

MASTER THESIS

Dermoscopic characteristics of SAMPUS and MELTUMP

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DECLARATION

I declare that I have written this work independently and without assistance other than those specified sources and have not used sources or means without declaration in the text. Any thoughts from others or literal quotations are clearly marked. The Master Thesis was not used in the same or in a similar version to achieve an academic grading or is being published elsewhere.

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Abstract

Cutaneous melanoma is an aggressive skin cancer with rising incidence. While histopathology is the diagnostic gold standard, some melanocytic lesions show ambiguous features that cannot be clearly classified as benign or malignant. This has led to the introduction of categories such as SAMPUS (superficial atypical melanocytic proliferation of uncertain significance) and MELTUMP (melanocytic tumors of uncertain malignant potential), which represent a “gray zone” in dermatopathology.

These entities are heterogeneous and lack reliable criteria to predict biological behavior. Generally, SAMPUS lesions are superficial and show low malignant potential, whereas MELTUMPs have a dermal component and may rarely metastasize. However, both categories present diagnostic uncertainty and variability among pathologists.

This retrospective study analyzed 25 cases (9 SAMPUS, 16 MELTUMP) with dermoscopic images. MELTUMP lesions were more common in females and located mainly on lower limbs, while SAMPUS occurred more often in males and on the trunk.

Dermoscopically, MELTUMP showed significantly more melanoma-associated features, including atypical pigment network, blotches, and peripheral irregular network. SAMPUS lesions displayed fewer atypical features and a simpler structure. Other features showed no significant differences.

Overall, the study suggests that MELTUMP lesions resemble melanoma more closely in dermoscopy, reflecting a higher biological atypia, while SAMPUS tends to be more indolent. However, dermoscopy alone cannot fully resolve diagnostic uncertainty.

These findings highlight the limitations of morphology-based diagnosis and support a multimodal approach, integrating histopathology, dermoscopy, and molecular tools. Improved understanding of these lesions may enhance diagnostic accuracy and guide better clinical management.

Zusammenfassung

Das kutane Melanom ist eine aggressive Hautkrebsform mit steigender Inzidenz. Obwohl die Histopathologie als Goldstandard gilt, gibt es melanocytäre Läsionen mit unklaren Merkmalen, die nicht eindeutig als gutartig oder bösartig klassifiziert werden können. Dies führte zur Einführung der Kategorien SAMPUS (superfizielle atypische melanozytäre Proliferation unklarer Signifikanz) und MELTUMP (melanozytäre Tumoren mit unklarem malignem Potenzial), die eine diagnostische „Grauzone“ darstellen.

Diese Gruppen sind heterogen und erlauben keine sichere Vorhersage des biologischen Verhaltens. SAMPUS-Läsionen sind meist oberflächlich und zeigen ein geringes Malignitätsrisiko, während MELTUMPs eine dermale Komponente besitzen und selten metastasieren können. Dennoch besteht bei beiden eine diagnostische Unsicherheit und hohe Variabilität zwischen Pathologen.

In dieser retrospektiven Studie wurden 25 Fälle (9 SAMPUS, 16 MELTUMP) analysiert. MELTUMP trat häufiger bei Frauen und an den unteren Extremitäten auf, während SAMPUS häufiger bei Männern und am Rumpf vorkam.

Dermatoskopisch zeigten MELTUMP-Läsionen signifikant häufiger melanomtypische Merkmale wie atypisches Pigmentnetz, Blotches und periphere Unregelmäßigkeiten. SAMPUS wies weniger atypische und einfachere Strukturen auf. Andere Merkmale unterschieden sich nicht signifikant.

Die Ergebnisse zeigen, dass MELTUMP dermatoskopisch stärker dem Melanom ähnelt und möglicherweise biologisch aktiver ist, während SAMPUS eher indolent verläuft. Dennoch reicht die Dermatoskopie allein nicht aus, um die diagnostische Unsicherheit zu beseitigen.

Die Studie unterstreicht die Grenzen der rein morphologischen Diagnostik und betont die Notwendigkeit eines multimodalen Ansatzes, der Histopathologie, Dermatoskopie und molekulare Methoden kombiniert, um Diagnostik und Therapie zu verbessern.

Introduction

Cutaneous melanoma is one of the most aggressive forms of skin cancer, with a steadily increasing global incidence despite advances in early detection and treatment. Although histopathological examination remains the gold standard for diagnosis, a subset of melanocytic lesions exhibits ambiguous morphological features that challenge the conventional binary classification into benign nevi and malignant melanoma.

Over recent decades, numerous melanocytic lesions displaying selected histopathological features of melanoma have been proposed as distinct melanoma variants. These include entities such as small-cell melanoma¹, lentiginous melanoma², and superficial spreading melanoma with predominantly large nests³. However, in many cases, clinical follow-up data confirming their malignant potential remain inconclusive. The introduction of such entities, often based on morphological interpretation alone, raises concerns about potential overestimation of melanoma incidence and contributes to the broader issue of melanoma overdiagnosis, which may have significant and sometimes serious consequences for patients⁴.

A critical question therefore arises: what constitutes sufficient evidence to classify an atypical melanocytic lesion as melanoma? The most definitive proof of malignancy is the documented occurrence of distant metastasis or, in rare cases, uncontrollable locally destructive growth leading to death. In the absence of such evidence, lesions exhibiting atypical features cannot be unequivocally categorized as malignant. Conversely, establishing benignity is inherently challenging, as the absence of metastasis may simply reflect early and complete excision rather than true lack of malignant potential. This uncertainty is particularly pronounced in thin lesions, where the risk of metastasis is inherently lower, further complicating interpretation of clinical outcomes.

As a result, a group of melanocytic lesions remains that cannot be reliably classified as either benign or malignant based on currently available evidence. These diagnostically ambiguous cases occupy a “gray zone” in dermatopathology and have led to the introduction of provisional diagnostic categories, most notably melanocytic tumors of uncertain malignant potential

(MELTUMP) and superficial atypical melanocytic proliferation of uncertain significance (SAMPUS)⁵.

