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EQUIPMENT FOR DYNAMIC ELECTRON CONTACT THERMOGRAPHY OF SKIN MELANOMA

The computer-assisted hardware complex for dynamic electron contact thermography of skin melanoma has been developed. A cooling device based on the Peltier cell, a matrix scanner with intellectual «temperature/digital code» converters, and an original customized software for visualizing and processing temperature maps have been created. The combined use of the complex and the dermatoscopy technique have been experimentally established to improve the validity of early diagnostics of skin melanoma.

Key words: skin melanoma, DCT-1 digital contact thermographer, and dynamic thermography.

In recent years, there has been a trend towards an increase in the incidence of malignant neoplasms (MN) of the skin. The main causes of MN are the growing influence of solar radiation, as a result of ozone depletion, the widespread uncontrolled use of artificial ultraviolet radiation, and the toxic chemicals. Therefore, the problem of premalignant and malignant diseases of the skin has become a priority in public health research and practice.

The most frequent pathologies are skin melanocytic neoplasms recorded for 80% of the population [1, 2]. The melanocytic dysplastic nevi are precursors of skin melanoma (SM), one of the most dangerous and aggressive tumors that are prone to metastasizing to different organs.

Despite the fact that among malignant diseases of the skin the share of SM is only 12—14%, its early diagnostics is of paramount importance because of high mortality. According to the materials of the 8th Congress of European Association of Dermatologists, annually, worldwide, 160 thousand people sicken with melanoma and 48 thousand die from this disease. Over the past 20 years, the incidence of SM increased 4 times. According to the National Cancer Registry of Ukraine, in 2011, 3.3 thousand cases of SM (7.1 cases per 100 thousand population) were registered, and 1.2 thousand patients were reported to die. In the past 25 years, annual growth of SM incidence is 5%. The highest incidence has been observed in the southern regions of Ukraine [3]. Among the patients who sickened in 2011, 12.6% of patients died within a period less than a year. High mortality is caused by the late detection of disease, usually at an extensive (III-IV) stage, rather than by the lack of adequate therapy. Only early diagnostics of SM can reduce the mortality.

The melanocytic nevi are reported for 3/4 Caucasians and are benign tumors of melanogenous system. Only some of them are transformed into melanoma or are a marker of increased risk of SM development [4]. Therefore, differential diagnostics of benign and malignant melanocytic skin neoplasms is of crucial importance for the

dermatovenereologic practice.

It should be noted that there are a limited number of non-invasive instrumental methods that are widely used in clinical practice for early diagnostics of SM. The gold standard of diagnosis is dermatoscopy that is epifluorescent microscopy. This is a highly sensitive and highly specific method that makes it possible to recognize *in vivo* small structures of epidermis and papillary layer of the skin, which are indistinguishable to the naked eye. The method is easy to use and allows the researchers to store information in electronic database and to monitor the dynamics of tumor growth. According to the survey [5], for the integrated use of digital photography and dermoscopy sensitivity and specificity make up about 87 and 79%, respectively. High cost of modern digital dermoscopes prevents their wide use in practice. Other methods (X-ray, high-frequency ultrasound, radio phosphorous) are of secondary importance and cannot be broadly implemented because of high radiation exposure of the patient, high cost and difficult interpretation of the results. However, the combination of several techniques improves the accuracy of diagnosis [5, 6].

E-contact digital thermography can be a promising new method suitable for the use with dermoscopy in order to improve the reliability of early diagnosis. It is a cost-effective and harmless technique for mass screening of the population. A hardware complex based on *DCT-1* thermograph has been developed as part of NASU R&D project «Development and Mass Production of Digital Contact Thermograph for Diagnostics and Monitoring of Medical Treatment of Skin Tumor Diseases».

The *DCT-1* digital contact thermograph was developed earlier at O.O. Galkin DonIPhT of NASU, approved for the use and registered in the State register of medical equipment and medical products in Ukraine [7—9]. Currently, more than 40 devices are operated at the public and private health facilities of Ukraine. The device is manufactured by *Metekol* RPC (Nizhyn) and listed by the Ministry of Healthcare in the Suggested list of the materials and technical equipment of the primary healthcare center, which greatly simplifies the commercialization of the hardware and reduces the time required for the organization of its practical application.

THERMOGRAPHY IN DERMATOLOGY

In contrast to all the above methods of diagnosis, the thermal methods, thermometry and thermography, record the thermophysiologic changes accompanying the development of malignancy instead of the structural changes of tissues. They register local changes in skin temperature in the zone of pathological process (both surficial and deep) caused by enhanced metabolism and angiogenesis. As the breast practice has showed, such changes are often registered before their clinical manifestations [10, 11].

