

**PERFECT BIOPSY METHODS FOR THE DIAGNOSIS OF MALIGNANT MELANOCYTIC SKIN NEOPLASMS (A LITERATURE REVIEW)**<sup>1</sup>National Pirogov Memorial Medical University (Vinnytsya, Ukraine)<sup>2</sup>Ukrainian Military Medical Academy (Kyiv, Ukraine)<sup>3</sup>Danylo Halytsky Lviv National Medical University (Lviv, Ukraine)

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*Malignant neoplasms of the skin are quite common tumors in the world population among the population of Ukraine. Biopsy remains the main and definitive method of diagnosing such tumors. It is, actually, biopsy that makes it possible to establish a diagnosis in the early stages and provides a favorable prognosis for the survival of patients.*

*Today, the most common biopsy methods are: punch biopsy, shave biopsy, excisional and incisional biopsy. Most guidelines recommend full-thickness excisional biopsy as the preferred procedure for suspected melanoma. To this day, there is no unification in the types of biopsy given the clinical diversity of benign melanocytic skin formations, non-melanoma malignant skin tumors and melanoma.*

*The most inaccurate method turned out to be the punch biopsy method, which is associated with an increased risk of a low level of melanoma diagnosis. Excisional complete biopsy is the most justified in most cases of diagnosis. But definitely a skin biopsy remains the first step to establish a final diagnosis. Rational biopsy technique remains an issue that needs further study.*

**Key words:** skin biopsy, nevus, melanocytic skin neoplasms, malignant neoplasms of the skin, melanoma, technique, complications, dermato-oncology.

**Connection of the publication with planned research works.**

The work is a part of the research work "Development of modern methods of diagnostic and treatment of purulent-septic complications in managing surgical trauma" (state registration number 0120U101834).

**Introduction.**

Although skin biopsy is simple and easy to perform, it is a significantly important clinical method of diagnosing most lesions and neoplasms in the practice of a GP, dermatologist and oncologist [1]. Due to the widespread prevalence of the malignant neoplasms of the skin and other skin diseases in the general population, the question of choosing a skin biopsy method is gaining more and more popularity. The punch biopsy, shave biopsy, excisional and the incisional biopsies are considered to be most frequently used today [2]. The choice of biopsy method depends on the prognosis of the pathology and the location of the lesion which is of great importance in the diagnosis of malignant neoplasms of the skin.

Biopsy can be a quick and comfortable method of diagnosis, as well as provide the necessary level of diagnostic information, provided that it is adequately used, which allows for the formation of the further treatment tactics. The question of the best «ideal» method of the skin biopsy for the differentiation of the malignant neoplasms is still debatable, which on the one hand ensures the accuracy of the diagnosis and adequate therapy for the patient, and on the other - should be the least traumatic procedure, taking into account the risk of the tumor spread and the absence of complications considering the economic factor [3]. Modernity offers us many new methods of melanoma diagnosis, even with the involvement of artificial intelligence, with fairly high and accurate visualization [4-6]. However, it is the skin biopsy that occupies the central place in the diagnosis and treatment of the malignant neoplasms of the skin [7-9].

**The aim of the work.**

To review modern sources on the biopsy technique in the rational diagnosis of malignant skin neoplasms with the involvement of electronic databases MEDLINE/PubMed, EMBASE/Excerpta Medica, Cochrane Library, PubMed and Google Scholar. 48 publications were analyzed over the past 10 years and included in our review.

**Main part.**

Technical aspects of performing a biopsy are described in detail in many clinical guidelines and recommendations [1, 2, 10]. Nevertheless, some other aspects of this method are no less important and quite controversial. Timely diagnosis and treatment of melanoma is of crucial importance and are the most important factors that increase the patient's survival rate [11]. According to the statement of the majority of authors in 2022, the indication for referral to a specialist was uncertainty in the choice of the biopsy method [2].

The purpose of our work on the biopsy method in the rational diagnosis of malignant skin neoplasms was a review of modern literary sources with the involvement of electronic databases. We built the following literature search strategy: the search was conducted in MEDLINE/PubMed, EMBASE/Excerpta Medica, Cochrane Library, PubMed and Google Scholar bibliometric data using such keywords as: skin biopsy, malignant skin neoplasms, melanoma, complications. The search depth was 10 years, preference was given to Scopus and Web of Science indexed sources. Exclusion criteria were: works without statistical analysis, descriptions of individual cases, articles without conclusions, sources with duplicate results.

In our review, 48 publications that met our declared criteria over the past 10 years were used.

The use of the adequate skin biopsy techniques minimizes diagnostic error with serious medical and legal consequences. It is a well-known fact that the major-

ity of errors occur when biopsies are not performed on time, rather than when unnecessary biopsies are performed [12]. On the one hand, biopsy is indicated for all suspicious neoplasms, but on the other hand, a large percentage of suspicious pigmented skin formations sent for research turn out to be benign [13]. Accurate histological examination is the next stage in case of confirmation of malignancy of the process. It is, actually, this kind of examination that provides full verification of the diagnosis and is the basis for carrying out appropriate and the adequate therapy [14].

The implementation of urgent excisional biopsy to a sufficient depth when a malignant melanoma is suspected is considered to be a classic approach [15], which allows histological assessment of the Breslau tumor thickness. But in the cases of an acral melanoma or the location of the tumor on the face, it is recommended to use an incisional biopsy or a punch biopsy. Though, performing a shave biopsy is not recommended in such cases due to the impossibility of determining the stage of the pathology, namely the Breslau thickness. Failure to comply with such requirements can lead to a delay in diagnosis, incorrect subsequent treatment tactics and negatively affects the prognosis of the course of the disease. In addition, the difference in results depending on what doctor performs the biopsy - a general practitioner, a dermatologist or an oncologist - turned out to be insignificant [15].

