

Dermatoscopy for Students

A concise outline of:

Revised Pattern Analysis: a method for the accurate diagnosis of pigmented skin lesions

And

Chaos and Clues: a decision algorithm for routine practice to detect pigmented skin malignancy of any type

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Revised Pattern Analysis

Revised pattern analysis (RPA) is a stepwise algorithmic method for the diagnosis of pigmented skin lesions, pigmented either by melanin, significant blood pigment (as in structureless blood or red clods), or discoloured keratin [1,2]. The method of pattern analysis was first published in 1987 by Pehamberger et al [3] and no method has since been shown to be more accurate, but there was no stepwise process and the language of dermatoscopy evolved with a myriad of poorly-defined or un-defined metaphorical terms that in many cases carried preconceived diagnostic implications. RPA uses a limited number of clearly defined geometric terms and provides a clear stepwise process of analysis, assessing patterns then colours and finally clues, leading the clinician to a specific provisional diagnosis or alternatively a limited differential diagnosis.

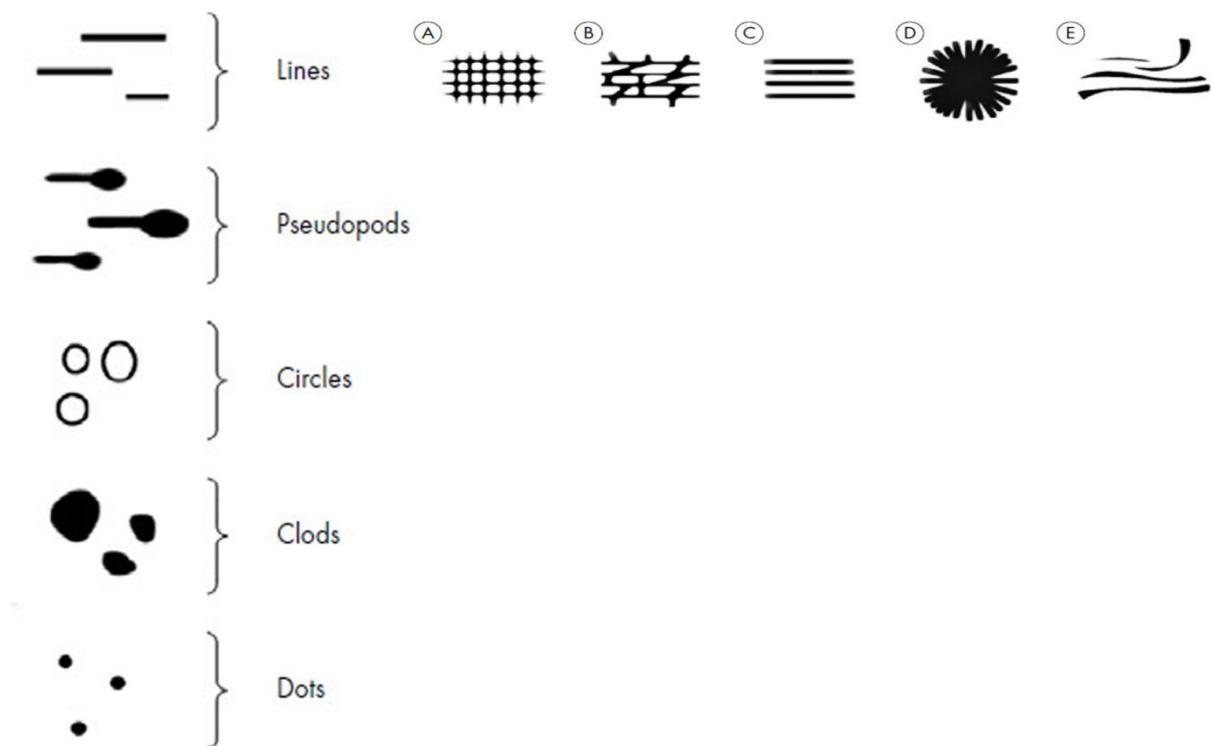


Figure 1: There are five basic structures in RPA: Lines (A reticular, B branched, C parallel, D radial and E curved), pseudopods, circles, clods, and dots.

In the language of RPA there are five basic structures: lines, pseudopods, circles, clods and dots (figure 1 vertical). Because lines are a very specific structure they are further subdivided into five different types: reticular, branched, parallel, radial and curved (figure 1 horizontal). A pattern is an area made up of multiple repetitions of a basic structure. The terms used are clearly defined:

A **line** is a structure with length greatly exceeding width.

A **pseudopod** is a line with a bulbous end.

A **circle** is a curved line sensibly equidistant from a central point (this includes ellipses).

A **clod** is a well-defined, solid object larger than a dot and it can be any colour and any shape.

A **dot** is an object too small to have a discernable shape (at 10 times magnification).

A **structureless** area is an area covering a significant portion of a lesion with no basic structure predominating.

A pattern is formed by multiple repetitions of a basic structure and it must cover a significant portion of a lesion to be regarded as a pattern. For example a few reticular lines covering 5-10% of a lesion with an otherwise structureless pattern would constitute a clue rather than a pattern. If however reticular lines covered 30% of an otherwise structureless lesion then the lesion would be regarded as having two patterns (figure 2). It is best as far as possible to avoid arbitrary rules of degree, but for the purpose of consistency it is reasonable to define the minimum area of a pattern as 20% of the surface area of a lesion. In figure 2 the right hand side of the lesion has a pattern of lines reticular. There are a few lines and dots on the left side but as none of these structures predominate this portion of the lesion is termed structureless. Note that structureless does not necessarily equate with featureless.

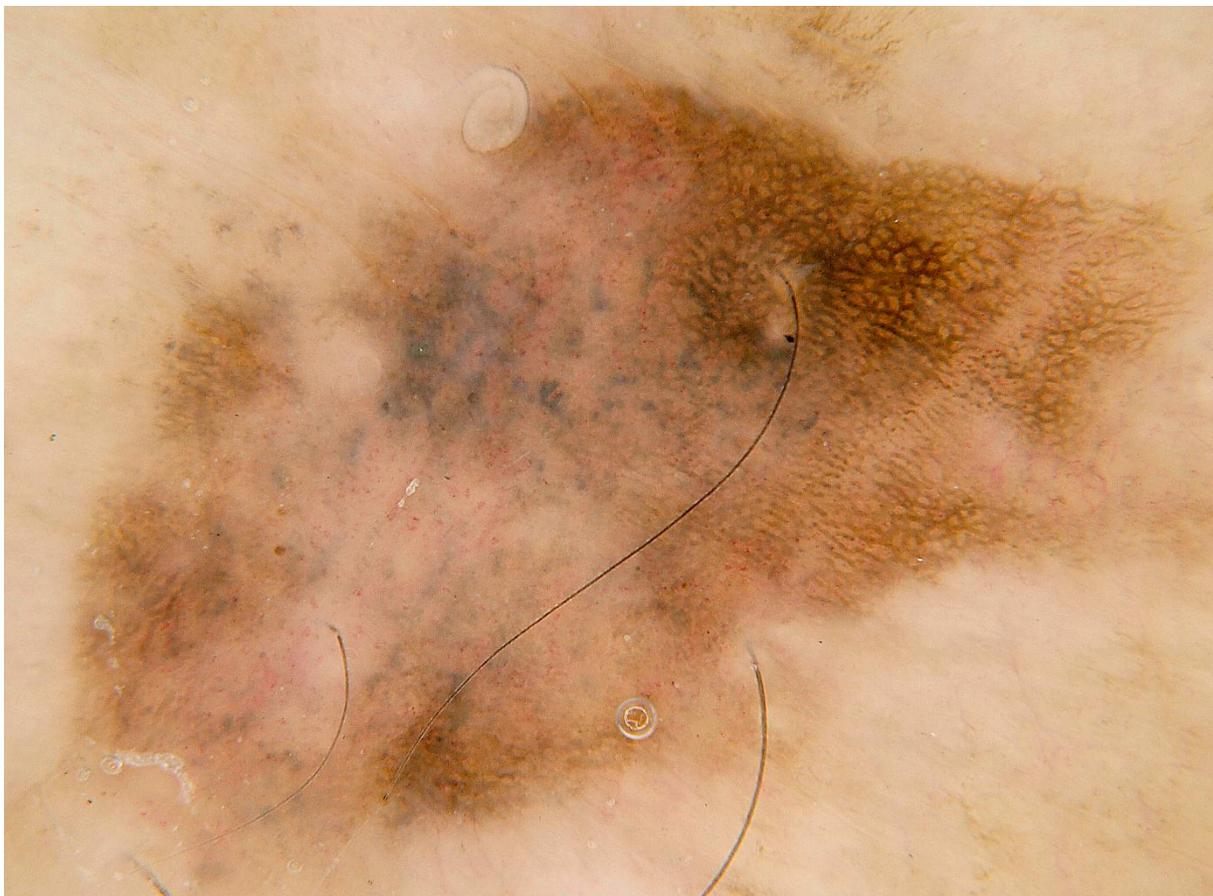


Figure 2: A pigmented skin lesion with a pattern of lines reticular on the right. Although there are some lines and dots on the left, none of these predominate, so the pattern is structureless. This is a solar lentigo on the right hand side in collision with a pigmented squamous cell carcinoma in situ on the left hand side.

Patterns should be assessed as such and a few structures out of synchrony do not destroy a pattern. For example looking at the right side of figure 2 you may recognise a few circles but that does not interfere with the description of a pattern of reticular lines. It must be remembered that we are

describing biological material rather than an architect's design and it is appropriate to tolerate reasonable variation.

Why the 2-step method of dermatoscopy is not used in revised pattern analysis

The 2-step method of dermatoscopy requires that melanocytic status be determined by dermatoscopy as a first step before the lesion is assessed for clues to melanoma as a second step [4,5]. The so-called melanocytic criteria (network, pseudonetwork, aggregated brown globules, radial streaming, pseudopods, homogenous blue pigmentation and parallel lines on acral skin) are not melanocytic criteria at all. They are just melanotic criteria and can occur in any pigmented lesion whether it has a proliferation of melanocytes or not. The lesion in figure 2 has clear pigment network but it is a solar lentigo in collision with a pigmented squamous cell carcinoma (SCC) in situ, neither of which are melanocytic. So-called pseudonetwork is commonly seen in solar lentigo (see figure 7 right) and pigmented actinic keratosis, neither of which are melanocytic. Lines radial segmental are seen in pigmented basal cell carcinoma (BCC) (see figure 17 lower images) and in pigmented SCC in situ (see figure 18 lower images), neither of which are melanocytic. The sensitivity and specificity of the first step of the 2-step process were evaluated in a study on consecutive lesion in a practice in Europe, compared to a practice in Australia [6]. The specificity was found to be 67.9% in Europe and 33.6% in Australia.