The differential thermometric methods involve measuring the skin temperature with a single thermometer in a limited number of points, both directly on the neoplasm and near it, on the skin areas subjectively deemed healthy. For example, according to [12], the temperature of the nevus and the average temperature of the four points around it at a distance of 1 cm are measured. The malignancy criterion is a difference between them exceeding 0.6 °C. The thermometric methods, despite their simplicity, have a significant disadvantage: the arbitrary choice of the few points on which the findings may critically depend. For this reason, they have not been widely used so far.

Much more widespread are skin MN diagnostic methods based on infrared (IR) thermography, i.e. the visualization of temperature maps of the body surface with the help of thermal imager [5, 13—15]. In these studies, the temperature maps were recorded in a static mode after the establishment of thermal equilibrium between the naked body of the patient and the environment. Having compared the images of neoplasms and the temperature maps a number of qualitative and quantitative diagnostic parameters such as shape and size of the hyperthermic area and the

magnitude of hyperthermia have been obtained. Thus, according to [5], the average hyperthermia of the patients with SM is 2.5 °C, while that of the patients with benign tumors is 1 °C. Hyperthermia in the form of strands is prognostically unfavorable. The observed temperature distribution facilitates the planning of surgery. In [14], having made a survey of 245 patients using a dermatoscope and an IR imager, the authors concluded that thermography could complement dermatoscopy. The average hyperthermia has been established to be 1.1 ± 0.3 °C for the benign nevi; 1.39 ± 0.28 °C for the dysplastic nevi, and 1.6 ± 0.4 °C for the malignant melanomas. It is believed that the nevi with hyperthermia more than 1.4 °C should be removed surgically. In [15], the authors determined sensitivity and specificity of the diagnosis of tumors of different sizes by IR imager. These parameters have been established to be 39—100% for the neoplasms having a size up to 5 mm; 58—98% for the neoplasms having a size of 5—15 mm, 95—100% for those whose size ranging from 15 to 30 mm; and 78—89% for the newly growing tissues greater than 30 mm. It is concluded large malignant and benign neoplasms are distinguished very well.

Nevertheless, static thermal imaging diagnostics of skin MN has significant shortcomings. *Firstly*, the room temperature should be comfortable and stable, with all sources of infrared radiation (heaters, powerful incandescent lamps, direct sunlight) shielded. *Secondly*, to prepare the patient, namely, to reach the thermal equilibrium with the environment, takes 15—20 min, which reduces the productivity of the survey. These deficiencies especially complicate the mass screening.

Recently, dynamic infrared thermography of skin neoplasms has been intensively developed in order to raise sensitivity and specificity, especially for the study of pigmentary disorders of small size (5 mm). The dynamic method implies that a selected portion is forcibly cooled and then, while it is warming up to the room temperature, a series of consecutive shots is made by IR imager. Inasmuch as thermal radiation is the dominant mechanism of heat exchange between the human body and the environment (80%), the thermal contrast in the temperature map intensifies as the temperature difference between the body and the environment increases. In addition, the cooling is a physiological factor that emphasizes the temperature difference in the body areas with different rate of blood circulation. From a series of pictures it is necessary to select those in which hyperthermia of MN is displayed most prominently.

In [16], dynamic thermography has been realized for the first time in dermatological practice. A skin area of 10 cm × 10 cm was cooled using a packet of aqueous gel having a temperature of 20 °C. The research has showed based on the specific features of temperature map transformation it is possible to distinguish the benign and the malignant neoplasms.

This technique was further studied in a series of research at the John Hopkins University, Baltimore, USA. The results of research [e.g., 17, 18] have been summarized in [19] and in patents [20, 21]. In [17, 18], skin was cooled down to 10—15 °C using compressed air blown through a vortex cooler, while in patent [20], the authors proposed to use for this purpose cold water, ice or pre-chilled plate. The temperature distribution was recorded by IR imager or by IR confocal microscope. The temperature difference between the small nevus and the healthy skin area has been showed to reach its maximum within a few minutes after the removal of the cooling device, with hyperthermia of suspicious nevus having a diameter of only 2 mm detected.

A positive quality of dynamic thermography is the fact that the time of patient preparation decreases to 1—2 minutes (time of cooling the skin area) as compared with 15—20 min required by the static method for the patient adaptation to the room temperature. However, both the general shortcomings of IR thermography (high requirements to room condition, temperature stability, and qualifications of technical personnel, high

cost of advanced matrix IR imagers) and the specific difficulties (the need for a computer compensation of involuntary movements of the patient in the process of shooting a sequence of temperature maps) hinder the introduction of thermography in clinical practice [17—19].

THE HARDWARE PART OF THE DEVELOPED COMPLEX

To implement dynamic contact thermography of skin neoplasms using *DCT-1* thermograph a specialized temperature scanner, a cooling unit with temperature control and a software have been developed. The block diagram of the complex is showed in Fig. 1.