A number of publications over the next 10 years contain conflicting data regarding the type of biopsies used in the diagnosis of the melanoma.

In the studies reflected in the 2022 UK national guidelines for the treatment of melanoma, it was found that incisional biopsy is not indicated in the diagnosis of the malignant melanoma [16]. Although, partial biopsy can sometimes be used for the diagnosis of the melanoma, as noted by the most authors in order to save time and money compared to the excisional biopsy technique. At the same time, as the authors suggested, the impact on further treatment of melanoma remained unpredictable, which negatively affected the prognosis.

As shown by the results of the other retrospective studies, [17] in 2020, using the Victorian Cancer Registry, those diagnosed with melanoma in 2005, 2010 and 2015, the preference for partial biopsy over excisional biopsy was not influenced by diagnostic suspicion. The use of partial biopsy in patients older than 50 years exceeded the use of excisional biopsy compared with patients younger than 50 years old. Tumors diagnosed by the punch biopsy and shave biopsy had ratios of 34% and 17%, respectively, and required three procedures instead of two for definitive removal, compared with 5% of the excisional biopsies. It was emphasized that when using a partial biopsy, patients more often needed an additional stage of removal. Based on the results of these studies, it was concluded that the use of partial biopsy in the diagnosis of melanoma often requires an additional procedure for definitive treatment compared to the excisional biopsy. In addition, a partial biopsy was unreasonable in a third of patients.

An additional systematic review [18] examining the relationship between the types of biopsy used in the diagnosis of cutaneous melanoma and four clinically important outcomes: melanoma mortality, all-cause mortality, Breslau tumor thickness as well as melanoma

recurrence had similar results as found in the punch biopsy group (risk ratio [RR], 1.520;  $P=0.02$ ), according to the aggregated data, significantly higher mortality due to other causes is shown. A similar high rate of mortality due to melanoma (HR, 1.96;  $P=0.22$ ) and melanoma recurrence (HR, 1.20;  $P=0.186$ ) was also found in the punch biopsy group. However, these studies had limited evidence of differences in clinically important outcomes across the spectrum of the most common methods used by physicians in their clinical practice for the primary diagnosis of the cutaneous melanoma. The small but significant increase ( $P=0.02$ ) in other-cause mortality observed in the punch biopsy group was not supported by the other outcomes, so the authors attributed this fact to the small sample size.

The work that was devoted to the study of the influence of the shave biopsy on the stage of the tumor also attracts attention, especially in terms of further recommendations for treatment and prognosis [19]. It is emphasized that there is a high heterogeneity of all results in the cited and analyzed studies. Four studies reported survival: while none found a significant difference in complication-free or comorbidity-free survival or overall survival between shave biopsy and the other biopsy methods. The conclusion appeared naturally: slightly more than 40% of the melanomas diagnosed during a shave biopsy have sufficient thickness. This approach changed tumor stage in 7.7% of patients and treatment recommendations in a relatively small cohort of patients – 2.3%, respectively. However, this did not affect relapse or survival [19].

Next, the results of the analysis of the diagnosis of pigment formations by the method of the shave biopsy in the order to exclude malignant neoplasms of the skin [20] are given. Only neoplasms excised by the method of shave biopsy with complete removal of the lesion were included. A total of 349 pigmented tumors were included, 50 (14%) of which were melanomas, and none of them had lesions at the deep margin of resection, while 13 (26%) had lesions at the lateral margin [20].

In particular, another retrospective study [21] established the high diagnostic value of the subtotal diagnostic biopsy, which allowed to identify melanoma with an increased risk of progression with such clinicopathological characteristics as an anatomical location on the head, neck, arms, feet, genitals, or pretibial area of the leg. Cross-sectional study of 1332 cases of melanoma in situ to stage T4a, which were treated by the method of wide local excision proved that preoperative diagnostic biopsies (OR 1.89,  $P=0.004$ ) increase the risk of melanoma progression.

However, there are studies that do not support the effect of the melanoma biopsy technique on the overall survival. Thus, in one retrospective study [22] regarding the diagnosis and treatment of melanoma from 2004 to 2016, there were 42,272 cases of melanoma, of which 27,899 (66%) were diagnosed by the shave biopsy method, 8,823 (20.9%) by the method punch biopsies and 5,550 (13.1%) using the excisional biopsy method. The researchers concluded that incisional biopsy was highly likely to result in a decrease in overall 5-year survival, but no difference was observed between the shave biopsy and punch biopsy cohorts. It also turned out that their results confirm already existing recommendations

regarding the diagnosis and treatment of melanoma [22].

The results of the analysis of the complications' indicators and residual diseases after the use of a partial biopsy and the level of subsequent survival are the addition to the aforementioned material [23]. Comparing the period from 1994 to 2014, 3,939 patients were included in these studies and 874 (22%) were diagnosed using partial biopsy methods. The following clinicopathologic features were generated: melanoma-specific survival, distant disease-free survival, and disease-free survival in patients with residual invasive melanoma and those without residual melanoma. In conclusion, the authors note that the survival rate of patients with primary melanoma is not worse or lower in cases where a partial biopsy is performed and residual invasive tumor is later found in the excised skin sample.

