Master thesis

Dermatoscopic features of acral melanocytic lesions – a review of literature

submitted by

Benjamin David Gasser

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under supervision of

Ao. Univ.-Prof. Dr.med.univ. Rainer Hofmann-Wellenhof

Linz, 29.07.2024

Statutory declaration

I declare that I have authored this thesis independently, that I have not used other than the declared sources / resources, and that I have explicitly marked all material that has been quoted either literally or by content from the used sources.

Linz, 29.07.2024	Gasser Benjamin David
(Date)	(Signature)

Abstract

Background:

Acral melanomas are challenging to diagnose and therefore often diagnosed at later stages with worse prognosis. For this reason, early recognition of specific patterns is important, to obtain early diagnosis and avoid unnecessary excisions and biopsies.

Materials and Methods:

Research of literature was performed by using PubMed and Google Scholar databases. By titles and abstracts, matching the search terms, suitable scientific papers have been selected and further evaluated for their references. Also, books have been included in the introduction. After the literature was collected it was subsequently reviewed for the dermatoscopic patterns of acral melanocytic lesions.

Results:

Typical patterns for benign and malignant acral melanocytic lesions have been defined and shown their usefulness in the diagnosis of acral melanoma.

Conclusion:

Further education on typical dermatoscopic patterns in acral melanoma as well as raised awareness is needed for physicians using dermatoscopy to allow earlier diagnosis and to improved outcome.

Zusammenfassung

Hintergrund:

Akrale Melanome sind eine diagnostische Herausforderung und werden daher auch häufig erst in fortgeschrittenen Stadien mit schlechterer Prognose diagnostiziert. Aus diesem Grund ist die Früherkennung typischer dermatoskopischer Muster essenziell, um eine frühzeitige Diagnose stellen zu können und unnötige Exzisionen und Biopsien zu vermeiden.

Material und Methoden:

Eine Literaturrecherche wurde mittels Verwendung der Datenbanken von PubMed und Google Scholar durchgeführt. Anhand von Titeln und Abstracts, welche mit den Suchbegriffen übereinstimmten, wurden Artikel identifiziert und auch deren Quellen analysiert. Für die Einleitung wurde auch Fachliteratur verwendet. Nachdem die Sammlung von Literatur abgeschlossen war, wurden die Artikel nachfolgend auf typische dermatoskopische Muster von akralen melanozytären Läsionen untersucht.

Ergebnisse:

Typische dermatoskopische Muster benigner und maligner akraler melanozytärer Läsionen wurden in der Literatur definiert und ihren Nutzen in der Diagnostik von akralen Melanomen bewiesen.

Konklusion:

Vertiefende Kenntnisse der auflichtmikroskopischen Zeichen und Muster von akralen Melanomen und auch erhöhtes Bewusstsein über die Erkrankung von dermatoskopierenden Ärztinnen und Ärzten ist benötigt um eine frühzeitigere Diagnose zu erlauben und die Prognose zu verbessern.

Acknowledgments

First, I would like to thank my supervisor, *Ao. Univ.-Prof. Dr. Rainer Hofmann-Wellenhof* for giving me the opportunity to conduct my thesis about this interesting topic and the possibility to perform my training in a center of excellence at the Department of Dermatology and Venereology in Graz, and further for his corrections and the provision of clinical and dermatoscopic images.

Special appreciations go, once again, to my parents *Dietmar* and *Daniela Gasser* who supported another project financially.

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I. Introduction

Melanoma is a malignant tumor of melanocytic origin, which predominantly arises on skin but has also been found in mucosal areas, the meninges and the eye. It tends to metastasize early lymphogenic and/or hematogenic. If early detected it is a curable type of cancer, in later stages the prognosis is significantly worse. The incidence of melanoma increased in the last decades, but the average thickness by the time of the diagnosis decreased, which is also the most important initial marker for the prognosis (and thus further treatment). The initial treatment consists of surgical excision and depending on the histological findings followed by further resection of margins and exclusion of lymph node metastasis or distant metastasis. Based on these results adjuvant therapy (chemotherapy, immunotherapy, radiotherapy etc.) might be recommended. (1–3)

Due to anatomic differences of acral skin compared to other anatomic regions, the classic dermatoscopic features of melanoma are very uncommon and so rules like the ABCDE rule are not applicable. Other criteria and patterns have been evaluated for palmar and plantar skin and have proven themselves. Dermatoscopy has shown to be useful and non-invasive to differentiate acral lentiginous melanoma from acral nevi (or other benign lesions) and in evaluation of the nail unit – and facilitates earlier diagnosis. (4)

I.i. Acral melanoma

Acral melanoma is a subtype arising on palms, soles and nail units. The diagnosis of acral melanomas is often delayed by different appearances which might imitate benign conditions. These tumors could be pigmented or amelanotic, but also appear nodular or as an ulcer – and patients might underestimate new lesions and consult specialists at later stages. Symptoms might be unspecific and appear as pruritus, pain, bleeding or might be missing and might lead to misdiagnosing. (1,5)

In most publications, the terms acral melanoma and acral lentiginous melanoma are used synonymously, while acral melanoma is defining a clinical subtype, depending on localization on peripheral body parts, and acral lentiginous melanoma describes

a histological subtype. It is important to notice that not all melanomas arising on acral sites are of lentiginous subtype, especially if they had been exposed to UV rays frequently. (6)

In Caucasian patients the ALM is uncommon, but it represents the most common subtype in patients of Latin American (or Hispanic), African and Asian descent – while other subtypes are more uncommon. Vice versa other subtypes such as superficial spreading melanoma, nodular and lentigo maligna melanoma are usually more common in people of the Caucasian race. (1,3,5,7)

An Australian single center study identified risk factors for plantar melanomas, these included high nevus count, preexisting nevi on the soles, history of penetrating injury and exposure to agricultural chemicals. (2,8)

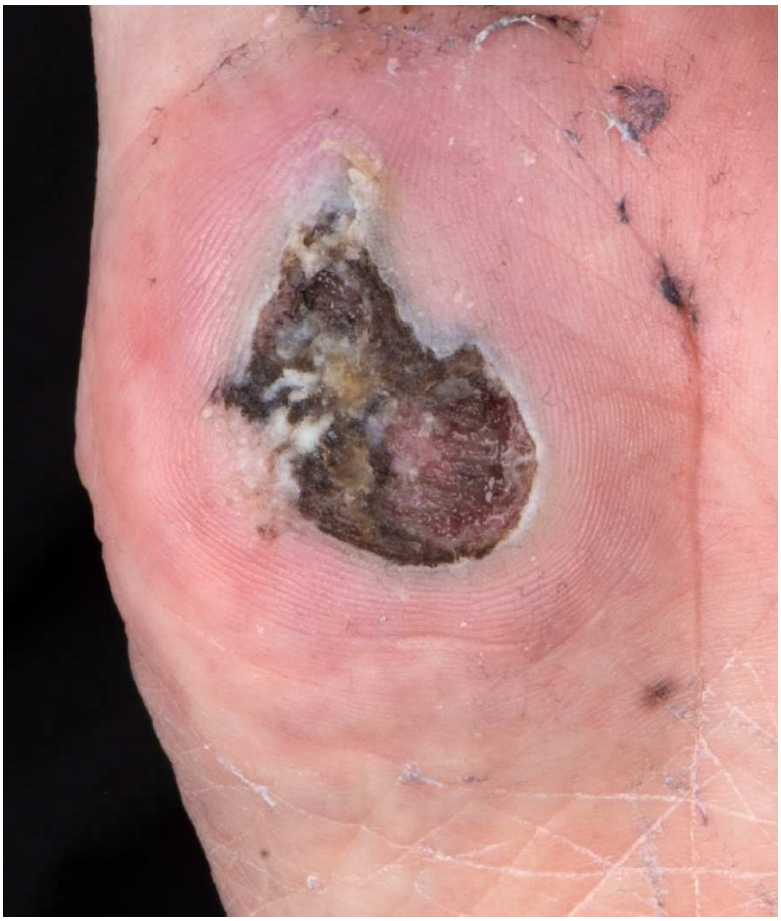

Figure 1: Clinical presentation of an acral melanoma with adjacent clinically suspicious lesions for satellite- respectively in-transit metastases (Courtesy ao. Univ.-Prof. Dr. Rainer Hofmann-Wellenhof, Department of Dermatology and Venereology, Medical University of Graz)