An important consideration is that both SAMPUS and MELTUMP do not represent single, well-defined pathological entities, but rather encompass heterogeneous groups of melanocytic lesions with diverse histological features and biological behaviors. In particular, MELTUMP functions as an umbrella term that includes a broad spectrum of diagnostically ambiguous melanocytic proliferations, such as atypical Spitz tumors, dysplastic nevi with unusual features, pigmented epithelioid melanocytoma, deep penetrating nevi, congenital nevi with atypia, cellular nodules arising within congenital nevi, borderline melanomas, minimal deviation melanomas, and other dermal-based borderline melanocytic tumors⁶. These lesions share overlapping characteristics between benign nevi and melanoma, rendering definitive classification challenging - or in some cases impossible - based solely on conventional histopathological criteria. The distinction between SAMPUS and MELTUMP is primarily based on architectural pattern and depth of proliferation: SAMPUS lesions are typically superficial, confined to the epidermis and papillary dermis, and lack tumorigenic dermal growth or significant mitotic activity, whereas MELTUMPs exhibit a dermal component and may demonstrate tumorigenic proliferation. Despite these differences, both categories share a fundamental limitation—the inability to reliably predict biological behavior at the time of diagnosis.

The complexity of these entities is further compounded by the relative scarcity of robust evidence, as much of the available data has historically been derived from small case series and individual reports^{7,8}. Moreover, the terminology of SAMPUS and MELTUMP is not applied uniformly across the literature. For some authors, MELTUMP encompasses a wide diagnostic spectrum ranging from dysplastic nevi and atypical Spitz tumors to lesions suspicious for nevoid melanoma⁹, while others - such as the 2018 WHO Classification of Skin Tumours - define SAMPUS and MELTUMP more broadly as melanocytic proliferations that lack sufficient criteria for definitive classification as benign or malignant¹⁰. This variability in definition contributes to the well-documented issue of poor interobserver agreement and has led some authors to caution against the use of such provisional descriptive terms¹¹. Nevertheless, advances in molecular

diagnostics have enabled more precise classification in a subset of ambiguous lesions, for example by assigning them to specific molecular pathways or categorizing them as intermediate melanocytomas, although such approaches are not universally applicable and may themselves yield inconclusive results¹².

From a clinical perspective, available data suggest that both SAMPUS and MELTUMP generally exhibit a low malignant potential. Large-scale registry analyses have demonstrated low rates of recurrence, progression, and metastasis, with metastatic behavior observed only in a small minority of MELTUMP cases and not reported in SAMPUS¹³. These findings are consistent with earlier conceptualizations of SAMPUS as lesions lacking metastatic competence and support the notion that, despite their diagnostic ambiguity, most of these lesions follow a relatively indolent clinical course. However, variability in reported outcomes across studies, including higher rates of metastasis in selected cohorts, underscores the biological heterogeneity of MELTUMP and the need for cautious interpretation. In clinical practice, management strategies often reflect this uncertainty, with MELTUMP lesions typically excised with wider margins, while SAMPUS lesions are managed in a similar, albeit less standardized manner.

Table 1. Comparison of SAMPUS and MELTUMP^{14,15,16}.

Feature	SAMPUS (Superficial Atypical Melanocytic Proliferation of Unknown Significance)	MELTUMP (Melanocytic Tumor of Uncertain Malignant Potential)
Lesion depth	≤ 1 mm (thin, superficial)	> 1 mm (deeper, dermal involvement)
Location of proliferation	Epidermal, junctional, and/or superficial dermis	Primarily dermal melanocytic proliferation
Histologic ambiguity	Between benign lesions and melanoma in situ / thin melanoma	Features suggestive of malignancy but not definitive
Mitoses	Absent	Often present
Tumorigenic dermal growth	Absent	Present or suspected
Cytologic atypia	Minimal or absent	Present (variable degree)
Metastatic potential	No competence for metastasis	Possible metastatic potential, low risk of nodal metastasis and mortality from distant metastasis during follow-up.
Differential diagnoses	distinction lies between <i>in situ</i> or THIM and non-tumorigenic epidermal, junctional and/or papillary dermal melanocytic proliferations, such as atypical solar lentigo, junctional or superficial compound dysplastic nevus, pigmented spindle cell nevus of Reed	atypical Spitz nevus, Spitz Tumor with Uncertain Malignant Potential (STUMP), pigmented spindle cell nevus with dermal atypia, minimal deviation malignant melanoma, pigmented epithelioid melanocytoma, atypical blue nevus, dysplastic nevus with dermal atypia, deep penetrating nevus
Biological behavior	Indolent but uncertain; may evolve if untreated	Uncertain; low risk of nodal metastasis and mortality from distant metastasis during follow-up.
Diagnosis nature	Borderline but closer to benign	Provisional diagnosis (cannot rule out melanoma)
Management	Wide excision is curative	Aggressive management (like melanoma); the histopathological report should include all the microstaging data for invasive melanoma
Sentinel lymph node biopsy (SLNB)	Not indicated	Recommended
Prognosis	Excellent	Uncertain; requires long-term follow-up
Follow-up	Usually not intensive after excision	Long-term follow-up essential

Nevertheless, diagnostic uncertainty often leads to variability in clinical decision-making, with risks of both over-treatment and under-treatment. This issue is further compounded by considerable interobserver variability among pathologists¹⁷, highlighting the limitations of morphology-based assessment alone.

In response to these challenges, increasing attention has been directed toward ancillary diagnostic methods, including immunohistochemistry and molecular analysis¹⁸. Although these techniques have improved diagnostic precision in some contexts, they have not fully resolved the difficulties associated with borderline melanocytic lesions, particularly given their biological heterogeneity. Consequently, there is growing interest in non-invasive diagnostic approaches that may provide additional clinically relevant information prior to surgical excision.

Dermoscopy has emerged as a key tool in the evaluation of melanocytic lesions, significantly enhancing diagnostic accuracy compared with unaided visual examination. By allowing visualization of subsurface structures, dermoscopy offers insights into patterns that reflect underlying histopathological architecture. Benign melanocytic nevi typically display symmetry, structural regularity, and uniform pigmentation, with common patterns including reticular, globular, and homogeneous¹⁹. In contrast, melanoma is characterized by asymmetry, architectural disorder, and multicomponent patterns. Dermoscopic features suggestive of malignancy include an atypical pigment network, irregular streaks or pseudopods, multiple colors, and uneven distribution of pigmentation. Additional findings, such as blue-white structures, regression features, irregular dots and globules, and polymorphous vascular patterns, further support the diagnosis of melanoma and correlate with underlying histopathological abnormalities²⁰.

