

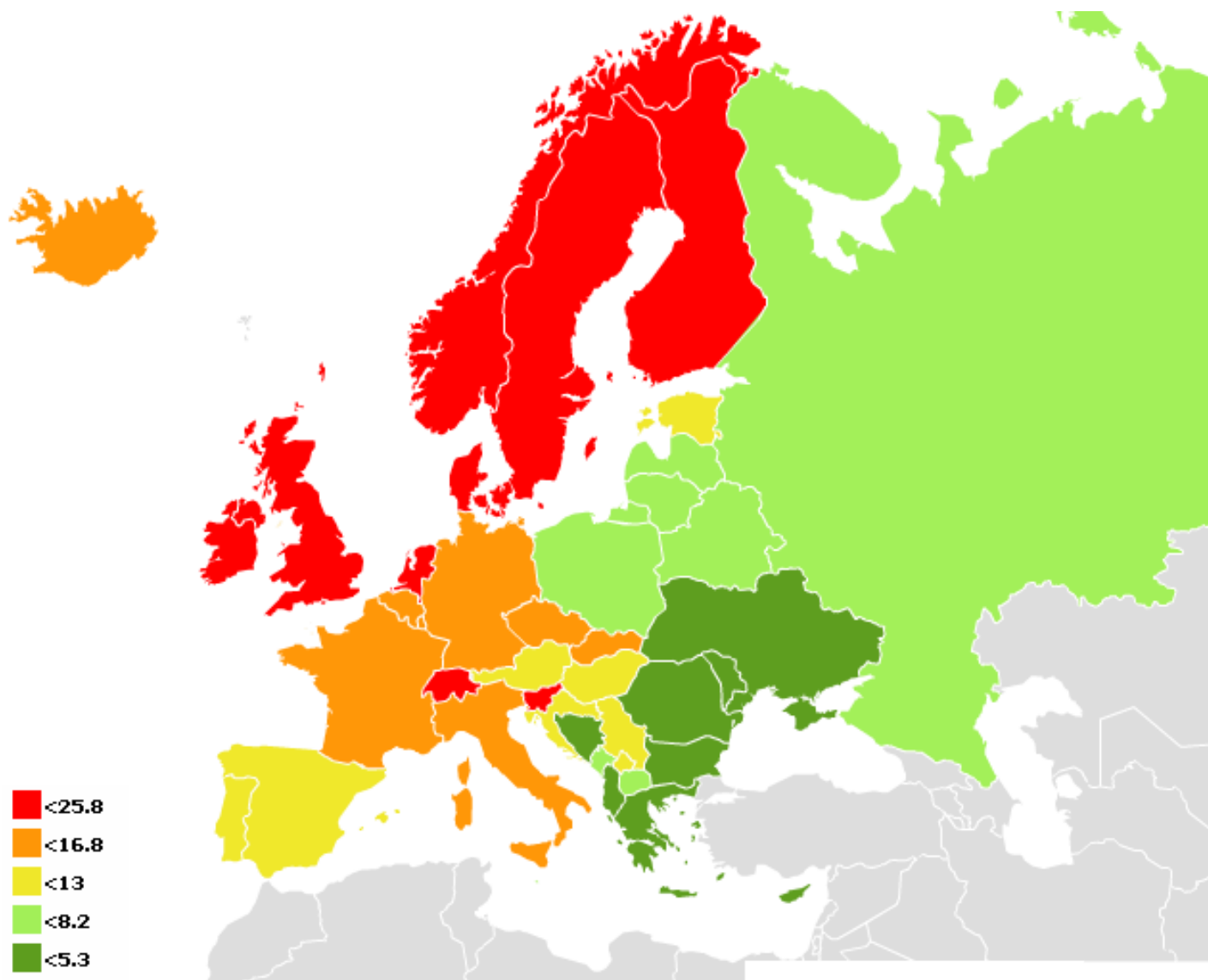
# Malignant Melanoma

Juraj Hegyi  
LF MU

- Originates from melanocytes
  - Melanin producing cells
  - Basal membrane, hair follicles
- 
- 8 most common malignant tumor in CR
  - In the last 30 years 4x increased incidence
  - 2500 new cases per annum (450 deaths)
  - Every 4 diagnosed patient <50r.
  - Cca 25.000 patients with dg. MM in anamn.