Regarding the issue of melanoma diagnosis by the shave biopsy method it should be stated that this is a rather controversial procedure. On the one hand, it is affordable and cost-effective for the diagnosis of various skin lesions. But on the other hand, there remains the risk of incomplete diagnosis and further rapid spread of the tumor. This is shown by one prospective study in which the use of this technique was shown in 26% of patients with melanoma and where signs of incomplete diagnosis were reliably established [24]. On the other hand, there is a statement that the use of the shave biopsy contributes to the earlier detection of atypical manifestations of melanoma [25].

Another retrospective study [26] assessed the impact of the initial biopsy technique and the provision of adequate and complete clinical information to pathologists on the accuracy of the histopathological diagnosis of the melanoma and its subsequent progression. It was found that partial shave biopsy had more false-negative results (OR 5.19, 95% CI 2.89-9.32;  $P < 0.001$ ) and, as a result, false-positive diagnosis of (OR 1.95, 95% CI 1.45-2.63;  $P < 0.001$ ) melanoma, compared with classic elliptical excisional biopsy. Odds ratios were compared with those found in puncture biopsy. Accordingly, the researchers concluded that the correct and accurate histopathological diagnosis of melanoma of the skin depends on the choice of the initial biopsy technique and the provision of complete and adequate clinical information to pathologists, and therefore significantly prevents the further progression of the disease.

Modern recommendations emphasize [27] that in the vast majority of cases it is possible to use an excisional biopsy of a neoplasm with minimal clear edges. Therefore, punch biopsy may be an option only in cases of large neoplasms located in important functional or certain cosmetic areas, such as the face, limbs or genitals, which is associated with a high risk of developing a cosmetic defect. In particular, the American Joint Commission on Oncology (AJCC), according to the most recent revision of the staging system, recommends sentinel lymph node biopsy (SNB), but only in the case of a primary lesion  $> 0.8$  mm thick or for thinner, high-risk lesions. Sentinel node (SN) score is commonly used to determine tumor stage but it does not affect survival.

As reported by the results of the meta-analysis, the choice of the biopsy technique showed no difference between the risk of death from melanoma, the rate of survival and the absence of recurrence (RFS) related

to melanoma (MRS). However, the current trend is in favor of excisional biopsy in terms of reducing the risk of recurrence ( $P=0.09$ ) [28]. A partial biopsy can be performed in special situations, such as the large size of the primary tumor, the location in surgically inconvenient areas, without changing the long-term consequences, according to the conclusions of some researchers. But other studies [29] found that in most cases, a correctly performed partial biopsy (especially a shave biopsy) can provide enough information to further plan the necessary surgical treatment of melanoma. While therapy planning it should be taken into account that puncture and incisional biopsies have an equally high rate of staging. Desmoplastic and acral lentiginous melanomas have a high tendency to progress, especially after partial biopsy, so they should be completely excised before definitive treatment. In addition, it has been reported [30] that the use of excisional biopsy is the gold standard even in cases of the premelanoma conditions, such as dysplastic nevi with positive histological margins. This approach prevents the potential development of the melanoma.

Summarizing all the above facts about the use of the shave biopsy, we can draw the conclusions. The positive effect, which is based on economic benefit, is overshadowed by higher costs for additional procedures carried out to verify the diagnosis. Regarding the impact on the survival rate, an important point is the timely establishment of the correct stage for the further appointment of the adequate therapy, which in turn ensures a high survival rate. However, the diagnosis of the pathology can be difficult and this should be taken into consideration, especially since up to 9.2% of the biopsies of the melanocytic formations are not verified. The choice of the initial biopsy technique and the provision of adequate and sufficient clinical information to pathologists are essential and important for the correct histopathological diagnosis of melanoma of the skin, which allows timely prevention of further progression of the disease [31].

In comparison with the use of a partial biopsy, the adverse consequences and the probability of a false diagnosis with a complete excisional biopsy are significantly reduced. It has been suggested [32] that there is a direct relationship between the increase in the use of the shave biopsy as well as the increase in adverse effects directly related to this technique. When considered at the population level, this technique does not have sufficient efficiency in the diagnostic biopsy of invasive melanoma. The accuracy of the pathological diagnosis and the adequate assessment of the tumor thickness are the two most important goals that are ensured by a complete excisional biopsy [32].

While summarizing, we should note that most dermatologists support the general opinion that melanoma should not be diagnosed by taking part of the sample but by complete excision.

Though, the shave biopsy is a quick, simple and affordable procedure that can be achieved with minimal conditions and equipment [33]. And because it is considered a one-day procedure, liability issues are minimized. In addition, there is no need for a second visit for monitoring the scar and removal of the sutures and it also gives quite acceptable and good functional and the cosmetic results. But despite the fact that the risk of local recurrence or metastasis is minimized, giving prefer-

ence to the shave biopsy method is a controversial fact, since studies show a high frequency of an excision of the base even in superficial (34% >0.5 mm) melanomas [34]. However, according to some retrospective studies, the probability of base excision in eligible neoplasms is extremely low for lesions that do not show clear signs of deeper invasion (pale blue veil, ulceration, nodules), are large (>1 cm), or are not amenable to shave biopsy (not on the face). The shave biopsy may be the first choice and should be used for less risky lesions because it is safer and more cost-effective [34].