I.i.i. Acral lentiginous melanoma

Due to its initially radial growth phase, before it invades deeper layers of the glabrous skin it is called acral lentiginous melanoma. While the etiology is still controversial this subtype of melanoma is the most prevalent type of melanoma on acral skin. Although there is no clear evidence, studies discussed genetic factors and association with other cancers. History of plantar trauma has been associated with the diagnosis of acral lentiginious melanoma and suggested that they might be triggered by mechanical injuries or pressure – other studies did not prove this thesis. Because of these suspected risk factors and the uncertain triggers that have not been associated regularly with acral lentiginious melanoma, it is believed to be of multifactorial origin. (5,7,9)

In people of European ethnicity acral lentiginious melanoma only represents a small share of overall diagnoses, while the percentage is much higher in people of African, Asian or Hispanic descent and accounts for up to 75% of melanoma cases. Despite this incidence rates show similar results, regardless of ethnicity. (3,7)

Since early clinical and dermatoscopic patterns are often subtle, lesions are often hard to detect, and therefore acral lentiginious melanoma is often diagnosed at advanced stages, which is associated with increased tumor thickness and a worse outcome. Also lesions with obvious clinical changes might be misdiagnosed as ulcers, warts or benign neoplasms. Furthermore, delays have been linked to lower socioeconomic status, a lack of availability of qualified dermatologists and missing skin examinations by primary care doctors. (7)

I.i.ii. Less common subtypes of melanomas on acral skin

Even though the most commonly diagnosed subtype of melanoma on acral skin is acral lentiginious melanoma, also those of nodular, superficial spreading or amelanotic subtypes have been reported. (5,10,11)

The proposed “EFG” (Elevation, Firmness and Growth) acronym has been created for amelanotic melanomas and their clinical features, so they do not get missed in clinical inspections. (7)

I.i.iii. Nail unit melanoma

Nail unit melanoma is a rare subtype and like other acral located melanomas they are often diagnosed at later stages. They are further categorized as subungual, ungual or periungual. Since melanocytes are primarily located at the nail matrix, most of nail unit melanomas are thought to originate from here, but also a smaller percentage arises from the nail bed or the adjacent epidermis. In retrospective studies more than half of these melanomas of the fingers were located at the thumb (followed by the index finger) and more than 80% of those on the toes were found at the hallux. Especially those of the toes have been linked to trauma but the relation to trauma is still unclear (or if it is just a coincidence that leads to more frequent examinations of the toes). Also, these larger digits have a relatively bigger nail matrix area for nail unit melanomas to arise from, but these melanomas have been reported in all digits. Sun exposure does not seem to be a risk factor since the nail plate absorbs most of UV-A light and totally blocks UV-B light, aside from that many cases have been reported in people who usually do not walk without footwear. (12)

Nail unit melanoma has been thought to be a subtype of acral lentiginious melanoma, but research has shown that they differ in clinical and molecular features. Like in acral lentiginous melanomas they are more likely to appear in non-caucasian patients and the etiology is also thought to be multifactorial. (12,13)

Clinically about two-thirds of melanomas of the nail apparatus appear as so-called longitudinal melanonychia, while it is reported that up to every fourth nail unit melanoma are found to be amelanotic. (12)

The American Joint Committee on Cancer (AJCC) uses the same staging system for cutaneous melanomas and acral melanomas, although the differences no separate system has been published yet. (12)

I.ii. Acral nevi

Nevi are defined as benign melanocytic tumors and can also appear on volar skin. They are divided into congenital and acquired subtypes. Typical benign dermatoscopic patterns have been described and published. (14,15)

I.iii. Non-melanocytic acral lesions

There are also acral lesions, which are non-melanocytic, that might delay the diagnosis of acral melanoma. An ulcerated or amelanotic melanoma might initially be misdiagnosed as a diabetic or traumatic foot ulcer because of its fleshy appearance. In unclear clinical presentations, which do not respond to adequate therapy a biopsy should be performed to rule out malignancy. (5,7,16)

If lesions are found at the nail unit onychomycosis, subungual hemorrhage and trauma should also be kept in mind as possible origin of clinical changes and if suspicious they should be evaluated further. (7,16)

Infectious diseases such as fungal infections might also mimic flat acral melanocytic lesions, while smaller tumors could present like warts, poromas or pyogenic granuloma. (5,7,16,17)

Drug-induced hyperpigmentation is another cause for diffuse and acral pigmentation, for example after therapy with Cyclophosphamide. (18)

I.iv. Diagnosis

Early diagnosis of acral melanoma is crucial to improve the outcome of the disease and can be facilitated by dermatoscopy, especially in pigmented lesions, and knowledge of possible differential diagnosis if the initial treatment of a supposedly benign condition fails. In doubtful cases a biopsy should be performed. (5,7)

Since the plantar foot and the interdigital area are difficult for oneself to see podiatrists can be helpful to detect lesions of feet and legs. (2)

I.iv.i. Diagnostic algorithms

The established “ABCDE” rule is an accepted tool for the evaluation of lesions that are suspicious for cutaneous melanomas but is hardly applicable to acral lesions. Differences in clinical presentation and anatomy of the nail unit and acral skin required a different approach. Another acronym for the assessment of these lesion was proposed called CUBED. (7,16)

The CUBED acronym stands for: Colored lesions, Uncertain diagnosis, Bleeding lesions, Enlargement, Delay in healing. Colored lesions are defined as such which are not of the same color as the surrounding skin. The category of bleeding lesions also includes oozing ones, and those which could be clinically diagnosed as chronic "granulation tissue". Enlarging or worsening of acral lesions despite of so thought adequate therapy. Also, a delay of healing beyond two months is suspicious and should raise the awareness of differential diagnoses. If two or more features of the acronym apply, the patient should be referred to a specialized center. (2)

I.iv.ii. About dermatoscopy

Dermatoscopy (or dermoscopy) allows early detection of skin cancer, reduces the number of unnecessary excisions, and is a cost-effective and non-invasive tool. It is a diagnostic approach based on microscopy of the upper skin layers. (19)

Dermatoscopy as it is known today, has been developed since the 17th century, when Pierre Borel used an early version to evaluate capillaries in the nail apparatus. After a longer gap the term "Diascopy" was introduced by Paul Gerson Unna, and in the 1920s after multiple publications of Johann Saphier the word "Dermatoscopy" was used for the first time. In the 1950s Lean Goldman started to publish his studies that focused on the dermatoscopic possibilities to distinguish malignant and benign melanocytic lesions. It has developed even further, and in the late 20th century the first handheld dermatoscope was introduced – followed by the first one with polarized illumination without the need of an immersion fluid. Newer dermatoscopes are able to switch between polarized and non-polarized light, and allow optimal visualization of different structures. Since the introduction of the first handheld dermatoscope, dermatoscopy had an impressive rise in popularity and is now used widely by most dermatologists. (19,20)

This increase in acceptance results in factors like increased sensitivity and specifity, but also speed, efficiency, cost and the widespread indications to use dermatoscopy (inflammatory diseases, infectious diseases, skin neoplasms and skin appendages). (20)

Another valuable improvement is the invention of digital dermatoscopy which allows a feasible and precise follow-up in high-risk patients, but also facilitates

dermatologic telemedicine if it is not possible or unreasonable for the patients to travel to specialized doctors or clinics. Studies have shown that digital follow-up led to improved detection of in-situ and thinner melanomas than normal follow-up. It can also be combined with total-body photography. (19)