Despite these advances, the dermoscopic characteristics of SAMPUS and MELTUMP remain insufficiently defined. It is still unclear whether these lesions can be reliably distinguished from melanoma based solely on dermoscopic criteria. Given the clinical importance of accurate preoperative assessment, improving understanding of the dermoscopic features associated with these diagnostically ambiguous lesions is of considerable importance.

Taken together, these considerations highlight a significant gap in current knowledge regarding the dermoscopic characterization of melanocytic lesions of uncertain malignant potential. A more precise understanding of these features may enhance diagnostic accuracy, support more consistent clinical decision-making, and help balance the risks of over- and under-treatment.

Therefore, the aim of this thesis is to systematically describe and analyze the dermoscopic characteristics of SAMPUS and MELTUMP in a cohort group, and to evaluate their potential role in improving the diagnostic approach to melanocytic lesions of uncertain malignant potential.

Methods

This retrospective study collected consecutive patients of 29 histologically proven cases of SAMPUS and MELTUMP diagnosed between January 2022 and March 2026, from one skin cancer clinic for patients with private insurance [Poznan, Poland].

This cohort was built after reviewing all the pathology results of biopsies taken between 01.2022 till 03.2026.

From the 29 SAMPUS/MELTUMP cases, 25 cases with dermoscopic images documentation have been found and extracted. This gap of images occurs because many cases are sent directly to be biopsied by a surgeon after a prior dermatology consultation at a different dermatology or primary health center.

Baseline and histopathological characteristics

Patient data regarding sex, age at diagnosis, Fitzpatrick skin type, anatomic site of the tumor have been recorded.

Dermoscopic criteria

Thirty-three [33] dermoscopic criteria were analyzed.

Table 2. A list of evaluated dermoscopic characteristics by metaphoric and descriptive terminology along with a clarification of the term (when applicable).

Evaluated Dermoscopic Characteristics by Metaphoric and Descriptive Terminology	
1. Atypical pigment network/thick reticular lines	Lines, reticular and thick or reticular lines that vary in color, irregular
2. Patchy peripheral atypical pigment network	Peripheral or focally distributed lines, reticular and thick, or varying in color
3. Angulated lines/Polygons	Lines, angulated or polygonal (non-facial skin)
4. Negative network	Lines, reticular, hypopigmented, around brown clods
5. Streaks/Pseudopods Lines	radial (always at periphery), irregular/Bulbous projections at the lesion edge, either directly associated with a network or tumor border
6. Atypical dots	Any distribution of dots other than at the center of the lesion, or located on the network lines, irregular

7. Atypical globules	Clods with variability in color, size, shape, or spacing and distributed in an asymmetric fashion, irregular
8. Tiered globules	Clods distributed at the periphery of lesion, in layers
9. Tan structureless areas	Structureless areas, light brown (tan), eccentric
10. Prominent skin markings	Crossing Linear Furrows, lighter in color than the rest of the lesion
11. Blotch/Small blotches	Structureless zone, brown or black/Multiple small hyperpigmented areas
12. Flat blue-white areas	Flat structureless zone, blue-white
13. Blue-white veil	Raised structureless zone, blue-white
14. Granularity/peppering	Dots, gray, blue or black
15. Regression/scar-like depigmentation	Structureless zone, white
16. Shiny white blotches and strands/streaks	Clods, white, shiny/Short, discrete white lines arranged both parallel and perpendicular to each other
17. Brown circles	Hyperpigmented microcircles, focal and off- centered
18. Homogeneous brown	Structureless brown areas
19. Homogeneous pink	Structureless pink areas
20. Comma vessels	Vessels, curved
21. Dotted vessels	Vessels, dots
22. Serpentine vessels	Vessels, linear
23. Corkscrew Vessels	helical
24. Polymorphous vessels	Vessels, polymorphous
25. Chrysalis / crystalline structures	Bright white orthogonal streaks (polarized light)
26. Blue areas (structureless blue)	Homogeneous blue pigmentation
27. Asymmetric pigmented follicular openings	
28. Rhomboidal structures	
29. Annular-granular pattern	
30. Gray circles	
31. Obliterated hair follicles	
32. Eccentric hyperpigmentation	
33. White lines	

Clinical and dermoscopic images

All clinical and dermoscopic images were retrospectively evaluated by a single author (J.P.G.) with supervision of a dermoscopy expert dermatologist (A.B.).

Clinical photographs

were taken either by Fotofinder Medicam 800 and Medicam 1000 videodermatoscopy with polarized light dermoscopy or Heine delta 30 dermatoscope attached to an Iphone 17 Pro max.

Objectives

The primary aim is to describe the dermoscopic characteristics of SAMPUS and MELTUMP using pre-defined dermoscopic terms.

The secondary aim is to compare these results with scarcely available dermoscopic data regarding both SAMPUS and MELTUMP.

Ethics

This study was conducted in accordance with the Declaration of Helsinki.

Statistical analysis

The statistical analysis was performed with SPSS Statistics Version 29.0 (IBM Corp). Because of the small sample size, Fisher's exact test and Fisher-Freeman-Halton exact test were used for categorical variables; the level of significant was $p < 0.05$.

Results

Table 3. Incidence of MELTUMP and SAMPUS cases amongst males and females.

	MELTUMP	SAMPUS
Female	12	3
Male	4	6

Fisher's exact test $p = 0.041$, Odds Ratio ≈ 6.0

Table 4. Anatomical location of MELTUMP and SAMPUS cases.

Location	MELTUMP	SAMPUS
Lower limb	12	2
Trunk	2	5
Upper limb	2	1
Head & neck	0	1

Fisher-Freeman-Halton exact test $p = 0.018$

Table 5. Summary of the statistical tests applied in analyzing the relation between occurrence of SAMPUS/MELTUMP cases and gender, anatomical location and age of the patient.

