# Clinicopathologically Defined Naevus Subtypes and **Associated Melanoma Risk**

Clauwaert V<sup>1,2</sup>, Verhaeghe E<sup>2</sup>, De Schepper S<sup>2</sup>, Haspeslagh M<sup>1,2</sup>, Brochez L<sup>2,3</sup>

<sup>1</sup> Dermpat, Ghent, Belgium <sup>2</sup> Department of Dermatology, University Hospital Ghent, Belgium <sup>3</sup> Cancer Research Institute Ghent, Belgium

#### Introduction

- The technique of ex vivo dermoscopy and derm dotting (EVD-DD) allows targeted sectioning of skin biopsies. In this way, atypical dermoscopical features can be marked and selected for histopathological examination. This improves diagnostic accuracy and efficiency drastically.
- A large collection of mainly flat naevi that were excised for displaying suspicious dermoscopical features were processed and divided into 12 naevus subtypes through the EVD-DD method. These subtypes were compared in terms of associated age, gender, location and diameter.
- Moreover, we examined whether the subtypes differ in terms of relative risk. On the one hand, we examined the frequency of a positive melanoma history among their patient groups to identify potential melanoma markers, and on the other hand, we examined histological atypia and melanoma occurrence within naevi to identify potential melanoma precursors.

#### Ex vivo dermoscopy





#### **Conclusion**

- Based on targeted sectioning through EVD-DD, we differentiate 12 mainly flat naevus subtypes in a collection of more than 7000 excised, clinically suspicious naevi.
- These naevus subtypes differ significantly in associated age and gender of the patient, as well as location and diameter of the lesion.
- Our results show significant differences in histological atypia and melanoma risk among these subtypes. Notably, atypical lentiginous naevi and orange pulverocytic flat naevi are associated with higher proportions of (severe) atypia and melanoma within the lesion, as well as higher proportions of a positive melanoma history among their patients. Hypermelanotic naevi however, accounting for about half of the collection, infrequently demonstrate atypia and
- We believe these subtypes may reflect different tumoural and/or germline genetic entities with different risk of melanoma development. The clinician may discriminate these subtypes dermoscopically and based on demographic information.
- Further research of these subtypes (including genetic testing) can lead to better follow-up of high-risk patients, less unnecessary excisions and new insights in melanoma pathogenesis.

### Naevus subtypes

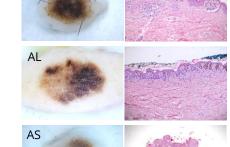
Most commonly excised subtypes (N ≥ 100)

Actively growing naevus (N = 213)

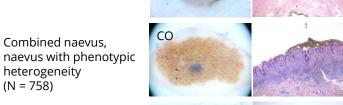
Atypical lentiginous

(N = 102)

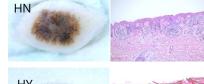
naevus of the elderly



Naevus with asymmetrical shoulder (N = 137)

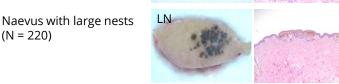


Hypermelanotic naevus, mainly nested (N = 232)



Hypermelanotic naevus, mainly lentiginous (N = 3377)

(N = 220)



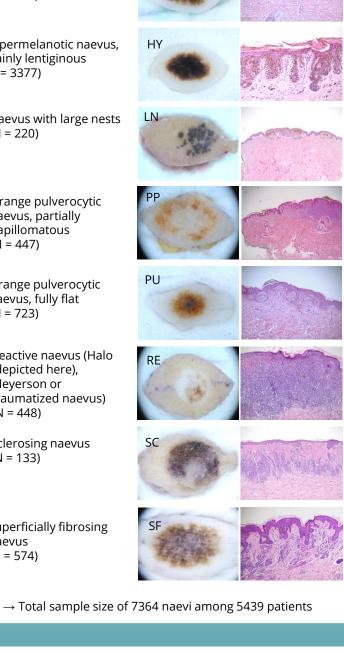
Orange pulverocytic naevus, partially papillomatous (N = 447)



