Dermoscopy for pigmented genital lesions - Systematic review of non-malignant and malignant features of genital melanoma, nevi and melanosis

Masterthesis

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ABSTRACT

Objectives: The aim of this study was to assess dermoscopy criteria of pigmented genital melanoma and common benign counterparts to better differentiate between benign and malignant pigmented genital lesions.

Materials and Methods: A systematic literature review of MEDLINE (PubMed) and bibliographic cross-referencing was performed to identify articles covering dermoscopy features of common and atypical nevi, melanosis and melanoma. Articles were included if dermoscopy was performed on genital lesions and dermoscopy features of pigmented genital lesions were described and extractable.

Results: A total of 19 articles with 455 dermoscopy cases of genital lesions could be extrapolated from the published literature. Identified dermoscopy criteria for genital melanoma included asymmetry of color and/or structure (92%), followed by blue/white or blue/grey veil (69.2%). Genital melanosis showed a diffuse pigmentation in 51.4% and a ringlike pattern in 27.8% of described cases. Features identified in common genital nevi included a homogeneous brown-gray pigmentation or brown structureless areas and were described in 35.1%. A globular pattern was described in in a total of 35.7% of common nevi.

Conclusion: Clinically pigmented genital lesions may look alarming, however the application of dermoscopy may help to differentiate benign melanosis and common genital nevi from melanoma.

1. INTRODUCTION

Diseases of the genital area cover a broad spectrum of benign and malignant disorders, that range from benign inflammatory conditions to malignant and potentially lethal diagnoses (i.e melanoma) (Figure 1).

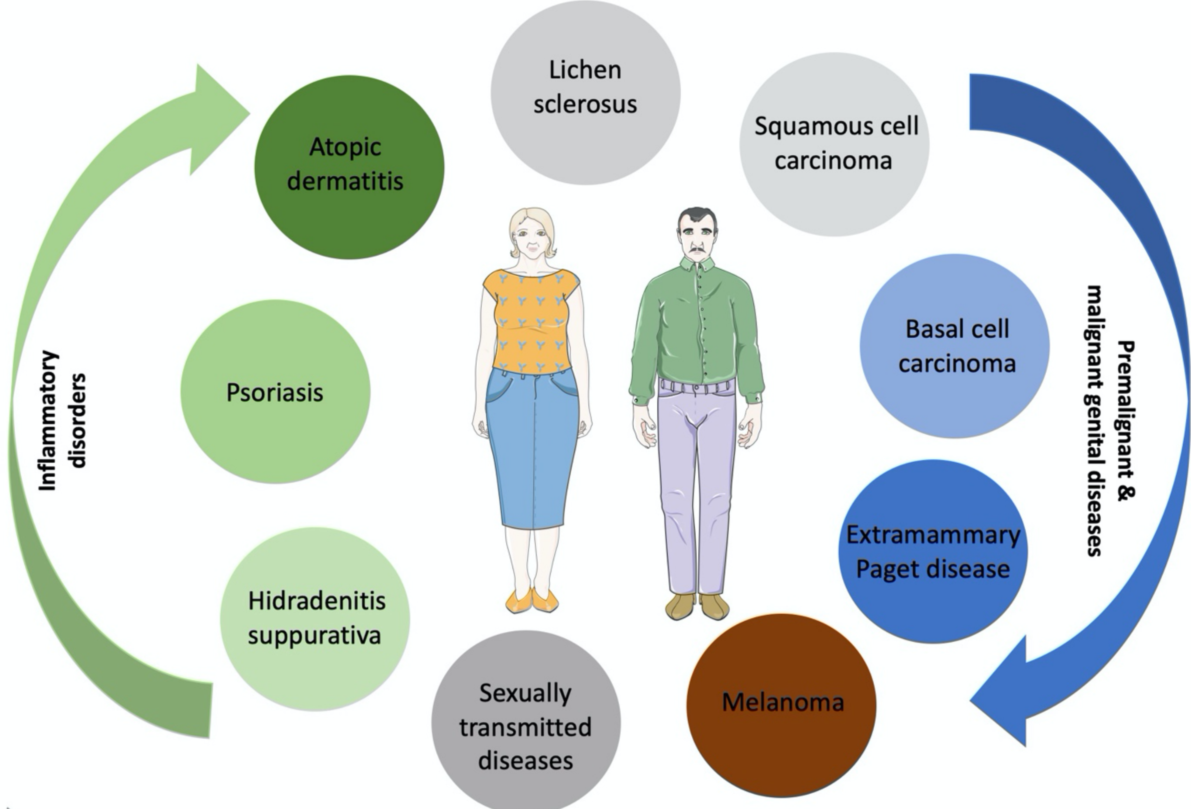
Besides melanoma, pigmented skin neoplasms of the genital area include melanocytic naevi (common and atypical nevi), melanosis, and less often pigmented Bowenoid papulosis, pigmented basal cell carcinoma or pigmented extramammary Paget's disease, which all may mimic melanoma on clinical and dermoscopic examination.

The diagnosis of pigmented genital lesions imposes some diagnostic challenges for several reasons; first, patients might not be aware of the existence of their skin condition due to a lack of self-screening or self-awareness and second, women might seek help from a gynecologist and men might consult a urologist first, before being referred to a specialized clinic (ideally an interdisciplinary vulva or male genital disease clinic) (1).

Non-invasive diagnostic tools for the evaluation of pigmented lesions have improved over the last years and the role of dermoscopy has been well established and is now recognized as a valuable diagnostic tool in both clinical and research settings (2).

This thesis focuses on the description of dermoscopy criteria for melanoma and its most common differential diagnosis (i.e common and atypical nevi and melanosis).

Figure 1. Spectrum of genital disorders



Own image. The images of the persons used were modified from Servier Medical Art under the Creative Commons Attribution 3.0 Unported License.

1.1 Dermoscopy – a brief historical overview

Dermoscopy or dermatoscopy is a non-invasive diagnostic tool, that uses a polarized or non-polarized light source coupled with a magnifying glass (10-fold magnification), that allows to view sub-microscopic structures at the level of the epidermis and upper level of the dermis (3,4). Historically in 1655 Pierre Borel a French physician, used a microscope to visualize the capillaries of the nailbed. Eight years later in 1663, Johan Christophorus Kolhaus a German doctor followed his desire to visualize skin structures and published his findings of the visualization of the vessels in the nail matrix (5,6). In 1878, Ernst Karl Abbe a German optometrist and physician improved this technique by adding oil immersion to create a layer between the skin and the microscope and thus increased the resolution of microscopic images by reducing backscattered light from the skin surface (5,6). Unna used the technique of adding oil to the skin lesion of patients with lupus to better study their skin conditions, he then introduced the term “Diaskopie” in an article published in 1893 (3,5,6). In 1913, Darier utilized this knowledge to describe Wickham-striae in patients with Lichen ruber planus - an important diagnostic clue that still aids the diagnosis of Lichen ruber planus today (6). Saphier a Viennese dermatologist shaped the term “dermatoskopie” and applied this new technique to identify criteria to distinguish cutaneous tuberculosis from syphilis (5,6). It took nearly 80 years of further research from the investigations made by Borel and Kolhaus until the first portable dermatoscope was introduced in 1958 by Lean Goldman who applied the technique to evaluate melanocytic nevi and melanoma (Figure 2) (7). In the 1980s several Austrian dermatologists including Pehmberger (8) and Soyer (9), published their data on the correlation of dermoscopic features with histopathology (3,10,11). In 2003 the International Dermoscopy Society was founded in Graz, Austria which set standards in the field of dermoscopy and connected researchers around the globe (2).

