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Diagnostics of Early Signs of Surface-Spreading Melanoma Using A Robotic Complex

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ABSTRACT

The article presents a brief analysis of the state of diagnosis of skin melanomas in the region. It is shown that the incidence of this pathology has increased more than 1.5 times over the past decade. The percentage of nodular skin melanomas is 47%, requiring expensive treatment than the early surface-spreading forms. In order to detect skin melanomas earlier and activate pigment nevi, we have developed a non-invasive method of ZOOM diagnostics using a portable USB microscope with digital transmission to a robotic complex with a touch screen and pre-staining the pigment nevus using the Van-Gieson type-picrofuxin (positive decision to grant a patent for invention no. 2019136711/14 (072500 of 14.11.2019). In this case, connective tissue fibers are colored yellow and collagen (reticular) in bright red, creating a diamond-shaped network. When activating or transforming pigment nevi, structural changes occur that can be recorded on the screen and a library with standards can be created. For the purpose of interpretation, two lines from one corner to the other, provided for in the computer insert, were "water" on the segments. The method is simple, tested in 40 patients and can be used at the primary care stage or sent for remote counseling.

Keywords: Pigment nevi, USB microscope, Picrofuxin, Digital transmission to the screen of a robotic complex

There is not a single person who does not have 10 pigment nevi. The frequency of skin melanomas (MC) has increased almost 2 – fold over the past decade, mainly among middle-aged and elderly people due to sunburn and an increase in the high frequency of advanced cases and 1-year mortality, respectively, by 10% and 19% [1].

According to many authors [2,3] the phase of horizontal growth (usually up to 6 mm) replaces the phase of radial growth and is a manifestation of progression. MC is more likely to develop in women aged 30-60 years. Its manifestations are diverse. MC in the 2nd phase can rapidly develop and metastasize. To prevent this, it is important to diagnose the neoplasm in the horizontal growth phase.

MC can develop both on the background of an existing nevus and on unchanged skin. There are the following signs of malignant transformation of skin pigment formations (ABCDE method): A-asymmetric form of formation; B (borders) - irregular, indistinct outlines of the edge; C (color)- heterogeneous color D (diameter) - diameter of the formation E (evolution) - evolution/development (changes occurring in the pigment formation). However, clinical signs are not always early, so any pigment formation should be mandatory examined by a specialist. In addition to the visual examination, a dermatoscopy is performed, which increases the effectiveness of the diagnosis of primary melanoma. A number of authors allow biopsies to be performed by scraping or taking a piece of tissue for morphological examination for the diagnosis of primary MC [2]. However, this is an invasive method and should only be performed by a specialist before surgery. At the primary level, you must adhere to the principle of "Non tange me" (don't touch me).

In Russia, over the past 10 years, the incidence of MC has increased from 5.46 to 7.76 (almost 1.5 times).

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PURPOSE OF RESEARCH

Assess the state of skin melanoma diagnosis in the region and develop a non-invasive method for detecting signs of activation of pigment nevi and surface-spreading melanomas.

MATERIALS & METHODS

From 2014 to 2018, 276 patients with skin melanomas aged 22 to 75 years (101 men and 182 women) were registered in the Novgorod region. The number of cases of MC in the last 5 years with certain fluctuations shows a tendency to stabilize with an excess of the incidence among women by 8.2%. However, if compared over a longer period (since 2009 **Table 1**) the number of cases increased by more than 1.6 times, which is associated with a change in lifestyle, fashion trend to tan led to a significant increase in the total time and area of exposure to UVF on human skin, which is not evolutionarily adapted to this.

Table 1. Comparative data on morbidity and mortality from skin melanoma in the Novgorod region (2009-2018 in abs. tsch.).