- Malignant melanoma is usually diagnosed early approx. 85%
- High 5 year survival rate
- Stage I. – 90/100 patients
- Stage IV. - 15/100 patients
  
- **Characteristic horizontal growth phase followed by penetrating vertical phase**
  
- Most cases Sweden, Estonia, Denmark, Holand and Australia.

# Standardized mortality of MM per 100 000 capita



- **Genetics**

- Mutation of CDKN2A, CDK4, MCN1
- Aneuploidia of chromosomes 1,6,7,9,10,11
- BRAF, N-RAS mutations

- **Enviromental factors (UVA, UVB)**

- Intermittent sun exposure (short but intensive) ↑
- Long term sun exposure (slow but steady) ↓
- Solariums +/-

- **Sensibilisation**

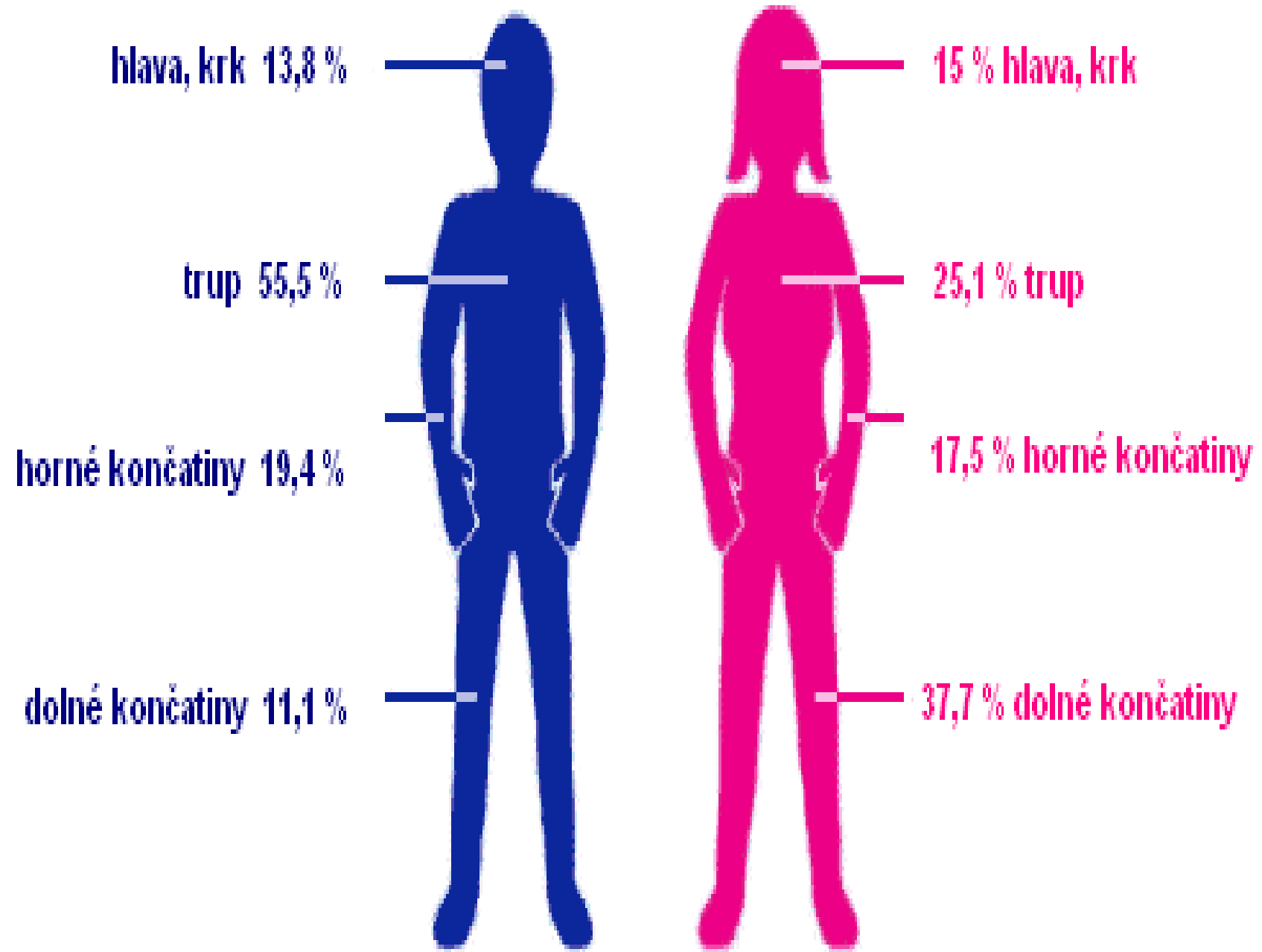
- Plants (furocoumarines, lime)
- Tar
- Medication (furosemide, diclofenac, TTC, ketoprofen)