Today, the search for new biopsy methods is underway based on the principles of minimal invasiveness and reduction of trauma having the main goal of high diagnostic value of the obtained materials. Consequently, it is proposed to improve the punch biopsy, which has an advantage among other methods in obtaining skin samples for the entire thickness. In addition, the post-biopsy wound heals with primary or repeated tension much faster, especially in conditions of location in hard-to-reach parts of the body [35]. Also presented [36] is the technique of precision biopsy, which is currently a new method that facilitates direct histopathological correlation of a dermoscopy with signs of the melanoma. Its principle is based on minimally invasive excision of the tissue under the control of the optical imaging devices, which achieves high accuracy of the diagnosis.

It was concluded that the biopsy technique is more important for the timely diagnosis of melanoma than the time between the initial diagnosis and the radical treatment followed by the removal of sentinel lymph nodes. No study found a difference in melanoma-specific survival or disease-free survival even after a delay of more than 30 days and those patients who received early or delayed therapy [37].

There are also significant issues considering the limits of removal, which is actually a sensitive technical point when conducting a biopsy. For thin, low-risk melanomas, there is absolutely no benefit or rationale for wide local excision. One study evaluated morbidity after wide local excision. The results showed [38] a significant increase in morbidity due to local excision with a width of 1.0 cm, which clearly affects the physical, psychological and social well-being of the patients. Therefore, the need for repeat 1-cm-wide local excision procedures for thin melanomas should be reassessed since this technique does not provide a survival advantage and margins are increasingly reduced in cosmetically sensitive areas. This is especially true in cases where 95% of malignant melanomas have been removed with the primary biopsy alone.

National recommendations established the size of the margins during wide excision surgery for invasive treatment of melanoma. However, the recommendations of some specialists for wider excision margins than it is recommended are still quite often observed. Thus, in an analysis of 26,440 patients, it was established [39] that wider excision margins were used for the localization of the melanoma on the trunk in certain groups with Breslau tumor thickness ( $p < 0.05$ ). However, the practice of applying wider limits than recommended was not associated with improved survival.

The New Zealand guidelines for the treatment of the cutaneous melanoma require the excisional biopsy specimens of the suspicious lesions to be 2 mm in

horizontal and deep margin in the upper subcutaneous compartment. Although a diagnostic review [40] in New Zealand of deep margin biopsy is not subjected to significant audit and adherence to horizontal margin size recommendations was low. However, the clinical significance of this remains unclear.

Last but not least, there is still the question of choosing a doctor and medical institution where the biopsy should be performed. Taking into account the steady increase in the incidence of skin cancer over the past decades and the search and implementation of modern diagnostic tools and innovative therapies, skin cancer incidence and mortality still remain a major burden on society [41]. Today, dermatologists play a central role in improving diagnostics and approaches to modern treatment. When it comes to conducting an adequate biopsy, dermatology should be considered as a separate specialization of the dermatovenerology. Especially considering the knowledge and experience of the dermatologists, new diagnostic approaches and the methods of the treatment of the skin cancer in early and later stages, as well as taking into account the wide range of different skills that are required to treat this heterogeneous group of diseases [42].

The choice of biopsy method in the issue of melanoma diagnosis is also influenced not only by the type of medical institution but also by such demographic indicators as the patient's age and race [43]. The use of a partial excisional biopsy ratio was higher in patients older than 50 years than in patients younger than 50 years [relative risk ratio (RRR) 1.5; 95% CI from 1.0 to 2.2;  $P = 0.03$ ]. Tumors diagnosed by punch biopsy and shave biopsy required three procedures instead of two for definitive removal in 34% and 17%, respectively, compared with 5% of the excisional biopsies. But when partial biopsy was used, there was a greater risk of needing three-stage excision after adjusting for age, anatomic location, melanoma subtype, and thickness (RRR 6.7; 95% CI 4.4-10.1;  $P < 0.001$ ). The use of the partial biopsy for the diagnosis of melanoma often requires an additional procedure for definitive treatment compared to excisional biopsy [17].

In the biopsy technique, an important issue is the choice of the operator. A biopsy should be performed by a primary care physician or a dermatologist or oncologist. There is debate as to whether diagnostic excision of melanoma in primary care is safe and informative. For example, the European guidelines do not make any recommendations on this, and the United Kingdom guidelines for melanoma require that all suspicious skin neoplasms have to be treated in secondary care from the outset, as there is a lack of evidence that excision in primary care is high-quality or low-quality treatment [44, 45]. A presented Scottish population-based study suggests that patients undergoing melanoma excision in primary care do not have reduced survival or increased morbidity compared with those initially diagnosed and treated in secondary care [44]. However, there are no randomized controlled trials on this issue.

Currently, there are works assessing whether the length of training of a clinician or the type of internship affects the average size of the biopsy and the adequacy of the sample [46]. Differences in biopsy size between training levels were found to be statistically significant, despite qualitatively similar biopsy sites and categories

of final diagnosis for each clinician training group. A greater number of inadequate and poor-quality samples concerned the group of clinicians with the least experience in dermatology. Therefore, according to the results of this study, a connection between the reduction in the size of the biopsy and the increase in the training experience of dermatologists was established [47]. Although there is no evidence that this trend is now threatening the quality and adequacy of samples.

Concluding our review, we note that we deliberately conducted research excluding, in general, national guidelines and protocols, as they are duplicative of international recommendations [48, 49] and did not meet the purpose of the work. Also, the heterogeneity of the populations in the above-mentioned sources does not allow to conduct a full-fledged meta-analysis regarding the rational method of biopsy.

### Conclusions.

An excisional biopsy is the best way to get complete information about a skin lesion.