In acral lentiginous melanoma dermatoscopy improves the diagnostic accuracy by about 30% if it is performed by a qualified professional. (7)

I.v. Typical dermatoscopic features of acral melanocytic lesions

The usefulness of dermatoscopy in the evaluation of melanocytic lesions on acral skin is widely accepted. Patterns and algorithms have been proposed to assist clinicians. (21)

I.v.i. Benign lesions

Most acral melanocytic nevi show a parallel furrow pattern, lattice-like pattern or fibrillar pattern in dermatoscopy – these patterns have been described as low-risk patterns. If lesions are unpigmented, the analysis of their vascular pattern can aid the diagnosis and does not differ from lesions on non-acral skin. (7,15)

In a retrospective analysis, benign lesions with a regular fibrillar pattern had the highest rate of biopsy. So, knowledge of typical benign melanocytic lesions and their patterns could reduce the rates of unnecessary biopsies. (15)

The fibrillar pattern can be further divided in regular and Irregular. (21)

Typical benign melanocytic lesions of the nail apparatus are divided in melanocytic activation (hypermelanosis), lentigo (melanocytic hyperplasia) and nevi. Hypermelanosis is the most common cause of benign melanonychia which can be caused by pregnancy, trauma, medication and genetic diseases. Melanocytic hyperplasia is characterized by proliferation of melanocytes – clinically appearing as longitudinal band. (22)

Typically, melanocytic nevi appear clinically as pigmented longitudinal bands in the nail-plate. The most common subtype are junctional nevi, but rarely also blue nevi, Spitz nevi or compound nevi can be found in the nail apparatus. (22)

I.v.ii. Malignant lesions

High-risk patterns that usually might be seen in acral melanoma are the parallel ridge pattern and the multi-component pattern – these lesions are more likely to be malignant. (15)

Also, intermediate-risk patterns, which are more likely to be seen in benign acral lesions, have been described – these are reticular, globular, homogenous and non-typical (not fitting with a classical pattern). It has been recommended that they should be biopsied if they are larger than 7mm. (15)

A newly re-revised version of the 3-step algorithm has been proposed in 2022, to facilitate the detection of acral melanomas, and included Lallas' earlier research on acral melanoma. Congenital and nodular lesions are excluded from this algorithm. In the first step a lesion has to be evaluated for high-risk patterns as a parallel ridge or multicomponent pattern – if one of these patterns is found biopsy is recommended or otherwise it leads to the second step. If the lesion has one of the most common benign patterns as typical parallel furrow, latticelike or regular fibrillar pattern the lesion is classified as benign and no follow up is needed, but if it shows any other pattern, it must be evaluated for its size in the third step. Lesions larger than 7mm in diameter should be biopsied for histopathologic evaluation, smaller lesions must be followed up and be biopsied if an enlargement to more than 7mm in diameter occurs or if the pattern changes to one of those so-called high-risk patterns. (21)

Sometimes it might be not so easy to differentiate between furrows and ridges, in these cases it can be useful to perform the furrow ink test. Basically, ink gets applied on the lesion of interest and after a few seconds the ink is wiped off. Ink in the furrows will stay visible after wiping and facilitate the dermatoscopic differentiation between these structures. (23)

If typical acral dermatoscopic patterns of melanocytic lesions are missing, asymmetry, multiple colors and classical melanoma clues (blue-whitish-vail, irregular vascular structures, irregular dots or streaks, abrupt edges) should raise awareness for melanoma. Also, clinical information might be helpful to assess the risk for these lesions to be melanoma. (24)

Most melanomas of the nail apparatus appear clinically as longitudinal melanonychia and up to 25% of nail unit melanomas have been described as amelanotic. These melanomas present as pink, red or flesh colored lesions. In contrast to longitudinal melanonychia, amelanotic lesions present as longitudinal erythronychia – which might be accompanied by symptoms of bleeding, ulceration or nail damage. The most affected fingers are thumb, hallux and index fingers while these tumors have been reported in all digits. (12)

For longitudinal melanonychia the ABCDE rule has been adapted to ABCDEF and has been proposed to assist the diagnosis of nail unit melanomas. In this acronym A stands for Age (but also for the racial most affected groups like Africans, Asians and native Americans), while B stands for Bands with breadth > 3mm, brown-black discoloration and irregular borders. Change is abbreviated by C. D stands for the typically most affected Digits, which are thumb, hallux and index fingers. E for Extension of pigment, while F stands for Family history. Since this rule has not been validated, it might not be as reliable as other widely accepted acronyms in dermatology. (12)

Other clinically concerning features of longitudinal melanonychia are color band heterogeneity, change of width or darkening, proximal widening, bleeding, nail destruction, and extension of pigmentation to the surrounding skin (Hutchinson's sign). (12)

Longitudinal melanonychia, which is no safe sign for malignancy, can also be caused by nonmalignant reasons such as infections, subungual hematoma, benign melanocytic lesions. Typical dermatoscopic findings in melanomas that appear as longitudinal melanonychia are irregularities in color, width, spacing, loss of parallelism or asymmetry, when compared to benign lesions. (12)

The gold standard for the definite diagnosis of nail unit melanoma is a matrix biopsy with histopathologic evaluation of the specimen but always has the associated risk of permanent nail dystrophy. (12,25)

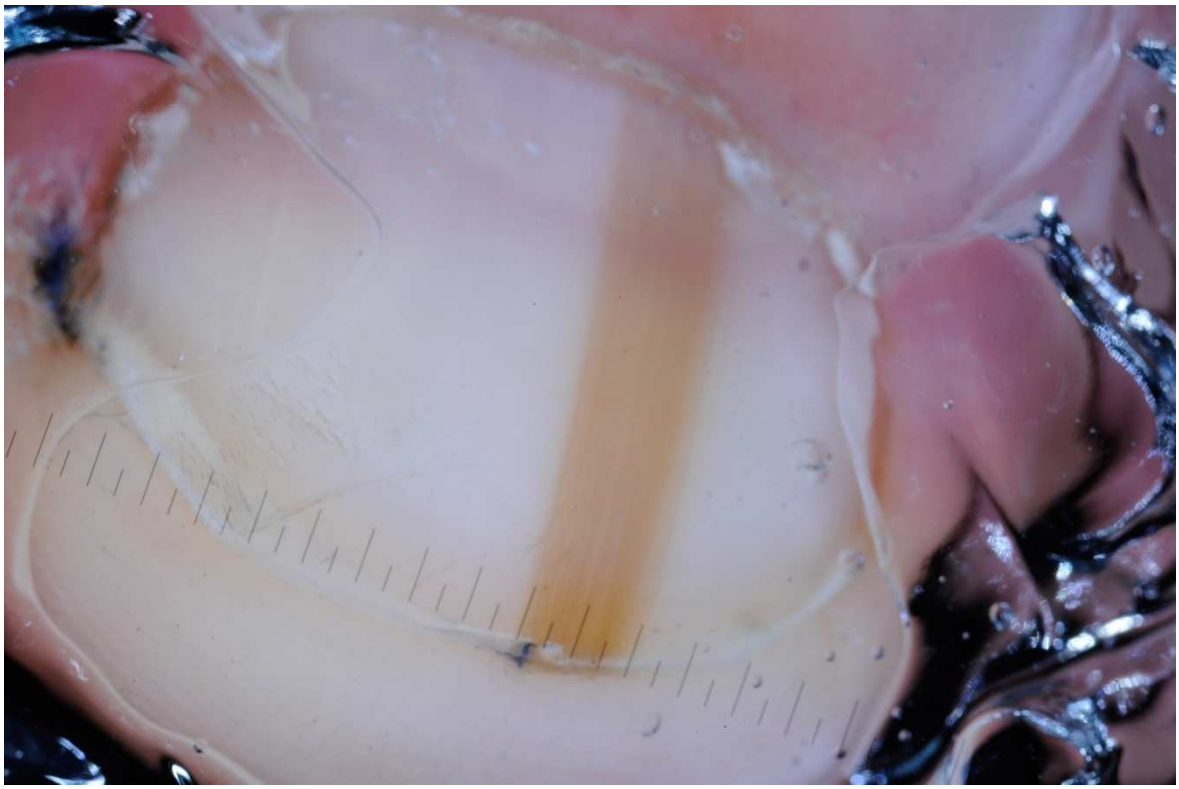

Figure 2: Dermatoscopic image of longitudinal melanonychia with homogenous width and color (Courtesy ao. Univ.-Prof. Dr. Rainer Hofmann-Wellenhof, Department of Dermatology and Venereology, Medical University of Graz)