- **Imunosupression**

- Transplanted patients
- Systemic treatment of autoimmune diseases

- **Ethnicity**

- Pale skin (phototype I. a II.) Pigmented nevi
- ↓ incidence in darker skin



# Most common forms of MM

- Superficial spreading melanoma (SSM)
- Nodular melanoma (NMM)
- Acral lentiginous melanoma (ALM)
- Lentigo maligna melanoma (LMM)



# Rarer types of MM

- Amelanotic melanoma
- Nevoid melanoma
- Malignant blue nevi
- Desmoplastic melanoma
- Mucous membrane melanoma
- Ocular melanoma
- Juvenile melanoma

# Superficial spreading melanoma (SSM)

- Most common form (approx. 70%)
- Often between 3 and 5 decade
- Women most often feet
- Men most often upper body
- Depigmentation (regression) – signs of interaction with immune system

# Superficial spreading melanoma (SSM)



# Superficial spreading melanoma (SSM)



# Nodular melanoma (NMM)

- 15-30% of all melanomas
- Often in 6 decade of life
- Chest, neck, face
- Blue or black nodules
- Often without horizontal phase

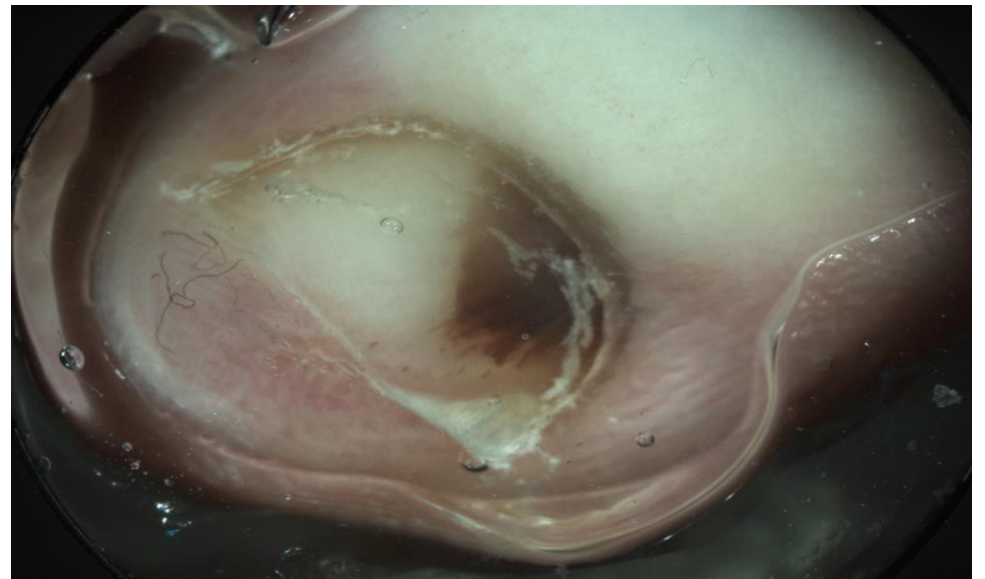
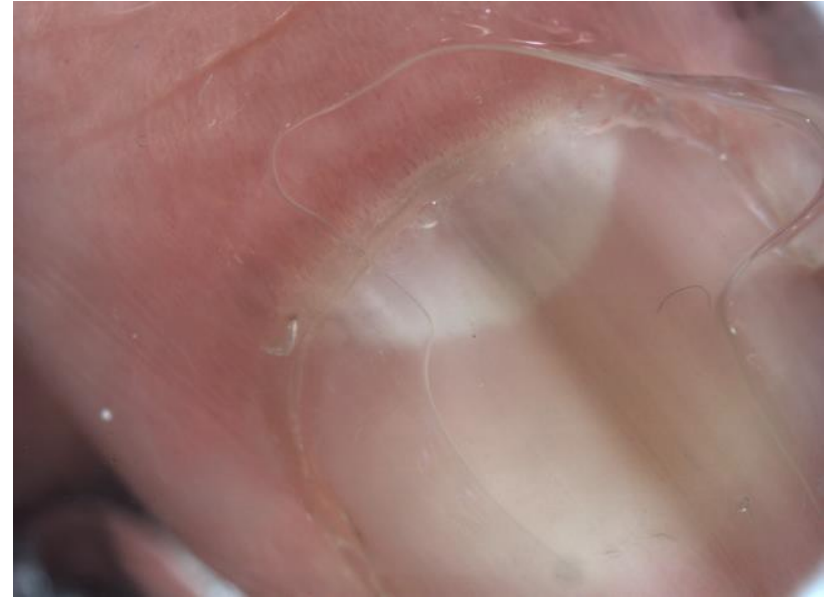
# Nodular melanoma (NMM)



# Acral lentiginous melanoma (ALM)

- Less common form of melanoma (5-10%)
- Most common form in asians and blacks (45%/70%)
- Palms, soles of feet, **nails**
- Due to location hard to diagnose

# Acral lentiginous melanoma (ALM)





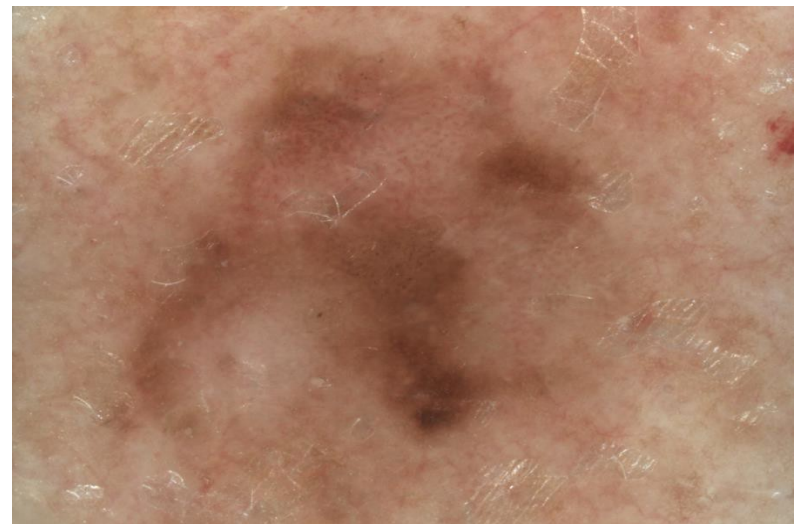
# Acral lentiginous melanoma (ALM)



# Lentigo maligna melanoma (LMM)

- Approx. 15% of all melanoma
- Locations of chronic sun damage
- Usually 7 decade of life
- Most often head, face and nose
- Differential diagnosis with sun damage