Regarding the neoplasms in cosmetically sensitive areas or their large size, preference should be given to incisional biopsy.

The other methods, such as punch-biopsy and shave-biopsy, are rather inaccurate methods of diagnosis, although they do not affect the spread of the tumor or deterioration of the results of therapy.

The experience of the operating physician and the choice of medical institution have little influence on the choice of technique and the quality of diagnosis. However, priority should be given to an examination by a dermatologist for a more rational diagnosis and treatment.

### Prospects for further research.

A clear definition of the biopsy technique, its technique (excision depth and edges) for the diagnosis of malignant skin neoplasms requires further clarification, comprehensive approach following modern world concepts and standards.

## References

- Ramsey ML, Rostami S. Skin Biopsy. Treasure Island (FL): StatPearls Publishing; 2022.
- Greenwood JD, Merry SP, Boswell CL. Skin Biopsy Techniques. *Prim Care*. 2022;49(1):1-22. DOI: [10.1016/j.pop.2021.10.001](https://doi.org/10.1016/j.pop.2021.10.001).
- Messina JL, Gibbs J. Pathologic analysis of melanocytic neoplasms. *Semin Cutan Med Surg*. 2018;37(2):88-100. DOI: [10.12788/j.sder.2017.054](https://doi.org/10.12788/j.sder.2017.054).
- Phillips M, Marsden H, Jaffe W, Matin RN, Wali GN, Greenhalgh J, et al. Assessment of Accuracy of an Artificial Intelligence Algorithm to Detect Melanoma in Images of Skin Lesions. *JAMA network open*. 2019;2(10):e1913436. DOI: <https://doi.org/10.1001/jamanetworkopen.2019.13436>.
- Navarrete-Dechent C, Cordova M, Sahu A, Liopyris A, Rishpon A, Chen C, et al. Optical imaging guided- 'precision' biopsy of skin tumors: a novel approach for targeted sampling and histopathologic correlation. *Arch Dermatol Res*. 2021;313(7):517-529. DOI: [10.1007/s00403-020-02126-6](https://doi.org/10.1007/s00403-020-02126-6).
- Chuchu N, Dinnes J, Takwoingi Y, Matin RN, Bayliss SE, Davenport CE, et al. Teledermatology for diagnosing skin cancer in adults. *Cochrane Database Syst Rev*. 2018;12(12):CD013193. DOI: [10.1002/14651858.CD013193](https://doi.org/10.1002/14651858.CD013193).
- Kilic A, Kilic A, Kivanc AE, Sisik A. Biopsy Techniques for Skin Disease and Skin Cancer: A New Approach. *J Cutan Aesthet Surg*. 2020;13(3):251-254. DOI: [10.4103/JCAS.JCAS\\_173\\_19](https://doi.org/10.4103/JCAS.JCAS_173_19).
- Knackstedt T, Knackstedt RW, Couto R, Gastman B. Malignant Melanoma: Diagnostic and Management Update. *Plast Reconstr Surg*. 2018;142(2):202e-216e. DOI: [10.1097/PRS.0000000000004571](https://doi.org/10.1097/PRS.0000000000004571).
- Davis LE, Shalin SC, Tackett AJ. Current state of melanoma diagnosis and treatment. *Cancer Biol Ther*. 2019;20(11):1366-1379. DOI: [10.1080/15384047.2019.1640032](https://doi.org/10.1080/15384047.2019.1640032).
- Beard CJ, Ponnarasu S, Schmieder GJ. Excisional Biopsy. Treasure Island (FL): StatPearls Publishing; 2021.
- Naik PP. Cutaneous Malignant Melanoma: A Review of Early Diagnosis and Management. *World J Oncol*. 2021;12(1):7-19. DOI: [10.14740/wjon1349](https://doi.org/10.14740/wjon1349).
- Hartman RI, Lin JY. Cutaneous Melanoma-A Review in Detection, Staging, and Management. *Hematol Oncol Clin North Am*. 2019;33(1):25-38. DOI: [10.1016/j.hoc.2018.09.005](https://doi.org/10.1016/j.hoc.2018.09.005).
- Dorrell DN, Strowd LC. Skin Cancer Detection Technology. *Dermatol Clin*. 2019;37(4):527-536. DOI: [10.1016/j.det.2019.05.010](https://doi.org/10.1016/j.det.2019.05.010).
- Chopra A, Sharma R, Rao UNM. Pathology of Melanoma. *Surg Clin North Am*. 2020;100(1):43-59. DOI: [10.1016/j.suc.2019.09.004](https://doi.org/10.1016/j.suc.2019.09.004).