Figure 2. Historic image of the instrumentation of cutaneous microscopy

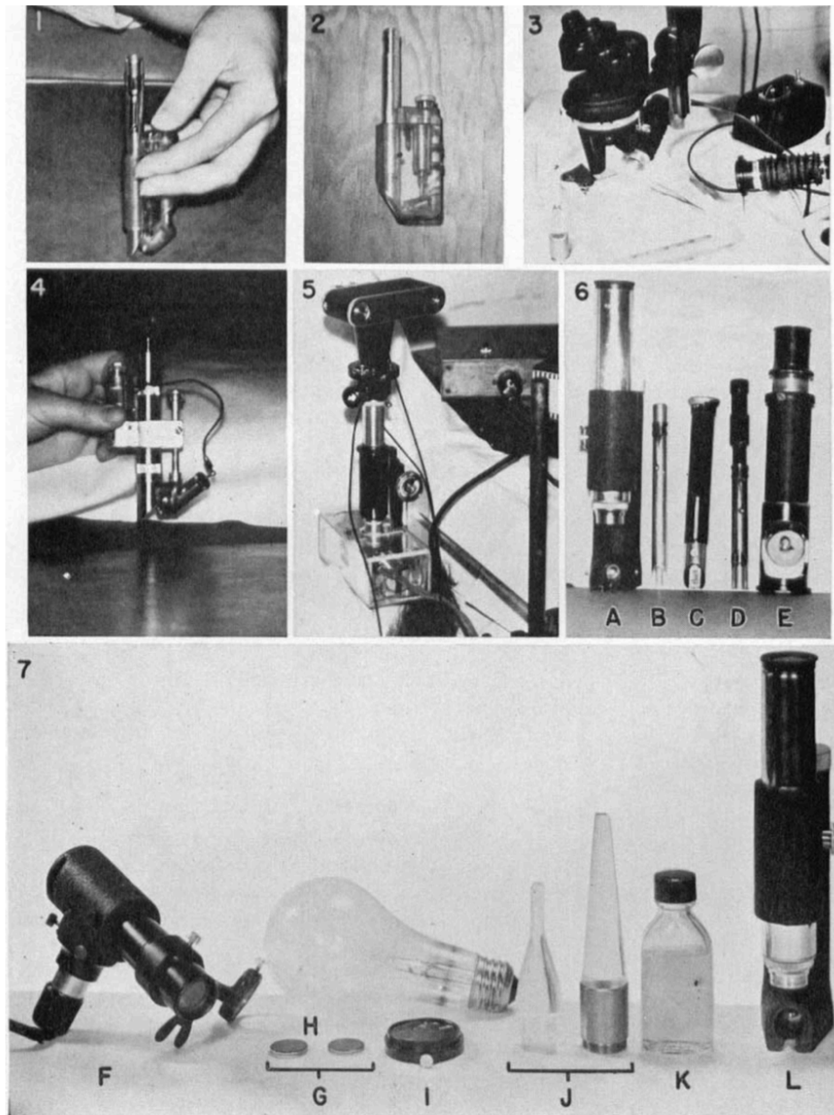


Fig. 1. Instrumentation of cutaneous microscopy.

1. 20× microscope with attached battery illuminator source.
2. 40× microscope with simple attached battery illuminator source—this type preferred for routine clinical work.
3. Showing technic of examining excised tissue under binocular microscope; illumination can be varied.
4. 40× microscope with flexible illumination source—to vary direction of light reaching surface of skin.
5. Photomicrographic apparatus of Siebentritt for photography of surface of skin at magnifications of 40× and 100×.

From Goldman L. Some investigative studies of pigmented nevi with cutaneous microscopy. J Invest Dermatol. 1951 Jun;16(6):407-27.

1.2 The science behind dermoscopy

Visible light is mainly reflected by the skin surface, thus visual information from subsurface structures of the skin is mostly lost to the observer (4,12) (Figure 3A). Hand-held dermatoscopes overcome this effect as they are composed of a glass plate, a standard magnifying objective and a transilluminating light source (12). The skin is flattened when the glass surface of a dermatoscope is directly applied on the skin.

By adding some kind of immersion liquid (i.e mineral oil, alcohol, ultrasound gel or water) air-pockets within the stratum corneum are reduced to a minimum and structures at a deeper lever become visible. The light source helps to illuminate the skin and thus aids in the visualization of subsurface structures, while the magnifying glass allows to view the dermo-epidermal junction (13).

1.3 Polarized and non-polarized dermoscopy

Two different modes of dermoscopy exist; nonpolarized dermoscopy (NPD) and polarized dermoscopy (PD) which differ in the way that colors and certain patterns are visualized (4,14). Light is reflected by the skin surface, due to the higher refractive index of the stratum corneum (1.55) compared with that of air (1.0) (4). NPD requires an immersion liquid to reduce the reflection, thus allowing for increased light penetration into the skin (4). While the first available dermatoscopes were nonpolarized and set the standard for years, polarized devices are available since 2000 (14). PD uses 2 polarizers with orthogonal axes which intersect at 90° and allow to collect the light returning from deeper layers of the skin, thus allowing to better visualize deeper structures compared with NPD, which is better at visualizing superficial structures (Figure 3B). For example, milialike cysts (a superficial structure and an important clue to the diagnosis of a seborrheic keratosis) are better

appreciated with NPD (14). Vascular structures on the other hand are better appreciated with PD, since direct contact with the skin compresses the vessels (13). Other than NPD, where an immersion liquid is required, PD does not require the utilization of a liquid interface and direct contact with the skin is not needed (4). This can be an advantage when rapidly performing a full-body skin exam.

Knowing these differences between NPD and PD helps to choose which method to use for selected criteria. Switching between NPD and PD does not necessarily mean to change devices, as hand-held dermatoscopes, which allow to toggle between these methods are commercially available and frequently used in the clinical setting.

Figure 3. Regular light reflection and Polarized dermoscopy

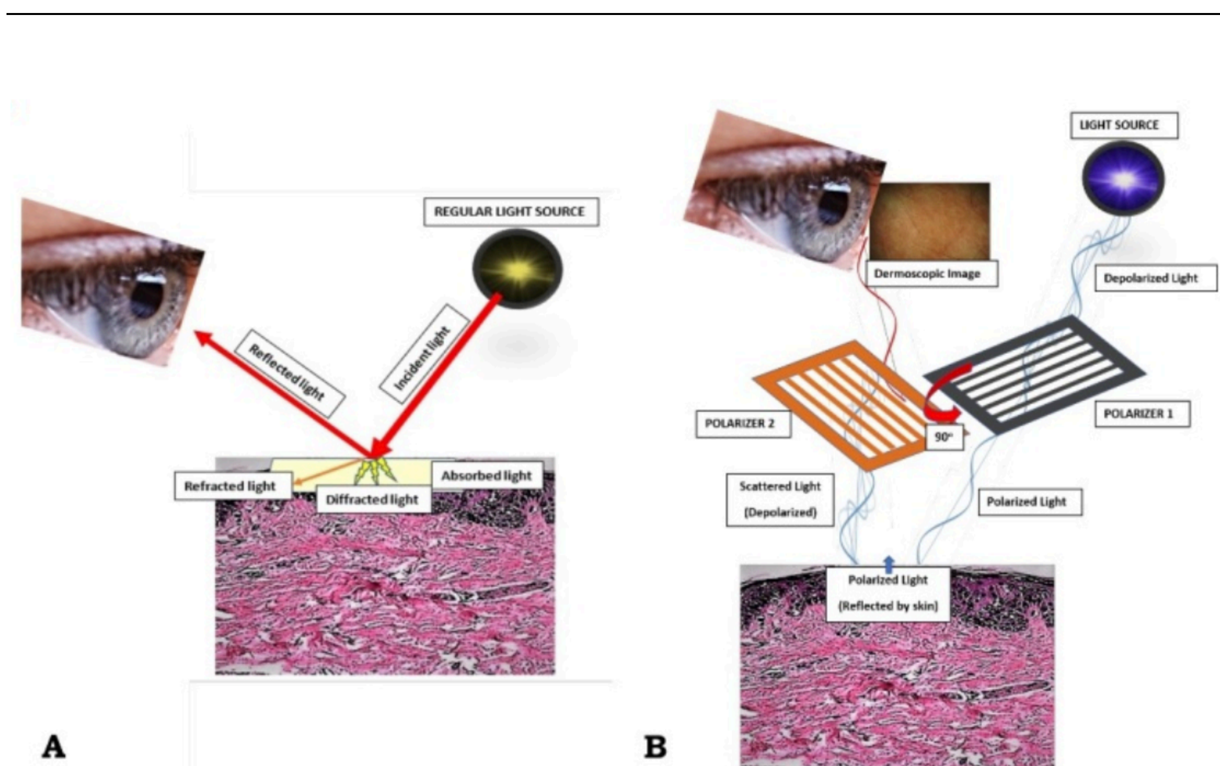


Figure 3 (A) Most of the light is reflected by skin surface. With the unaided eye only the reflected surface of the skin is appreciated. **(B)** Polarized dermoscopy uses 2 polarizers with orthogonal axes which intersect at 90 that allow to collect the reflected light returning from deeper layers of the skin. Image reproduced under the Creative Commons Attribution 4.0 International License, Sonthalia S, Yumeen S, Kaliyadan F. Dermoscopy Overview and Extradiagnostic Applications. [Updated 2022 May 15]. In: StatPearls. Treasure Island (FL): StatPearls.