No.	Indicators	2009	2014	2015	2016	2017	2018
1	Number of cases	37	61	51	62	41	61
2	Number of deaths	15	18	18	15	19	16

According to the results of statistics in the region, most of them are registered nodal MC (47%), characterized by primary vertical growth, this is due to untimely diagnosis and late treatment of patients and waiting for the "open day", held once a year. However, despite the current situation, the number of deaths in recent years has increased slightly, due to more expensive treatment (increased volume of plastic surgery, the use of adjuvant immunotherapy and targeted drugs).

The most common method for diagnosing MC is dermatoscopy, which usually allows for a 10-fold increase in the surface structures of the tumor. The doctor applies special immersion oil to the mole and applies a Dermatoscope to it. The light source is fed from the side at an angle resulting in some surface structures being reflected, which are then analyzed.

The main disadvantages of this option of dermatoscopy are: the inability to examine deeper layers with a Dermatoscope; the lack of own lighting; inspection by a single specialist; the inability to document photos and conduct telemedicine consultation in the "op-line" mode with leading specialists [4].

To study the structures of connective tissue, we used a brush to paint Van-Gieson when a nevus transformation was suspected for 5-10 min. The dye was a mixture of acid fuchsin and picric acid (picrofuxin). For surface forms of pigment neoplasms, the dye penetrates the skin epithelium, while fuchsin stains the collagen fibers in a bright red color, located in the dermis in the normal form of rhombs **(Figure 1)**, picrin adds yellow and other colors to other tissue structures that become randomly or asymmetrically arranged in melanoma - Jocelyn H. Bruce-Gregorios, M. D.: carried out a histopathologic techniques, JMC Press Inc., Quezon City, Philippines, 1974.; Wikipedia.

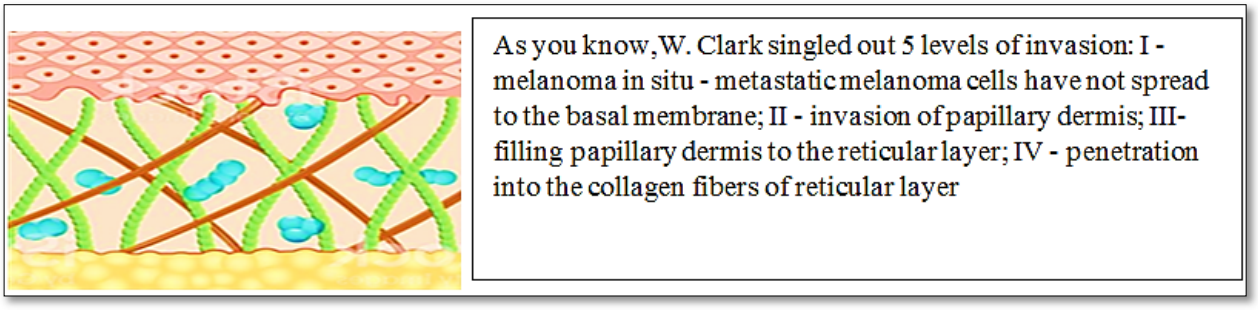


Figure 1. Schematic representation of the skin structure (collagen fibers are located in the IV layer, forming a diamond-shaped frame of bright red color under the influence of the dye).

Using a robotic complex and interviewing the patient with illustrations in the section "Pigmented nevi" according to standards, the presence of a nevus with signs of activation or high risk (borderline, Dubreuil's melanosis, etc.) is established. A trained nurse paints the studied nevus with picrofucxin for 5-7 min with a brush. The patient, under the control of the nurse, takes a sleeve with a portable USB microscope with an adjusted focus and puts the tube on the pathological process, which is displayed on the monitor screen with full-screen magnification. In connection with staining with a special dye, we get information from deeper layers (where the collagen fibers are located). For the purpose of topographic assessment, two "water" lines are applied to segments from one corner to the other, provided in the computer insert. The lines were superimposed on a fixed digital photo (**Figure 2**; positive decision to grant a patent for invention no. 2019136711/14 (072500 of 14.11.2019).