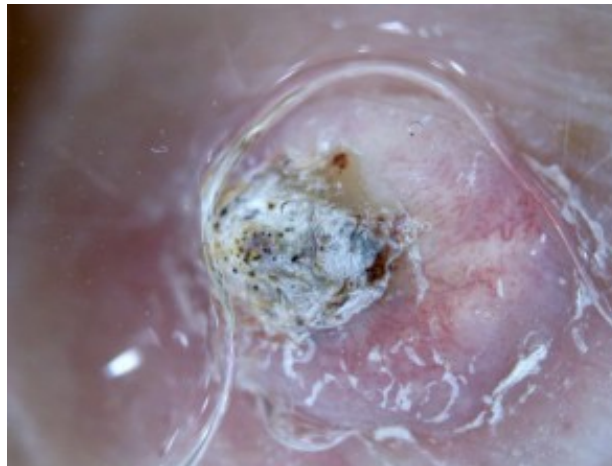
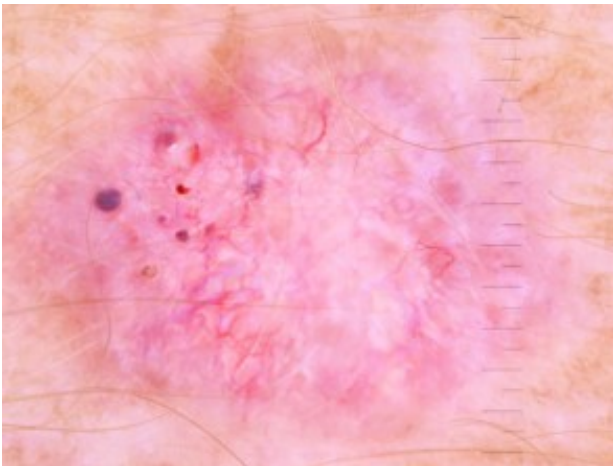
# Lentigo maligna melanoma (LMM)



# Amelanotic melanoma

- Rare form of pigmented
  - Approx. 2-20% of all diagnosed melanomas
- Often misdiagnosed (BCC, verruca, fibroma)
- Very hard to diagnose (3R method)
  - Raised
  - Red
  - Recent