To measure the temperature of a large number of points on the skin surface an advanced system of digital contact thermography is used. It is based on miniature microprocessor telemetric temperature sensors that convert *temperature* into *digital code*. These converters are arranged in a matrix scanner and through the common three-wire bus and the hardware interface block with galvanic isolation are connected to the signal processor, a personal computer with which they communicate. This thermography system has several advantages as compared with the IR imaging technique. Since the measurements are made by direct contact method, the effect of interference from external heat sources significantly decreases and the requirements for room condition soften. The sensors have stable metrological characteristics and do not require any calibration. The scanners based on them have small dimensions, and the thermograph is much cheaper and easier to use than the infrared imager. The availability of ready information in digital form (without analog-to-digital converters) facilitates the visualization of temperature distribution (i.e. the creation of temperature maps) and the calculation of quantitative statistical temperature parameters (hypo- or hyperthermia) and geometrical parameters (area of temperature zones).

To produce undistorted temperature maps the matrix scanners for contact thermography should meet the following mandatory thermodynamic and structural requirements:

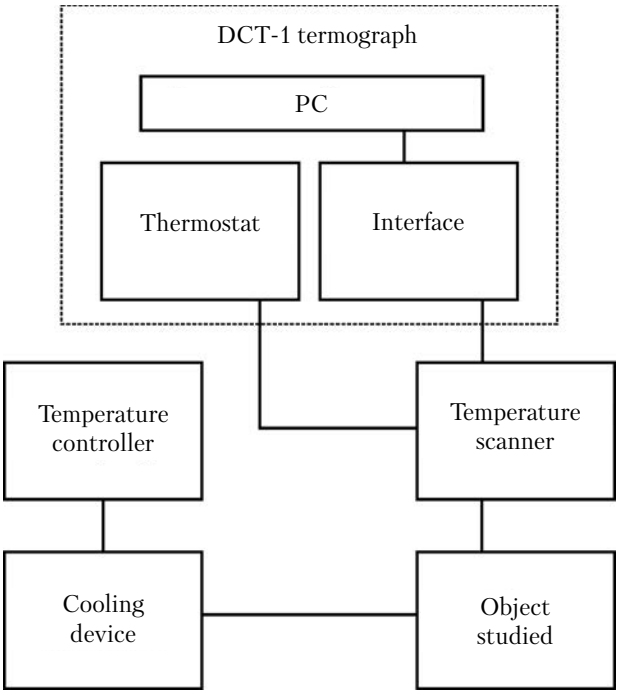

Fig. 1. Block diagram of the developed complex apparatus

- Thermal conductivity between adjacent sensors of the scanner by structural components and connecting conductors should be minimized;
- The stray heat flux from the sensors into the environment should be minimized;
- Mass and heat capacity of the structural elements on which the sensors are mounted should be minimized to reduce thermal inertia;
- Stable thermal contact of the sensors with the patient's body should be ensured;
- The matrix should be reliably protected from external radiation and thermal noises.

The main design requirements are as follows:

- The sensor matrix pitch should be consistent with the expected size of the thermal irregularities in the temperature map to obtain the necessary spatial resolution;
- The matrix design should be consistent with the geometry of studied body surface;
- The connecting wires between the sensors and the bus should accommodate a large number of measurement cycles;

✦ The scanner must be ergonomic.

The scanner of *DCT-1* thermographer meets all these requirements for screening the mammary glands [22], but is unsuitable for the study of temperature fields in the vicinity of pigmented nevi of small size (3—5 mm). Furthermore, melanocytic neoplasms often rise above the skin surface, therefore, to ensure thermal contact the scanner matrix should not be rigid.

The scanner square matrix is formed by intelligent converters DS18B20U manufactured by *Dallas Semiconductor* (USA) with sensitivity 0.0625 °C. The sensors have miniature plastic body of μSOP type (dimensions: 3 × 3 × 0.85 mm), with the leads increasing one size parameter to 4.9 mm. The sensor weighs approximately 23 mg, the thermal inertia is less than 10 seconds. The MicroLAN technique [23] in which all the sensors are connected to common three-wire bus is used for ensuring communication between the sensors and the computer.

Fig. 2 shows the scanner square matrix. To minimize the matrix pitch the adjacent sensors are arranged at an angle of 90° to each other, in staggered order. Such arrangement with a gap of 1 mm between the sensors makes it possible to realize a pitch of 5 mm, whereas if the sensors were aligned unidirectionally the pitch would be 6 mm. In addition, this arrangement prevents bridging between the leads of neighboring sensors.

The polymeric base of the matrix to which the sensors are attached with the contact glue is formed of three layers of EVA (ethyl vinyl acetate) flexible porous material bonded together and having a thickness of 7 mm. In the outer layer, to which the sensors are glued, there are 1.5 mm diameter holes through which the bundles of three twisted wires leading out of each sensor, and the other two layers have 3.5 mm diameter holes that allow the bundles shaped as helix to freely change their shape when the scanner is pressed. This flexible design ensures a long service life of the scanner without lead breaks and reliable results of thermography of convex neoplasms. In addition, the porous base matrix provides a low inertia and a low thermal conductivity between the densely packed sensors.