- Tadiparthi S, Panchani S, Iqbal A. Biopsy for malignant melanoma--are we following the guidelines? *Ann R Coll Surg Engl*. 2008;90(4):322-325. DOI: [10.1308/003588408X285856](https://doi.org/10.1308/003588408X285856).
- NICE 2022. Melanoma: assessment and management. NICE; 2022. Available from: <https://www.nice.org.uk/terms-andconditions#notice-of-rights>.
- de Menezes SL, Wolfe R, Kelly JW, Farrugia H, Mar VJ. Think before you shave: Factors influencing choice of biopsy technique for invasive melanoma and effect on definitive management. *Australas J Dermatol*. 2020;61(2):134-139. DOI: [10.1111/ajd.13227](https://doi.org/10.1111/ajd.13227).
- Shellenberger RA, Fayyaz F, Sako Z, Schaeffer M, Tawagi K, Scheidel C, et al. Impact of Biopsy Technique on Clinically Important Outcomes for Cutaneous Melanoma: A Systematic Review and Meta-analysis. *Mayo Clin Proc Innov Qual Outcomes*. 2020;4(4):373-383. DOI: [10.1016/j.mayocpiqo.2020.04.005](https://doi.org/10.1016/j.mayocpiqo.2020.04.005).
- Ahmadi O, Das M, Hajarizadeh B, Mathy JA. Impact of Shave Biopsy on Diagnosis and Management of Cutaneous Melanoma: A Systematic Review and Meta-Analysis. *Ann Surg Oncol*. 2021;28(11):6168-6176. DOI: [10.1245/s10434-021-09866-3](https://doi.org/10.1245/s10434-021-09866-3).
- Shao E, Blake T, Po-Chao F, Pool L, Carew B, Yong-Gee S, et al. Prospective study of pigmented lesions managed by shave excision with no deep margin transection of melanomas. *Australas J Dermatol*. 2020;61(3):269-272. DOI: [10.1111/ajd.13312](https://doi.org/10.1111/ajd.13312).
- Etzkorn JR, Sharkey JM, Grunyk JW, Shin TM, Sobanko JF, Miller CJ. Frequency of and risk factors for tumor upstaging after wide local excision of primary cutaneous melanoma. *J Am Acad Dermatol*. 2017;77(2):341-348. DOI: [10.1016/j.jaad.2017.03.018](https://doi.org/10.1016/j.jaad.2017.03.018).
- Liszewski W, Stewart JR, Vidal NY, Demer AM. Incisional Biopsy Technique Is Associated With Decreased Overall Survival for Cutaneous Melanoma. *Dermatol Surg*. 2022;48(5):486-491. DOI: [10.1097/DSS.0000000000003430](https://doi.org/10.1097/DSS.0000000000003430).
- Ramiscal JAB, Stern SL, Wilson AK, Lorimer PD, Lee NA, Goldfarb MR, et al. Does Residual Invasive Disease in Wide Local Excision after Diagnosis with Partial Biopsy Technique Influence Survival in Melanoma? Matched-Pair Analysis of Multicenter Selective Lymphadenectomy Trial I and II. *J Am Coll Surg*. 2022;235(1):49-59. DOI: [10.1097/XCS.0000000000000263](https://doi.org/10.1097/XCS.0000000000000263).
- Shao E, Blake T, Po-Chao F, Pool L, Carew B, Yong-Gee S, et al. Prospective study of pigmented lesions managed by shave excision with no deep margin transection of melanomas. *Australas J Dermatol*. 2020;61(3):269-272. DOI: [10.1111/ajd.13312](https://doi.org/10.1111/ajd.13312).
- Pitney T, Shao E, Muir J. A Reply to 'Think before you shave: factors influencing choice of biopsy technique for invasive melanoma and effect on definitive management'. *Australas J Dermatol*. 2021;62(1):96-97. DOI: [10.1111/ajd.13389](https://doi.org/10.1111/ajd.13389).
- Kok Y, Scott K, Pham A, Liu W, Roberts H, Pan Y, et al. The impact of incomplete clinical information and initial biopsy technique on the histopathological diagnosis of cutaneous melanoma. *Australas J Dermatol*. 2021;62(4):e524-e531. DOI: [10.1111/ajd.13697](https://doi.org/10.1111/ajd.13697).
- Testori AAE, Blankenstein SA, van Akkooi ACJ. Primary Melanoma: from History to Actual Debates. *Curr Oncol Rep*. 2019;21(12):112. DOI: [10.1007/s11912-019-0843-x](https://doi.org/10.1007/s11912-019-0843-x).