1.4 Digital and hand-held dermatoscopes

Most dermatoscopes used in the clinical routine are simple hand-held devices that do not possess an inbuilt camera. However, for most of the dermatoscopes used today, adaptors are available that allow to connect the dermatoscope with a smartphone or digital camera (13,15). Special image-capturing dermatoscopes (lenses) possess a special lens that is connected to a digital camera. These lenses cannot be used for direct skin examinations without a camera and thus always require the clinician to appreciate the skin lesion using the digital camera. The resolution of the captured image depends on the resolution of the digital camera used. Images can easily be stored on the camera`s memory card and can then be exported (15).

In addition to the above-mentioned hand-held devices, video-dermatoscopes are equipped with a high-resolution camera that is built in a handpiece that can be placed on the skin lesion with the image being visualized on a computer screen.

Dermoscopy images and videos can thus be easily stored and visualized with a greater magnification. With the use of a digital zoom function diagnostic challenging sections of a lesion can be extrapolated and better visualized (13,15). Captured digital images can be easily stored to provide an adequate resource for patient follow-up or to exchange images in the setting of teledermatology or teleconsultation with an expert in the field of dermoscopy (15).

Newest advances in dermoscopy include automated diagnostic tools that use artificial intelligence systems that allow the analyzation of skin lesions and even assist the clinical decision making (16).

1.5 Dermoscopic alphabet

1.5.1 Basic elements

Five basic elements have been identified, to describe and evaluate a lesion using dermoscopy: (I) lines (elements with a parallel edge with a greater length than width), (II) dots (small round elements), (III) clods (round elements, diversely formed), (IV) circles (lines or dots arranged in a circular fashion), (V) pseudopods (short pigmented lines with a bulbous end) (17).

1.5.2 Patterns

A pattern is composed of repetitions of one or more basic elements, that requires to constitute at least 25% of the lesion.

According to the five basic elements, five patterns constituting of a basic element can be differentiated: a pattern of lines, a pattern of dots, a pattern of clods, a pattern of circles and a pattern of pseudopods. Lesions with no identifiable basic elements but with a homogeneous appearance (for example brown) represent a structureless pattern.

A pattern of lines can be further broken down into five types of differently arranged lines: reticular lines (thin lines that are arranged in a net-like fashion), branched lines (thin and thick lines that intersect with each other), parallel lines (straight lines that are arranged in parallel fashion), radial lines (lines the run of the center or a single point in a radial fashion – this pattern is only found in combination with another pattern) and curved lines (curved lines have few intersections that run either in a parallel fashion or randomly).

Pigmented lesions can be composed of either a single pattern or a combination of multiple patterns (17).

1.5.3 Colors

The application of dermoscopy allows to visualize different shades of pigmentation that correspond with the layer of skin in which melanin is located. Melanin in the cornified layer appears black, whereas melanin located in the basal layer appears brown. Gray color corresponds with melanin in the papillary dermis and blue color with melanin located in the reticular dermis (3).

The density of melanin and the thickness of the epidermis also affect the observed color. Very dense aggregates of melanin in the basal layer of the epidermis may also appear dark brown (3).

1.5.4 Symmetry & Asymmetry

When assessing a lesion using dermoscopy, it is important to differentiate between a symmetrical or an asymmetrical overall appearance. The above-mentioned patterns can be combined in a symmetrical or asymmetrical fashion. A symmetric lesion can be mirrored in any perpendicular axis, this criterion does not apply for asymmetrical lesions.

1.6 Algorithms

To facilitate the analysis of a pigmented lesion, several algorithms have been established (3). These diagnostic methods can be broken down into semiquantitative models (i.e the ABCD rule (18), seven-point checklist (19), the three-point checklist (20) and the CASH-algorithm (21)) and qualitative diagnostic models (i.e Menzies' method (22), pattern analysis (8), chaos and clues method (17)). These algorithms from the basis of our understanding of dermoscopy, especially in the process of learning, however most algorithms cannot be easily applied for the diagnosis of pigmented genital lesions.

1.6.1 ABCD rule

By applying the ABCD rule, four different criteria of a melanocytic lesions are systematically analyzed (18). “A”, the first criterion stands for asymmetry. To assess a lesion for its symmetry, the lesion is divided by two perpendicular 90° axes. If both axes show features of irregularity regarding shape, color and/or dermoscopic structures an asymmetry score of 2 will be given. If the lesion is asymmetric in one axis it scores 1 point. If the lesion is symmetric in both axes it scores 0 points.
The letter “B”, the second criterion stands for boarder. The lesion is subdivided into eight segments and each segment is analyzed for an abrupt cut-off of pigment pattern at the periphery. Every segment is analyzed individually, thus the maximum sore for border is 8 and the minimum score is 0. The letter “C” stands for color.
Six different colors (white, red, light-brown, dark-brown, blue-gray, and black) are counted to determine the score. Each color scores one point. If all six colors are present the color score is 6. The last criterion is “D”, which stands for dermoscopic structures (i.e. network, structureless or homogeneous areas, branched streaks, dots and globules), of which each criterion scores one point (18).
The ABCD-score is then calculated using the following formula, which takes into account the different diagnostic weight of the individual criteria:

Formula: $(A \times 1.3) + (B \times 0.1) + (C \times 0.5) + (D \times 0.5) = \Sigma$

Lesions that score less than 4.75 point are deemed benign, lesions that score between 4.8 – 5.45 points are deemed suspicious and lesions that score more than 5.45 points are deemed malignant (18).

1.6.2 Seven-point checklist

With the seven-point checklist, a pigmented lesion is evaluated for the presence of the following dermoscopic patterns and structures: atypical network (major criterion), blue-white veil (major criterion), atypical vascular pattern (major), irregular dots/ globules (minor criterion), irregular streaks (minor criterion), irregular blotches (minor criterion) and regression structures (minor criterion). Every major criterion scores two points and every minor criterion scores one point. A lesion is deemed to be benign if the total score is less than 3, a score of 3 or higher is considered malignant (19).

1.6.3 Three-point checklist

The three-point checklist is a simplified algorithm that can be easily applied by non-expert medical professionals, including primary care physicians and nurses, to quickly assess and decide whether a lesion should undergo a profound examination by an expert in the field of dermoscopy.

For this purpose, every lesion is screened for asymmetry in dermoscopic colors and/or structures, presence of atypical network, and blue white structures. The presence of more than one criterion is suspicious for malignancy and requires further evaluation or excision (20).

1.6.4 CASH-algorithm

The acronym “CASH” stands for: color, architecture, symmetry and homogeneity. Pigmented skin lesions are screened for different dermoscopic colors (light brown, dark brown, black, red, white, blue). Each color scores one point. Architectural disorder is divided into none or mild (0 points), moderate (one point) and marked (two

points). Symmetry of dermoscopic structures/colors in both axis scores 0 points, asymmetry in one axis scores 1 point and asymmetry in two axis scores 2 points. The last criterion “homogeneity” is based on the number of the following dermoscopic structures: network, dots and globules, streaks and pseudopods, blue-white veil, regression, blotches, polymorphous vessels. The presence of each of these features scores one point. A total CASH-score of eight or more is suggestive of melanoma (21).

1.6.5 Menzies’ method

The Menzies` method is a qualitative diagnostic model. A skin lesion is analyzed for the presence of negative features and positive features in dermoscopy. The two negative features are symmetry of pattern and presence of only a single color. The nine positive features include: blue-white veil, multiple brown dots, pseudopods, radial streaming, scar-like depigmentation, peripheral black dots and/or globules, multiple colors (five to six), multiple blue and or gray dots, broadened network. A lesion is suspicious for a diagnosis of melanoma if it has neither of both negative features and one or more positive feature (22).

1.6.6 Pattern analysis

Pattern analysis refers to the assessment of the “overall gestalt” of a pigmented lesion with dermoscopy: each pigmented lesion is evaluated based on all dermoscopy features (symmetry, general patterns, local structures, and colors) shown (1.5.1 - 1.5.4). As a rule of thumb, benign lesions have few colors and patterns, regular local structures and are symmetrical.