Figure 2. Robotic complex. USB microscope, schematic execution of photos and interpretation (without coloring). Then we performed visual interpretation of enlarged and colored structures of the pigment nevus by segments. To objectify the assessment of signs of malignancy of pigmented skin tumors, the mathematical sum of micromorphological signs (MMS) presented in **Table 1** was used.

We sum up the points and get mathematical micromorphological features (MMS):

1. Benign neoplasm-from 0 to 5 points
2. Borderline neoplasm-from 5 points
3. Malignant neoplasm-from 6 points

This method was tested in 40 patients at the regional clinical Oncology center.

As a result of the clinical examination, it was concluded that 9 patients have intradermal nevus, 2 have senile keratosis, and 8 have mixed nevus. In 2 cases, Dubreuilmelanosis was established. 13 people have border nevi. In addition, 6 patients were suspected of activating the process **(Table 2)**.

Table 2. Weight of signs or changes in points (last 3-6: months).

No.	There are no signs of pigmented neoplasm	No	On one side of the axis	On both sides of the axis
1	Asymmetry and/or changes in the external contours of the entire nevus	0	1	2
2	Asymmetry of collagen and other fibers around the nevus	0	1	2
3	Asymmetry in color: grey-blue, black, beige, red, white	0	1	2
4	Lack of skin pattern, structureless formations, sometimes the appearance of Shine	0	1	2
5	Collagen fibers that form partitions-in thickness and color, abruptly break off along the periphery of the hearth	0	1	2
6	Globular model. Globules of different size and color, appearance of gray-blue and/or reddish tones	0	1	2
7	Globules are randomly arranged, borders abruptly break off	0	1	2
8	Formation of blurry spots, dots, blotches. Different colors	0	1	2
9	The appearance of blacker globules on the periphery signs of growth of the nevus	0	1	2
10	Atypical collagen network with the formation of glomeruli and spots-signs of the beginning of satellite formation	0	1	2

As can be seen from **Table 3**, according to our data, including on the "Open doors" day, the use of ZOOM diagnostics with staining in 11 patients (28.2%) revealed signs of transformation into a malignant neoplasm, of which in 1 case, a histological study after surgery turned out to be melanocytic dysplasia.

As an illustration, we give several examples **(Figures 3,4 and 5)**.

Table 3. Results ZOOM the diagnosis staining with fuchsin.

No. Nosology	Number of patients	Diagnosis	
		Confirmed	The transformation is set
1 Senile keratosis	2	2	-
2 Border nevus	13	9	4
3 Intradermal nevus	9	9	-
4 The compound nevus	8	7	1
5 Dubreil's Melanosis	2	-	2
6 Activation of the nevus	6	2	4
Total	**40**	**29**	**11**

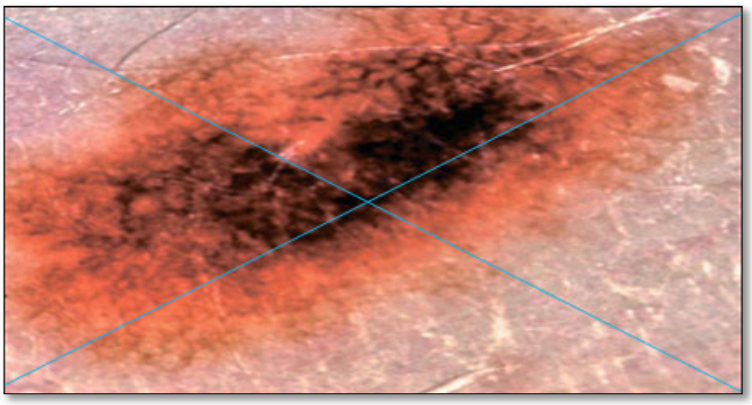


Figure 3. Borderline pigment nevus with the first signs of transformation-a pigment network of unevenly dark color is located in the center-2; around collagenosis is bright red without structure-2; in the upper segment, collagenosis asymmetrically shines through in the center-2. Conclusion: potentially malignant neoplasm. MMS = 2 + 2 + 2 = 6 bals.