Before RPA is applied a lesion must be identified as pigmented. Although pigmentation may be obvious it is important to understand that the presence of any visible pigment at all should, as a rule, lead to the lesion being assessed as a pigmented lesion. Pigmented structures are far more specific as diagnostic clues than non-pigmented structures such as blood vessels, and should always be given priority when present [1].

Step 1: Pattern and Colours: Once a lesion is recognised as pigmented the first step is to assess the pattern(s) with a decision made as to whether there **is one pattern or more than one pattern**. Defining a precise number of patterns does not additionally assist the diagnostic process and so the simple decision on whether there is one pattern or more than one is adequate. If a lesion has more than one pattern the dermatoscopist goes straight to step 2 without analysing colours. If there is only one pattern then colour must be considered in the decision about symmetry so the decision is made as to whether there is **one colour or more than one colour**.

The colours seen in dermatoscopy include the colours of melanin (black, brown, grey and blue), the colours of keratin (orange and white), and the colour of collagen (also white) as well as the colours of blood (blue, purple and black). **Shades of brown (dark brown and light brown) are only recognised if there is an abrupt transition with a high degree of variation.**

Step 2: Symmetry: After assessing whether there is one pattern or more than one pattern, and in the case that there is a single pattern, whether there is one colour or more than one colour, a decision must be made as to whether the lesion is **symmetrical or not**. Symmetry is decided on the basis of pattern and colour, regardless of shape.

In the case of only one pattern, symmetry is decided on the basis of colour. If there is one pattern and one colour then by definition the lesion is symmetrical. If there is one pattern but more than one colour and the colours are combined asymmetrically the lesion is asymmetrical.

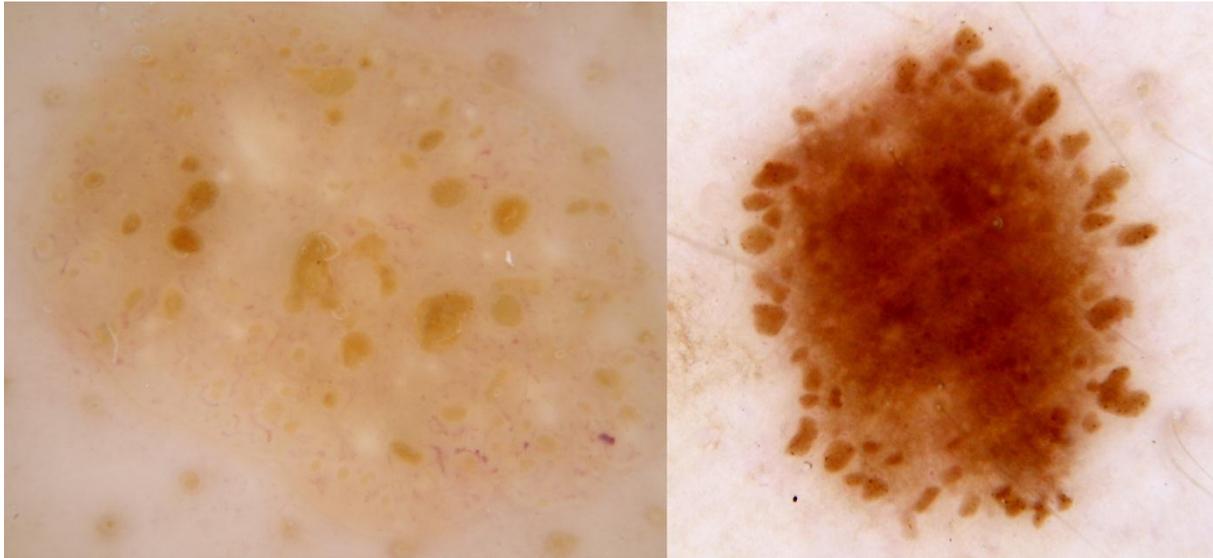


Figure 3: The lesion on the left has one pattern clods and one colour yellow. By definition it is symmetrical. The lesion on the right has two patterns: central structureless and peripheral clods, combined in a symmetrical concentric pattern.

In figure 3 the lesion on the left has a pattern of yellow clods. There is one pattern and one colour. The background does not constitute a structureless pattern because it is overlaid by the pattern of yellow clods. A couple of white clods have no impact on the *pattern* although they are additional *clues* to the diagnosis of seborrhoeic keratosis. With one pattern and one colour the lesion is symmetrical.

In the case of more than one pattern, symmetry is determined by the structures and colour is disregarded in the assessment of symmetry (figure 3). The lesion on the right in figure 3 has two patterns, a central structureless pattern and peripheral clods combined symmetrically in a concentric arrangement. It does not matter that there are a few clods missing at the top. Such variation is acceptable in biological tissue. Another way of understanding this is to realise that *such a degree of variation is not consistent with the disorganised behaviour of malignant tissue.*

Step 3: Clues: Having assessed the patterns, colours and symmetry of a pigmented skin lesion, RPA then proceeds in a stepwise fashion according to *clues*.

Interpreting various dermatoscopic patterns

Clues to naevus versus solar lentigo

This distinction is not always possible without dermatopathology, but as a rule a naevus is expected to have a gradual border over the total periphery, while a solar lentigo is expected to have a sharply demarcated border (like its older brother seborrhoeic keratosis) which is often scalloped.

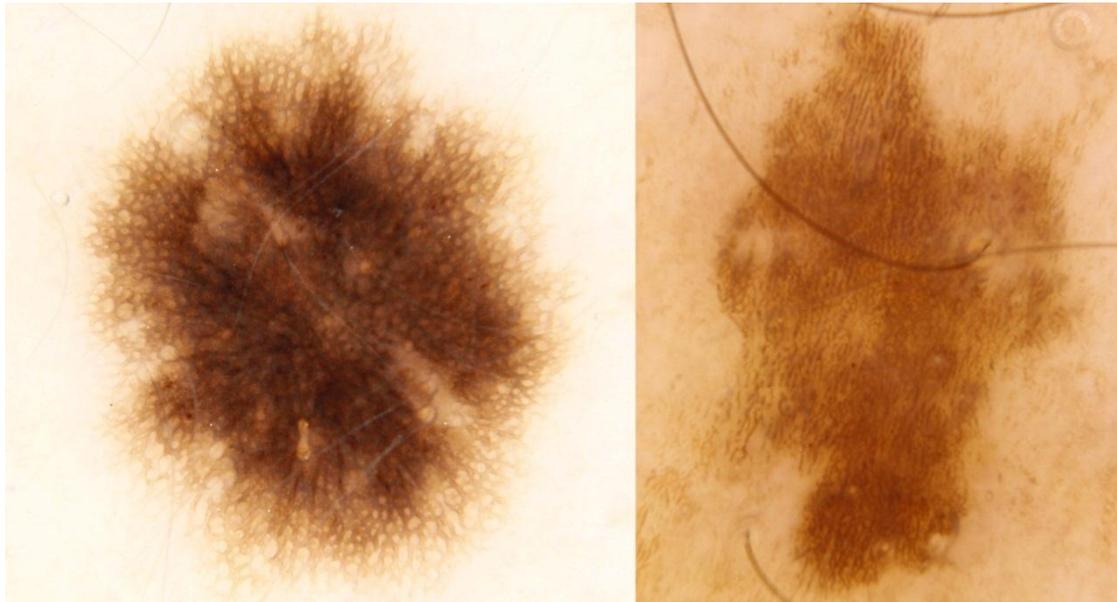


Figure 4: The lesion on the left has one pattern lines reticular and one colour brown. The gradual (non-abrupt) border points to a diagnosis of nevus. The lesion on the right has one pattern lines curved and with an abrupt border this is most consistent with the diagnosis of solar lentigo.

Patterns with a peripheral pattern of lines



Figure 5: Each of these three lesions has a pattern of lines peripherally combined in the lesions in the left and right with a central structureless area and in the lesion in the middle with a central pattern of clods. The lesion on the left is symmetrical and has the clue of white dots to support a diagnosis of congenital nevus. The lesion in the middle is also symmetrical and the pattern of peripheral lines combined with central clods is also consistent with congenital nevus. The fact that the lines at one end are branched and at the other end curved (or as the clinician thought radial) lead to excision but in retrospect this variation was not consistent with the chaotic behaviour of malignant tissue. The lesion on the right is asymmetrical, the central pink structureless area extending to the periphery on one side but not the other. In addition to the clue of an eccentric structureless area (not skin-coloured) there is the clue of lines radial segmental at the upper border of the dermoscopic image. The asymmetry of this lesion, although it has a central structureless area and peripheral pattern of lines like the other two lesions, is due to a degree of disorganisation which is quite consistent with the chaotic behaviour of malignant tissue. It was an invasive melanoma.

A pattern of lines radial/pseudopods circumferential

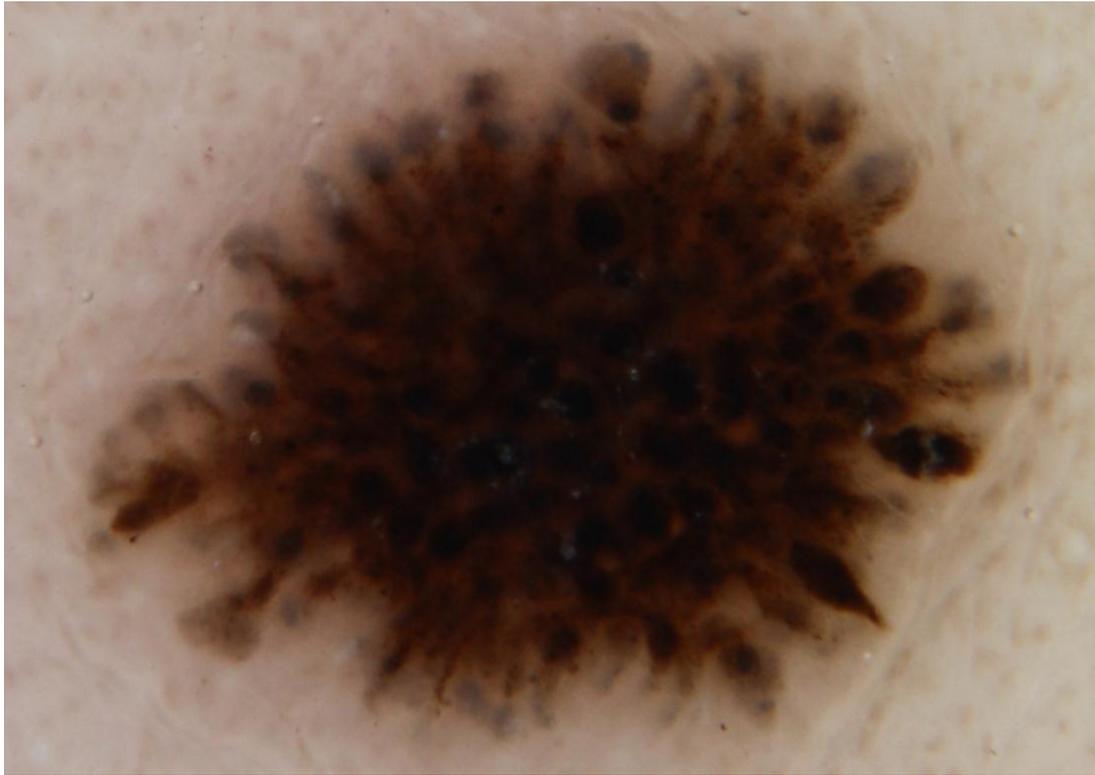


Figure 6: This lesion on the forearm of a 9 year old child has a peripheral circumferential pattern of lines radial and pseudopods combined symmetrically with a pattern of clods, of equally dark pigmentation compared to the centre of the lesion from which they project. When radial lines and pseudopods are combined in a concentric pattern they are regarded as one pattern, defaulting to the more specific structure of pseudopods (order of specificity: lines, pseudopods, circles, clods, dots and structureless). The differential diagnosis includes Reed nevus and melanoma. Histology confirmed this as a Reed nevus which was the expected diagnosis in a child.