An important factor is the choice of material of which the sensor leading cables are made. The use of conventional copper wires of PEV, copper flexible electric conductor and other types results in unacceptable heat dissipation from the sensors, which can distort the natural temperature distribution over the skin. The developers of hardware complex have used Manganin wires with a low thermal conductivity having a diameter of 0.1 mm, the thermal conductivity of which is 13 times less than that of conventional copper wires having the same diameter. Increased active resistance of wires (as compared with the copper wires) does not impair the metrological characteristics of the scanner, inasmuch as the sensors are digital microprocessors, with resistance of their leads not affecting the conversion of temperature into digital code.

The scanner has an odd number of sensors (5 × × 5 = 25), with one of them located directly in the center of the matrix. In the course of thermography of the thermal field around the small pigment neoplasm (having a size of about 3—5 mm), the scanner is positioned in the target area of the skin so that the central sensor is placed exactly over the nevus and records its temperature, with the rest of the sensors measuring the thermal field around the neoplasm. This prevents any loss of data caused by discrete nature of the matrix.

To protect the scanner matrix from external radiation thermal noise it is placed within the shield made of polished aluminum alloy D16 that provides an isothermal environment around the matrix. On the surface of the shield, there is a label that in the course of thermography orients itself toward the patient's head. This eliminates the ambiguity of thermogram interpretation. An ergonomic polymer handle allows the operator to hold the scanner comfortably. For the aseptic purpose, the scanner matrix is coated with a thin disposable polymer film that does not affect the measurement accuracy. The scanner general view is showed in Fig. 3.

The hardware includes a single digital contact thermometer (Fig. 4). It is also based on *DS18B20U* thermal converter. The thermometer applies to thermography of suspicious neoplasms by the differential static method in the remote places of the body surface, where the thermal imaging technique is difficult to realize.

The developed hardware provides for cooling the skin area with the neoplasm by the dynamic thermography technique using a Peltier semiconductor cell whose area covers the area of the skin. This advanced method of cooling is very convenient, insofar as it eliminates the use of gaseous, liquid or solid refrigerants and refrigerators used in [16-21]. This is a particularly valuable advantage in the view of mobile screening. The heat flux from the skin is proportional to the electric current flowing through the Peltier cell. This makes it easy to control the processes of cooling and temperature stabilization by conventional electronic techniques. The temperature of cooled skin surface at the end of the cooling process is equalized in a similar easy way. The developed cooling device is lightweight, compact, and easy to maintain.

The complex incorporates a *TES1-127040-40* Peltier cell with an area of 40 × 40 mm, which overlaps the scanner matrix having an area of 25 × 25 mm. The element is sandwiched between the aluminum shoe and the radiator. The shoe is made of material with high thermal conductivity and is located on the surface of one of the elements. It is intended for obtaining a uniform temperature distribution and for ensuring a good contact with the skin. The radiator is designed to withdraw heat from the opposite (hot) surface of the element. To improve the heat withdrawal the radiator is equipped with a small-sized fan. On the cold surface of the element, there is a thermistor involved in stabilizing the temperature of the shoe and, consequently, of the cooled skin area. All this structure is placed within the case equipped with an ergonomic handle and is connected to the thermocontroller unit via cable.

The thermocontroller is a similar device in which the thermistor is incorporated into one of the legs of resistor bridge, with a K140UD17 amplifier used for enhancing the error signal. The key element controlling the current through the Peltier cell is an *IRF630* field transistor. The controller is equipped with a LED indicator of temperature of 15 °C that does not cause any patient's discomfort. The tests have showed that to obtain a uniform temperature distribution over the skin area it suffices to cool it for 2 minutes. This testifies to the effectiveness of the proposed cooling technique. General view of the cooling device is showed in Fig. 5.

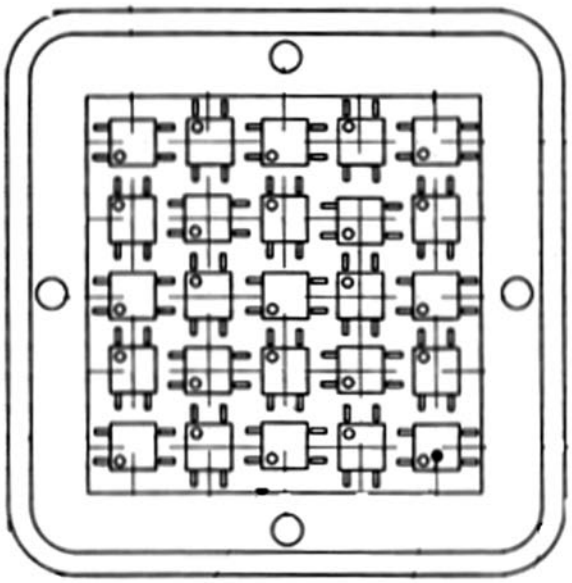

Fig. 2. Arrangement of sensors on square matrix of temperature scanner

The scanner and the cooling device are precisely positioned with respect to the suspicious nevi using a stencil made of transparent resin plate. On the stencil, there is a crosshair, the center of which coincides with the center of the nevus. On the four beams forming the crosshair, there are the four holes corresponding to the size of the scanner's square screen and the four holes corresponding to the size of the cooler's case. Through these holes the operator makes positioning marks on the patient's body using a surgical marker. These marks help to match the scale of digital