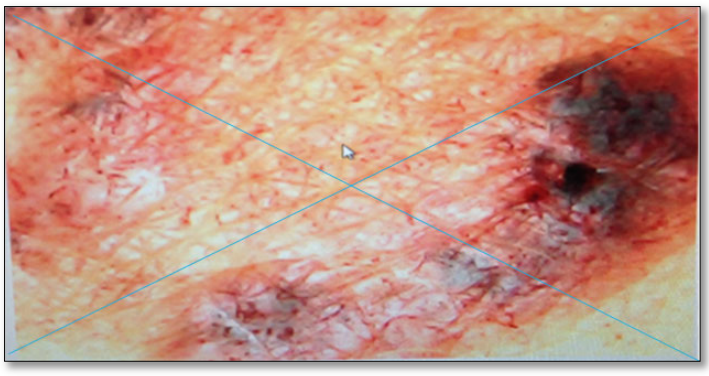
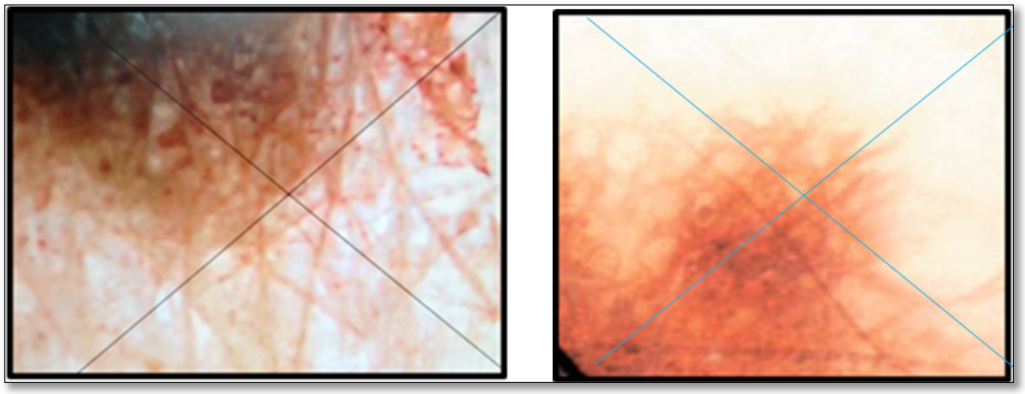


Figure 4. Surface-spreading melanoma with different degrees of pigmentation -2 and irregular borders from Dubreil's melanosis-2; bright red uneven collagen fibers and yellow connective tissue in different segments-2; tissue forms a chaotic network with areas of their breakage-2, lumps of pigment, whitish spots mainly in the lower and left segments-2. MMP= 2+ 2+ 2+ 2+ 2 = 10; histology #30174 from 16.10.19. Diagnosis: Surface-spreading melanoma. The thickness of the pigment neoplasm is 0.6 mm.



a) b)

Figure 5. Edge pigmented tumors after staining with fuchsin: a) collagen fibers relatively uniformly away from a benign pigmented nevus; b) collagen fibers depart randomly, break and form a ball with pinpoint inclusions, indicating the early appearance of the satellites.

CONCLUSION

1. Preliminary data on microscopy of surface-spreading pigment formations with a special dye are a real breakthrough in the diagnosis of melanomas. The use of this technique can be used for remote counseling.

2. Evenly rhomboid arrangement of collagen fibers in the nevus and their departure from the edge characterizes a benign pigment nevus, chaotic location, their breakage, the formation of glomeruli at the edge with dot inclusions, indicates, respectively, malignization and the beginning of the appearance of satellites.

3. An important aspect of improving the effectiveness of diagnosis of early forms of melanoma is training the population in self-examination methods and contacting a specialized institution directly.

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