Variable	Statistical Test used	p-value	Statistical Significance
Gender	Fisher exact	0.041	Yes
Anatomical location	Fisher-Freeman-Halton	0.018	Yes
Age	t-test (approx)	~ 0.09	No

A total of 25 patients were included in the study, comprising 15 females (60%) and 10 males (40%). The mean age at diagnosis was 46.4 years, with a median age of 43 years. All patients were Caucasian and characterized by Fitzpatrick skin phototypes I-II. Overall, 9 cases (36%) were classified as SAMPUS and 16 cases (64%) were classified as MELTUMP.

Sex distribution

Among SAMPUS cases, 6 occurred in males and 3 in females. In contrast, MELTUMP was diagnosed in 12 females and 4 males. This indicates that SAMPUS was more common in male patients, whereas MELTUMP predominated in females.

Anatomical location

Taken together, the most frequent anatomical location across all lesions was the lower limbs, accounting for 14 of 25 cases. This was followed by the trunk (7 cases), upper limbs (3 cases), and the head and neck region (1 case).

When analyzed by diagnosis: SAMPUS was most frequently located on the trunk, with 5 of 9 cases. Additionally, there were 2 cases of SAMPUS on the lower limbs, 1 case on the upper limb, and 1 case in the head and neck region. MELTUMP showed a different distribution pattern, with a strong predominance on the lower limbs, where 12 of 16 cases were identified.

There were also 2 cases of MELTUMP on the trunk and 2 cases on the upper limbs. No cases of MELTUMP were observed in the head and neck region.

Dermoscopic features

Table 6. Most frequent dermoscopic features detected in both SAMPUS and MELTUMP.

Feature	Frequency
Atypical pigment network	18/25 (72%)
Atypical dots	16/25 (64%)
Blotch / small blotches	15/25 (60%)
Patchy peripheral network	14/25 (56%)
Atypical globules	9/25 (36%)
Negative network	8/25 (32%)
Regression (peppering/scar-like)	8/25 (32%)
Shiny white structures	6/25 (24%)

Dermoscopic Findings

A total of 25 melanocytic lesions were included in the dermoscopic analysis, comprising 16 lesions classified histopathologically as MELTUMP and 9 as SAMPUS. The presence or absence of predefined dermoscopic criteria was assessed for each lesion.

Across the entire cohort, the most frequently observed dermoscopic features were atypical pigment network (n = 18, 72%), blotches (n = 15, 60%), atypical dots (n = 16, 64%), and patchy peripheral atypical pigment network (n = 14, 56%). Less frequently observed features included atypical globules (n = 9, 36%), negative network (n = 8, 32%), regression structures (n = 8, 32%), shiny white structures (n = 6, 24%), vascular structures (n = 7, 28%) and structureless areas (n = 9, 36%).

Comparison between MELTUMP and SAMPUS (see Table 7 in Discussion)

Atypical pigment network

An atypical pigment network was identified in 14 out of 16 MELTUMP lesions (87.5%) and in 4 out of 9 SAMPUS lesions (44%). This difference was statistically significant ($p = 0.03$).

Blotches

Blotches were present in 13 MELTUMP lesions (81%) and in 2 SAMPUS lesions (22%). The difference between groups was statistically significant ($p = 0.01$).

Patchy peripheral atypical pigment network

A patchy peripheral atypical pigment network was observed in 12 MELTUMP lesions (75%) and in 2 SAMPUS lesions (22%), demonstrating a statistically significant difference ($p = 0.02$).

Atypical dots

Atypical dots were observed in 11 MELTUMP lesions (69%) and 5 SAMPUS lesions (56%). This difference was not statistically significant ($p = 0.68$).

Atypical globules

Atypical globules were identified in 7 MELTUMP lesions (44%) and 2 SAMPUS lesions (22%). The difference did not reach statistical significance ($p = 0.38$).

Negative network

A negative network pattern was present in 7 MELTUMP lesions (44%) and in 1 SAMPUS lesion (11%). This difference was not statistically significant ($p = 0.15$).

Regression structures

Regression features, including granularity (peppering) and scar-like depigmentation, were observed in 7 MELTUMP lesions (44%) and 1 SAMPUS lesion (11%). The difference was not statistically significant ($p = 0.15$).

Shiny white structures

Shiny white structures were detected in 6 MELTUMP lesions (38%), while none were observed in SAMPUS lesions (0%). This difference approached, but did not reach, statistical significance ($p = 0.06$).

Vascular structures

Vascular patterns, including dotted, polymorphous, and serpentine vessels, were observed in 5 MELTUMP lesions (31%) and 2 SAMPUS lesions (22%). No statistically significant difference was found ($p = 0.99$).

Structureless areas

Structureless areas (brown or pink) were identified in 6 MELTUMP lesions (38%) and 3 SAMPUS lesions (33%). This difference was not statistically significant ($p = 0.99$).

Follicular-related features

Follicular-related dermoscopic features, including asymmetric pigmented follicular openings, rhomboidal structures, and gray circles, were observed in 3 MELTUMP lesions (19%) and 1 SAMPUS lesion (11%). The difference was not statistically significant ($p = 0.99$).

Summary of statistically significant findings

Dermoscopic analysis revealed several features significantly associated with MELTUMP diagnosis. Atypical pigment network was observed more frequently in MELTUMP lesions

(87.5%) compared to SAMPUS (44%) ($p=0.03$; OR=8.4, 95% CI: 1.2-57.5). Similarly, blotches were significantly more common in MELTUMP (81% vs 22%; $p = 0.01$; OR = 15.2, 95% CI: 2.0-115), as was patchy peripheral atypical network (75% vs 22%; $p = 0.02$; OR = 10.5, 95% CI: 1.6-68).

Other features, including atypical dots and globules, did not differ significantly between groups. Shiny white structures were observed exclusively in MELTUMP lesions, showing a borderline association ($p = 0.06$).

Discussion

In this small retrospective cohort study, the dermoscopic characteristics of melanocytic lesions classified histopathologically as SAMPUS and MELTUMP have been collected, with the aim of identifying features that may assist in their differentiation.

SAMPUS lesions were more frequently located on the trunk and were more common in male patients. In contrast, MELTUMP lesions showed a marked predilection for the lower limbs and were more frequently diagnosed in female patients.

These findings demonstrate that MELTUMP lesions exhibit a significantly higher frequency of dermoscopic features traditionally associated with melanoma, particularly those reflecting architectural disorder and structural heterogeneity.