I.vi. Treatment

Most trials about melanoma therapy included various subtypes of melanoma and mostly tumors on non-acral locations, also many publications do not distinguish between acral melanoma and acral lentiginous melanoma. This leads to a lack in evidence-based treatment recommendations on this specialized subtype. (6)

I.vi.i. Surgical treatment

Surgical treatment of acral melanoma is more difficult compared to other body parts. This is because of its unique anatomic circumstances and limitations in resection as small distances to adjacent structures. Partial biopsies can be performed for confirmation of diagnosis in pigmented lesions of the nail unit. Also, amputation of digits is an option for a total resection, but newer approaches focus on complete resection while preserving the digital function and thereby quality of life. In non-invasive melanoma of the nail apparatus, a more conservative excision did not affect

the prognosis compared to amputation of the digit. Advanced melanoma of the nail unit may not be suitable for function preserving surgery, but still surgeons should try to amputate at the most distal joint possible. Mohs micrographic surgery showed good efficacy. (12,26)

Recommended margins have been defined but might be limited by anatomical circumstances. Nagore and colleagues recommended that deep margins should be resected either to the fascia, or in subungual melanoma to the adjacent periosteum or bone, while lateral margins should be as in other cutaneous melanomas up to a Breslow thickness of 1.0 mm. In thicker melanomas of the nail apparatus a distal amputation is recommended. (12,26)

A sentinel node biopsy might be recommended, depending on Breslow thickness and additional risk factors, and allow clinicians to identify high risk patients, that might profit from adjuvant therapies. (26)

A 2021 published retrospective cohort study showed that acral lentiginous melanoma had high rates of sentinel node positivity and suggested that a sentinel biopsy should be performed in clinical stages IB and II. Due to this higher risk for regional metastasis in this study it is further suggested to analyze the rates of sentinel node positivity in clinical stage IA. (27)

I.vi.ii. Adjuvant treatment

Patients with advanced acral melanoma may be eligible for adjuvant therapy with targeted and immune therapy. (12)

Most therapy options used for acral melanoma and melanoma of the nail unit are adapted from well-established therapies used in the treatment of cutaneous melanoma. (28)

I.vi.ii.i. **Targeted therapies**

BRAF mutations are more common in non-acral melanomas and occur in only 15-20%. The data for BRAF- and MEK-inhibitors in the treatment of acral melanomas is limited, but it may be considered as therapies in these melanomas. (12)

Acral lentiginous melanoma have less somatic mutations, so in general these therapies have limited usefulness. (28)

Tyrosine kinase inhibitors are another therapeutic approach since tyrosine kinases are involved in metastasis and growth of melanoma. But data on long term toxicity is still not studied in detail. Another possibility for treatment of advanced melanoma is high-dose interferon alfa-2b. (12)

I.vi.ii.ii. **Immunotherapies**

Immunotherapeutic agents target important steps in the surveillance of melanoma cells. While CTLA-4 (cytotoxic T-lymphocyte antigen 4) inhibitors promote T-cell activity and thereby persuade tumor regression. PD-1 (Programmed cell death protein 1) inhibitors block the PD-1 ligand which normally inhibits T-cell activity and results in higher anti-tumor activity of the immune system. (12)

Anti-PD-1 may be used as a monotherapy or in combination with CTLA-4 inhibitors or LAG-3 inhibitors (lymphocyte activation gene-3). Immune checkpoint inhibitor treatment is well established in the treatment for cutaneous melanoma, but separate regimens for acral melanoma or melanoma of the nail apparatus have not been published yet. (12)

The combination therapy for advanced acral lentiginous melanoma, has proven better efficacy than monotherapy and is now standard of care. Most of the regimens included PD-1-inhibitors in combination with CTLA-4-inibitors, while some included other agents. (28)

I.vi.iii. Neoadjuvant treatment

Neoadjuvant treatment has been investigated for cutaneous melanoma in several studies, but histologic subtypes have not been reported. (28)

The SWOG S1801 phase II trial focused on patients with resectable stage IIIB – IVC cutaneous melanoma, it has been stated that 6% of the patients suffered from acral lentiginous melanoma. A benefit in event-free survival has been reported in both groups, in the group that has been treated with neoadjuvant pembrolizumab and the other group that received adjuvant pembrolizumab. (28)

Further studies and more, that focus on the response of different melanoma subtypes are needed to evaluate the usefulness of adjuvant and neoadjuvant systemic therapy in advanced melanoma. (28)

I.vii. Regional and intralesional treatment

The anatomic site of acral lentiginous melanoma and its typical recurrence in distal extremities allows the possibility of regional or intralesional treatment. Current methods are isolated limb infusion, intralesional talimogen laherparepvec, radiotherapy and electrochemotherapy. Further studies are needed to determine their potential roles in the treatment of acral melanoma. (28)

II. Aim and Method

II.i. Background

Acral melanomas are often diagnosed at a later stage and with poor prognosis. Besides clinical findings that should raise concerns about a benign diagnosis, also dermatoscopic clues could facilitate to differentiate between malignant and benign melanocytic lesions, and lead to earlier diagnosis, less unnecessary excisions and a better outcome.

II.ii. Aim

The aim of this thesis is to review relevant scientific literature and the dermatoscopic features of acral melanocytic lesions.

II.iii. Method

Research of literature was performed by using PubMed and Google Scholar databases. By titles and abstracts, matching the search terms, suitable scientific papers have been selected and further evaluated for their references. Also, books have been included in the introduction. After the literature was collected it was subsequently reviewed for the dermatoscopic patterns of acral melanocytic lesions.

III. Results

III.i. Typical dermatoscopic patterns in melanocytic lesions

Many specific dermatoscopic patterns that are suggestive of benign and malignant acral melanocytic lesions have been published and help to distinguish between those. (29)
Lesions crossing the Wallace-Line between glabrous and non-glabrous skin might be challenging for physicians and should be evaluated clinically, but also for their specific acral and non-acral patterns seen in dermatoscopy. (30)

III.i.i. Acral melanomas

III.i.i.i. **Parallel Ridge Pattern**

The most common and most important high-risk pattern that can be detected in acral melanoma is the parallel ridge pattern. Like the parallel furrow pattern, which is mostly seen in acral nevi, it is composed of parallel band-like pigmentation. Typically, the color shades of brown to black are lighter in early acral melanoma and are usually denser in advanced melanoma. (31)

Another important detail in differentiating between benign and malignant lesions is that acral melanoma tends to obliterate the eccrine gland ducts seen on the pigmented ridges in this pattern. (32)

According to literature the sensitivity and specificity of this pattern are 86% and 99% respectively, also in early tumors, which makes it a very important tool in detection of early acral melanoma. (31)

Despite its undoubtful usefulness it has also been observed in benign acral lesions like lentiginosis, melanocytic nevi, subcorneal hemorrhage, drug induced hyperpigmentation and dye-related pigmentation. (32)