Patterns on facial skin

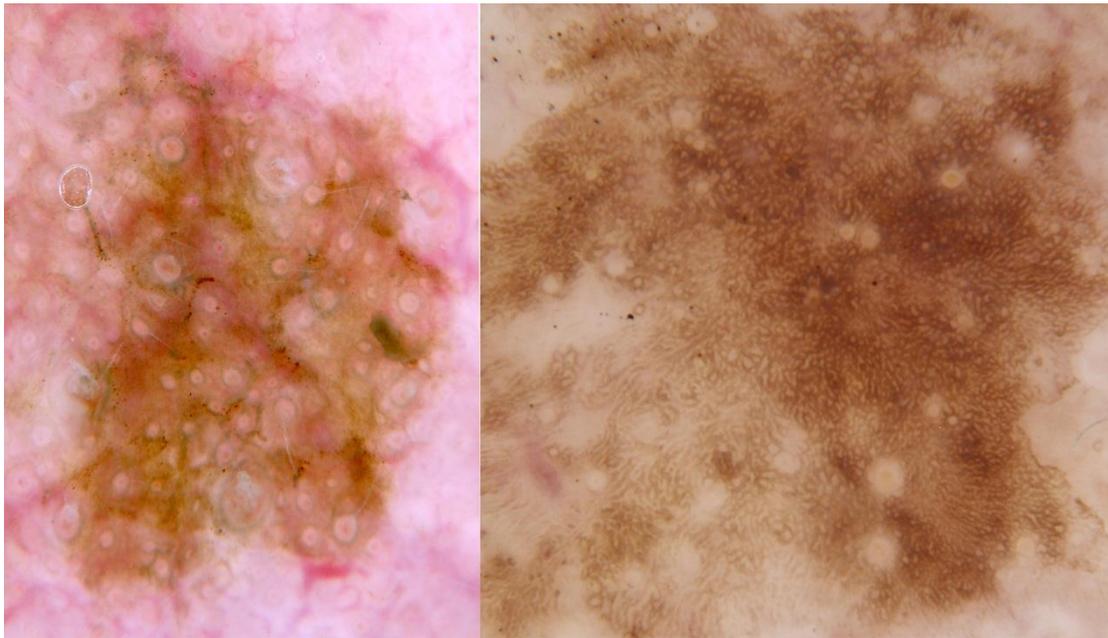


Figure 7: Both of these pigmented lesions are located on facial skin so as predicted, the pigment is interrupted by follicular openings. On the left a pattern of grey circles is a compelling clue to melanoma while on the right a pattern of curved lines interrupted by follicular openings is simply assessed as one pattern lines curved, one colour brown with a sharply demarcated scalloped border as an additional clue to solar lentigo. *Follicular opening do not rate as either a pattern or a clue, and unless defined by a circular line they should be ignored.*

Patterns of circles on non-facial skin

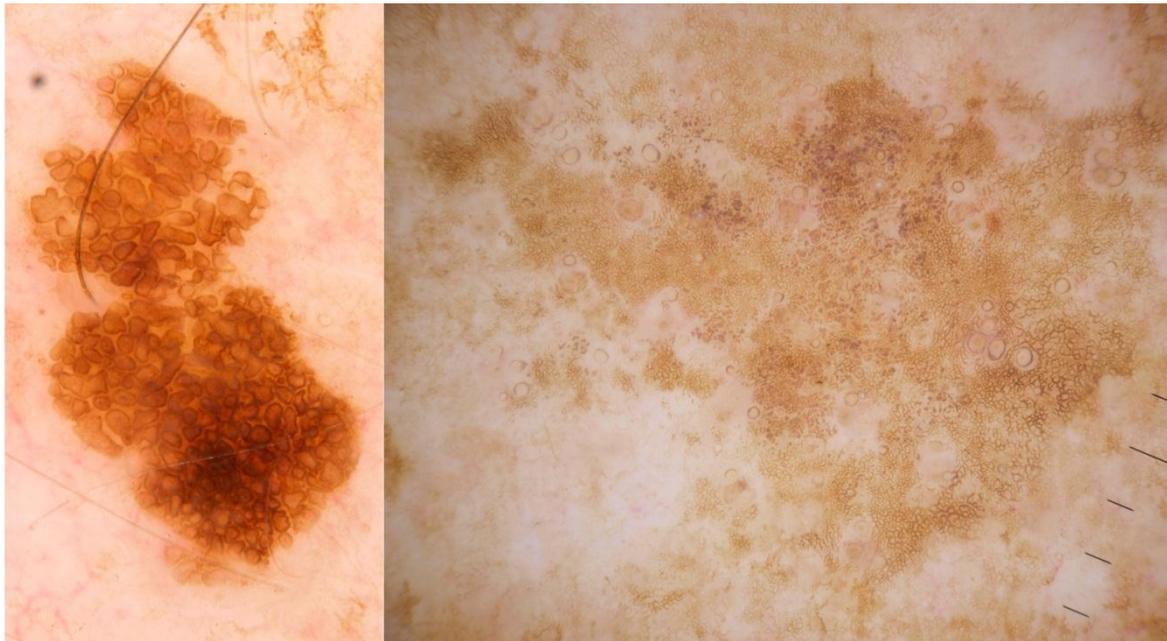


Figure 8: Both of these lesions on the torso contain pigmented circles. The lesion on the left consists of one pattern circles (they are not clods because the centre is lightly pigmented compared to the periphery), one colour brown (there is no abrupt transition between the shades of brown). The circles are not related to follicles and are caused by basal hyperpigmentation of acanthotic rete ridges (a pattern which would otherwise project as a reticular pattern can project as a pattern of circles when the rete ridges are widened by acanthosis). Such a lesion is predictably a seborrhoeic keratosis and the sharply demarcated border is an additional clue to that diagnosis. The lesion on the right has a pattern of reticular lines interrupted by a few pigmented circles which are related to follicles. Although there is some grey colour and the lesion is not perfectly symmetrical, the diagnosis of seborrhoeic keratosis was made with confidence due to the very regular fine pattern of the reticular lines, a pattern which is not consistent with the chaotic behaviour of malignant tissue. The lesion also had a palpably rough surface texture uniformly over its surface as an additional clue to seborrhoeic keratosis.

Clues to seborrhoeic keratosis

Seborrhoeic keratoses can have varied morphology which can include patterns of lines, circles, clods dots as well as structureless patterns. They frequently are asymmetrical and may have clues to melanoma but even so, if they can be reliably diagnosed by pattern analysis they do not need to be excised to exclude melanoma. Clues to seborrhoeic keratosis include the clinical clue of a raised lesion with a rough surface texture (figure 8 right) as well as multiple grouped morphologically identical or similar lesions. Dermatoscopic clues to seborrhoeic keratosis include multiple orange clods (figure 3 left, figure 10 left), multiple white clods (figure 3 left), fine or thick curved lines (figure 4 right), a pattern of circles not related to hair follicles (figure 8 left) and a sharply demarcated border over the total periphery (figure 3 left, figure 4 right, figure 8 left). Malignant conditions can have one or even more of these clues. In summary if chaos and clues to malignancy are present there must be compelling clues to seborrhoeic keratosis *including a palpable rough texture and/or a sharply demarcated border over the total periphery*, for excision biopsy to be avoided.

Patterns of clods

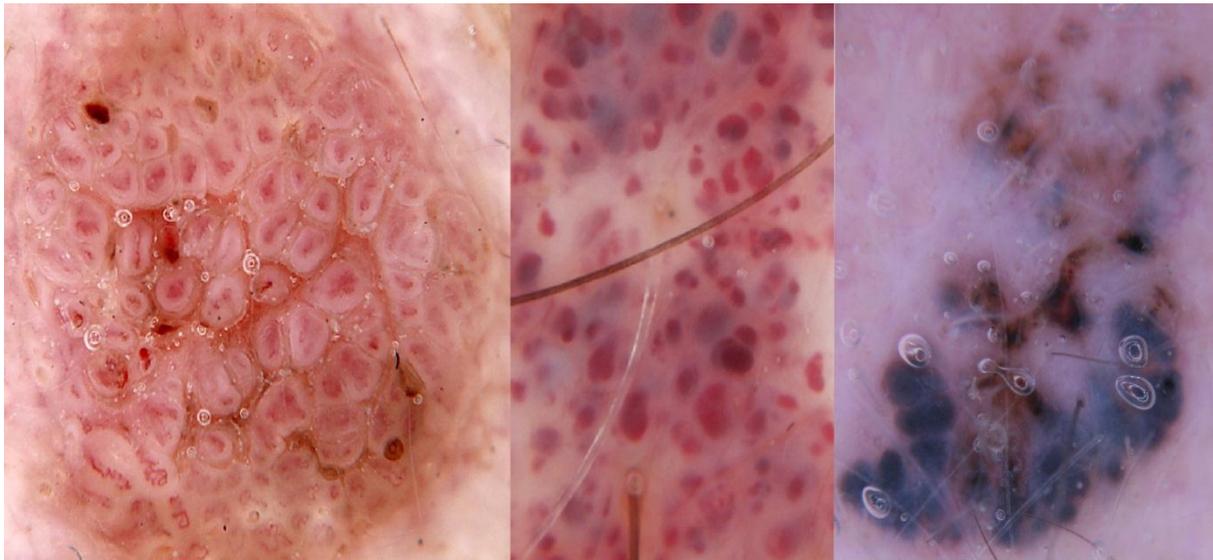


Figure 9: These three lesions all have one pattern clods. On the left a pattern of skin-coloured clods with centred vessels is consistent with either a seborrheic keratosis or congenital nevus. In the centre a pattern of red and purple clods, with no linear vessels is consistent with a haemangioma. On the right a pattern of blue clods points confidently to the diagnosis of BCC.