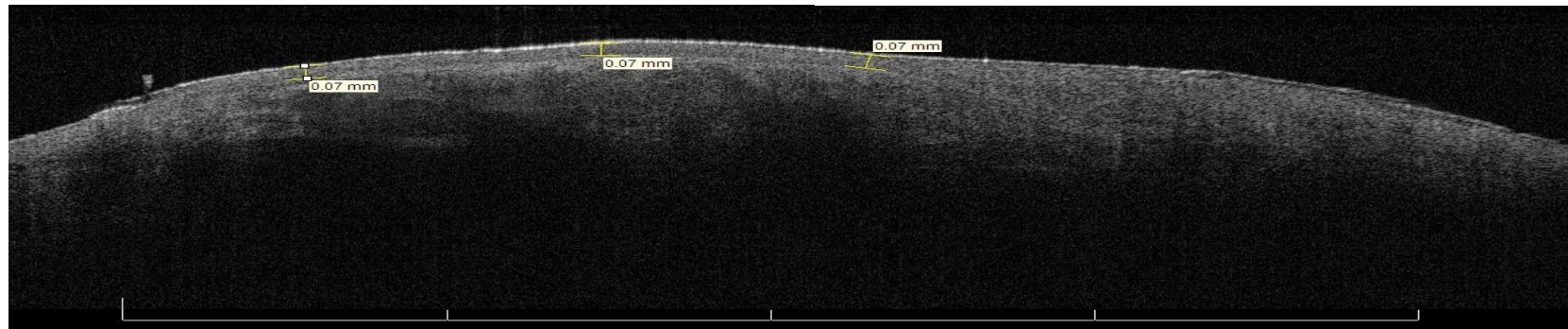
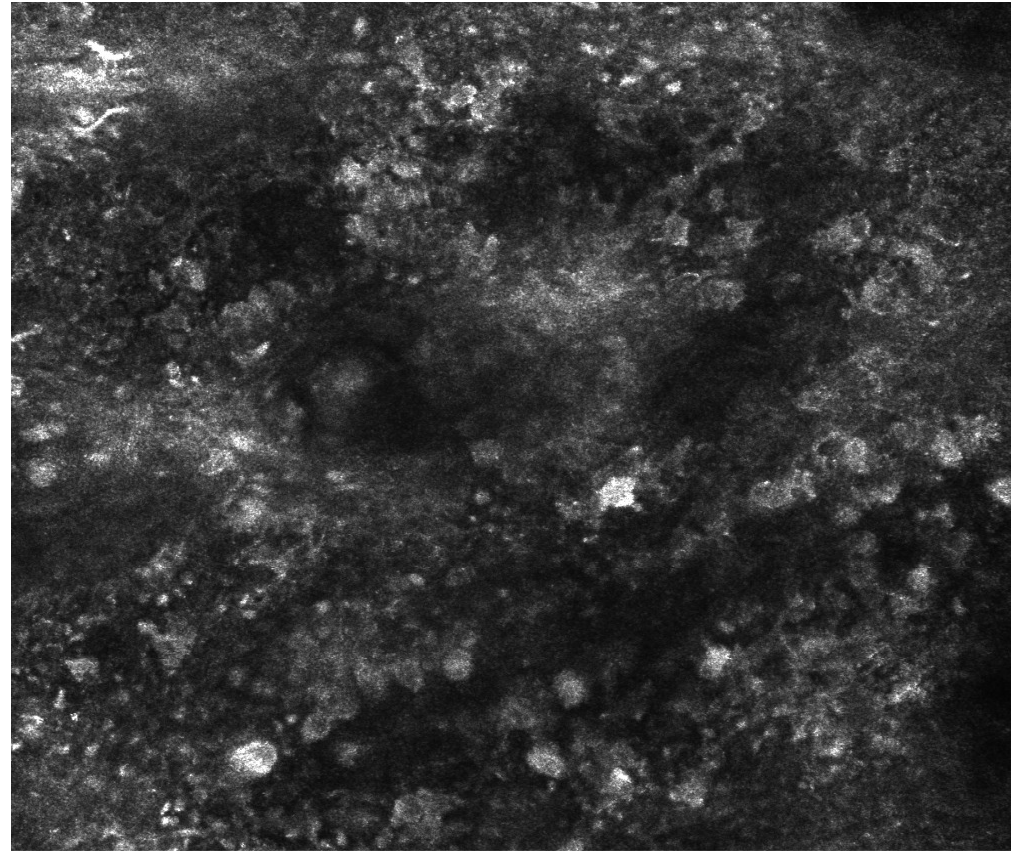