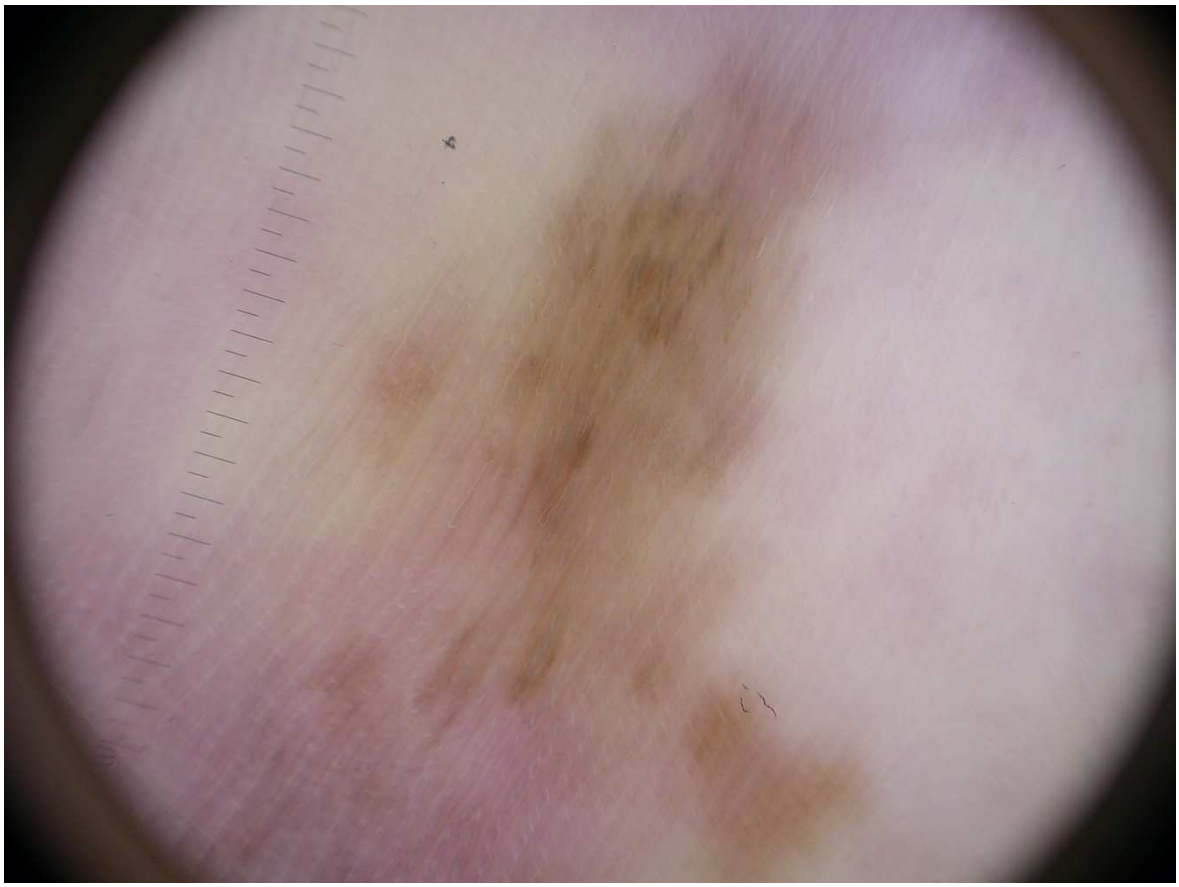

Figure 3: Dermatoscopic image of an acral melanoma with a parallel ridge pattern and irregular shades of brown troughout the lesion (Courtesy ao. Univ.-Prof. Dr. Rainer Hofmann-Wellenhof, Department of Dermatology and Venereology, Medical University of Graz)

III.i.i.ii. **Multi-Component Pattern**

The multi-component pattern (also called irregular diffuse pigmentation or bizarre pattern) shows diffuse and irregular pigmentation, combining structureless features and variable shades of brown and black, sometimes with a grayish color (these findings correspond with melanocytes in various layers of the skin) and is consequently more frequent seen in advanced melanoma. (30,31)

Sensitivity and specificity are 69% and 97% for in situ melanoma and 94% and 97% in invasive ones respectively. (31)

Some authors describe diffuse pigmentation with variable shades of brown as an own pattern, while most sum it up as multi-component pattern. (30)

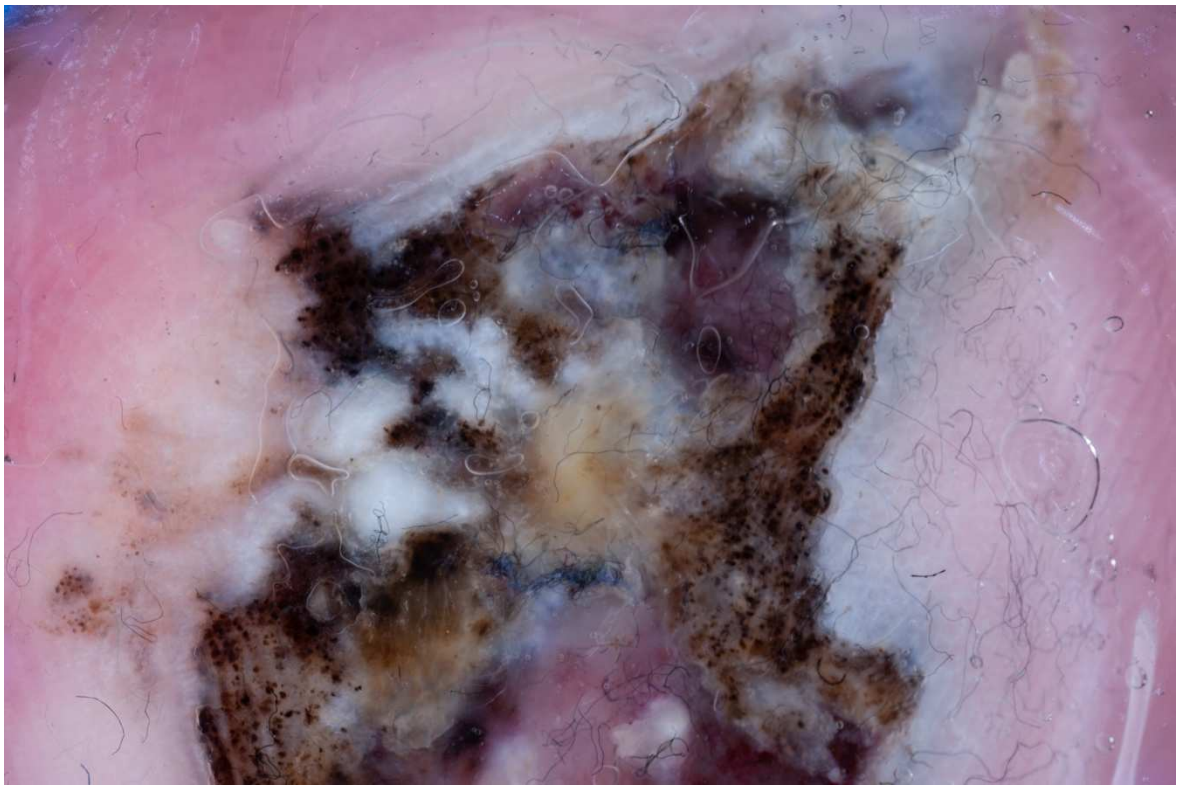

Figure 4: Multi-component pattern with various dermatoscopic features and ulceration, suspicious for acral melanoma (Courtesy ao. Univ.-Prof. Dr. Rainer Hofmann-Wellenhof, Department of Dermatology and Venereology, Medical University of Graz)

III.i.i.iii. **Irregular Fibrillar Pattern**

In the irregular fibrillar pattern fibrils are irregularly distributed and show a variability not only in color-shades but also in thickness. This pattern might also be found focally inside of another lesion. (21)

By turning the dermatoscope slightly sideways and using gel as a contact medium the fibrillar pattern might appear as a parallel ridge pattern, this method is called oblique dermatoscopy. (33) Typically fibrillar pattern is seen in weight bearing areas and is induced by mechanical pressure that deforms the cornified skin layer. (34)