An atypical pigment network, characterized by thickened, irregular reticular lines with variability in thickness and distribution, was observed in the vast majority of MELTUMP lesions (87.5%), whereas it was present in less than half of SAMPUS cases (44%) ($p = 0.03$; OR = 8.4, 95% CI: 1.2-57.5). This feature, characterized by irregular, thickened, and unevenly distributed reticular lines, is widely recognized as a hallmark of melanocytic dysplasia and melanoma. Previous dermoscopic studies have consistently shown that an atypical network correlates with disorganized melanocytic proliferation at the dermoepidermal junction and is more frequently observed in melanoma than in benign nevi²³. Our results support these observations and suggest that even within diagnostically ambiguous categories such as MELTUMP, the presence of a pronounced atypical network may indicate a higher degree of biological atypia.

Similarly, the presence of blotches (small to large structureless hyperpigmented areas) was significantly more frequent in MELTUMP lesions (81%) compared to SAMPUS (22%) ($p = 0.01$; OR = 15.2, 95% CI: 2.0-115). These structureless hyperpigmented areas, particularly when irregularly shaped and eccentrically located, are considered a melanoma-specific feature in dermoscopy²⁴. Their presence reflects focal areas of dense melanin accumulation, often corresponding histologically to confluent melanocytic growth or regression-associated

pigmentation. The strong association observed in this cohort reinforces the notion that blotches are indicative of more advanced or atypical melanocytic proliferation.

Another distinguishing feature was the patchy peripheral atypical pigment network, seen in 75% of MELTUMP cases versus 22% of SAMPUS lesions ($p = 0.02$; OR = 10.5, 95% CI: 1.6-68). Peripheral network irregularity is often interpreted as a sign of radial growth and lesion expansion. In melanoma, such peripheral structures are typically asymmetrical and discontinuous, reflecting uneven lateral proliferation of atypical melanocytes²⁵. The significantly higher prevalence of this feature in MELTUMP lesions suggests that these tumors may share dermoscopic characteristics with early radial growth phase melanoma, further supporting their intermediate biological behavior.

In contrast, features such as atypical dots and globules, although commonly observed in both groups, did not show a statistically significant difference between MELTUMP and SAMPUS. While these structures are commonly associated with melanocytic lesions and may indicate focal nests of melanocytes, they are known to have limited specificity when considered in isolation²⁶. This aligns with previous studies indicating that dots and globules must be interpreted in the broader context of lesion symmetry and overall dermoscopic pattern.

Interestingly, shiny white structures, visible under polarized dermoscopy and associated with dermal fibrosis, were observed exclusively in MELTUMP lesions. Although this finding did not reach statistical significance ($p = 0.06$), it represents a clinically relevant trend. Their presence may reflect underlying dermal remodeling, regression, or increased stromal response, features more commonly associated with biologically advanced or evolving melanocytic lesions²⁷ and not features that were expected to be observed in purely intraepidermal lesions such as SAMPUS.

These structures have been increasingly recognized as important indicators of melanoma and are thought to correspond to altered collagen in the dermis²⁸. Their exclusive presence in MELTUMP in this cohort may reflect a higher degree of stromal remodeling or regression, features more commonly seen in biologically active or evolving lesions.

Additional features such as regression structures (peppering and scar-like depigmentation) and negative network were more frequently observed in MELTUMP compared to SAMPUS, although these differences as well did not achieve statistical significance. Both features are well-described in melanoma and are associated with tumor-host interaction and architectural disruption²⁹. The lack of statistical significance in this cohort study might be attributable to the limited sample size.

Additional vascular features, including dotted vessels, polymorphous vessels, and serpentine vessels, were observed sporadically across both groups without a clear discriminatory pattern. Similarly, structureless areas (brown or pink), prominent skin markings, and follicular-related features (e.g., asymmetric pigmented follicular openings, rhomboidal structures) were present in both MELTUMP and SAMPUS lesions, reflecting variability in dermoscopic presentation but lacking statistical significance.

The observation that MELTUMP lesions are significantly associated with: atypical pigment network, blotches and peripheral irregular network is consistent with well-established dermoscopic criteria for melanoma. Although direct dermoscopic studies on MELTUMP are scarce, melanoma literature consistently links these features to architectural disorganization and radial growth. Importantly, MELTUMP lesions have been shown to carry a small but real risk of progression or metastasis (approximately 0.7-2%), supporting the notion that their dermoscopic resemblance to melanoma may reflect underlying biological potential rather than mere morphological overlap.

In contrast, SAMPUS lesions in our cohort demonstrated fewer melanoma-specific structures and lower frequency of asymmetry and architectural disorder. This aligns with the concept that SAMPUS may correspond to high-grade intraepidermal nevus with dysplasia without clear invasive potential.

Table 7. Summary of the incidence of dermoscopic features in SAMPUS and MELTUMP.

Dermoscopic feature	MELTUMP (n=16)	SAMPUS (n=9)	p-value	OR (95% CI)
Atypical pigment network	14 (87.5%)	4 (44%)	0.03	8.4 (1.2-57.5)
Blotch / small blotches	13 (81%)	2 (22%)	0.01	15.2 (2.0-115)
Patchy peripheral network	12 (75%)	2 (22%)	0.02	10.5 (1.6-68)
Atypical dots	11 (69%)	5 (56%)	0.68	-
Atypical globules	7 (44%)	2 (22%)	0.38	-
Negative network	7 (44%)	1 (11%)	0.15	-
Regression structures	7 (44%)	1 (11%)	0.15	-
Shiny white structures	6 (38%)	0 (0%)	0.06	-
Vascular structures*	5 (31%)	2 (22%)	0.99	-
Structureless areas (brown/ pink)	6 (38%)	3 (33%)	0.99	-
Follicular-related features**	3 (19%)	1 (11%)	0.99	-

- *Vascular structures include dotted, polymorphous, and serpentine vessels
- **Follicular-related features include asymmetric pigmented follicular openings, rhomboidal structures, and gray circles
- OR calculated only for statistically significant variables
- P-values obtained using Fisher's exact test

The present retrospective cohort study provides novel insights into the clinicopathological and dermoscopic characteristics of melanocytic lesions classified as SAMPUS and MELTUMP, contributing to a still limited body of evidence on these diagnostically ambiguous entities. By systematically evaluating dermoscopic features in correlation with histopathological

classification, this study offers an additional layer of understanding regarding the biological spectrum that these lesions occupy.