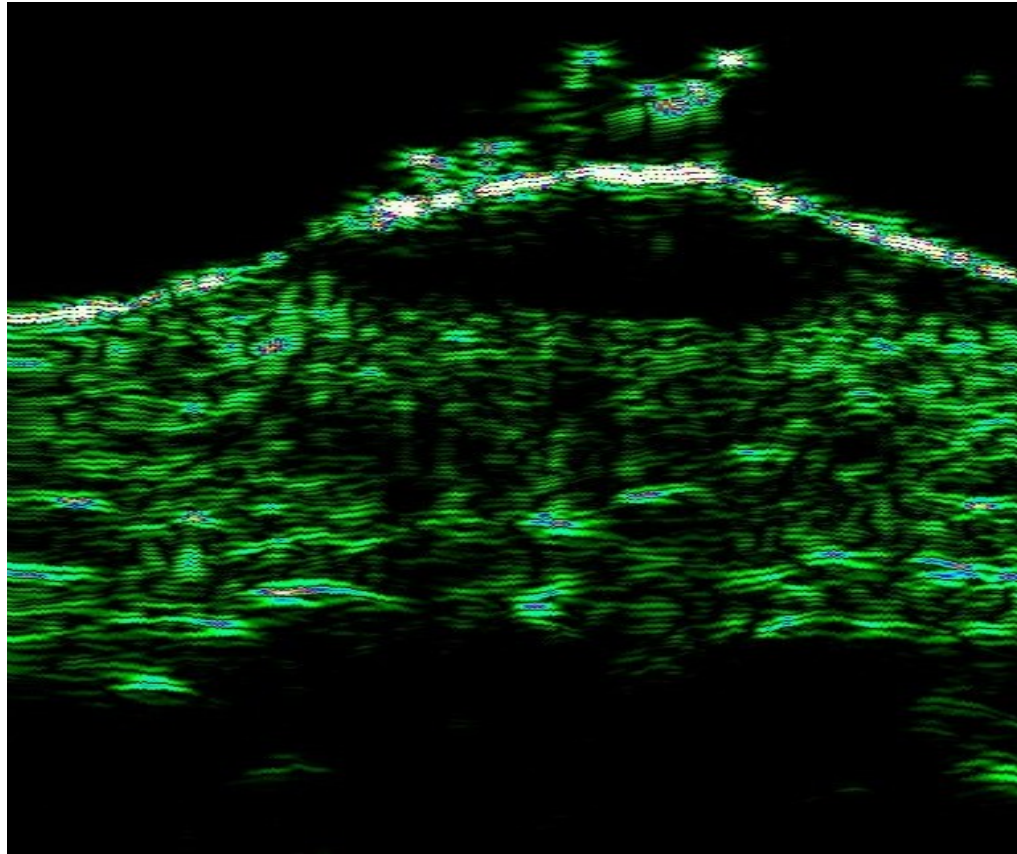
# Amelanotic melanoma