Pigmented lesions might also exhibit a negative fibrillar pattern with parallel distributed whitish rods on fibrillar or dark structureless areas. (21,35)

III.i.i.iv. **Typical dermatoscopic findings associated with malignancy**

Besides the previous high-risk patterns there are also other dermatoscopic findings that have been associated with malignant lesions as abrupt edges, serrated pattern, peripheral irregular dots and globules, atypical streaks, blue-whitish veil, milky red areas, regression, pseudopods and radial streaming. (30,36)

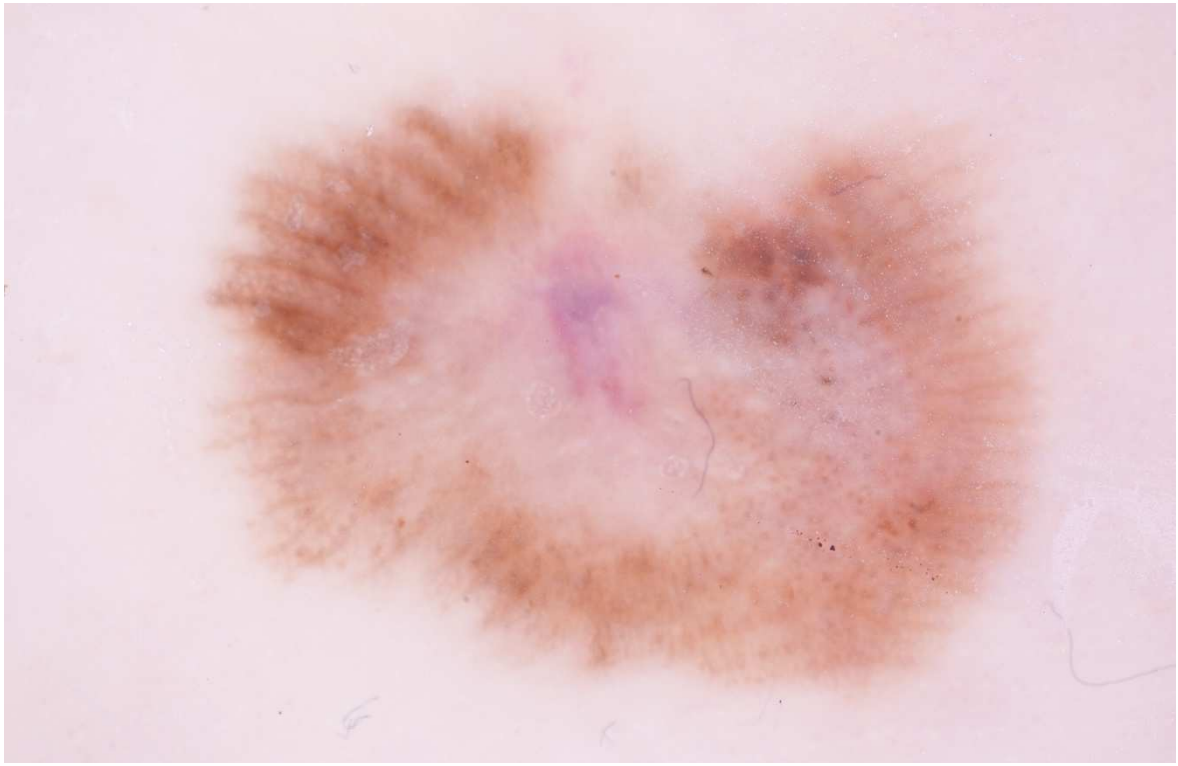

Figure 5: Dermatoscopic image of an acral melanoma with multi-component pattern, milky red center and radial streaming (Courtesy ao. Univ.-Prof. Dr. Rainer Hofmann-Wellenhof, Department of Dermatology and Venereology, Medical University of Graz)

III.i.ii. Nail unit melanoma

The typical presentation of melanoma of the nail apparatus is longitudinal melanonychia of variable width and color-shades from brown to black. (25)

After clinical assessment for typical signs as the presence of pigmentation, macroscopic proximal or distal extension of pigmentation, onycholysis, ulceration, nodules, nail dystrophy or hemorrhage. (25)

Periungual pigmentation is called Hutchinson's sign, if only visible with dermatoscopy it is defined as micro-Hutchinson's sign.

Dermatoscopy is also a useful tool to distinguish blood from melanin, subungual hemorrhage usually shows reddish to brown globules. That the cause of the bleeding might be a tumor must always be considered. (37)

A lesion is suggestive to be benign if the longitudinal pigmentation consists of regular parallel lines of the same color, regular spacing and width, even though most benign lesions observed are not always like this. Irregularities in these parameters are suggestive for malignant melanoma. An important factor is the homogeneity of those individual longitudinal lines. Changes in width and color along their length is suspicious for malignancy. In adults those melanomas often show a diffuse dark background and longitudinal lines might be barely visible, then a change of color-shade along its extension is the suggestive for melanoma. The decision to excise should not only be based on dermatoscopic patterns, but also on clinical criteria and patient history. (37)

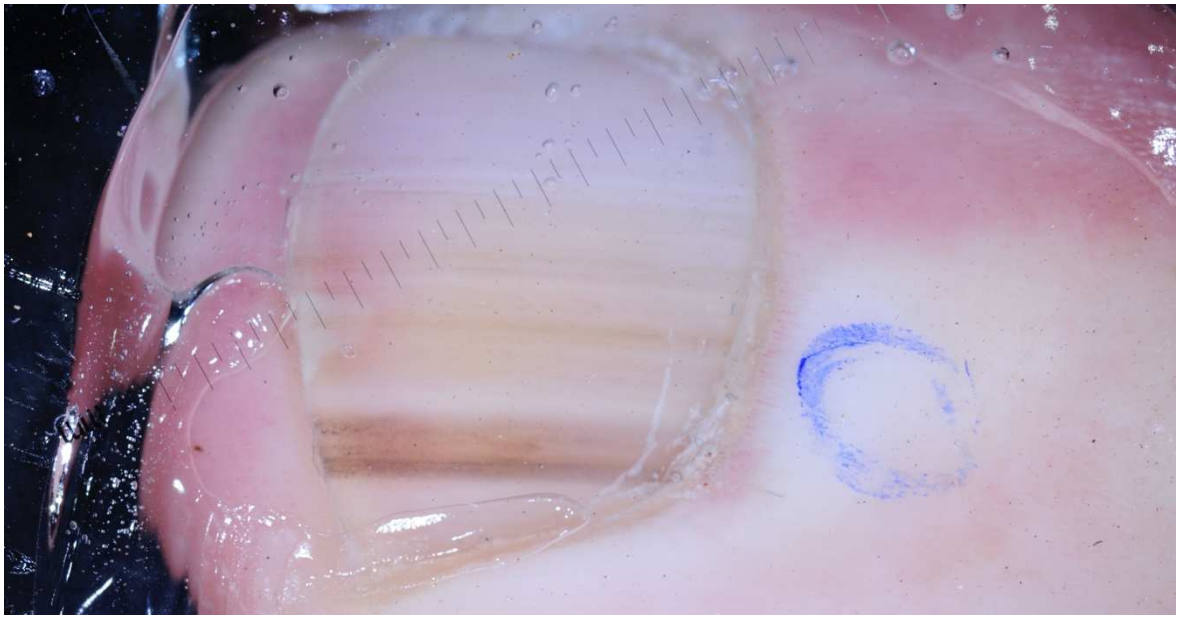

Figure 6: Irregular melanonychia in a nail unit melanoma (Courtesy ao. Univ.-Prof. Dr. Rainer Hofmann-Wellenhof, Department of Dermatology and Venereology, Medical University of Graz)

III.i.iii. Benign melanocytic lesions

III.i.iii.i. **Acral nevi**

Various patterns can be detected in the dermatoscopy of acral nevi, but most of them show one of these three major patterns: parallel furrow pattern, latticelike pattern or regular fibrillar pattern. (31)