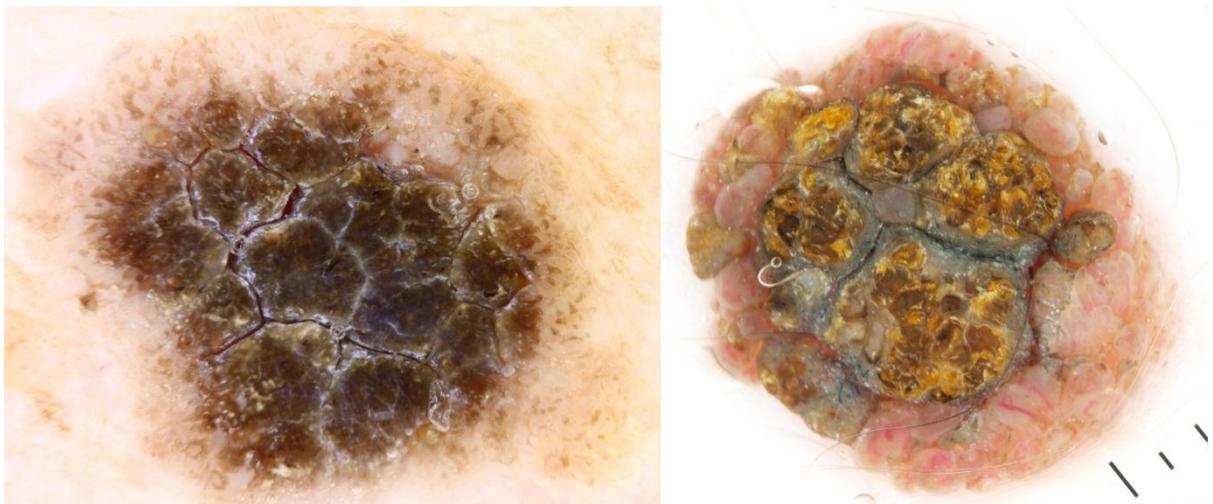


Figure 10: The lesion on the left has a pattern of orange keratin clods only, this being compelling evidence for seborrheic keratosis. The lesion on the right also has a pattern of clods-only, including a symmetrical combination of both central keratin clods (both orange and grey), and peripheral skin coloured clods. Terminal hair is a clue that this is in fact a congenital nevus. It had been present since childhood.

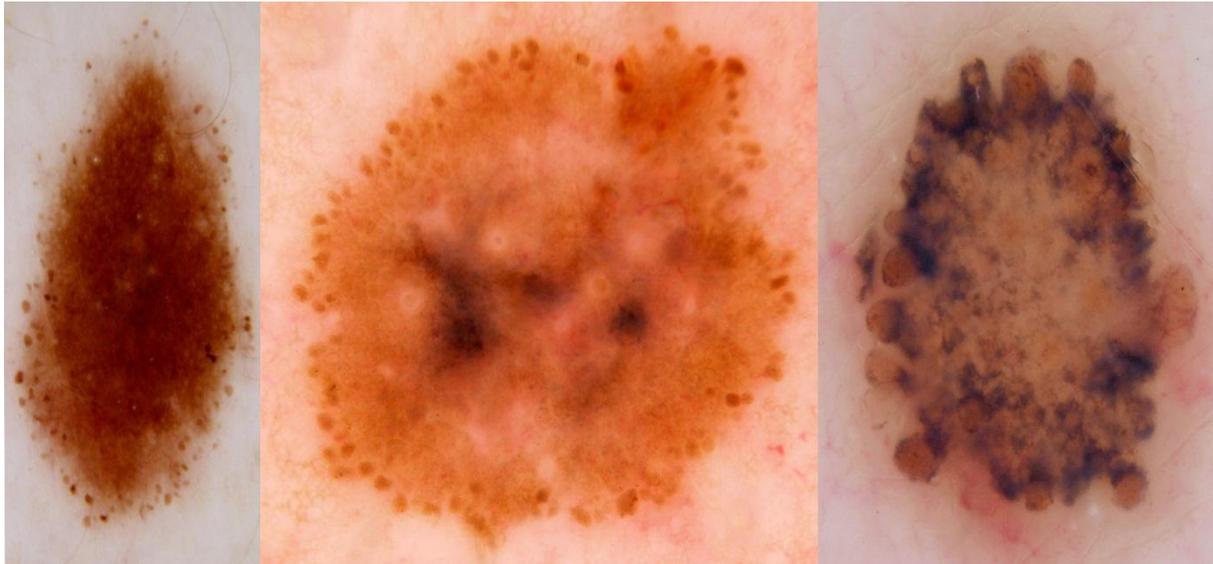


Figure 11: On the left a symmetrical lesion with central pattern of reticular lines and peripheral pattern of clods (or dots depending on perception), on a 30 year-old man, is predictably a growing Clark nevus. The middle lesion may appear similar but the central structureless area has an asymmetrical distribution of colours and one of these colours, grey, is a clue to melanoma. In this case on the chest of a 50-year-old man the peripheral clods or dots are not a clue to a growing nevus but to a growing melanoma in situ. Similarly the lesion on the right, on the chest of a 60 year old lady, with peripheral clods surrounding a structureless centre is not a nevus but is in fact a nodular melanoma, 3mm in diameter and 1mm thick [7].

A pattern of dots

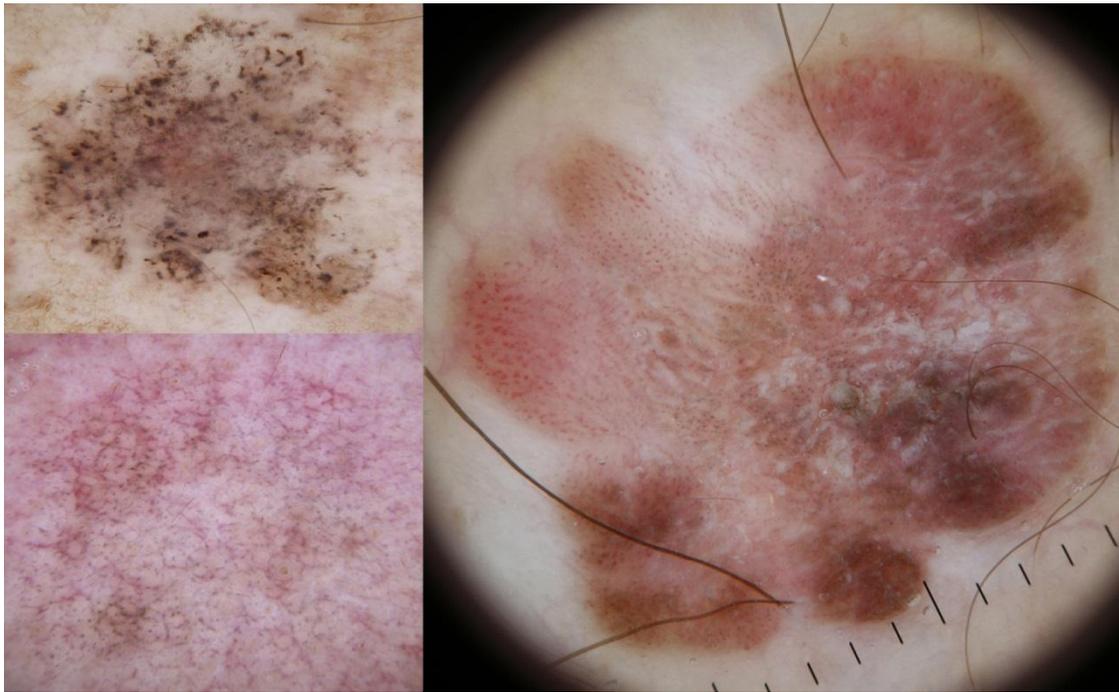


Figure 12: Both lesions on the left have one pattern dots and one colour grey. The upper lesion is located on the back and this pattern on the torso or limbs is consistent with the confirmed diagnosis of lichen-planus-like keratosis (LPLK). The lower lesion is on the face and at this location any lesion with dermatoscopic grey will have melanoma in the differential diagnosis [8]. This lesion was an in situ melanoma. The lesion on the right has a pattern of dots (left side of image) combined asymmetrically with a structureless pattern on the right side. Red dots, (not on their own constituting a pattern in RPA) merge into brown dots. The linear arrangement of the dots was consistent with the confirmed diagnosis of SCC in situ.

Dermatoscopic Clues to Specific Malignancies

Clues to melanoma

With respect to colour these clues depend on the fact that melanin appears as different colours depending on its depth in the skin [9]. Melanin, being a very efficient pigment, absorbs all light and therefore it appears black at the level of the stratum corneum. At the dermo-epidermal junction and the epidermis, the normal location of melanin in healthy skin, some light is reflected back by cells in the epidermis so it appears near-black, which is brown. Due to the fact that the collagen particles of the dermis scatter back short wave-length (blue) light preferentially to long wave length (red) light, while blocking the colour of haeme from below, melanin in the superficial and deep dermis appears grey and blue respectively.

Grey or blue structures correlate with melanin in the superficial and deep dermis respectively. In melanomas blue correlates with immature nested pigmented melanocytes in the deep dermis and in an asymmetrical lesion it is a strong clue to invasive melanoma. In melanomas grey dots usually correlate with melanophages in the papillary dermis and they are a common finding in the majority of in situ melanomas as well as being common in invasive melanomas.

An eccentric structureless area must cover a sufficient portion of the lesion for form a pattern, it much exist in contrast to a structured pattern somewhere within the lesion and it must be a colour other than skin-coloured. In melanomas, if coloured with the colours of melanin, it is produced by the chaotic behaviour of malignant melanocytes, if pink it is caused by increased blood flow and if white it may correlate with fibrosis after regression.

Thick lines reticular are defined when the lines are as thick as, or thicker than, the holes that they surround. In melanomas they correlate with rete ridges which are widened by pigment laden malignant melanocytes.

Peripheral black dots and clods in melanomas correlate with pigmented pagetoid melanocytes and nests of melanocytes which have moved close to the stratum corneum by pagetoid spread, where melanin is expected to appear black.

White lines must be whiter than normal surrounding skin and may be polarising-specific or alternatively white lines that are seen in both modalities. Polarising specific white lines are shiny white lines orientated perpendicularly to each other but not crossing. They are only seen with polarising dermatoscopy but they may correlate with reticular white lines seen with non-polarised dermatoscopy. Polarising-specific white lines can also be seen commonly in BCC as well as dermatofibroma (DF) and Spitz nevus. They are not specific to these lesions but their presence is not expected in any other type of nevus or in seborrhoeic keratoses. If they are seen in such lesions they should be excised to rule out malignancy even if there is a history of preceding trauma, which occasionally results in polarising-specific white lines in these lesions. Polarising-specific blue lines have the same diagnostic significance as polarising-specific white lines.

