# AA015 - Predictive models of melanoma metastasis based on dermatoscopy. An international human reader study

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#### Introduction

- Current melanoma prognosis tools have limited clinical utility, highlighting the need for more effective biomarkers<sup>1</sup>.
- Dermatoscopy is a non-invasive examination that correlates with established prognostic markers obtained through invasive procedures, such as Breslow thickness and ulceration<sup>2</sup>.
- However, the evidence directly linking specific dermatoscopic structures to melanoma spread at locoregional or distant sites remains limited.

### Methodology

#### Setting and study design – inclusion criteria

- Patients with cutaneous melanoma with pathologic stage IB and above (AJCC 8<sup>th</sup> edition)
- Available dermatoscopic image of the primary tumor
- Sufficient follow-up time for metastasis development (minimum follow-up of 36 months for non-metastatic lesions).

#### **Procedures**

Procedures of the study and the workflow are presented in Figure 1.

#### Outcomes

- **Primary**: to investigate the association between dermatoscopic features of primary melanoma and metastasis of any type (either regional or distant metastatic spread).
- **Secondary**: to develop 3 models and to compare their accuracy of metastasis prediction:
- 1) Model 1: a model based on dermatoscopy
- 2) Model 2: a model incorporating Breslow thickness and ulceration
- 3) Model 3: a combined model integrating both dermatoscopic and histologic predictors Also, to compare the diagnostic accuracy of all three models in predicting recurrence-free survival (RFS) and distant metastasis-free survival (DMFS) in early-stage tumors at diagnosis.

#### **Statistical analysis:**

- Risk of metastasis and RFS/DMFS was assessed by multivariable logistic and Cox regression analysis, respectively.
- Dataset split into training and test sets, stratified by TNM stage, age, and sex was conducted. A 5-fold cross-validation approach was applied to the training set, followed by independent validation in the test set.
- Accuracy of the models was expressed as the Area under Curve (AUC) and DeLong's method was used to compared AUC values.

# Results

### **Baseline characteristics**

- 524 patients with cutaneous melanoma were included.
- Metastasis occurred in 222 patients (42.4%), either at the time of initial diagnosis or during the follow-up period (median follow-up 50 months (range: 1-228 months).

#### **Reader analysis**

- 776 dermatoscopic images of primary melanomas assessed by 30 readers [median of 104 images (range: 21–208) per reader].
- Interrater agreement ranged from *fair* (color assessment) to *moderate* (pigmentation grade, ulceration, and vascular structures).

### Dermatoscopic predictors of metastasis (Multivariable analysis) (Table)

- **Negative predictors**: heavy pigmentation, regression structures
- **Positive predictors**: extensive ulceration, blue-white veil

# Comparative analysis of the accuracy of models in predicting metastasis

- Model 1: AUC 0.798 (95%CI: 0.754 0.841)
- Model 2: AUC 0.768 (95%CI: 0.721 0.816)
- Model 3: AUC 0.826 (95%CI: 0.786 0.866)
- These patterns persisted during independent validation in the test set.

### **RFS - DMFS in early-stage melanoma**

- Model 1: extensive ulceration and blue-white veil (reduced RFS), extensive regression (increased RFS).
- Model 2: only Breslow thickness deemed a significant predictor,
- Model 3: Breslow thickness and dermatoscopic ulceration (reduced RFS).

# Accuracy for predicting RFS and DMFS (Figure 2,3)

**Training set**: similar AUC values for all three models in RFS and DMFS. **Test set**: Model 3 showed a numerically higher AUC compared to Models 1 and 2.





#### Table: Multivariable analysis for the prediction of metastasis based on dermatoscopy (N=524)

	Model 1		Model 2		Model 3	
	OR	95%CI	OR	95%CI	OR	95%CI
Breslow thickness	-	-	1.37	1.23 – 1.52	1.23	1.11 – 1.35
Ulceration	-	-	2.94	1.90 - 4.56	2.30	1.37 - 3.83
Pigmentation						
Absent	Ref.				Ref	
2	.5 0.89	0.38 - 2.06	-	-	1.03	0.43 - 2.49
5	0 0.42	0.17 - 1.01	-	-	0.54	0.21 - 1.37
7	0.12	0.05 - 0.30	-	-	0.20	0.08 - 0.51
10	0 0.07	0.03 - 0.15	-	-	0.10	0.04 - 0.25
Dermatoscopic Ulceration						
Absent	Ref.		-	-	Ref.	
1-49	1.56	0.95 - 2.56	-	-	1.15	0.67 – 1.95
>50	3.84	1.79 - 8.23	-	-	1.67	0.72 - 3.87
Regression structures						
Absent	Ref.		-	-	Ref.	
1-49	0.81	0.48 - 1.35	-	-	0.87	0.51149
>50	0.41	0.19 - 0.87	-	-	0.35	0.15 - 0.80
Blue – white ve	il 6.10	3.65 - 10.17	-	-	5.46	3.20 - 9.33

Figure 3: a) 1.1mm Breslow non-metastatic (heavy pigmentation b) 1.1mm Breslow metastatic with blue-white veil





# References

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