The following general patterns are taken into consideration: reticular pattern (if typical, indicative for a benign nevus) globular pattern (prevalence of globules,

indicative for compound or intradermal nevi); cobblestone pattern (dermal nevi); homogeneous pattern; parallel pattern; star “burst” pattern (indicative for Reed nevus); multicomponent pattern (three or more parts of a lesion showing different dermoscopic features is suspicious for melanoma) (3).

1.6.7 Chaos and clues method

This algorithm evaluates a pigmented lesion based on the principle of “chaos” and “clues to the diagnosis of melanoma”.

“Chaos” is defined as asymmetry of dermoscopic structures or colors. If a lesion appears “chaotic” the investigator needs to search for one or more of the following clues: grey or blue structures, eccentric structureless area, thick lines (reticular or branched), peripheral black dots or clods, segmental radial lines or pseudopods, white lines, polymorphous vessels, parallel lines (or ridges if the lesion is acral). A biopsy or further investigation by an expert in the field of dermoscopy should be considered if both “chaos” and one or more “clue” are present (17).

1.7 Pigmented genital lesions

Pigmented genital lesions occur in about 10% of the general population and include common nevi, melanotic macules (melanosis), angiokeratomas, seborrheic keratosis, squamous cell carcinoma, pigmented basal cell carcinomas and melanomas (23,24). Genital nevi and melanosis are common mimickers of melanoma on clinical and/or dermoscopic evaluation.

1.7.1 Genital nevi

Genital nevi predominantly affect patients at younger ages (25,26). Although their clinical appearance might be suspicious for melanoma, most genital nevi exhibit a single dermoscopic pattern (reticular, clod or structureless), which helps to differentiate them from malignant melanoma (25).

1.7.2 Melanosis

Genital melanosis of the vulva or penis is a benign condition, characterized by the presence of single or multiple light brown to blue-black, poorly demarcated macules. Vulvar melanosis affects predominantly perimenopausal women and is sometimes found in patients with resolved annular lichen planus (27) or in patients with lichen sclerosus (28).

The clinical appearance of genital melanosis can be highly alarming to both the patient and the physician. Common dermoscopy algorithms are not reliable in ruling out melanoma in this specific anatomic site, thus a skin biopsy is performed in most patients (29).

1.7.3 Melanoma

Genital mucosal melanomas are rare malignancies with a poor prognosis (30,31). While melanoma incidence is rising for cutaneous melanoma, incidence of mucosal melanoma has remained stable over the last years (Figure 4) (30). Survival curves contradict this trend and indicate that survival of cutaneous melanoma has drastically improved, while the prognosis of genital melanoma still remains poor.

Studies have found that the differing tumor biology, delayed diagnosis and poorer response to current treatment modalities could explain these discrepancies (30,32,33). The majority of vulva melanomas are diagnosed in postmenopausal women with a median age at diagnosis of 68 years (30,32). Genital melanomas in men are extremely rare and, as in women, affect men in later stages of life (34). Differentiation of genital melanomas from benign pigmented lesions of the vulva or glans is often a challenging task and sometimes impossible to make based on the clinical judgment alone. However, early detection is key as surgery remains the mainstay of treatment today (30).

Figure 4. Change of melanoma incidence and survival over time.

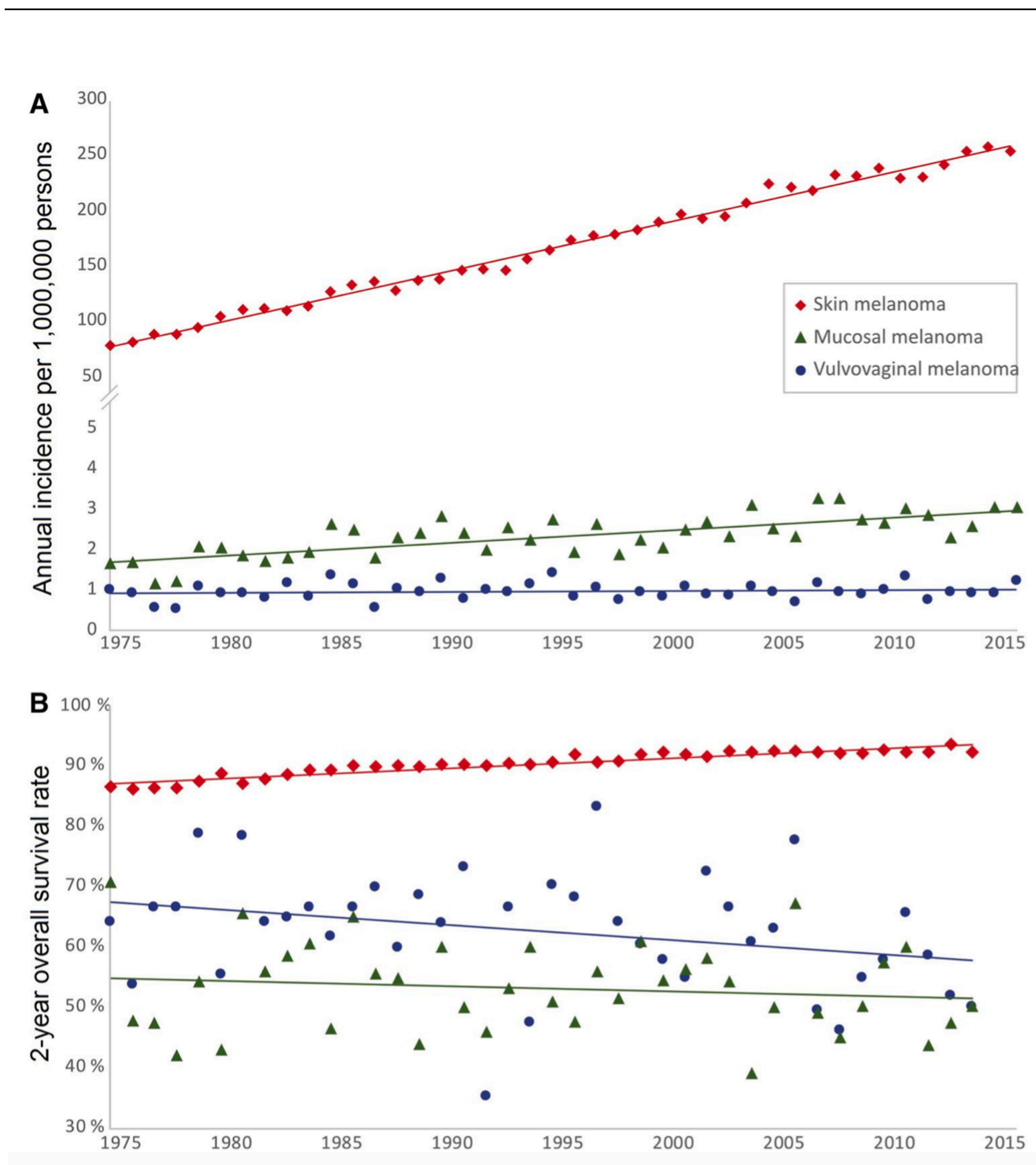


Figure 4 (A) Annual incidence of skin, mucosal, and vulvovaginal melanoma per 1,000,000 persons in the Surveillance, Epidemiology and End Results (SEER)-9 population. **(B)** Two- year overall survival rate of skin, mucosal, and vulvovaginal melanoma in the SEER-9 population.
Own publication. Reproduced with permission. Wohlmuth C, Wohlmuth-Wieser I et al. Malignant Melanoma of the Vulva and Vagina: A US Population-Based Study of 1863 Patients. Am J Clin Dermatol. 2020 Apr;21(2):285-295.

2. METHODS

2.1 Systematic Review

A systematic literature review of MEDLINE (PubMed) and bibliographic cross-referencing was performed to identify articles covering dermoscopy features of pigmented genital lesions. The following search terms were used: (dermoscopy AND penis), (dermoscopy AND vulva), (dermatoscopy [Mesh] OR dermoscopy [Mesh]) AND (genital [Mesh] OR genitalia [Mesh]). Titles and abstracts were screened for articles published from inception to 2021. Articles (case studies and case reports) were included if (I.) dermoscopy was performed on genital lesions; (II.) the dermoscopy features of genital melanoma and common mimickers (i.e melanoma, genital nevi and melanosis) were described and extractable. Pooled data of general mucous lesions were excluded if the location of the lesion was not explicitly specified. A total of 115 articles were retrieved from PubMed using the pre-defined search terms. After duplicate removal 85 articles were screened for inclusion in the study. Altogether, 19 articles met the inclusion criteria, comprising of 455 cases of pigmented genital lesions (386 vulva, 7 penis, 64 genital lesions with unspecified site) (Figure 5 – PRISMA Flowchart).