Fig. 3. General view of temperature scanner

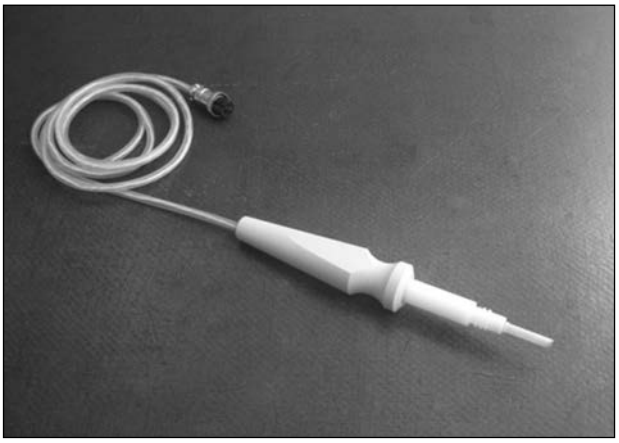

Fig. 4. General view of single contact digital thermometer

photography of the neoplasm and the scale of thermal map on the computer screen.

THE SOFTWARE

A computer program is written in Visual Basic v.6 for *Windows XP* and *Windows 7* and has three modes of operation: 1) the matrix mode without cooling the object of screening, 2) the matrix mode with pre-cooling of the object, and 3) the single thermometer mode.

The first mode is for thermographic study of extended objects whose area is larger than the size of the scanner matrix. The thermogram is obtained by sequential positioning of the scanner on adjacent areas of the skin and measuring the temperature distribution in these areas (positions). The complete thermogram is a sort of mosaic of the thermograms of positions. In this mode, the program carries out a dialogue with the sensors by MicroLAN protocol, verifies the sensor readings, composes a mosaic thermal image, matches the sizes and binds the thermograms and the photos of the object, calculates the statistical parameters of the thermogram (such as average, minimum and maximum temperature, isothermal zones and areas, etc.), controls data output to the screen, and saves them in a file.

The second mode (with pre-cooling) is for dynamic thermographic study of skin surface. In this mode, in addition to the above listed functions, the program controls cooling of the skin area and frame-by-frame shooting of thermograms in the process of skin warming. As the prechilled skin area warms, the thermogram photographs of the skin area, the statistical temperature parameters, as well as the graphs of scanner sensor readings grouped according to the algorithm are displayed on the screen in real time, in given intervals. These graphs help to illustrate the warming of the nevus area and the surrounding skin zone and to fix the time of maximum divergence of their temperatures. The magnitude of this maximum difference is one of the main parameters for concluding on the neoplasm nature.

The third mode (the single sensor mode) is used for operational control of skin temperature in hard-to-reach places. In this mode, the single sensor readings are displayed on the screen in regular intervals forming a map of the temperature. The sensor reading at any point of the graph can be displayed in digital form using a mouse or a keyboard.

DIAGNOSIS METHOD

The diagnosis method using the developed equipment reduces to the following sequence of

operations that must be performed before the dermatoscopy study:

1) Once, at the beginning of the shift, the scanner is «calibrated» to check the operation of 25 scanner sensors and to match their transmission characteristics up to a unit of discrete temperature conversion (0.0625 °C). For this purpose, the computer scans all scanner sensors placed in advance within the insulated thermostat of *DCT-1* thermographer [22] and makes individual adjustments calculated relative to the average temperature of the entire matrix; this procedure lasts two minutes, at most;

2) The selected skin area with suspicious neoplasm is marked in the following way: a stencil is placed so that its crosshair coincides with the center of the neoplasm; the operator puts marks on the skin for the Peltier element and the scanner matrix through the 8 holes of the stencil, using a surgical marker;

3) The operator makes digital photography of the skin area with neoplasm and the marks;

4) The marked area of the skin is cooled by the cooling device positioned with respect to the outer marks;

5) The operator removes the cooling device and applies the matrix scanner to the chilled skin area pressing it very gently and positioning it with respect to the inner marks (while the skin area is warming, the signal processor scans all the sensors and builds intermediate thermograms in predetermined time interval (from 5 to 30));

6) The operator prints on the screen the resulting sequence of thermal images and selects one of them with maximum thermal contrast, i.e. with a clear thermophysiologic anomaly;

7) The operator displays the numerical statistical parameters such as the average, the minimum, and the maximum temperatures of the thermogram, the areas of temperature zones, etc.;

8) On the basis of the obtained temperature maps, respective photographs of the neoplasm and the statistical parameters the diagnostician makes conclusion on the absence or presence of pathology or the effectiveness of medical treatment.