Our findings demonstrate that, although both SAMPUS and MELTUMP fall within the grey zone of melanocytic pathology, they exhibit distinguishable clinical and dermoscopic tendencies. MELTUMP lesions were more frequently associated with dermoscopic features classically linked to melanoma, including atypical pigment network, blotches, and peripheral architectural disorder. In contrast, SAMPUS lesions more often displayed less pronounced atypia and a more limited spectrum of melanoma-associated features. These observations support the concept that MELTUMP lesions may represent a biologically more advanced or heterogeneous category within the continuum of melanocytic neoplasia.

Histopathological examination remains the gold standard for the diagnosis and classification of melanocytic lesions and continues to serve as the cornerstone of clinical decision-making in dermatology and dermatopathology. The distinction between a benign nevus and melanoma carries profound implications for patient management, influencing surgical margins, the need for sentinel lymph node biopsy, follow-up strategies, and overall prognosis. In the majority of cases, a definitive diagnosis can be established through detailed assessment of histomorphological features, supplemented, when necessary, by immunohistochemical markers and molecular diagnostic techniques.

Despite its central role, histopathology is not without limitations. A significant subset of melanocytic lesions demonstrates architectural disorder and cytological atypia that do not meet clear-cut criteria for either benignancy or malignancy. These diagnostically ambiguous lesions expose the inherent limitations in a morphology-based system and challenge the traditional binary classification model. Importantly, such diagnostic difficulty does not merely reflect observer inexperience or technical shortcomings, but rather underscores a fundamental issue: the limited specificity of histopathological criteria in capturing the full biological spectrum of melanocytic proliferations.

A pivotal conceptual advance in addressing this limitation was the introduction of the terms SAMPUS (superficial atypical melanocytic proliferations of uncertain significance) and MELTUMP (melanocytic tumors of uncertain malignant potential) by Elder and Xu in 2004²⁰. In their seminal manuscript, the authors explicitly recognized that a subset of melanocytic lesions cannot be reliably classified as either benign or malignant using existing histopathological criteria. Instead, they proposed a pragmatic and biologically oriented framework that acknowledges diagnostic uncertainty as an inherent feature of melanocytic pathology.

Within this framework, SAMPUS refers to predominantly junctional or superficially invasive melanocytic proliferations confined to the epidermis and papillary dermis, lacking evidence of tumorigenic growth or significant mitotic activity, and therefore associated with an excellent prognosis when completely excised. In contrast, MELTUMP encompasses dermal-based, tumorigenic melanocytic proliferations characterized by cytological atypia and/or mitotic activity, in which invasive melanoma cannot be definitively excluded and which carry a potential, albeit unpredictable - for metastasis.

Importantly, the introduction of these terms reflects more than a semantic refinement; it represents a fundamental shift in diagnostic philosophy. Rather than forcing ambiguous lesions into a binary benign–malignant framework, Elder and Xu in their manuscript emphasized the necessity of explicitly acknowledging uncertainty. They advocated for transparent reporting that includes a descriptive diagnosis, a clear differential diagnosis, and management guided by the most clinically significant possibility within that differential. This approach underscores that SAMPUS and MELTUMP are not definitive diagnostic entities, but operational categories that reflect the biological continuum of melanocytic neoplasia and the current limits of morphology-based assessment.

The conceptual limitations highlighted by Elder and Xu were later quantitatively substantiated in the landmark observer study by Joann G. Elmore et al.²¹, which systematically evaluated diagnostic concordance among pathologists using the MPATH-Dx classification criteria. While high levels of agreement were observed for unequivocally benign lesions and advanced invasive

melanoma, the study revealed markedly reduced reproducibility in intermediate diagnostic categories, including moderately atypical nevi, melanoma in situ, and thin invasive melanoma. Concordance rates in these groups ranged from approximately 25% to 43%, highlighting substantial interobserver variability.

At a population level, it was estimated that approximately 17% of melanocytic lesion diagnoses would be discordant upon expert review, with both overdiagnosis and underdiagnosis occurring at comparable rates. These findings emphasize that histopathological interpretation—particularly in borderline lesions—is inherently subjective and lacks the level of specificity often assumed in clinical practice. In this context, the framework of SAMPUS and MELTUMP gains particular relevance, as it provides a structured means of categorizing lesions that fall within this zone of diagnostic ambiguity.

The manuscript underpinning this discussion further reinforces these observations by emphasizing that even expert histopathological assessment may be insufficient for definitive classification in difficult melanocytic lesions. It highlights that diagnostic uncertainty arises not only from observer variability but also from intrinsic limitations in available criteria and incomplete biological information, with some lesions remaining fundamentally indeterminate despite exhaustive evaluation. Moreover, diagnostic accuracy is significantly enhanced when histopathological findings are interpreted in conjunction with clinical information, including patient age, lesion site, evolution, and macroscopic appearance. This concept of clinicopathologic correlation is particularly critical in borderline lesions, where static morphological features alone may not adequately reflect biological behavior. In this sense, histopathology should not be viewed as an isolated diagnostic endpoint, but rather as one component of a dynamic and integrative diagnostic process.

The challenges associated with these lesions extend beyond diagnosis to prognostication. A clinical series by Britta Kaltoft et al.²², involving 67 patients with MELTUMP, demonstrated that although these lesions are generally associated with a favorable prognosis, they are not entirely devoid of malignant potential. Approximately 6% of patients presented with regional lymph node

metastases at diagnosis, and a small proportion developed nodal or distant metastases during follow-up, including rare melanoma-related deaths. Notably, no specific histopathological features were identified that could reliably predict which lesions would behave aggressively. This lack of prognostic specificity further underscores the biological heterogeneity of MELTUMP and highlights the limitations of morphology alone in guiding clinical decision-making.

Taken together, these findings support the concept that uncertainty in lesions such as SAMPUS and MELTUMP is both diagnostic and biological. The imperfect correlation between histopathological appearance and clinical outcome suggests that these lesions occupy a transitional space within the spectrum of melanocytic neoplasia, where current diagnostic tools are insufficient to fully characterize their behavior.

