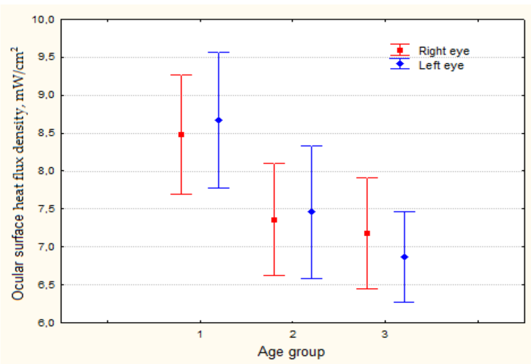


Fig.6. Parameters of temperature and heat flux density of the outer ocular surface of healthy individuals in three age groups.

In healthy individuals, 30 minutes after pupil dilation, an increase in heat flux density and a tendency to an increase in temperature of the ocular surface were noted. Such result is consistent with the data of other authors who studied the temperature of the outer ocular surface [38].

At the next stage, the dependences of temperature and heat flux density of the eye's outer surface on the age of the person were evaluated. The results are shown in Fig.6. A negative linear correlation between the age and the heat flux density was revealed (r = -0.5, p = 0.000).

The heat flux density of the eye in the first group averaged 8.6 ± 1.2 mW/cm^2, in the second group – 7.4 ± 1.1 mW/cm^2 (p = 0.003), and in the third – 7.0 ± 1.0 mW/cm^2 (p < 0.001 and p = 0.2 compared with groups 1 and 2, respectively).

In the first group, the temperature of the outer ocular surface averaged 34.9 ± 0.7 °C, in the second group, the temperature of the outer ocular surface was slightly lower and averaged 34.6 ± 0.6 °C (p = 0.07), in the third group, it was 34.3 ± 0.6 °C (p = 0.002 and p = 0.13 compared with groups 1 and 2, respectively). In these groups, mean temperature of the ocular surface according to infrared thermography was 35.3 ± 0.8 °C, 34.8 ± 0.6 °C (p = 0.3), and 34.4 ± 0.4 °C (p = 0.001 and p = 0.1 compared with groups 1 and 2, respectively). No significant differences were found between the ocular surface temperature measured by different methods in three age groups.

In the human eye, the blood circulation in the choroid is the main source of heat. With age, the choroid gets thinner [39]. Thus, age-related atrophic changes of the choroid and the associated decrease in blood supply to the vascular tract of the eye may be one of the reasons for the decrease in the heat flux density of the eyes of a healthy elderly person.

In our study, we also noted a decrease in the thickness of the choroid with age. The thickness was measured by optical coherence tomography. The heat transfer parameters of the eyes and the thickness of the choroid in three age groups are presented in Table 4.

Table 4. Parameters of heat transfer of the eyes and the thickness of the choroid in three age groups.

Parameter	Age groups		
	18-30 years, 11 people	31-60 years, 10 people	61-86 years, 11 people
Temperature [°C]	34.9±0.7	34.6±0.6	34.3±0.6*
Heat flux density [mW/cm^2]	8.6±1.2$^\#$	7.4±1.1*	7.0±1.0*
Thickness of the choroid [μm]	354±41	311±33	285±39*

Note: the table shows mean value and standard deviations (M ± SD).
*, significant difference (p < 0.05) compared to group 1;
$^\#$, significant difference (p < 0.05) compared to group 2.

The thickness of the choroid in healthy individuals averaged 307 ± 37 μm. There was a positive correlation between the thickness of the choroid with the heat flux density of the eye (r = 0.6, p = 0.000) and with the temperature of the cornea (r = 0.2, p = 0.1).

In patients with dry AMD the thickness of the choroid averaged 155 ± 60 μm ($p = 0.000$ compared with the third group of healthy individuals), the temperature of the outer ocular surface averaged 34.4 ± 0.7 °C ($p = 0.7$ compared with the third group of healthy individuals), and the heat flux density of the eye – 5.9 ± 1.1 mW/cm^2 ($p = 0.01$ compared with the third group of healthy individuals).

During the studies carried out using the developed thermoelectric device, no cornea injuries or other complications were observed. Real time measurements of the heat flux density of the eye were performed. The study of one eye lasts from 40 to 60 seconds.

The first results of clinical trials of the thermoelectric device in ophthalmology have shown that it is a simple and reliable device in operation. We would also like to underline the autonomy of the device, its versatility due to the possibility to connect the sensor to the conventional mounts of the Goldman tonometer, as well as the ability to carry out real time studies. The preliminary results of clinical piloting of the device have shown the safety of its use. It is provided both due to the special design of the contact thermoelectric sensor, and the use of the power supply of the device from a rechargeable battery. Thanks to the installation of the heat flow sensor in the standard mount of the Goldmann applanation tonometer, measurements were made quickly and comfortably in all cases due to the metered pressure of the sensor on the cornea, which also increases the stability of measurements.

5. CONCLUSION

For the diagnosis and treatment of ophthalmic diseases, it is important to understand the patterns of thermal processes that occur in the eye body and the relations between the parameters of such processes and changes in the structure of ocular tissues. It was for this purpose that a special device was developed and manufactured, which made it possible for the first time to measure the magnitude of the heat flux from the surface of the eye. In addition to the heat flux, the same device measures the temperature of the eye surface with high accuracy.

The design and technical parameters of the device described in the paper prove that this simple, compact, autonomous, easy-to-use and safe device can be useful in ophthalmic practice. Based on the results of the first clinical trials of the device in healthy and sick individuals, the dependences of temperature and heat flux from the ocular surface on the width of the pupil, thickness of the cornea, and age were defined.

A significant difference was revealed in choroidal thickness (155 ± 60 μm vs 285 ± 39 μm, $p = 0.000$) and density of heat flux from the ocular surface (5.9 ± 1.1 mW/cm^2 vs 7.0 ± 1.0 mW/cm^2, $p = 0.01$), but not in external ocular surface temperature (34.4 ± 0.7 °C vs 34.3 ± 0.6 °C, $p = 0.7$) between dry AMD patients and healthy individuals.

We believe that the developed device will improve the efficiency of early diagnosis of ophthalmic pathology associated with ocular hemodynamic disturbances (inflammatory processes, intraocular tumors, glaucoma, age-related macular degeneration).

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