IN-PATIENT TESTING OF THE HARDWARE COMPLEX

In-patient tests of the complex have been carried out in Donetsk Municipal Dermatovenereologic Dispensary no.1 both with the patients with pigmentary neoplasms found at primary medical examination and the patients with established diagnosis of *melanoma* involved. For applying the dynamic contact thermography method the skin area surrounding the neoplasm was thermally stimulated by cooling to 15 °C. More than 50 patients have been examined.

Figure 6 (see the color inset) shows a thermogram and a photo of neoplasm of a patient having a *dysplastic nevi*. Hereinafter, the reference grids on the photos and thermograms have the same geometric dimensions, with the scales of the photos and thermograms agreed by matching the marks made on the body by a surgical marker through a stencil and the marks (circles) on the reference grid of the photo. The color palette displays the temperature distribution from the minimum to the maximum using colors from blue to red, respectively [9]. The thermogram clearly shows that around the neoplasm there is no hyperthermic zone, which testifies to the absence of proliferative processes and therefore, the absence of malignant transformation of the neo-

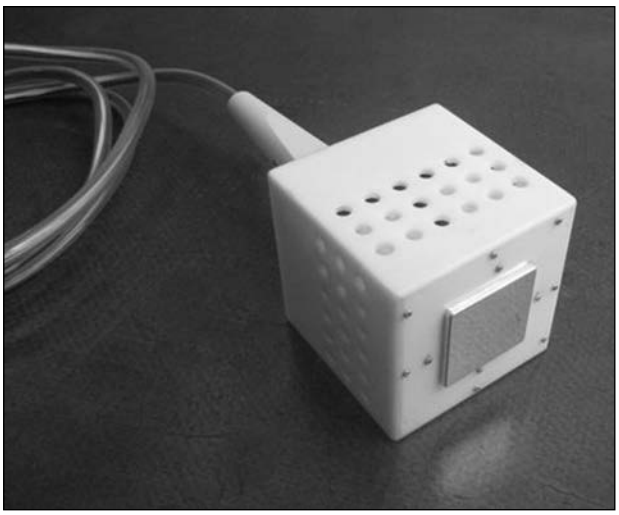

Fig. 5. General view of cooling device

plasm. This thermogram is typical for the benign pigmentary neoplasms.

Figure 7 (see the color inset) shows a thermogram having a substantial hyperthermia with a temperature difference of 3 °C. The hyperthermic zone coincides with the visible neoplasm but is much broader. Given a large magnitude of observed hyperthermia, its position, size, and shape the patient with suspected malignification is sent for further examination by traditional methods.

Figures 8 and 9 (see the color inset) show the data of patients with diagnosed *melanoma*. One can see clear hyperthermic zones with temperature differences of 3.8 °C and 5.7 °C, respectively.

Thus, it can be stated that the dynamic electronic contact thermography can distinguish the benign neoplasms and the malign tumors and is a promising new method that, if combined with dermoscopy, makes it possible to improve the accuracy of early diagnosis of skin melanoma.

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КОМПЛЕКС АПАРАТУРИ ДЛЯ ДИНАМІЧНОЇ ЕЛЕКТРОННОЇ КОНТАКТНОЇ ТЕРМОГРАФІЇ МЕЛАНОМИ ШКІРИ

Розроблено комп'ютеризований комплекс апаратури для динамічної електронної контактної термографії меланоцитарних новоутворень шкіри. Розроблено та виготовлено охолоджуючий пристрій на основі елемента Пельтьє, температурний матричний сканер з інтелектуальними перетворювачами *температура — цифровий код* і спеціалізоване програмне забезпечення для візуалізації температурних мап та їх первинної математичної обробки. Експериментально обґрунтована перспективність спільного застосування комплексу з дерматоскопією для підвищення достовірності ранньої діагностики меланоми шкіри.

Ключові слова: меланома шкіри, термограф контактний цифровий ТКЦ-1, динамічна термографія.

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КОМПЛЕКС АППАРАТУРЫ ДЛЯ ДИНАМИЧЕСКОЙ ЭЛЕКТРОННОЙ КОНТАКТНОЙ ТЕРМОГРАФИИ МЕЛАНОМЫ КОЖИ

Разработан компьютеризованный комплекс аппаратуры для динамической электронной контактной термографии меланоцитарных новообразований кожи. Разработаны и созданы охлаждающее устройство на основе элемента Пельтье, температурный матричный сканер с интеллектуальными преобразователями температура – цифровой код и специализированное программное обеспечение для визуализации тепловых карт и их первичной математической обработки. Экспериментально обоснована перспективность совместного использования комплекса с дерматоскопией для повышения достоверности ранней диагностики меланомы кожи.

Ключевые слова: меланома кожи, термограф контактный цифровой ТКЦ-1, динамическая термография.