Lines radial or pseudopods, segmental, in melanomas correlate with fascicles of pigmented melanocytes extending from the periphery of a lesion and they signify radial growth. In melanomas they should be distributed asymmetrically and should extend from reticular lines, clods or

structureless areas of equivalent pigmentation to the radial lines or pseudopods. This can sometimes distinguish them from the radial lines seen in BCCs which frequently extend from hypopigmented structureless areas.

Polymorphous vessels in melanomas are expected to include various types of linear vessels in raised portions, and patterns of dot vessel as well as any pattern of linear vessel in macular portions. Generally other clues apart from polymorphous vessels (pigment clues and/or white lines) are expected in a melanoma and the vessel -clues are then useful in differentiating melanoma from pigmented basal cell carcinoma (pBCC) and pigmented squamous cell carcinoma in situ (pSCC in situ).

Polygons [10] are defined as geometric polygonal shapes, complete or incomplete, bounded by straight lines, or by a straight pigment interface, meeting at angles and larger than the holes caused by individual follicles and larger by far than the holes bounded by reticular lines.

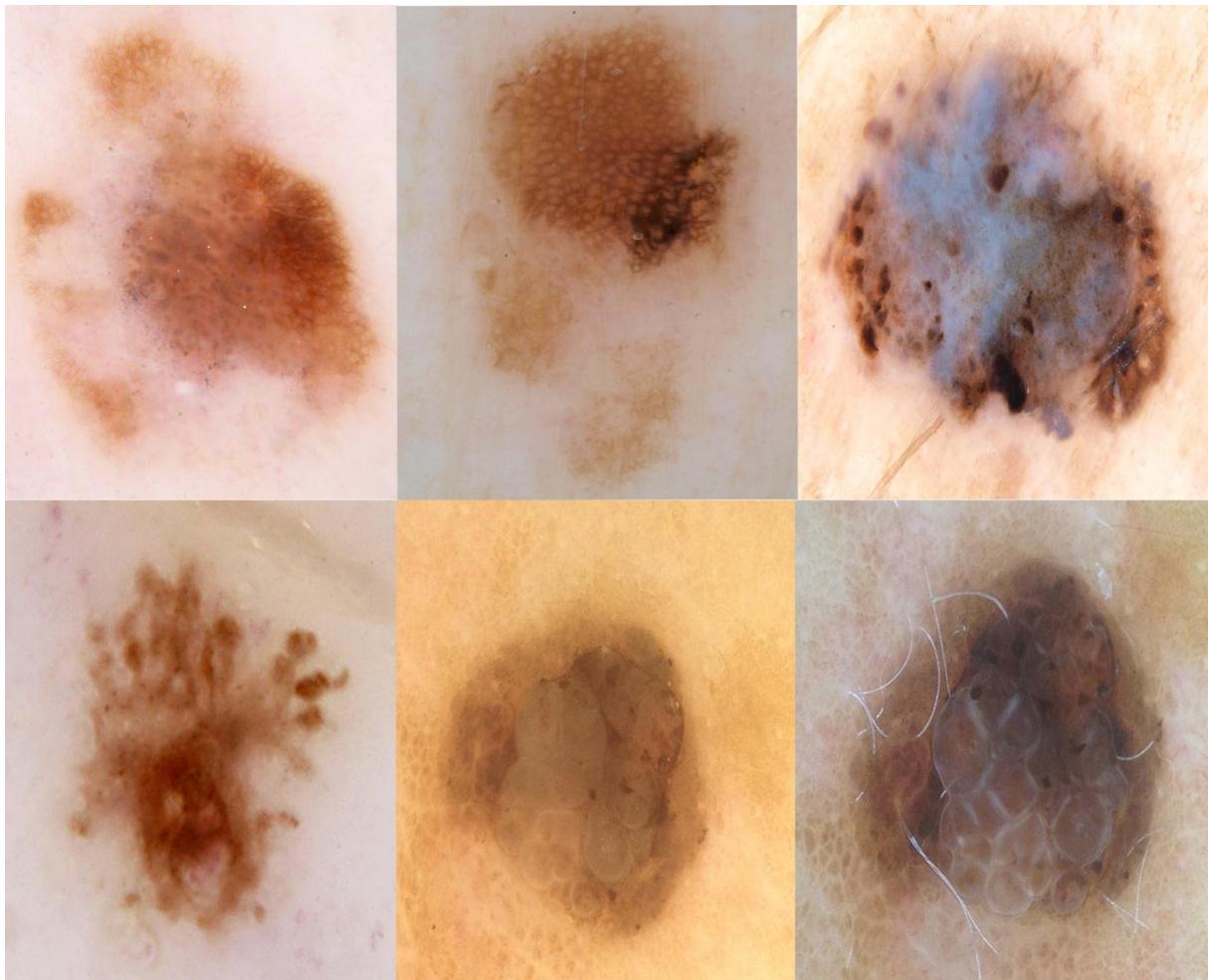


Figure 13: **Clues to melanoma:** Asymmetry plus: “grey dots” (upper-left); “thick lines reticular” and “eccentric structureless area light brown” (upper-centre); “eccentric structureless blue” and “black clods peripheral” (upper-right [7]); “lines radial and pseudopods, segmental” (lower-left); “polarising specific white lines” (lower-right with non-polarised dermatoscopy lower-centre [11]).

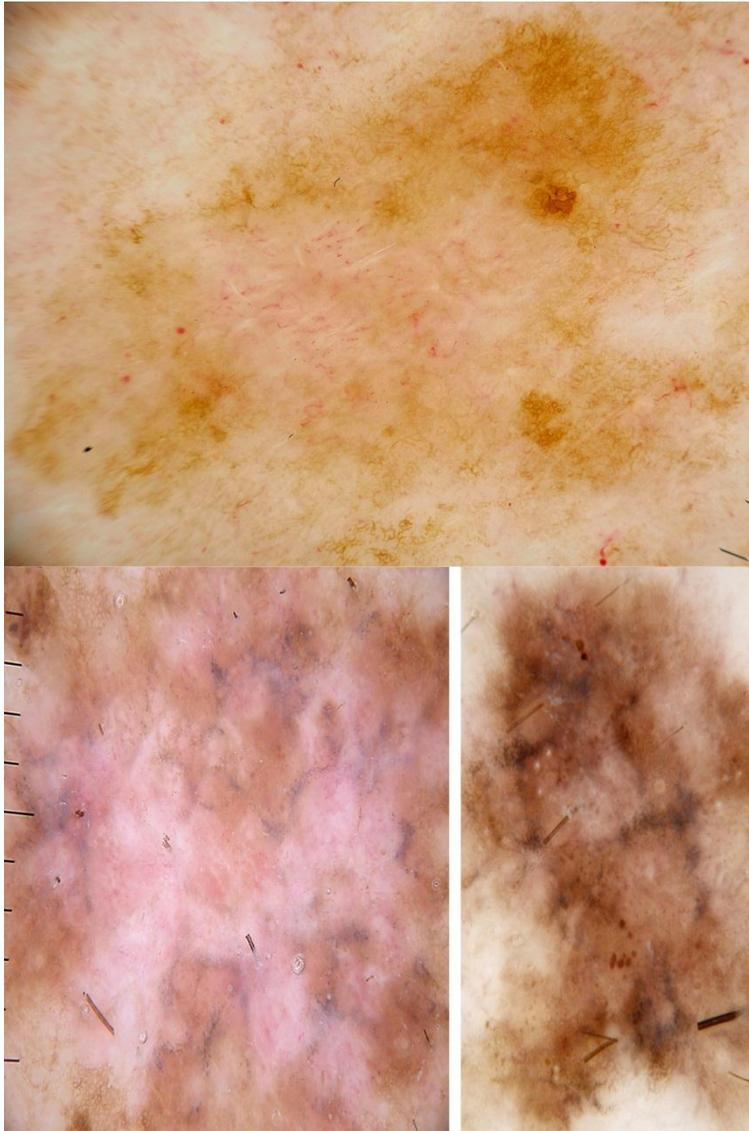


Figure 14: **Clues to melanoma:** Asymmetry plus: polymorphous vessels and polarising-specific white lines (upper); polygons (both lesions lower)

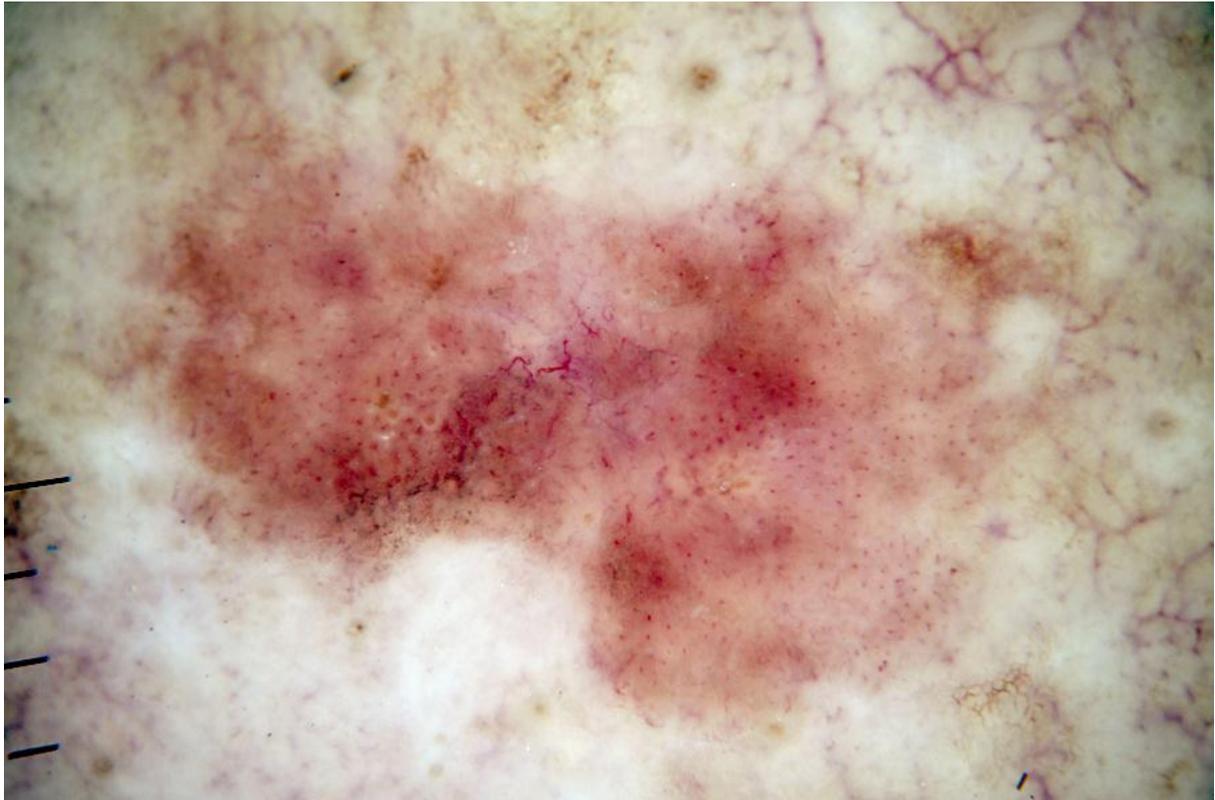


Figure 15: **Clues to melanoma:** a polymorphous pattern of vessels including a pattern of dot vessels. This lightly pigmented lesion has one pattern structureless, the small area of grey dots constituting a clue to malignancy although being insufficient for a pattern. In addition to the clues of asymmetry of colour (brown, grey, pink and white), this lesion has polymorphous vessels including patterns of both linear (serpentine) and dot vessels, pointing correctly to the diagnosis of (invasive) melanoma. Note the feature of peripheral structureless brown, this being reported as a clue to hypopigmented melanoma [12]. It should be noted that a significant proportion of melanomas, like this one, do not have any reticular lines.