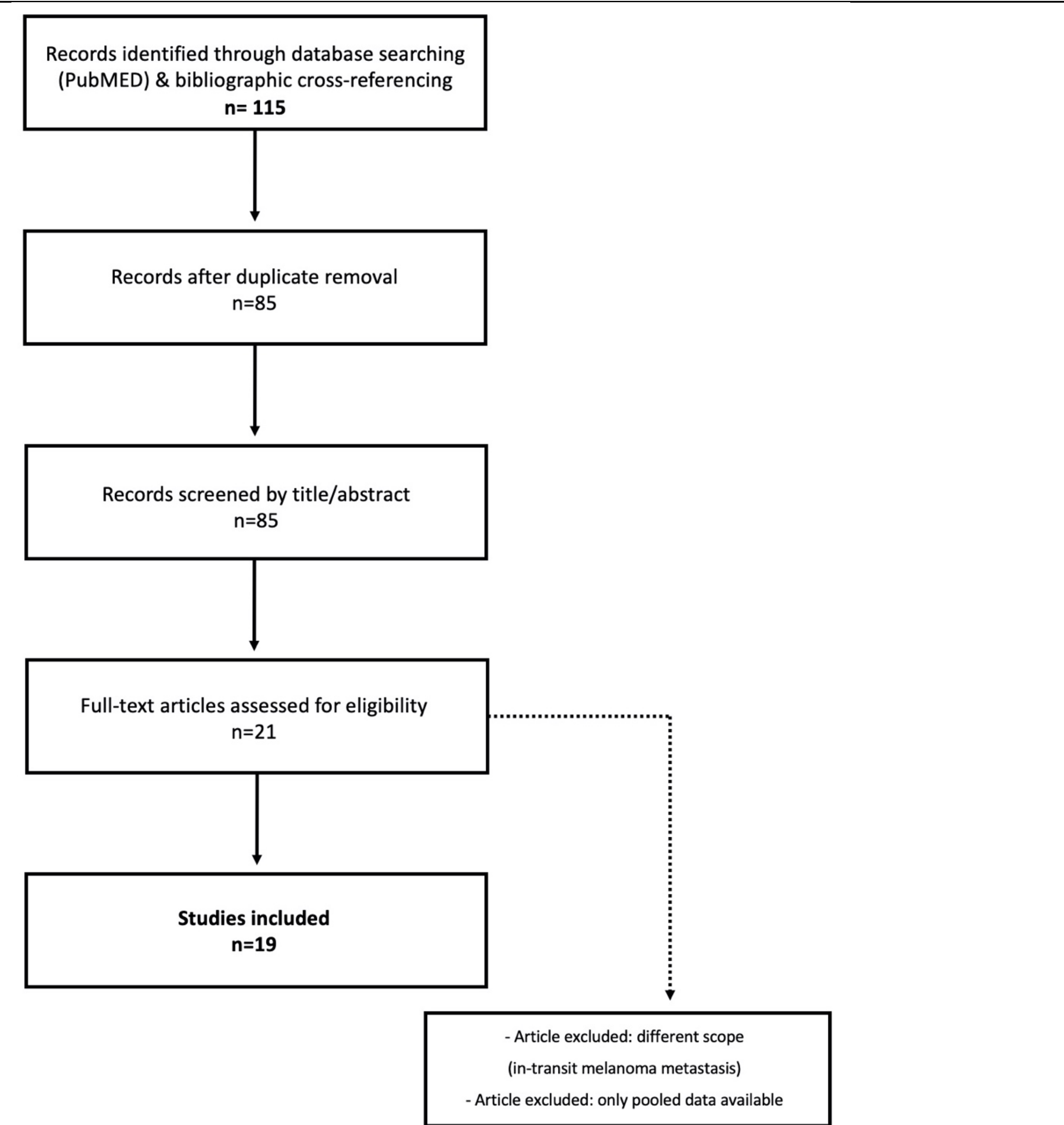
2.2. Data collection

Baseline data extracted included dermoscopy features and patterns of the different pigmented vulvar and penile entities (i.e common and atypical nevi, melanoma and melanosis). Data on the systematic literature review of vulvar melanoma have been previously published by the author (32), Table 1 has thus been modified with permission from Wohlmuth C and Wohlmuth-Wieser I et al. (32).

2.3 Statistical analysis

Descriptive statistics was used to report demographic data. Analyses were performed using software (IBM Corp. Released 2020. IBM SPSS Statistics for Macintosh, Version 27.0. Armonk, NY: IBM Corp).

Figure 5. PRISMA Flowchart



3. RESULTS

3.1 Systematic literature review

The systematic literature review of published articles in English language revealed a total of 19 articles, which met the inclusion criteria. Altogether, 455 dermoscopy cases of genital lesions could be extrapolated from the published literature and were included in the statistical analyses (Figure 5).

3.2 Melanoma of the vulva and penis

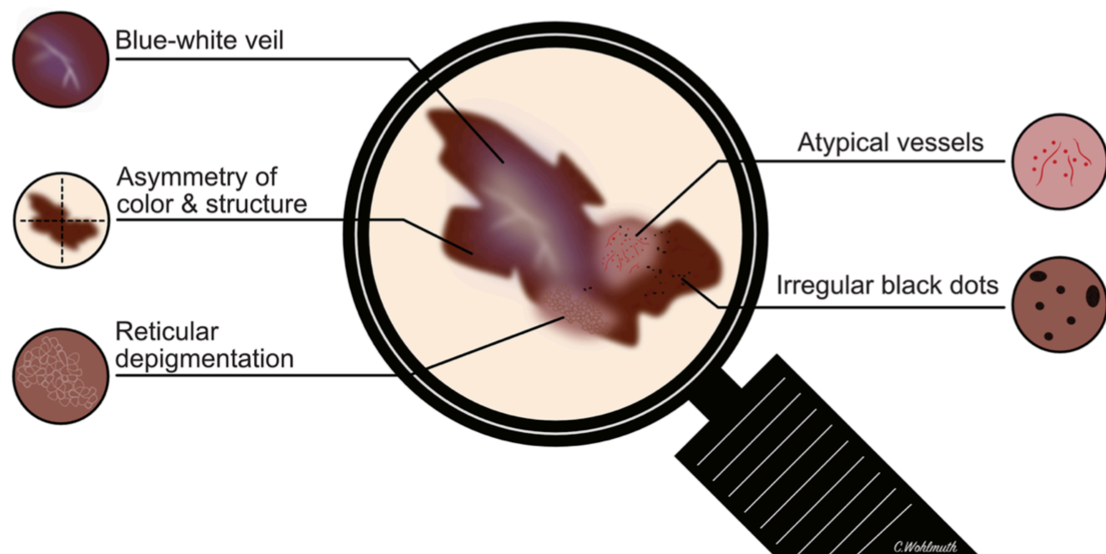
A total of 13 studies with a total of 39 cases (38 vulva melanoma and 1 penile melanoma) were identified (Table 1). The most commonly observed feature was asymmetry of color and/or structure and explicitly reported in 23 of 25 cases (92%), followed by blue/white or blue/grey veil (69.2%, 27/39). Structureless areas, atypical vessels and irregular dots and globules were found in 46.2%, 43.6% and 41% respectively. Reticular depigmentation was observed in 12.8% of all vulva melanomas and was identified in 80% (4/5) of vulva melanomas described by Ferrari et al. (35). Several melanoma-specific dermoscopy features were observed in the included case of penile melanoma; asymmetry of color and structure, blue/white veil, irregular streaks and regression structures (36). Collected dermoscopy features of vulva melanoma are summarized in Figure 6.