Depending on the opinion of the respective author of articles, the other patterns listed below besides the three major patterns may also be interpreted as intermediate risk patterns, since they are not exclusively seen in benign patterns. (15)

Congenital acral nevi might show variations of these patterns like bluish-gray pigmentation especially in nevi with intradermal components. (31)

Typical benign patterns as parallel furrow pattern or fibrillar pattern can also be observed in acral melanoma, but usually are located focally within the melanoma. In acral nevi the benign patterns are covering the whole area. (29)

III.i.iii.i.i.**Parallel Furrow Pattern**

In parallel furrow pattern the pigmentation is aligned to the furrows (sometimes also called sulci). Sometimes accompanied by pigmentation on the ridges, dots or globules or a variation seen as double-lined pigmentation. (31,36) The double lined parallel furrow pattern is also called ladder pattern by some authors. (30)

The double lined pattern seems to be more likely observed in younger patients. (38)

In congenital acral nevi the parallel furrow pattern can be accompanied by evenly distributed brown globules on the ridges. This unique pigmentation on the ridges is called peas-in-a-pod pattern. (31)

A rare combination of parallel furrow or latticelike with reticular pattern is called “transition” pattern, typically found around the fingers. (29,39)

Although this pattern is typically found in benign lesions; it has also been reported in a case association with an acral lentiginous melanoma in situ. The article

described the case of a 41-year-old female who had a slowly growing pigmented lesion on her left sole, previously partially biopsied and diagnosed as benign. The patient noticed progression in size and darkening with inhomogeneous pigmentation. Clinically the lesion was suspicious for melanoma, but in dermatoscopy a parallel furrow pattern was revealed. Histology confirmed acral lentiginous melanoma in situ. (40)

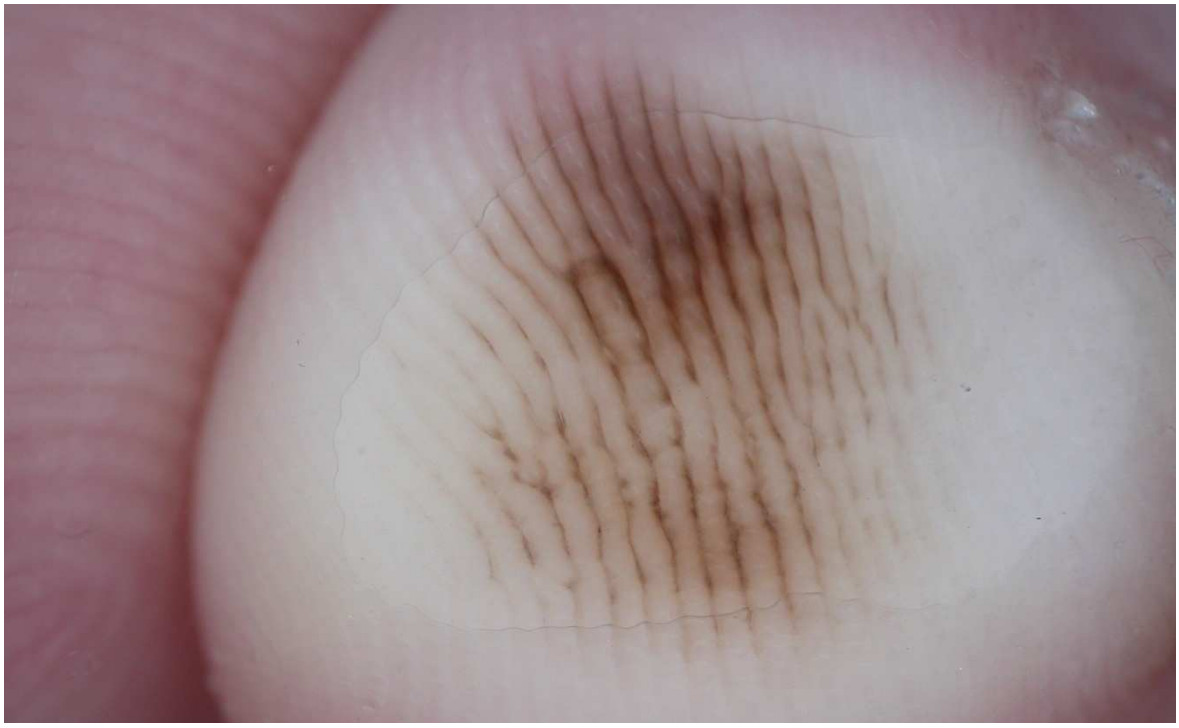

Figure 7: Typical parallel furrow pattern in an acral nevus (Courtesy ao. Univ.-Prof. Dr. Rainer Hofmann-Wellenhof, Department of Dermatology and Venereology, Medical University of Graz)

III.i.iii.i.ii.**Latticelike Pattern**

Like in the parallel furrow pattern the pigmentation is mainly seen in the furrows of glabrous skin, but with linear bands of pigment crossing them in between. Also, dots and globules can be present. (36)

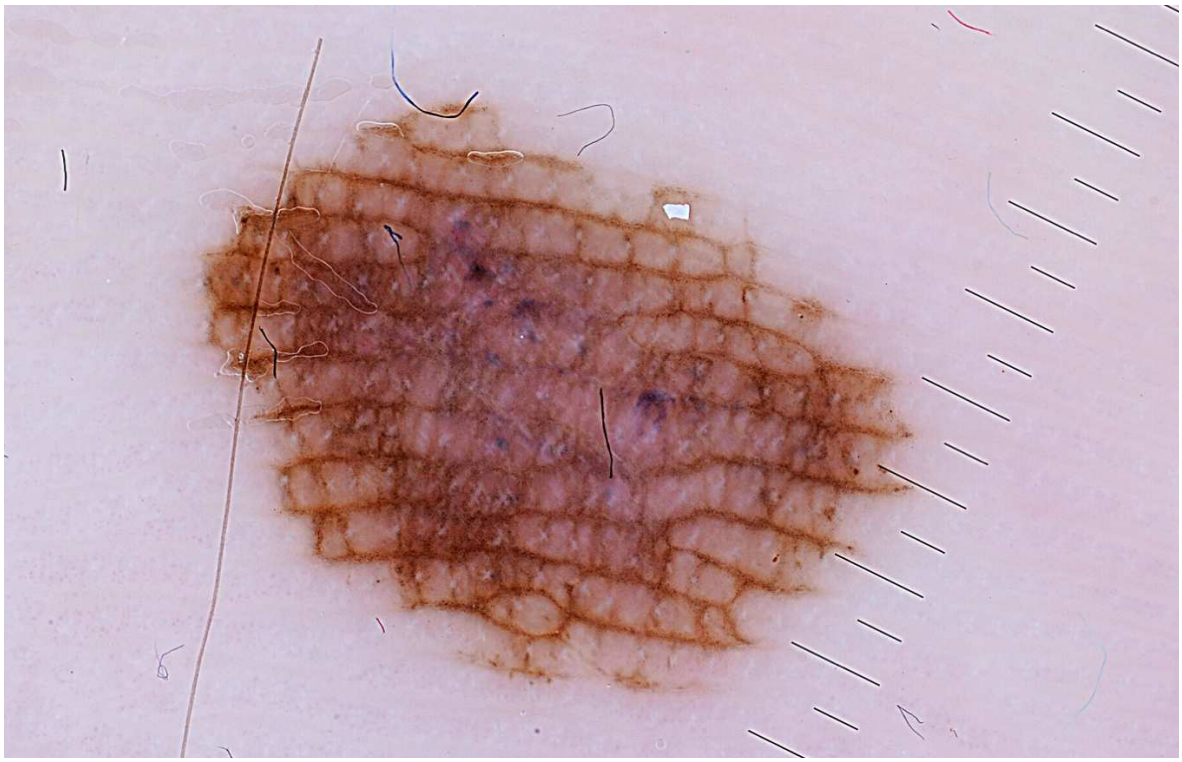

Figure 8: Latticelike pattern in an acral nevus (Courtesy ao. Univ.-Prof. Dr. Rainer Hofmann-Wellenhof, Department of Dermatology and Venereology, Medical University of Graz)