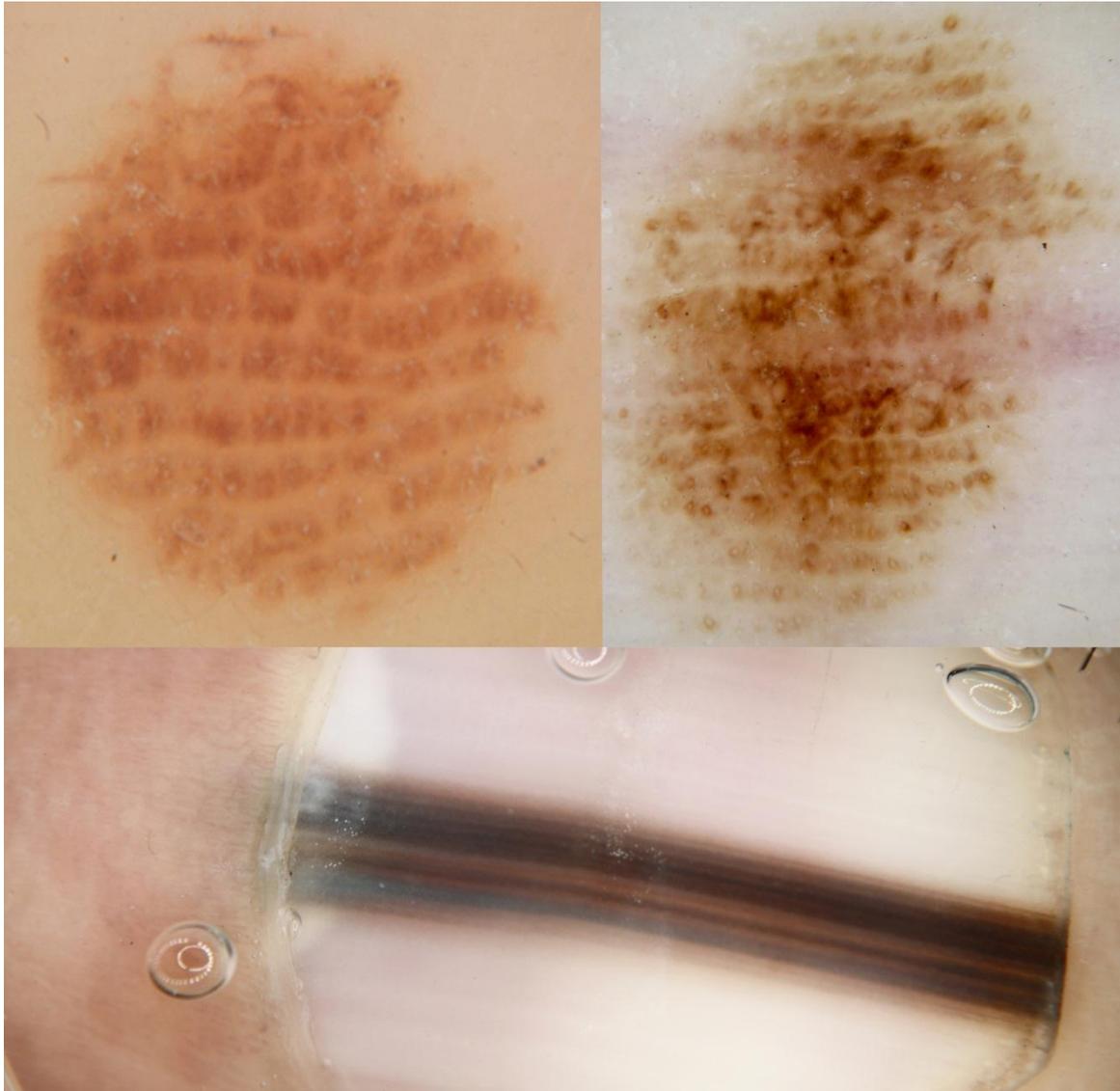


Figure 16: **Clues to melanoma on acral skin and the nail matrix:** The upper images are of patterns of parallel lines on the dermatoglyphic ridges on acral skin. Although the lesion on the upper-left was a corneal haemorrhage there were no satellite clods as a clue to that. The lesion had almost cleared after two weeks. The lesion on the upper-right was a small acral melanoma. The broad ridge pattern is best appreciated at the edges of the lesion, which is symmetrical. The lower lesion displays lines parallel varying in width, interval and colour (lines parallel chaotic) in the nail plate of a thumb and nail matrix biopsy confirmed the diagnosis on melanoma in situ.

Clues to BCC

Clues to BCC include lack of reticular lines plus one or more of: ulceration, blue or grey clods or dots, radial lines peripheral segmental converging, or radial lines central converging, and monomorphous serpentine or serpentine branched vessels. Basal cell carcinoma can also have polymorphous vessels but a polymorphous pattern including a pattern of dot vessels, makes the diagnosis of melanoma more likely. Polarising-specific white lines can support the diagnosis of both BCC and melanoma but they are much more frequently encountered in BCC.

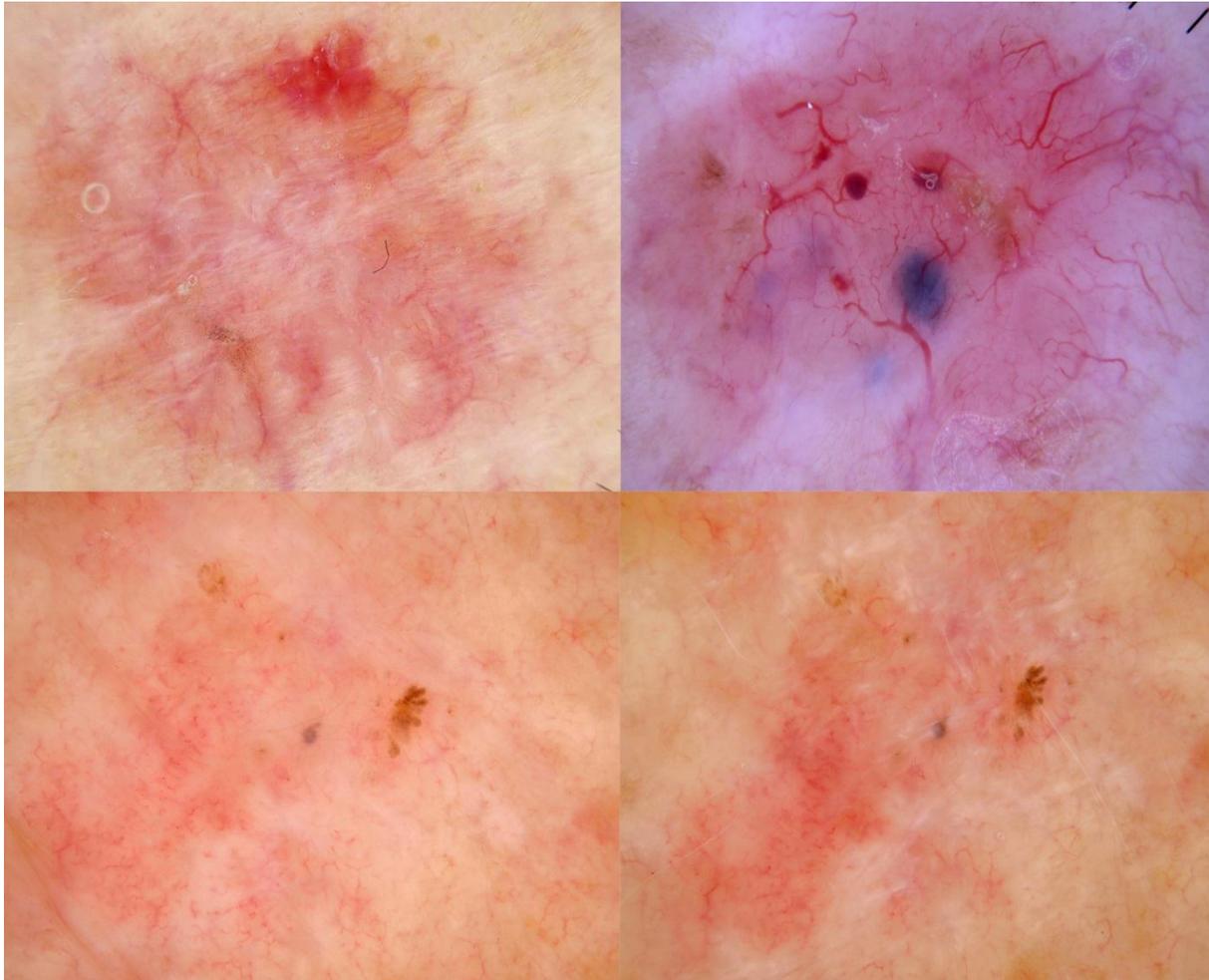


Figure 17: Clues to BCC include absence of reticular lines and: ulceration, polarising-specific white lines and linear serpentine vessels (upper-left). A small cluster of grey dots in the lower-left of the lesion makes this BCC pigmented for the purpose of analysis; blue clods and linear serpentine vessels in a branched arrangement with branches projecting from progressively thinner branches (upper-right); lines radial segmental converging which originate from a hypopigmented structureless area (lower-left) with the addition of polarising-specific white lines in the image lower-right of the same lesion taken with the dermatoscope in polarising mode.