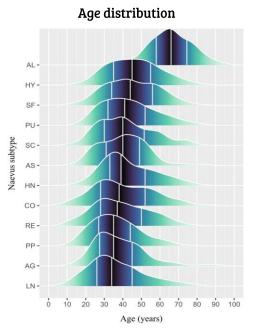
Reactive naevus (Halo (depicted here), Meyerson or traumatized naevus) (N = 448)

Sclerosing naevus (N = 133)

Superficially fibrosing (N = 574)

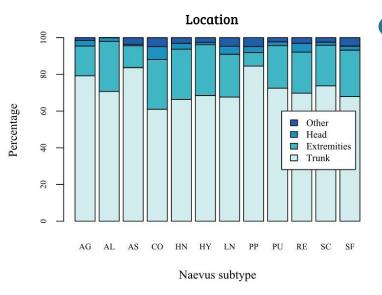


## Clinicopathological data



#### Gender

The majority of subtypes occurred more often on women. Atypical lentiginous naevi however, are more often found on men. Four subtypes have almost equal gender proportions. These include sclerosing, actively growing, reactive and fibrosing naevi. In general, there are more women in our patient population (dashed line).

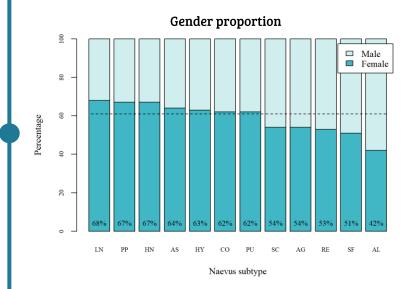


#### Diameter

In general, median diameter was 5mm. Significantly smaller subtypes included hypermelanotic and actively growing naevi (median 4 and 4.5 mm respectively). On the contrary, pulverocytic papillomatous naevi and atypical lentiginous naevi significantly larger (median 7 and 8mm).

#### Age

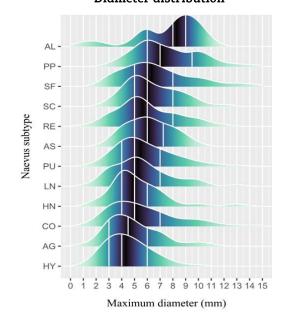
Median age at excision was 42 years in general. Naevi with large nests, actively growing naevi and pulverocytic papillomatous naevi occurred on younger patients (median ±35 years). On the other hand, pulverocytic flat naevi, fibrosing naevi and hypermelanotic naevi were found on significantly older patients (median ≥ 40 years). Atypical lentiginous naevi were observed in a substantially older group (median 66 years).



#### Location

In total, 68% was located on the trunk, 24% on extremities, 2% on the head, 3% on other locations (folds, anogenital, special, acral) and in 3% location was unspecified. Pulverocytic papillomatous naevi occurred significantly more often on the trunk and combined naevi more often on extremities.

#### Diameter distribution

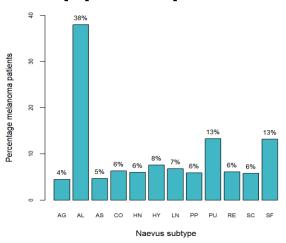


### Melanoma risk

#### Melanoma history among patients

Among patients with atypical lentiginous naevi, pulverocytic flat naevi and fibrosing naevi, there are significantly more patients with a positive melanoma history (38%, 13% and 13% respectively). Hence, these subtypes could be regarded as melanoma markers.

Patient proportion with a positive melanoma history



#### Histological atypia and melanoma occurrence within naevi

Atypical lentiginous naevi and pulverocytic flat naevi display high levels of histological atypia. Moreover, among these subtypes there is high occurrence of melanoma within the lesion (21 and 5% of cases respectively). Hence, these subtypes could be regarded as melanoma precursors. Pulverocytic naevi are more often associated with superficially spreading melanomas, while atypical lentiginous naevi co-occur more often with lentiginous melanoma type.

In our population, melanoma incidence is significantly higher within atypical lentiginous naevi and pulverocytic flat naevi compared to the others, independent of age and gender. Respective odds ratios and 95% credibility