28. Moscarella E, Pampena R, Palmiotti G, Bonamonte D, Brancaccio G, Piccolo V, et al. A meta-analysis on the influence of partial biopsy of primary melanoma on disease recurrence and patient survival. *J Eur Acad Dermatol Venereol.* 2020;34(2):279-284. DOI: [10.1111/jdv.15903](https://doi.org/10.1111/jdv.15903).
29. Doolan BJ, Robinson AJ, Wolfe R, Kelly JW, McLean C, McCormack C, et al. Accuracy of partial biopsies in the management of cutaneous melanoma. *Australas J Dermatol.* 2019;60(3):209-213. DOI: [10.1111/ajd.13004](https://doi.org/10.1111/ajd.13004).
30. Kim CC, Berry EG, Marchetti MA, Swetter S, Lim G, Grossman D, et al. Risk of Subsequent Cutaneous Melanoma in Moderately Dysplastic Nevus Excisionally Biopsied but With Positive Histologic Margins. *JAMA Dermatol.* 2018;154(12):1401-1408. DOI: [10.1001/jamadermatol.2018.3359](https://doi.org/10.1001/jamadermatol.2018.3359).
31. Kok Y, Scott K, Pham A, Liu W, Roberts H, Pan Y, et al. The impact of incomplete clinical information and initial biopsy technique on the histopathological diagnosis of cutaneous melanoma. *Australas J Dermatol.* 2021;62(4):e524-e531. DOI: [10.1111/ajd.13697](https://doi.org/10.1111/ajd.13697).
32. Menezes SL, Kelly JW, Mar V. The increasing use of shave biopsy for diagnosing invasive melanoma in Australia. *Medical Journal of Australia.* 2020;212(5):238-238.e1. DOI: [10.5694/mja2.50502](https://doi.org/10.5694/mja2.50502).
33. Ahmadi O, Das M, Hajarizadeh B, Mathy JA. Impact of Shave Biopsy on Diagnosis and Management of Cutaneous Melanoma: A Systematic Review and Meta-Analysis. *Ann Surg Oncol.* 2021;28(11):6168-6176. DOI: [10.1245/s10434-021-09866-3](https://doi.org/10.1245/s10434-021-09866-3).
34. Pitney T, Muir DJ. Single-center, single-operator, retrospective analysis of base transection rates in shave procedures for melanoma diagnosis. *J Am Acad Dermatol.* 2021;84(3):861-862. DOI: [10.1016/j.jaad.2020.10.049](https://doi.org/10.1016/j.jaad.2020.10.049).
35. Breslavets M, Lapa T. The tangential punch biopsy. *Dermatol Online J.* 2019;25(12):13030/qt1g60q188.
36. Navarrete-Dechent C, Cordova M, Sahu A, Liopyris K, Rishpon A, Chen C, et al. Optical imaging guided- 'precision' biopsy of skin tumors: a novel approach for targeted sampling and histopathologic correlation. *Arch Dermatol Res.* 2021;313(7):517-529. DOI: [10.1007/s00403-020-02126-6](https://doi.org/10.1007/s00403-020-02126-6).
37. Nelson DW, Stern S, Elashoff DE, Elashoff R, Thompson J, Mozzillo N, et al. Impact of Time Between Diagnosis and SLNB on Outcomes in Cutaneous Melanoma. *J Am Coll Surg.* 2017;225(2):302-311. DOI: [10.1016/j.jamcollsurg.2017.05.013](https://doi.org/10.1016/j.jamcollsurg.2017.05.013).
38. Lau KL, Bradish T, Rannan-Eliya S. 'Primum non nocere': how harmless is routine wide local excision for AJCC stage IA melanoma? *Ann R Coll Surg Engl.* 2020;102(7):483-487. DOI: [10.1308/rcsann.2020.0050](https://doi.org/10.1308/rcsann.2020.0050).
39. Huayllani MT, Bagaria SP, Restrepo DJ, Boczar D, Sisti A, Cochuyt JJ, et al. Wide Excisional Surgery in Invasive Melanoma Treatment: Factors Driving Non-compliance With National Guidelines. *Anticancer Res.* 2020;40(2):1065-1069. DOI: [10.21873/anticancerres.14044](https://doi.org/10.21873/anticancerres.14044).
40. Brian T, Jameson MB. Skin lesions suspicious for melanoma: New Zealand excision margin guidelines in practice. *J Prim Health Care.* 2018;10(3):210-214. DOI: [10.1071/HC17055](https://doi.org/10.1071/HC17055).
41. Chernyshov PV, Lallas A, Tomas-Aragones L, Arenbergerova M, Samimi M, Manolache L, et al. Quality of life measurement in skin cancer patients: literature review and position paper of the European Academy of Dermatology and Venereology Task Forces on Quality of Life and Patient Oriented Outcomes, Melanoma and Non-Melanoma Skin Cancer. *J Eur Acad Dermatol Venereol.* 2019;33(5):816-827. DOI: [10.1111/jdv.15487](https://doi.org/10.1111/jdv.15487).
42. Garbe C, Peris K, Soura E, Forsea AM, Hauschild A, Arenbergerova M, et al. The evolving field of Dermato-oncology and the role of dermatologists: Position Paper of the EADO, EADV and Task Forces, EDF, IDS, EBDV-UEMS and EORTC Cutaneous Lymphoma Task Force. *J Eur Acad Dermatol Venereol.* 2020;34(10):2183-2197. DOI: [10.1111/jdv.16849](https://doi.org/10.1111/jdv.16849).
43. Restrepo DJ, Huayllani MT, Boczar D, Sisti A, Gabriel E, Lemini R, et al. Biopsy Type Disparities in Patients With Melanoma: Who Receives the Standard of Care? *Anticancer Res.* 2019;39(11):6359-6363. DOI: [10.21873/anticancerres.13848](https://doi.org/10.21873/anticancerres.13848).
44. Garbe C, Amaral T, Peris K, Hauschild A, Arenberger P, Basset-Seguín N, et al. European consensus-based interdisciplinary guideline for melanoma. Part 2: Treatment – Update 2022. *Eur J Cancer.* 2022;170:256-284. DOI: [10.1016/j.ejca.2022.04.018](https://doi.org/10.1016/j.ejca.2022.04.018).
45. Nenclares P, Ap Dafydd D, Bagwan I, Miao B, Lu Y, Chen T. Head and neck mucosal melanoma: The United Kingdom national guidelines. *Eur J Cancer.* 2020;138:11-18. DOI: [10.1016/j.ejca.2020.07.017](https://doi.org/10.1016/j.ejca.2020.07.017).
46. Murchie P, Amalraj Raja E, Brewster DH, Iversen L, Lee AJ. Is initial excision of cutaneous melanoma by General Practitioners (GPs) dangerous? Comparing patient outcomes following excision of melanoma by GPs or in hospital using national datasets and meta-analysis. *Eur J Cancer.* 2017;86:373-384. DOI: [10.1016/j.ejca.2017.09.034](https://doi.org/10.1016/j.ejca.2017.09.034).
47. Dougher MC, Butt M, Helm KF, Helm MF. Impact of trainee experience on shave biopsy specimen size [published online ahead of print, 2022 May 14]. *Int J Dermatol.* 2022. DOI: [10.1111/ijd.16212](https://doi.org/10.1111/ijd.16212).
48. Voloshynovych M, Blaga I, Girnyk GY, Holotyiuk V, Kalmykova A. Melanoma shkiry: vid mayzhe nevydymoyi do vizual'no nezaperechnoyi. Okremi pryntsy py kerivnytstva ta ohlyad klinichnykh vypadkiv. *Ukr. Med. Chasopys.* 2020;3(137):1-5. DOI: [10.32471/umj.1680-3051.137.179285](https://doi.org/10.32471/umj.1680-3051.137.179285). [in Ukrainian].
49. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Melanoma, Version 3.2022. NCCN; 2022. Available from: [https://www.nccn.org/professionals/physician\\_gls/pdf/cutaneous\\_melanoma.pdf](https://www.nccn.org/professionals/physician_gls/pdf/cutaneous_melanoma.pdf).