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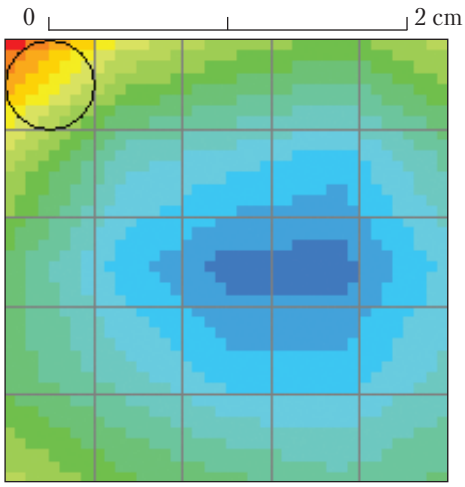


Standardized temperature-depth profile.
Frame 12

Photographic picture of the object

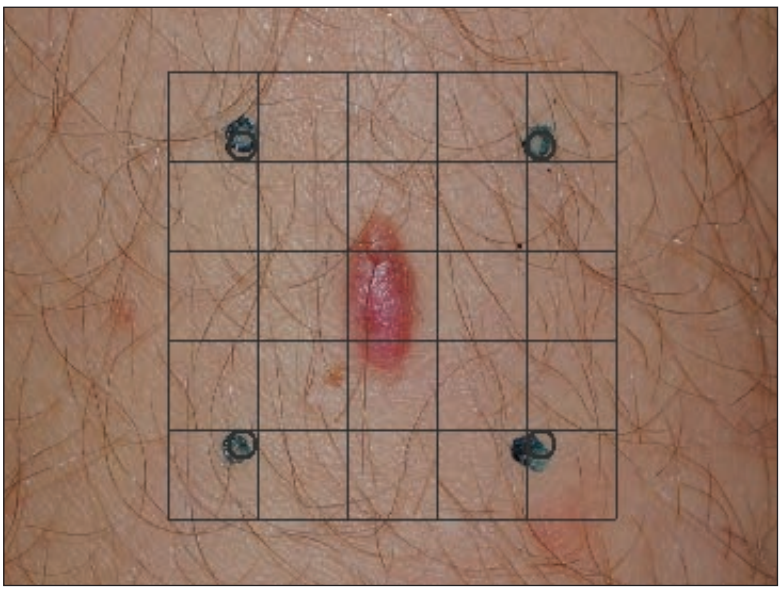
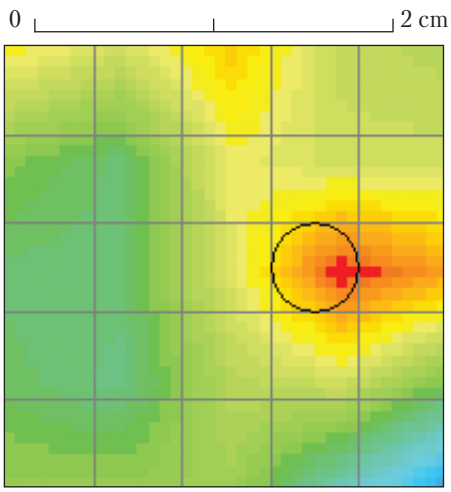


Fig. 6. Temperature-depth profile and photographic picture of neoplasm in patient with diagnosed dysplastic nevus without malignant transformation



Standardized temperature-depth profile.
Frame 7

Photographic picture of the object

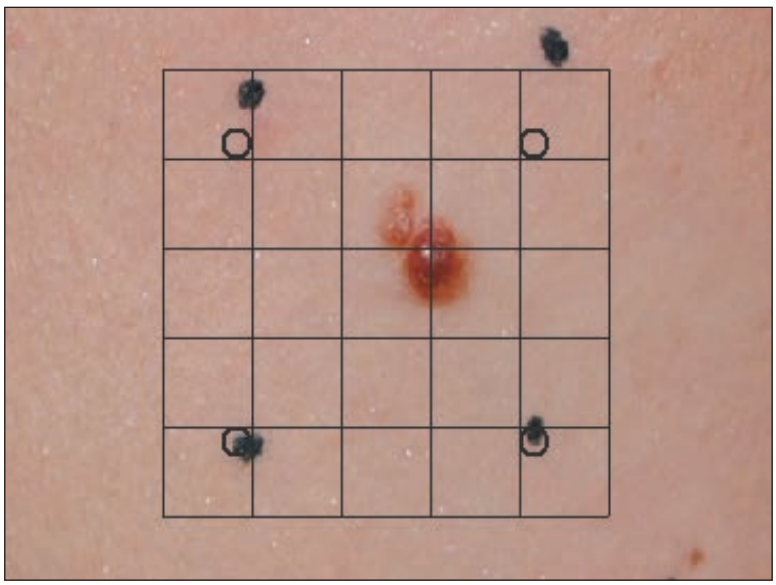
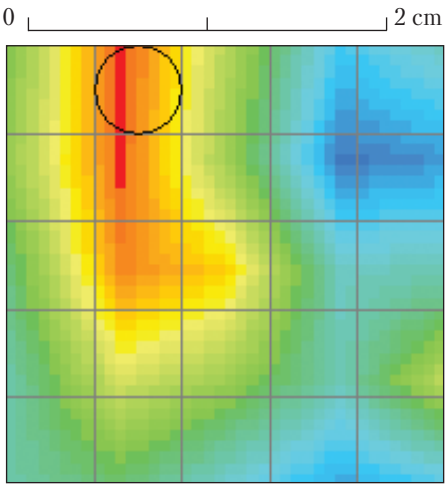