Clues to pigmented SCC in situ

In a study of 52 consecutive cases of pigmented SCC in situ (pigmented Bowen's disease) the lesions were typified by the absence of a pattern of reticular lines and by the presence of a pattern of dots and/or structureless zones [13]. A single pattern was present in 53.8% with 48.1% being only structureless. Hypopigmented (pink, skin coloured or white) structureless areas were present in 67.3%. The presence of brown or grey dots in a linear arrangement was present in 21.2% and the presence of a linear arrangement of coiled vessels was present in 11.5%.

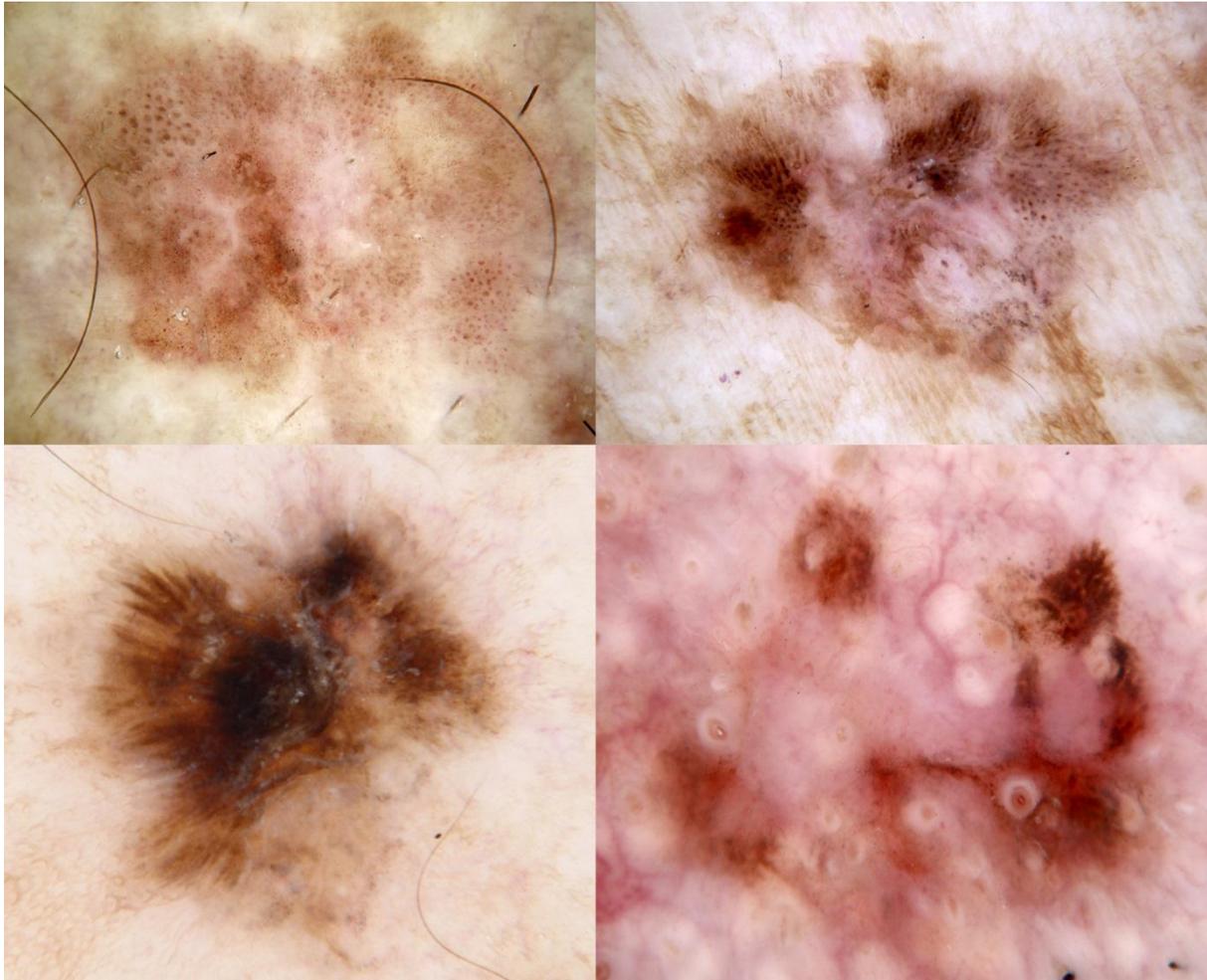


Figure 18: Four cases of pigmented SCC in situ: A pattern of brown dots in linear arrangement combined asymmetrically with a structureless area in the lower-left of the lesion (upper-left); a pattern of brown dots in linear arrangement combined asymmetrically with a structureless area in the lower half of the lesion (upper-right); a pattern of lines radial segmental composed of dots in linear arrangement, combined asymmetrically with a structureless area, partly hyperpigmented and partly hypopigmented (lower-left); a structureless pigmented lesion on the face with the clue of lines radial segmental on the upper-right of the lesion and the additional clues to SCC in situ on the face, of white circles, whiter than surrounding skin (lower-right).

Chaos and Clues: a decision algorithm for pigmented lesions based on revised pattern analysis

Revised pattern analysis is designed to lead to a provisional diagnosis in a logical stepwise process. Chaos and Clues is an algorithmic method which uses pattern analysis to guide the clinician in a stepwise process to the decision about whether (excision) biopsy is indicated [14].

The flowchart for the Chaos and Clues algorithm is shown in figure 19.

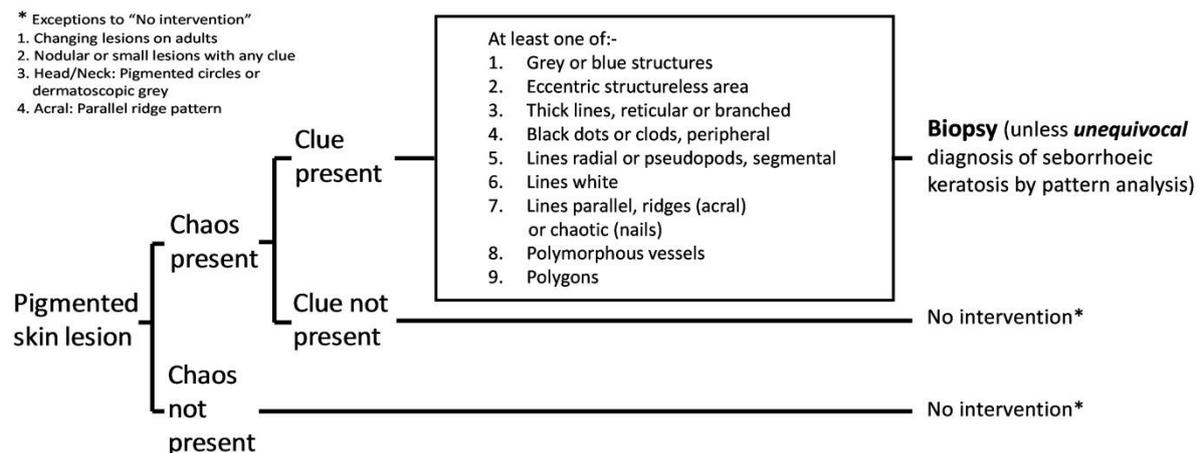


Figure 19: Flowchart for the chaos and clues algorithm. Pigmented lesions are first assessed for the presence of chaos (defined as dermatoscopic asymmetry of pattern and/or colour) and if chaos is present they are examined for any one or more of nine clues to malignancy. If a clue is present an adequate biopsy is considered unless an unequivocal diagnosis of seborrhoeic keratosis can be made by pattern analysis. There are four exceptions in which biopsy is considered even for non-chaotic lesions: any changing lesion on an adult, a nodular or small (<6mm) lesion which has any clue to malignancy, any lesion on the head or neck with either pigmented circles or dermatoscopic grey colour and any acral lesion with a parallel ridge pattern.

Chaos

Chaos is defined as the presence of dermatoscopic asymmetry of pattern and/or colour and it is assessed by the method described for revised pattern analysis. Any irregularity of the shape of a lesion is not relevant. Chaos of pattern requires that there be more than one pattern (a pattern covering a significant area of the lesion defined as at least 20%) with the patterns being combined asymmetrically. Chaos of colour requires that there be more than one colour (light and dark brown being regarded as different colours if the transition between them is abrupt), with those colours being combined asymmetrically. By definition if there is one pattern and one colour there can be no chaos. While natural laws (gravity, electrical and magnetic fields, surface tension and feed-back mechanisms) favour symmetry, malignant tissue defies natural laws and this is the basis for both dermatopathological and dermatoscopic chaos in malignant tissue.

Another feature which is an additional property of many malignant chaotic lesions is chaos of border abruptness*. While border abruptness is assessed in the ABCD method of dermatoscopy, this is given most significance in that method when the total border is abrupt. The ABCD method would

therefore allocate the highest score for border abruptness to an ink-spot lentigo or solar lentigo (see figure 4 right). Chaos of border abruptness is seen when parts of the border are abrupt and parts gradual (see all of the melanomas in figure 13 top row) and when this variation is asymmetrical. *Chaos of border abruptness is regarded as supporting evidence for malignancy, rather than as defining chaos. For the purpose of this algorithm, chaos is defined only by pattern and colour.*

* Chaos of border abruptness was first recognized and described by Francis Drugge, the 12 year old son of dermatologist, Rhett Drugge (Stanford, Connecticut, USA).