In this context, there is a clear need for adjunctive diagnostic approaches that can complement histopathological evaluation. Our manuscript points toward the potential value of non-invasive imaging techniques. Dermoscopy, in particular, represents a valuable intermediary modality, allowing in vivo visualization of subsurface structures and vascular patterns that reflect underlying histological architecture.

However, despite its established role in the evaluation of melanocytic lesions, the dermoscopic characterization of SAMPUS and MELTUMP remains poorly defined in the literature. This gap reflects the broader diagnostic uncertainty surrounding these entities and highlights the need for systematic investigation. The present thesis addresses this issue by examining the dermoscopic features of SAMPUS and MELTUMP and exploring their potential correlation with histopathological findings.

Importantly, the results of this study reinforce the notion that diagnostic uncertainty in melanocytic pathology is not merely a limitation of histopathological interpretation, but rather reflects the intrinsic biological variability of these lesions. The dermoscopic differences identified in this cohort suggest that non-invasive imaging may capture aspects of lesion architecture and evolution that are not fully appreciated on static histological examination. In this

sense, dermoscopy may serve as a valuable adjunctive tool, contributing to preoperative risk stratification and potentially guiding clinical decision-making in borderline cases.

The complexity of these entities is further compounded by the relative scarcity of robust evidence, as much of the available literature has historically been derived from small case series and individual reports.

The largest currently available analysis of SAMPUS and MELTUMP constitutes the nationwide Dutch retrospective cohort study by Vermariën-Wang et al.¹³, which identified 3642 primary cutaneous ambiguous melanocytic lesions, including 1685 MELTUMP and 1957 SAMPUS, from the Dutch Nationwide Pathology Databank. This represents a substantially larger dataset than any dermoscopy-focused cohort, including this small retrospective cohort study, and provides important epidemiological and outcome-based context. In that study, patients were predominantly female (59.7%), and lesions were most commonly located on the trunk (49.8%). In contrast, our cohort showed a more differentiated distribution between the two diagnostic categories, with SAMPUS more frequently located on the trunk and more common in male patients, whereas MELTUMP showed a marked predilection for the lower limbs and female patients.

Outcome data from the Dutch cohort support the concept that both entities generally have limited malignant potential. Among cases with at least three years of follow-up, metastatic behavior was observed in only 0.7% of initially diagnosed MELTUMP, while no SAMPUS cases developed metastases. Local recurrence or progression was also uncommon, occurring in 1.3% of MELTUMP and 0.2% of SAMPUS. These findings are consistent with the view that SAMPUS behaves in an indolent manner, whereas MELTUMP carries a small but real risk of adverse outcome.

Importantly, although this nationwide study provides the most robust epidemiological and prognostic data available for SAMPUS and MELTUMP, it does not include dermoscopic information. Therefore, no comparison regarding dermoscopic structures, global patterns, vascular features, regression, shiny white structures, or other non-invasive imaging criteria can

be made from this manuscript. This absence highlights the relevance of this cohort, which, despite its limited sample size, specifically addresses the dermoscopic differences between SAMPUS and MELTUMP and therefore contributes complementary information not available in the largest published outcome analysis.

In this context, the study by Pusiol et al¹⁵ provides valuable insight, describing a series of 14 MELTUMP cases, of which dermoscopic evaluation was available in five lesions. Notably, all five dermoscopically examined lesions demonstrated features suggestive of malignancy, including atypical pigment network, irregular diffuse pigmentation (blotches), gray-blue areas, regression structures, and atypical vascular patterns. As illustrated in the dermoscopic images and descriptions, these lesions frequently exhibited multicomponent global patterns, irregular streaks or pseudopodia, structureless hyperpigmented areas, and blue-whitish or regression-associated zones, all of which are well-established dermoscopic criteria associated with melanoma. Importantly, the authors emphasized that, despite these melanoma-like dermoscopic features, the biological behavior of MELTUMP in their series was generally favorable, further highlighting the disconnection between morphological appearance and clinical outcome. This is, according to our knowledge, the study with the highest number of SAMPUS/MELTUMP dermoscopic features published so far in scientific literature.

The consistency between our findings and those reported in this earlier case series is particularly noteworthy. Both studies demonstrate that MELTUMP lesions frequently display dermoscopic patterns that would typically raise strong suspicion for melanoma in routine clinical practice. However, the limited number of dermoscopic cases in the existing literature, including only five cases in the aforementioned study, underscores the need for larger, systematic investigations. By directly comparing MELTUMP with SAMPUS, this cohort study extends these observations by showing that such melanoma-associated dermoscopic features are significantly less frequent in SAMPUS lesions, which tend to exhibit a less complex and less atypical dermoscopic architecture. This supports the concept that, despite overlapping diagnostic uncertainty, SAMPUS and MELTUMP may occupy different positions along the biological spectrum of melanocytic neoplasia.

Taken together, these findings suggest that dermoscopy captures important aspects of lesion architecture and biological behavior that are not fully reflected by histopathological classification alone. While MELTUMP lesions often mimic melanoma dermoscopically, their clinical course is generally more indolent, emphasizing the need for cautious interpretation and integrative diagnostic approaches. Future studies incorporating larger cohorts and multimodal analysis - including dermoscopy, histopathology, and molecular techniques - will be essential to further refine the diagnostic and prognostic stratification of these challenging lesions.

Nevertheless, these findings must be interpreted in the context of this study's limitations, particularly the relatively small sample size and retrospective design. While statistically significant associations were identified for several dermoscopic features, other trends did not reach significance, likely reflecting limited statistical power. These observations highlight the need for larger, multicenter studies to validate and expand upon these preliminary findings.

Looking forward, it is increasingly evident that a purely morphology-based approach is insufficient to fully characterize melanocytic lesions of uncertain malignant potential.

In this context, recent advances in immunohistochemistry offer promising avenues for improving diagnostic precision in ambiguous melanocytic lesions. A comprehensive review published in 2026²⁹ has underscored the potential diagnostic value of combined p16 and MTAP immunohistochemistry, demonstrating that concurrent loss of both markers strongly correlates with melanoma or high-risk melanocytoma, whereas retained or discordant expression patterns are more frequently observed in borderline lesions.