Fig. 7. Temperature-depth profile and photographic picture of neoplasm in patient found at initial examination. Suspicious hyperthermia has been recorded



Standardized temperature-depth profile.
Frame 7

Photographic picture of the object

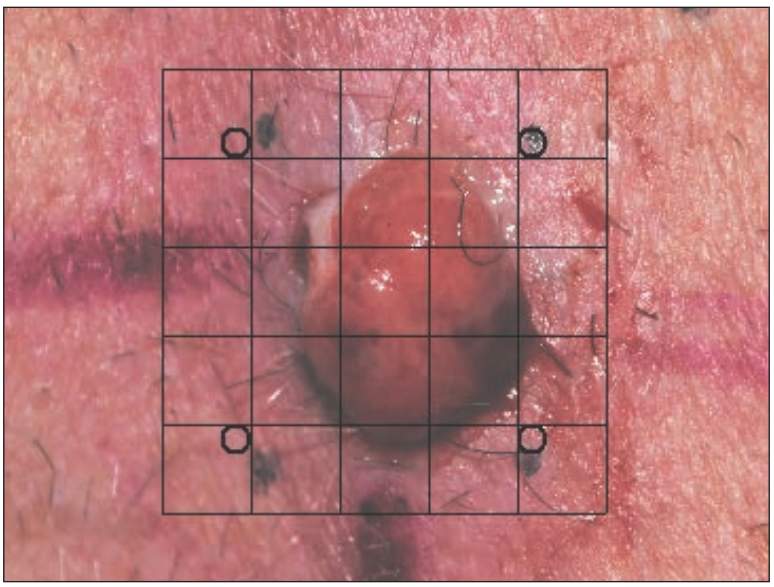
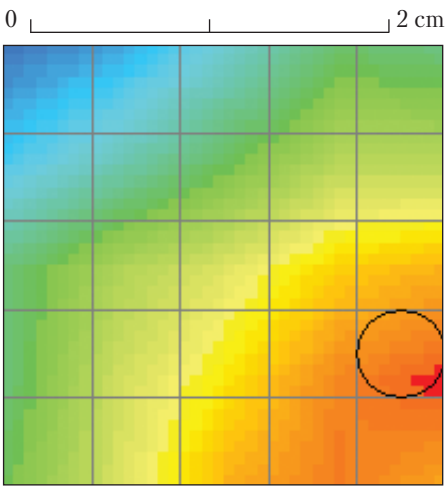


Fig. 8. Temperature-depth profile and photographic picture of tumor in patient N with diagnosed melanoma



Standardized temperature-depth profile.
Frame 3

Photographic picture of the object

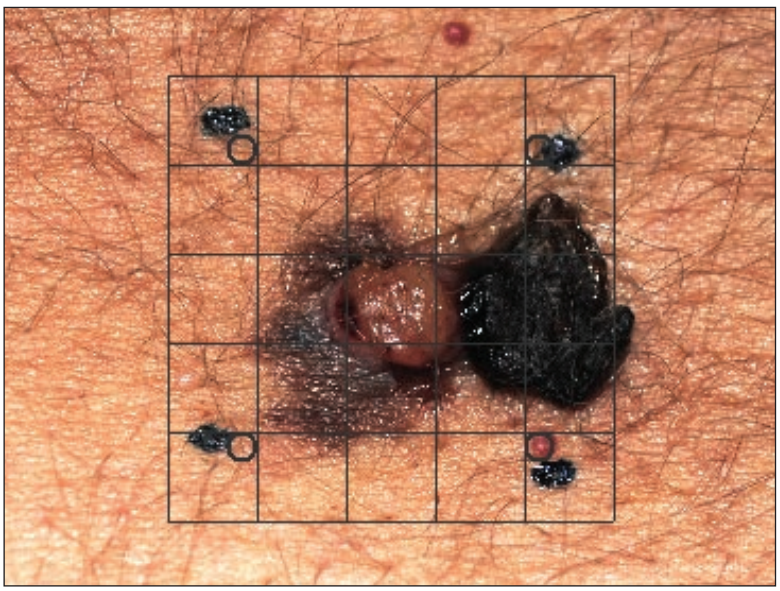


Fig. 9. Temperature-depth profile and photographic picture of tumor in patient NN with diagnosed melanoma