## МЕТОДИКА ІДЕАЛЬНОЇ БІОПСІЇ ДЛЯ ДІАГНОСТИКИ ЗЛОЯКІСНИХ МЕЛАНОЦИТАРНИХ НОВОУТВОРЕНЬ ШКІРИ (ОГЛЯД ЛІТЕРАТУРИ)

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**Резюме.** Основним методом діагностики злоякісних новоутворень шкіри, зокрема меланоми, вже давно залишається біопсія шкіри. Сучасні наукові пошуки присвячено актуальній проблемі клінічної дермато-онкології – пошуку найбільш оптимальних методів морфологічної верифікації злоякісних пухлин шкіри. Особливо актуальною залишається проблема визначення безпечних та ефективних методів біопсії меланоми в контексті доказової медицини. Найбільш популярними методами на сьогодні є ексцизійна та інцизійна біопсія, шейв-біопсія (shave-biopsy) та панч-біопсія. Більшість настанов рекомендують проводити ексцизійну біопсію на всю товщину, як бажану процедуру при підозрі на меланому, однак все частіше зустрічаються випадки в яких проведення ексцизійної біопсії є неможливим. Узгоджений консенсус щодо найкращої методики біопсії шкіри в діагностиці меланоми, на сьогодні не існує. Більшістю публікацій було зроблено висновок, що неправильне визначення достатньої глибини та товщини меланоми з високою ймовірністю призводить до неадекватної терапії, але основна небезпека полягає в неправильній постановці діагнозу. Найкращий та надійний спосіб для отримання інформації про ураження шкіри залишається ексцизійна біопсія. Перевага у виборі методу, при наявних новоутвореннях в косметично чутливих ділянках або при їх великому розмірі, схиляється до інцизійної біопсії. Інші методики, такі як панч-біопсія чи шейв-біопсія, визнані більш небезпечними щодо неточності діагностики, але при цьому не сприяють поширенню пухлини. Досвід лікарів та вибір лікувального закладу не мали будь-якого впливу на вибір методики та якість діагностики, однак вчасна консультація лікаря-дерматолога виявилась більш раціональною для своєчасної діагностики та подальшого лікування. Правильний вибір методу біопсії, її техніки (глибини та країв висічення) для діагностики злоякісних новоутворень шкіри потребують подальшого уточнення.

**Ключові слова:** біопсія шкіри, невуси, меланоцитарні утворення шкіри, злоякісні новоутворення шкіри, меланома, методика, ускладнення, дерматоонкологія.

### PERFECT BIOPSY METHODS FOR THE DIAGNOSIS OF MALIGNANT MELANOCYTIC SKIN NEOPLASMS (A LITERATURE REVIEW)

Fomina L. V., Aslanyan S. A., Gumeniuk K. V., Fomin O. O., Trutyak I.R.

**Abstract.** Skin biopsy has long been the main method of diagnosing malignant skin neoplasms, particularly melanoma. The modern scientific research is devoted to the actual problem of the clinical dermatology – the search for the most optimal methods of morphological verification of the malignant skin tumors. The problem of the determining safe and effective melanoma biopsy methods in the context of the evidence-based medicine remains particularly relevant. The most popular methods today are excisional and incisional biopsy, shave biopsy and punch biopsy. The most guidelines recommend full-thickness excisional biopsy as the preferred procedure for suspected melanoma, but there are increasing cases where excisional biopsy is not possible. There is currently no consensus on the best technique for skin biopsy in the diagnosis of melanoma. Most publications concluded that misdiagnosis of sufficient depth and thickness of melanoma is likely to lead to inadequate therapy, but the main danger lies in misdiagnosis. Excisional biopsy remains the best and most reliable way to obtain information about skin lesions. The advantage in the choice of the method, in the presence of neoplasms in cosmetically sensitive areas or their large size, is inclined to incisional biopsy. Other techniques, such as punch biopsy or shave biopsy, are recognized as more dangerous in terms of diagnostic inaccuracy, but at the same time do not contribute to the spread of the tumor. The experience of doctors and the choice of medical institution did not have any influence on the choice of methodology and the quality of diagnosis, however, timely consultation of a dermatologist proved to be more rational for timely diagnosis and further treatment. The correct choice of the biopsy method, its technique (depth and edges of excision) for the diagnosis of malignant neoplasms of the skin require further clarification.

**Key words:** skin biopsy, nevus, melanocytic skin neoplasms, malignant neoplasms of the skin, melanoma, technique, complications, dermatology.

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#### Conflict of interest:

The authors of the paper declare the absence of the conflict of interest.

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