Table 1. Dermoscopy features in malignant melanomas of the vulva and penis

Study	V/P(n)	Asymmetry of color / structure	Irregular dots / globules	Veil (blue/white, blue/grey, white)	Whitish-grey or grey areas	Irregular network / atypical pattern	Atypical vessels	reticular depig-mentation	Structure-less areas	Milky-red or red areas
Virgili et al.(37)	V (1)	100% (1/1)	100% (1/1)	0% (0/1)	0% (0/1)	100% (1/1)	0% (0/1)	0% (0/1)	0% (0/1)	0% (0/1)
De Giorgi et al.(38)	V (1)	100% (1/1)	0% (0/1)	100% (1/1)	0% (0/1)	0% (0/1)	0% (0/1)	0% (0/1)	0% (0/1)	0% (0/1)
Lin et al.(39)	V (2)	100% (2/2)	0% (0/2)	100% (2/2)	0% (0/2)	100% (2/2)	100% (2/2)	0% (0/2)	0% (0/2)	0% (0/2)
Blum et al.(40)	V (2)	100% (2/2)	0% (0/2)	100% (2/2)	0% (0/2)	0% (0/2)	0% (0/2)	0% (0/2)	100% (2/2)	0% (0/2)
Ferrari et al.(35)	V (5)	100% (5/5)	60% (3/5)	100% (5/5)	0% (0/5)	0% (0/5)	40% (2/5)	80% (4/5)	0% (0/5)	0% (0/5)
Ronger-Salve et al.(29)	V (5)	100% (5/5)	0% (0/5)	80% (4/5)	0% (0/5)	40% (2/5)	40% (2/5)	0% (0/5)	0% (0/5)	0% (0/5)
Rogers et al.(41)	V (1)	0% (0/1)	0% (0/1)	0% (0/1)	0% (0/1)	0% (0/1)	0% (0/1)	0% (0/1)	100% (1/1)	0% (0/1)
Oakley et al.(42)	V (3)	100% (3/3)	0% (0/3)	33% (1/3)	67% (2/3)	33% (1/3)	67% (2/3)	0% (0/3)	33% (1/3)	0% (0/3)
Blum et al.(43)	V (1)	0% (0/1)	0% (0/1)	0% (0/1)	0% (0/1)	0% (0/1)	100% (1/1)	0% (0/1)	0% (0/1)	0% (0/1)
Resende et al.(44)	V (2)	100% (2/2)	50% (1/2)	50% (1/2)	0% (0/2)	50% (1/2)	50% (1/2)	0% (0/2)	100% (2/2)	50% (1/2)
Theillac et al.(45)	V (1)	100% (1/1)	100% (1/1)	0% (0/1)	0% (0/1)	0% (0/1)	0% (0/1)	0% (0/1)	0% (0/1)	0% (0/1)
Vaccari et al.(46)	V (14)	n.a.	71% (10/14)	71% (10/14)	79% (11/14)	43% (6/14)	43% (6/14)	n.a.	86% (12/14)	14% (2/14)
De Giorgi et al.(36)	P (1)	100%(1/1)	0% (0/1)	100%(1/1)	100%(1/1)	100%(1/1)	100%(1/1)	100%(1/1)	0% (0/1)	0% (0/1)
Studies combined	**39**	**92.0% (23/25)**	**41.0% (16/39)**	**69.2% (27/39)**	**35.9% (14/39)**	**35.9% (14/39)**	**43.6% (17/39)**	**12.8% (5/39)**	**46.2% (18/39)**	**7.7% (3/39)**

Summary of dermoscopy features of vulvar and penis melanomas from previously published studies. Abbreviations: n, number; V, vulvar; P, penis.

Figure 6. Dermoscopy features of vulva melanoma



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Wohlmuth C, Wohlmuth-Wieser I. Vulvar Melanoma: Molecular Characteristics, Diagnosis, Surgical Management, and Medical Treatment. Am J Clin Dermatol. 2021 Sep;22(5):639-651.

Figure 7. Clinical and dermoscopy image of malignant melanoma of the vulva

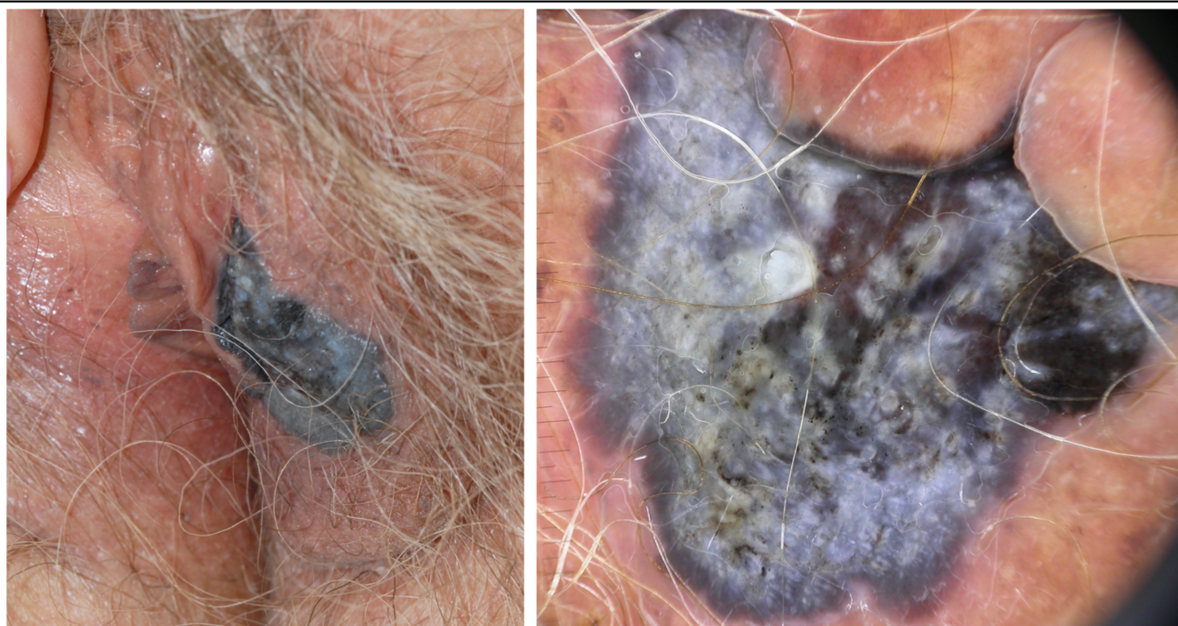

Image courtesy of Priv.-Doz. Dr. Verena Ahlgrimm-Siess

3.3 Common nevi of the vulva and penis

Dermoscopy features of common nevi of the genital area were reported in 4 studies and two case reports comprising of 97 patients (86 vulva cases, 2 penile cases and 9 genital cases not further specified). Table 2 summarizes all observed dermoscopy features of common genital nevi. Common observations included a homogeneous brown-gray pigmentation or brown structureless areas and were described in 35.1% (34/97) of all cases. A globular pattern was described in 35.7%. One of the two cases of common penile nevi which showed features of a globular pattern, was observed in an 8-year-old boy (26).

A cobblestone pattern was seen in 20.0%, a mixed pattern in 13.4% and a multi-component pattern in 8%. Globules and or clods were observed in a total of 25 cases and parallel lines in 5 patients. Melanoma-specific features, including a blue/white veil or reticular depigmentation were only observed in one patient respectively. Atypical vessels were not identified. A polycircular pattern was only described in one patient (29).