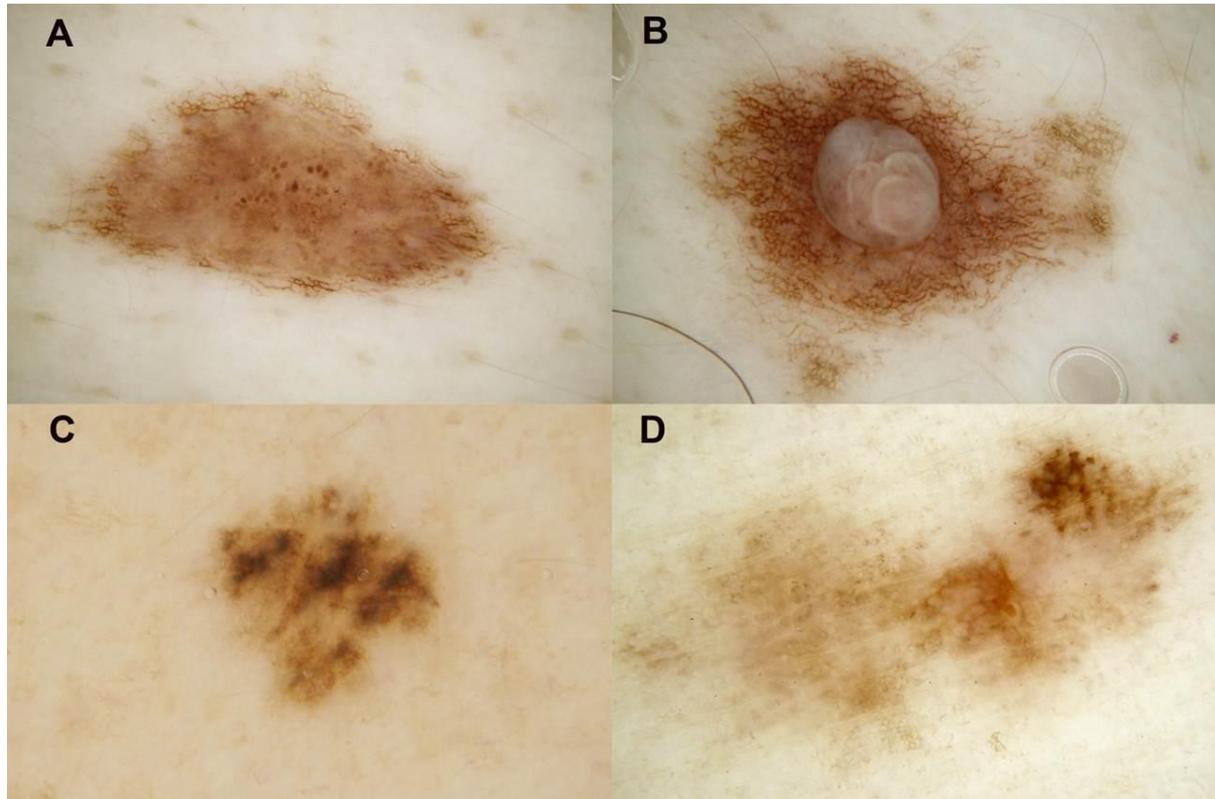


Figure 20: Assessment for the presence of chaos of four different lesions on the same patient: A- A concentric non-chaotic pattern with clods centrally surrounded by a structureless area which is surrounded by a pattern of lines; B- A concentric non-chaotic pattern with skin-coloured clods centrally and reticular lines peripherally. The shape of the lesion is irrelevant; C- A non-chaotic structureless pattern, hyper-pigmented centrally with relatively hypopigmented areas at the upper and lower extremities; D- A chaotic lesion, in this case by both structure and colour. This is also the only lesion with chaos of border abruptness, a feature which is recognised as a supporting clue to malignancy, rather than as a component of chaos as it is defined. Lesions A, B and C have not been excised but they have the morphology of congenital nevi. Lesion D, being chaotic and with the clue of pseudopods, was a melanoma in situ.

Clues

- 1. Grey or blue structures** (including grey or blue structureless). This clue, in a chaotic lesion, applies to both melanocytic and non-melanocytic malignancies. Grey colour is the most sensitive clue to malignancy and is seen in most in situ melanomas and many pBCC and pSCC. See figure 2, figure 13 upper-left, figure 14 lower images, figure 15, figure 16 lower image, figure 17 lower images and figure 18.
Blue colour correlates with pigment in the deep dermis, most commonly in melanocytes or nests of BCC. See figure 13 upper right and figure 17 upper right.
- 2. An Eccentric structureless area** *must cover a sufficient portion of the lesion for it to form a pattern, it must be contrasted to a structured pattern which is also within the lesion and it must be a colour other than skin-coloured.* If coloured with the colours of melanin it may have been produced by the chaotic behaviour of malignant melanocytes, if pink it is may be caused by increased blood flow and if white it may correlate with fibrosis after regression. This clue applies to both melanocytic and non-melanocytic malignancies.
See figure 2, figure 13 upper row, figure 20 D
- 3. Thick lines reticular** are defined when the lines are at least as thick as the holes that they surround and in melanocytic lesions they may correlate with rete ridges which are widened by pigment laden malignant melanocytes. They are a clue to malignancy in a chaotic lesion and will be focal rather than widespread evenly over the lesion. This clue is specific to melanoma as the presence of reticular lines rules out the diagnosis of BCC or SCC. Thick reticular lines frequently occur in seborrhoeic keratoses due to acanthotic rete ridges (due to a proliferation of keratinocytes) but they will be widespread and other clues to seborrhoeic keratosis will be present.
See figure 13 upper-middle.
- 4. Black dots and clods, peripheral**, correlate with pigmented pagetoid melanocytes and nests of melanocytes in melanomas and therefore this clue should be specific to melanomas. In reality, because dots are common in both pBCC and pSCC in situ, and because grey may be perceived as black, this clue can also be seen in those lesions. The reason for the designation that they be peripherally located is because black dots can be seen centrally in nevi which have been traumatised, correlating with pigment in ascending keratinocytes. Pagetoid spread can occur anywhere in a melanoma so when black dots or clods are seen peripherally they are regarded as a clue to malignancy.
See figure 13 upper right
- 5. Lines radial or pseudopods, segmental** are clues to malignancy, pseudopods being specific to melanoma and lines radial segmental being found in all three pigmented malignancies. In melanomas these structures correlate with fascicles of pigmented melanocytes extending from the periphery of a lesion and they signify growth. In melanomas they should be distributed asymmetrically and should extend from reticular lines, clods or structureless areas of equivalently dense pigmentation to the radial lines or pseudopods (see figure 13 bottom-left and figure 20 D). This can sometimes distinguish them from the radial lines seen in BCCs, which may project from hypopigmented structureless areas (see figure 17 bottom row). Lines radial segmental are also seen in pSCC in situ and they are usually created by dots in a linear arrangement (see figure 13 lower left and figure 18 upper-right and lower row)

6. **White lines** must be whiter than normal surrounding skin and they may be polarising-specific (polarising-specific blue lines have the same significance) or alternatively white lines that are seen with both modalities. Polarising specific white lines are shiny white lines orientated perpendicularly to each other but not crossing. They are only seen with polarising dermatoscopy but they may correlate with reticular white lines seen with non-polarised dermatoscopy. Polarising-specific white lines can be seen very commonly in BCC (pigmented or non-pigmented) and they are not unusual in melanoma (pigmented or non-pigmented). They are only rarely seen in pSCC in situ. They are also commonly seen in both DF and Spitz nevi but their presence is not expected in any other type of nevus (unless traumatised) or in seborrhoeic keratoses.

See figure 13 bottom right and figure 17 lower right.

7. **Polymorphous vessels** are a clue to both melanoma and pBCC but not to pSCC in situ. Pigmented BCC often has a monomorphous pattern of serpentine or serpentine branched vessels but it may have a pattern of polymorphous linear vessels, especially on the lower limb. A pattern of dot vessels is not expected in pBCC but ulceration, commonly present in BCC, and associated keratinisation may produce polymorphous vessels including looped vessels in radial arrangement and even dot vessels. In melanomas polymorphous vessels may include various types of linear vessels in raised portions, and a pattern of dot vessel as well as any pattern of linear vessel in macular portions. Generally other clues apart from polymorphous vessels (pigment clues and/or white lines) are expected in a melanoma and the vessel clues are then useful in differentiating melanoma from pBCC and pSCC in situ. Pigmented SCC in situ is expected to have a monomorphous pattern of coiled vessels which may resolve as dots depending on visual acuity.

See figure 15.

8. **Polygons** are defined as geometric polygonal shapes, complete or incomplete, bounded by straight lines, or by a straight pigment interface, meeting at angles and larger than the holes caused by individual follicles and larger by far than the holes bounded by reticular lines. This clue, in a chaotic lesion, is a valuable clue to melanoma but may also rarely be seen in pBCC. See figure 14 lower row.

9. **Lines parallel on the ridges (acral) or lines parallel chaotic on the nails**, is a clue to melanoma specifically on acral skin or in nail matrix respectively. This is the only one of the listed clues to malignancy which is specific to a particular anatomical site. It is important to remember that the longer an acral or nail-matrix melanoma remains untreated; the more likely it is to develop any of the other clues to melanoma. Melanoma may also arise in an acral naevus in which case any of the other 8 clues will override a benign parallel furrow pattern which may be present.

See figure 16 upper-right and lower.

Exceptions

Chaos and clues was tested on a consecutive series of pigmented lesions, the majority of melanomas in the series being in situ, and was found to have a diagnostic sensitivity of 90.6% (BCC 98.5%, SCC 86.5%, melanoma 79.3%) with a specificity of 62.7% for the diagnosis of malignancy, any type [15]. In an attempt to move the sensitivity closer to 100% the following exceptions are included, to *consider* lesions for biopsy, even if not chaotic:

1. Any changing lesion on an adult. This includes a lesion with a history of change, lesions with monitored change and lesions with dermatoscopic clues to change such as the presence of peripheral clods (see figure 11 middle and right) or symmetrical radial lines/pseudopods. The presence of peripheral clods must be considered in the context of the age of the patient. Peripheral clods in an otherwise unremarkable lesion with the morphology of a naevus, is consistent with the diagnosis of a growing naevus under the age of 30 but not over the age of 50. In between these ages the clues must be weighed and discretion exercised and if doubt remains then excision biopsy is prudent.
2. A nodular or small lesion which has any of the clues to malignancy. We define small, arbitrarily, as less than 6mm in diameter, this being the size cited in the clinical ABCD method of dermatoscopy(see figure 11 right: this 3mm diameter nodular melanoma was arguably symmetrical but in addition to peripheral clods as a dermatoscopic clue to change, it had the clue of grey colour).

*This particular exception should only be applied with respect to **small** lesions if there is an additional significant cause for concern.* Many naevi have grey colour or even patterns that could be interpreted as polygons, but if they are non-chaotic and a gradual border supports the diagnosis of naevus, there being no historical information to cause concern, a biopsy is *not* indicated. Also the common lesion, DF, is a small nodular lesion which frequently has central polarising-specific white lines and if DF can be diagnosed confidently by clinical and dermatoscopic criteria excision biopsy is not necessary.

3. Any lesion on the head or neck with pigmented circles and/or any dermatoscopic grey. This clue acknowledges that fact that young melanomas at these locations, possibly related to a physical barrier effect of numerous follicles, may be symmetrical (See figure 7 left).
4. Any lesion on acral skin with a parallel ridge pattern. This clue acknowledges that fact that young melanomas at these locations, possibly related to a physical barrier effect of numerous eccrine ducts, may be symmetrical (See figure 16 upper-right).

Chaos and clues is not a method designed for robots and it should not be regarded as an ultimate method, set in stone. It has been designed as a useful tool, avoiding tedious mathematical calculations, unburdened by a language of innumerable poorly defined metaphorical terms carrying preconceived diagnostic implications and it is suitable for seamless integration into routine practice. Individuals are encouraged to use it as a framework on which to organise their accumulated experience as they individualise the method for their own style and practice.

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