III.i.iii.i.iii.**Regular Fibrillar Pattern**

The regular fibrillar pattern shows parallel fine streaks that crossing the parallel skin markings in an aslant fashion. (36) Fibrils are evenly distributed, of homogenous color and of regular thickness. Also, it is often associated with lesions appearing with the parallel furrow pattern. (21)

Also, in the regular version of this pattern oblique dermatoscopy can be used. By turning the dermatoscope slightly sideways it might reveal a parallel furrow pattern. (33)

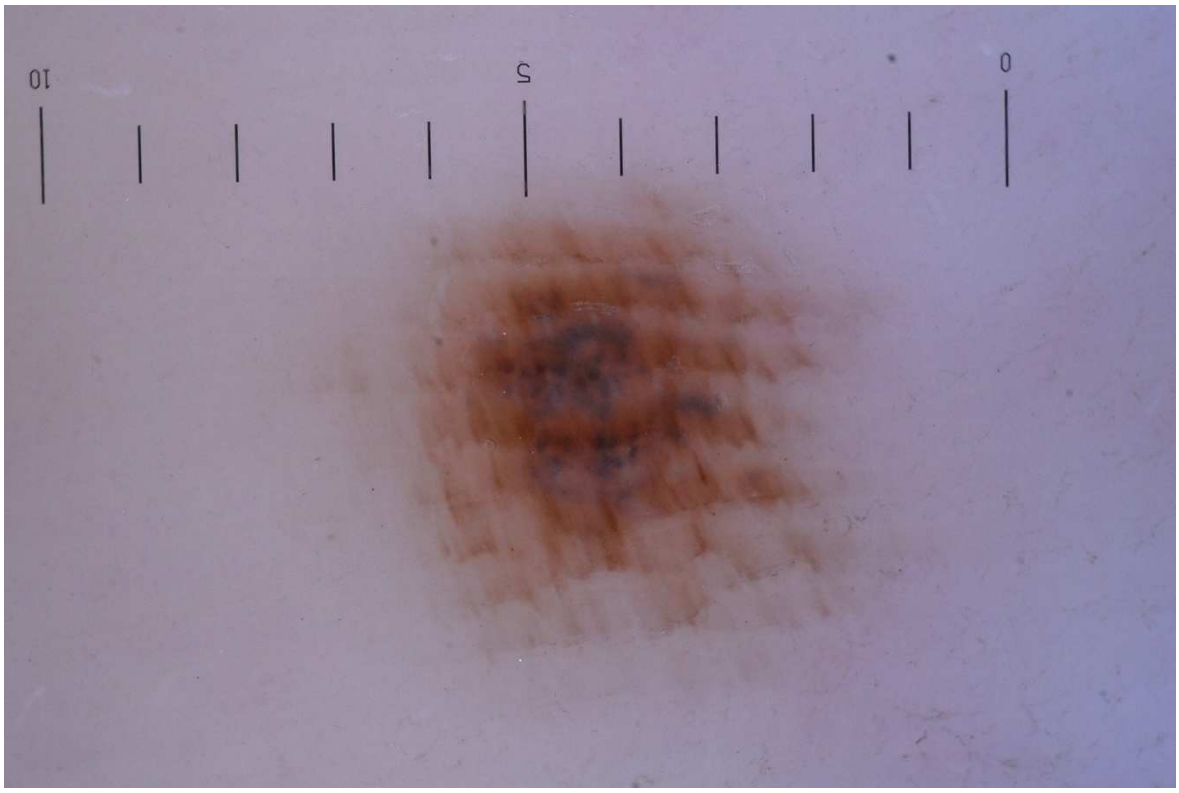

Figure 9: Regular fibrillar pattern in an acral nevus (Courtesy ao. Univ.-Prof. Dr. Rainer Hofmann-Wellenhof, Department of Dermatology and Venereology, Medical University of Graz)

III.i.iii.i.iv.**Homogenous Pattern**

This pattern shows an undefined monotone pigmentation without any structure inside of the pigmentated area. (36)

III.i.iii.i.v.**Globular Pattern**

The globular pattern consists of a usually light brownish area with pigmented globules and their distribution is nonparallel independent of skin markings. (36,39)

III.i.iii.i.vi.**Crista Dotted Pattern**

Composed of dots and globules with an evenly distribution on the ridges near to the openings of eccrine ducts. (39)

III.i.iii.i.vii.**Reticular Pattern**

This pattern describes a reticular pattern that looks very similar to those seen on non-glabrous skin, can be seen in acral skin. (39,41)

III.i.iii.i.viii.**Globulostreaklike Pattern**

This rare pattern has a mottled appearance of linear or curvilinear structures accompanied by bluish globules. (39,41)

III.i.iii.i.ix.**Nontypical Pattern**

Lesions of nontypical patterns cannot be classified by the typical patterns of acral nevi. No specific features of known benign or malignant patterns are seen in this subtype. (36)

IV. Discussion

Acral melanoma is the most frequent subtype in non-caucasian patients but has similar incidence rates in all races. (34) That's why many earlier conducted single center studies about dermatoscopic features and patterns of benign and malignant acral melanocytic lesions had a limited perspective on this subject. (30)

Since Saida and hist colleagues published their "Clinical guidelines for the early detection of plantar malignant melanoma" in 1990, in which dermatoscopy wasn't even mentioned once, a lot of research has happened. (42)

In acral melanocytic nevi the most common evaluated pattern is parallel furrow, followed by latticelike pattern, while the other observed patterns have been observed less frequently in people of European descent, therefore Altamura and colleagues analyzed 723 benign melanocytic lesions. (29) A multicenter study also analyzed dermatoscopic features in acral nevi that revealed the same patterns. (30) A Mexican study with 321 patients and 582 acral lesions had similar numbers of pattern distribution for Latin-American population as stated in previous studies, most commonly observing parallel furrow patterns. (43) Another study from Uruguay also stated similar results in Latin-Americans to previously published studies from Europe and Asia. (44)

Through all literature reviewed for this thesis the parallel ridge pattern and the multicomponent pattern have been noted as typical high-risk patterns in acral melanoma, without mentioning any racial differences. (21,30,34)

Additional methods facilitating the dermatoscopic diagnosis in acral skin have been developed, like the furrow ink test for easier differentiation of furrows and ridges, and oblique dermatoscopy for the closer evaluation of fibrillar patterns. (23,33)

In indistinct lesions and if neither benign nor malignant patterns can be observed a lesion should be excised to rule out melanoma, also not healing nodules and ulcers should be biopsied to avoid misdiagnosis. (5,30) Not only dermatoscopy, but also observations by the patient and clinical history might be helpful for diagnosis of melanoma, especially in lesions with a misleading dermatoscopic pattern and a history of clinical change, like in the case report by Akthar and colleagues that

reported a case of an acral lentiginous melanoma in situ while in dermatoscopy a parallel furrow pattern was observable. (40)

Another important message that has been spread by previous studies is, that lesions should always be evaluated entirely, since lesions that are partly exhibiting a classic benign pattern could focally show malignant features and therefore should be biopsied. (30)

V. Conclusion

Since dermatoscopy was invented characteristic dermatoscopic patterns have been defined to facilitate the diagnosis of malignant acral melanocytic lesions and to distinguish them from benign ones.

Various studies from different countries and different ethnical populations confirmed the prevalence of these patterns appearing in either benign or malignant melanocytic tumors.

The rise of awareness for acral melanoma and its typical dermatoscopic pattern is going to be needed to allow earlier diagnosis and to avoid unnecessary excisions, especially because by this time acral melanoma is diagnosed in later stages and worse prognosis, even though patterns with high specificity and sensitivity have been published.

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