Figure 8. Clinical and dermoscopy image of a common penile nevus

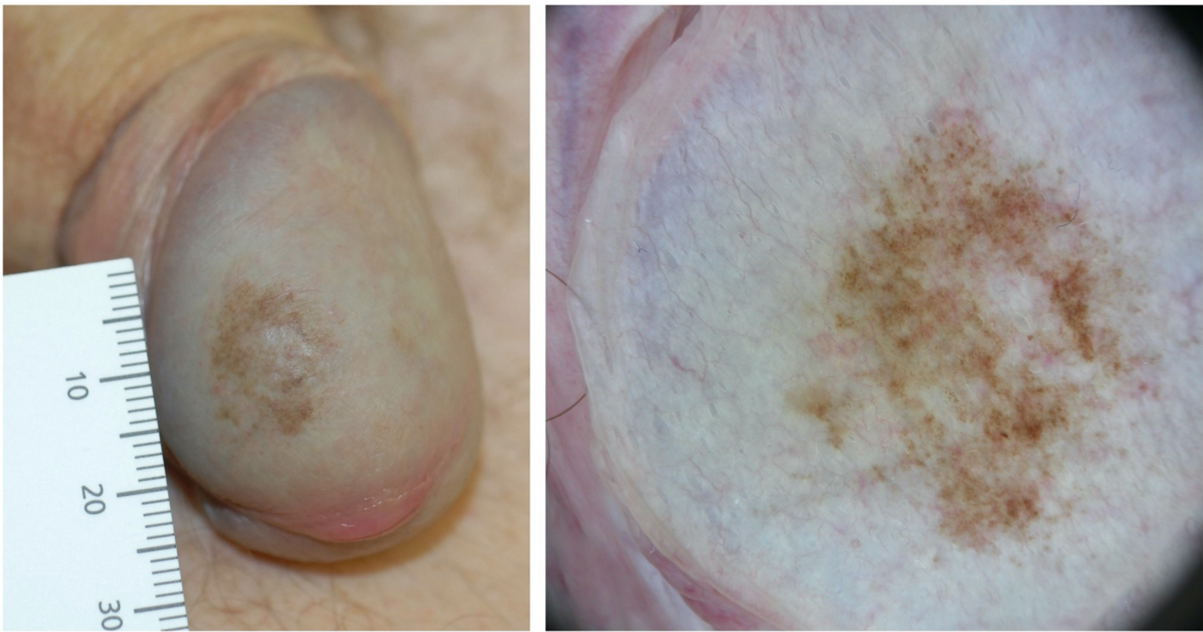

Image courtesy of Priv.-Doz. Dr. Verena Ahlgrimm-Siess

Table 2. Dermoscopy features in common nevi of the vulva and penis

Study	n	Globular pattern	Cobblestone pattern	Homogeneous pigmentation/ Structureless	Network	Mixed pattern	Multi-component pattern	Globules/Clods	Homogeneous brown-gray pigmentation	Parallel lines	Black dots	Blue-white veil	Atypical vessels	Reticular depigmentation	Polycircular
Ferrari et al.(35)	V (29)	41.4% (12/29)	17.2% (5/29)	17.2% (5/29)	3.4% (1/29)	17.2% (5/29)	6.9% (2/29)	13.8% (4/29)	10.3% (3/29)	13.8% (4/29)	3.4% (1/29)	3.4% (1/29)	0% (0/29)	3.4% (1/29)	n.a
Ronger-Salve et al.(29)	V (16)	43.8% (7/16)	n.a	43.8% (7/16)	12.5% (2/16)	31,2% (5/16)	6.3% (1/16)	43.8% (7/16)	n.a	6.3% (1/16)	n.a	n.a	n.a	n.a	6.3% (1/16)
Oakley et al.(42)	V (41)	n.a	n.a	46.3% (19/41)	0% (0/41)	0% (0/41)	7.3% (3/41)	29.3% (12/41)	n.a	n.a	n.a	n.a	n.a	n.a	n.a
Cengiz et al.(23)	n.s. (9)	0% (0/9)	33.3% (3/9)	33.3% (3/9)	0% (0/9)	33.3% (3/9)	n.a	n.a	n.a	n.a	0% (0/9)	0% (0/9)	n.a	0% (0/9)	0% (0/9)
Godinho et al.(47)	P (1)	0% (0/1)	0% (0/1)	0% (0/1)	0% (0/1)	0% (0/1)	100% (1/1)	100% (1/1)	0% (0/1)	0% (0/1)	0% (0/1)	0% (0/1)	0% (0/1)	0% (0/1)	0% (0/1)
Armengot-Carbó et al.(26)	P (1)	100% (1/1)	0% (0/1)	0% (0/1)	0% (0/1)	0% (0/1)	0% (0/1)	100% (1/1)	0% (0/1)	0% (0/1)	0% (0/1)	0% (0/1)	0% (0/1)	0% (0/1)	0% (0/1)
Studies combined	**97**	**35.7% (20/56)**	**20.0% (8/40)**	**35.1% (34/97)**	**3.1% (3/97)**	**13.4% (13/97)**	**8.0% (7/88)**	**28.4% (25/88)**	**9.7% (3/31)**	**10.6% (5/47)**	**5% (2/40)**	**2.5% (1/40)**	**0% (0/31)**	**2.5% (1/40)**	**3.7% (1/27)**

Summary of dermoscopy features of common nevi of the vulva and penis from previously published studies. Abbreviations: n, number; n.a; not applicable; n.s, not specified; P, penis; V, vulvar.

3.4 Atypical nevi of the vulva and penis

Dermoscopy features of atypical nevi of the genital area were reported in 3 studies comprising of 25 patients (8 vulva cases, 2 penile cases and 15 genital cases not further specified). Table 3 summarizes all observed dermoscopy features of atypical genital nevi.

Frequently observed features included, black dots (36%, 9/25) and parallel lines (40%, 4/10). A homogeneous pigmentation or structureless areas were found in 24% and a globular pattern was seen in 32% of all cases. A blue-white veil was observed in three of the twenty-five cases (12%). None of the cases showed features of atypical vessels, reticular depigmentation or a polycircular pattern.

Figure 9. Clinical and dermoscopy image of an atypical genital nevus

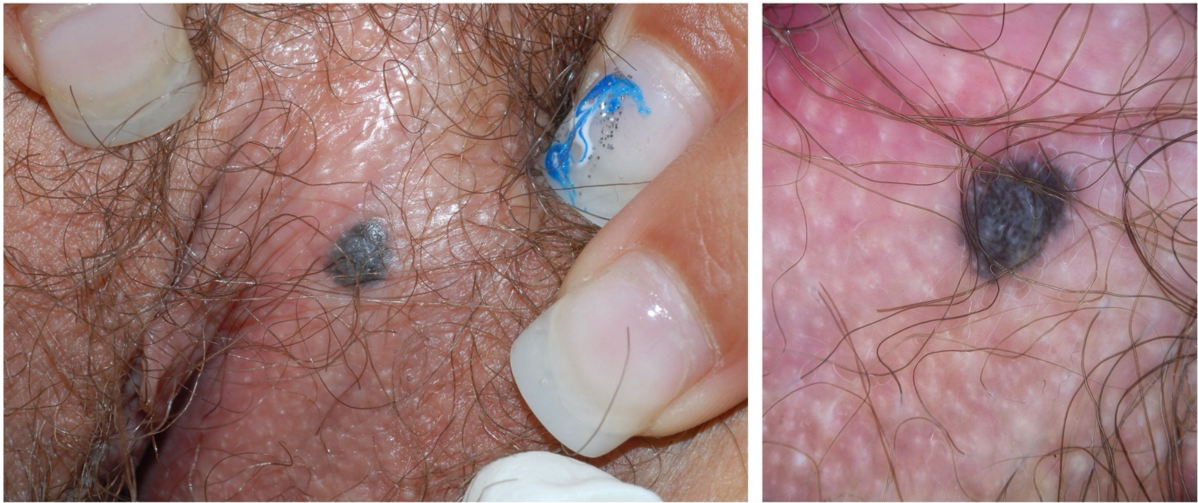

Image courtesy of Priv.-Doz. Dr. Verena Ahlgrimm-Siess

Table 3. Dermoscopy features in atypical nevi of the vulva and penis

Study	n	Globular pattern	Cobblestone pattern	Homogeneous pigmentation/ Structureless	Network	Mixed pattern	Multi-component pattern	Globules/Clods	Homogeneous brown-gray pigmentation	Parallel lines	Black dots	Blue-white veil	Atypical vessels	Reticular depigmentation	Polycircular
Ferrari et al.(35)	V (8)	25% (2/8)	0% (0/8)	25% (2/8)	0% (0/8)	37.5% (3/8)	0% (0/8)	25% (2/8)	37.5% (3/8)	37.5% (3/8)	0% (0/8)	0% (0/8)	0% (0/8)	0% (0/8)	n.a
Cengiz et al.(23)	n.s. (15)	40% (6/15)	0% (0/15)	20% (3/15)	0% (0/15)	40% (6/15)	n.a	n.a	n.a	n.a	9/15	13.3% (2/15)	n.a	0% (0/15)	0% (0/15)
Collgros et al.(48)	P (2)	0% (0/2)	0% (0/2)	50% (1/2)	0% (0/2)	0% (0/2)	0% (0/2)	50% (1/2)	0% (0/2)	50% (1/2)	0% (0/2)	50% (1/2)	0% (0/2)	0% (0/2)	0% (0/2)
Studies combined	**25**	**32% (8/25)**	**0% (0/25)**	**24.0% (6/25)**	**0% (0/25)**	**36% (9/25)**	**0% (0/10)**	**30% (3/10)**	**30% (3/10)**	**40% (4/10)**	**36% (9/25)**	**12% (3/25)**	**0% (0/10)**	**0% (0/25)**	**0% (0/17)**

Summary of dermoscopy features of common nevi of the vulva and penis from previously published studies. Abbreviations: n, number; n.a; not applicable; n.s, not specified; P, penis; V, vulvar.