These findings represent a significant step toward a more objective and reproducible diagnostic paradigm. Rather than relying solely on subjective morphological criteria, the integration of immunohistochemical surrogates such as p16 and MTAP allows for a biologically grounded assessment of melanocytic lesions. Furthermore, this approach aligns with the broader trend in dermatopathology toward molecularly informed classification systems that reflect underlying tumor biology rather than purely descriptive morphology.

However, it is important to recognize that even these advanced tools do not fully resolve the complexity of SAMPUS and MELTUMP. These entities encompass biologically heterogeneous lesions arising from distinct molecular pathways, and no single biomarker can serve as a universal discriminator. Instead, the greatest diagnostic value lies in the integration of multiple modalities - including dermoscopy and immunohistochemistry and possibly other techniques, interpreted within the clinical and pathological context of each individual case.

Conclusion

Taken together, the findings of this retrospective cohort study and the current body of literature reinforce the concept that melanocytic lesions such as SAMPUS and MELTUMP exist along a continuous biological and morphological spectrum rather than as clearly separable entities. The dermoscopic differences identified in this study likely reflect underlying biological variation between these lesions, providing a plausible explanation for the observed in vivo patterns.

Importantly, this work addresses a notable gap in the literature. While most previous studies have focused predominantly on histopathological features and clinical outcomes, dermoscopic criteria have not been systematically or quantitatively analyzed. In this context, our study contributes meaningful evidence by demonstrating measurable dermoscopic differences, offering practical clues that may aid in risk stratification and clinical decision-making.

However, consistent with existing evidence, our results also highlight a key limitation: dermoscopy alone is insufficient to reliably distinguish between SAMPUS and MELTUMP. Given their overlapping features and position within a biological continuum, histopathological evaluation remains indispensable for definitive diagnosis.

Overall, these findings support a shift toward a multimodal, integrative diagnostic approach. Dermoscopy provides valuable in vivo structural insight, but its optimal utility lies in combination with histopathology and emerging molecular and immunohistochemical techniques. Future research—particularly larger, prospective studies incorporating advanced diagnostic modalities—will be essential to further clarify the biological behavior of these ambiguous lesions and to refine their classification and management in clinical practice.

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Figure 1. Dermoscopic pictures of lesions classified as SAMPUS

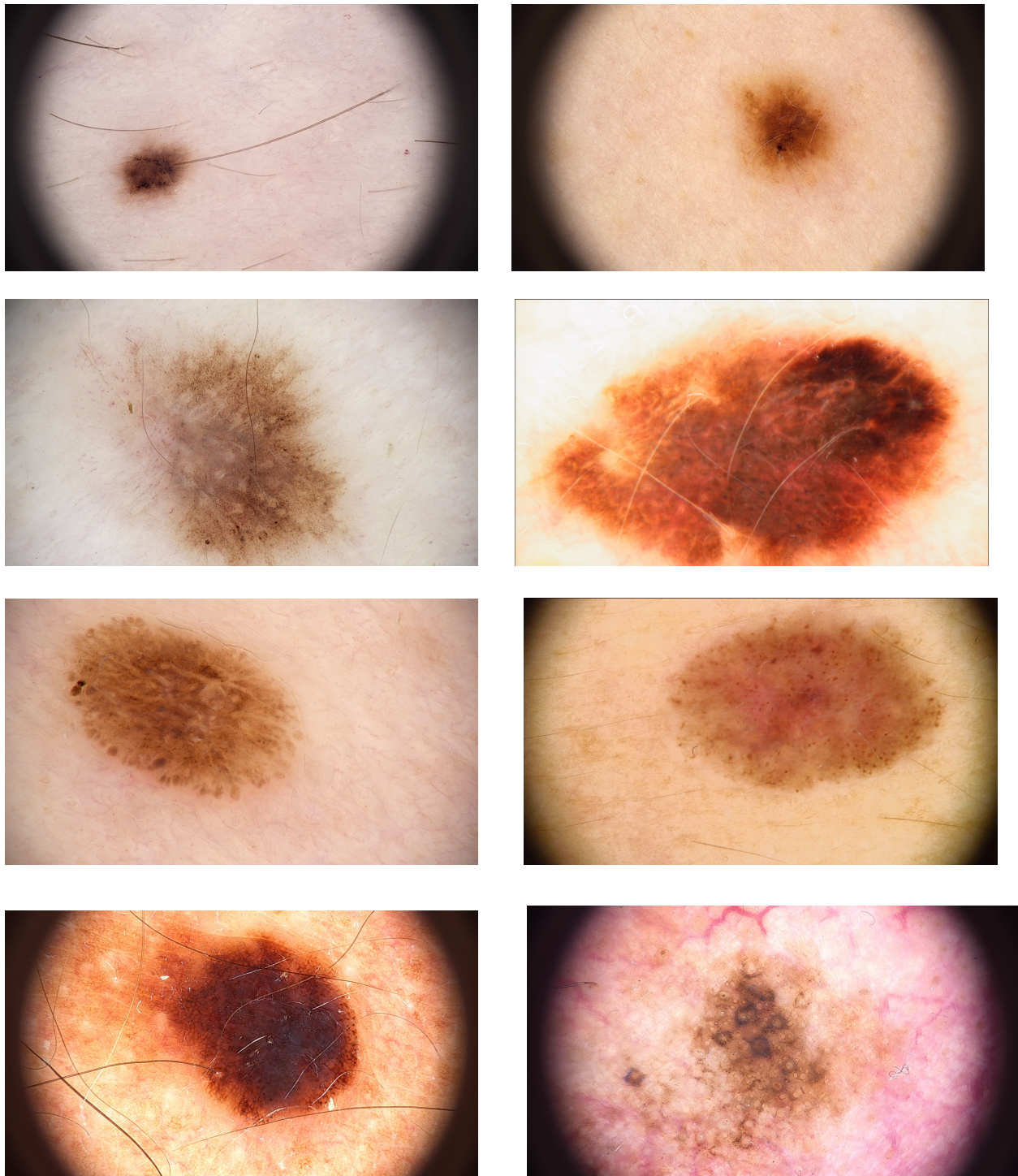




Figure 2. Dermoscopic pictures of lesions classified as MELTUMP