3.5 Melanosis of the vulva and penis

Dermoscopy features in melanosis of the genital area were reported in 6 studies comprising of 294 patients (252 vulva cases, 2 penile cases and 40 genital cases not further specified).

Table 4 summarizes all observed dermoscopy features in melanosis of the vulva and penis.

In the majority of melanosis cases, diffuse pigmentation or structureless pattern (51.4%, (151/294)) was observed. A parallel pattern was seen in 27.6% of all cases. A ringlike pattern was found in 27.8% (78/281) of all melanosis cases assessed but was not described in common or atypical genital nevi.

Dots and globules were seen in 12.1% (34/281) of melanosis cases. Other dermoscopy features, including pseudopods and streaks, blue-white veil, regression pattern or vascular pattern were not observed.

Figure 10. Clinical and dermoscopy image of penile melanosis

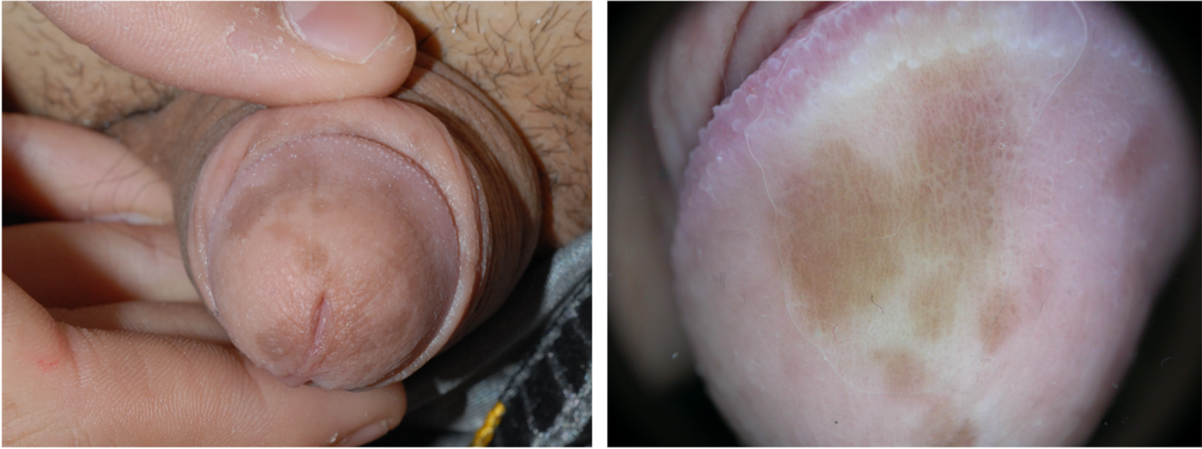

Image courtesy of Priv.-Doz. Dr. Verena Ahlgrimm-Siess

Table 4. Dermoscopy features in melanosis of the vulva and penis

Study	n	Diffuse pigmentation (homogeneous or dishomogeneous), Structureless Pattern	Parallel pattern	Nonspecific pattern	Ringlike pattern	Pigment network/ Reticular pattern	Dots and globules	Pseudopods and streaks	Blue-white veil	Regression (gray-blue areas, white areas, or peppering)	Vascular pattern	Polycircular
De Giorgi et al. (49)	V (129)	75.2% (97/129)	14.7% (19/129)	10.1% (13/129)	14.7% (19/129)	0% (0/129)	0% (0/129)	0% (0/129)	0% (0/129)	0% (0/129)	n.a	0% (0/129)
Ronger-Salve et al.(29)	V (12)	0% (0/12)	66.7% (8/12)	0% (0/12)	25% (3/12)	0% (0/12)	0% (0/12)	0% (0/12)	0% (0/12)	0% (0/12)	0% (0/12)	0% (0/12)
Mannone et al. (50)	V(11), P(2)	84.6% (11/13)	15.4% (2/13)	n.a	n.a	0% (0/13)	n.a	n.a	n.a	n.a	n.a	n.a
Ferrari et al.(51)	V (71)	25.4% (18/71)	21.1% (15/71)	n.a	39.4% (28/71)	5.6% (4/71)	25.4% (18/71)	n.a	n.a	n.a	n.a	n.a
Oakley et al.(42)	V (29)	17.2% (5/29)	55.2% (16/29)	n.a	27.6% (8/29)	n.a	10.3% (3/29)	n.a	n.a	n.a	n.a	n.a
Cengiz et al.(23)	n.s (40)	0% (0/40)	52.5% (21/40)	n.a	40.0% (20/40)	7.5% (3/40)	32.5% (13/40)	n.a	0% (0/40)	n.a	n.a	0% (0/40)
Studies combined	**294**	**51.4% (151/294)**	**27.6% (81/294)**	**9.2% (13/141)**	**27.8% (78/281)**	**2.6% (7/265)**	**12.1% (34/281)**	**0% (0/141)**	**0% (0/181)**	**0% (0/141)**	**0% (0/141)**	**0% (0/181)**

Summary of dermoscopy features of common nevi of the vulva and penis from previously published studies. Abbreviations: n, number; n.a; not applicable; n.s, not specified; P, penis; V, vulvar.

4. DISCUSSION

Ten percent of the general population harbor pigmented genital lesions, thankfully most of them are benign. Although melanoma of the genital tract is rare, melanoma of the vulva accounts for 1% of all melanomas diagnosed in women and accounts for 5% of all vulva malignancies (30,32). Genital melanoma in men (i.e melanoma of the glans or shaft of the penis, the urethral meatus, or on the scrotum) is even rarer and accounts for less than 1% of melanomas diagnosed in males per year (52).

While the incidence of cutaneous melanoma is rising, the mortality has dropped by 7% annually during the last 5 years. Unfortunately, prognosis and mortality of genital melanoma does not reflect this positive trend. The 5-year overall survival rate for vulva melanoma is 47% compared with 92% for cutaneous melanoma (30,53).

Recent studies have shown that the poor prognosis may be associated with a different tumor biology (c-KIT mutation), delayed diagnosis due to lack of self-screening and reduced response to current treatment regimens (30,32,33).

Large population-based data on more than 1500 patients with primary genitourinary melanomas, by Sanchez et al. indicate that both genders present late, when their disease has already progressed to advanced stages (54).

Early detection of melanoma is crucial, as surgical excision is still the mainstay of therapy (32). Awareness is key among patients but also among treating physicians (both dermatologists, gynecologists and urologists). Dermatologists need to perform a thorough full-body skin exam to identify suspicious lesions earlier (55).

Genital melanoma needs to be differentiated from benign melanosis and nevi. Both melanoma and melanosis occur predominantly in postmenopausal women, whereas nevi tend to occur during childhood and adolescence (25). Dermoscopy can aid in the differentiation between benign and malignant pigmented genital lesions (23,25).

The systematic review of the literature identified that asymmetry of color and/or structure and the presence of blue/white or blue/grey veil were the most common features observed in melanoma of the vulva or glans penis. In the study by Ferrari et al. the presence of reticular depigmentation was identified in 80% of all melanomas (35). This stands in contrast to genital melanosis, where the majority of cases had a homogeneous pigmentation or structureless pattern. A ringlike pattern was found in 27.8% of all melanosis cases and seems to be a signature pattern for the diagnosis of genital melanosis. Other melanoma specific features, including pseudopods, streaks, blue-white veil, regression pattern or vascular pattern were not observed in genital melanosis. Common genital nevi can be differentiated from melanoma by their homogeneous brown-gray pigmentation or brown structureless areas. A globular pattern was described in 35.7% of all cases. The differentiation of atypical genital nevi from genital melanoma based on dermoscopy alone is difficult and a reliable diagnosis can often only be made by skin biopsy, as several melanoma specific features, including the presence of blue-white veil have been observed in atypical genital nevi as well.

In summary, knowledge of specific dermoscopy features of pigmented genital lesions aids the differentiation between benign and malignant lesions and helps to decide whether a skin biopsy is necessary for the further work-up. As patients might not be aware of the presence of pigmented genital lesions, dermatologists need to include the examination of the genitals in their routine full-body skin exam to ensure early diagnosis of malignant melanoma.

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