# Diagnosis of MM

- Clinical image (ABCDE rule)
- Medical history
- Dermoscopy
  
- Histological examination (excision/biopsy)
  - “When in doubt, cut it out”
- FISH – detection of chromosomal aberrations

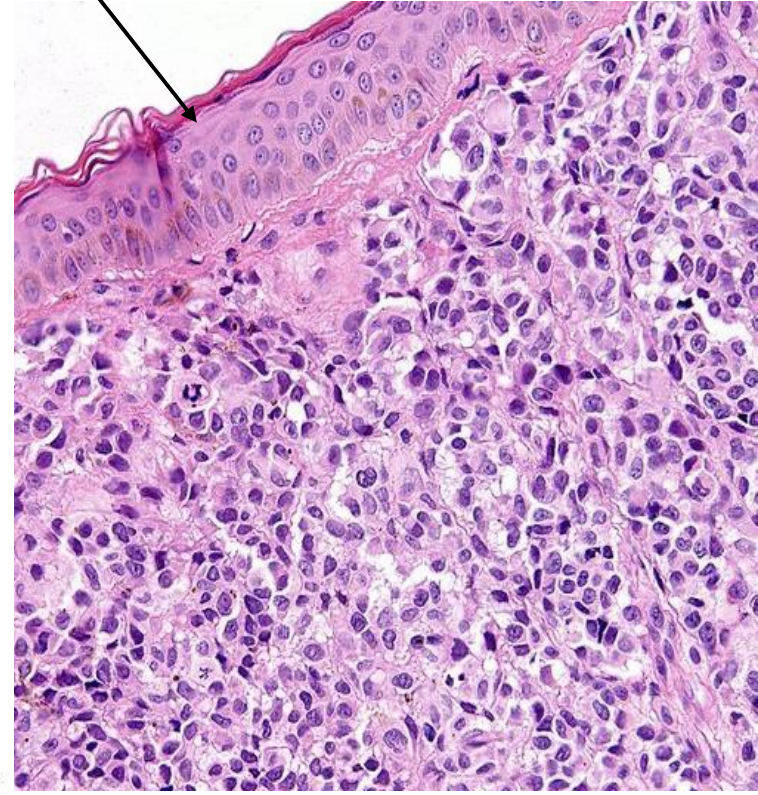
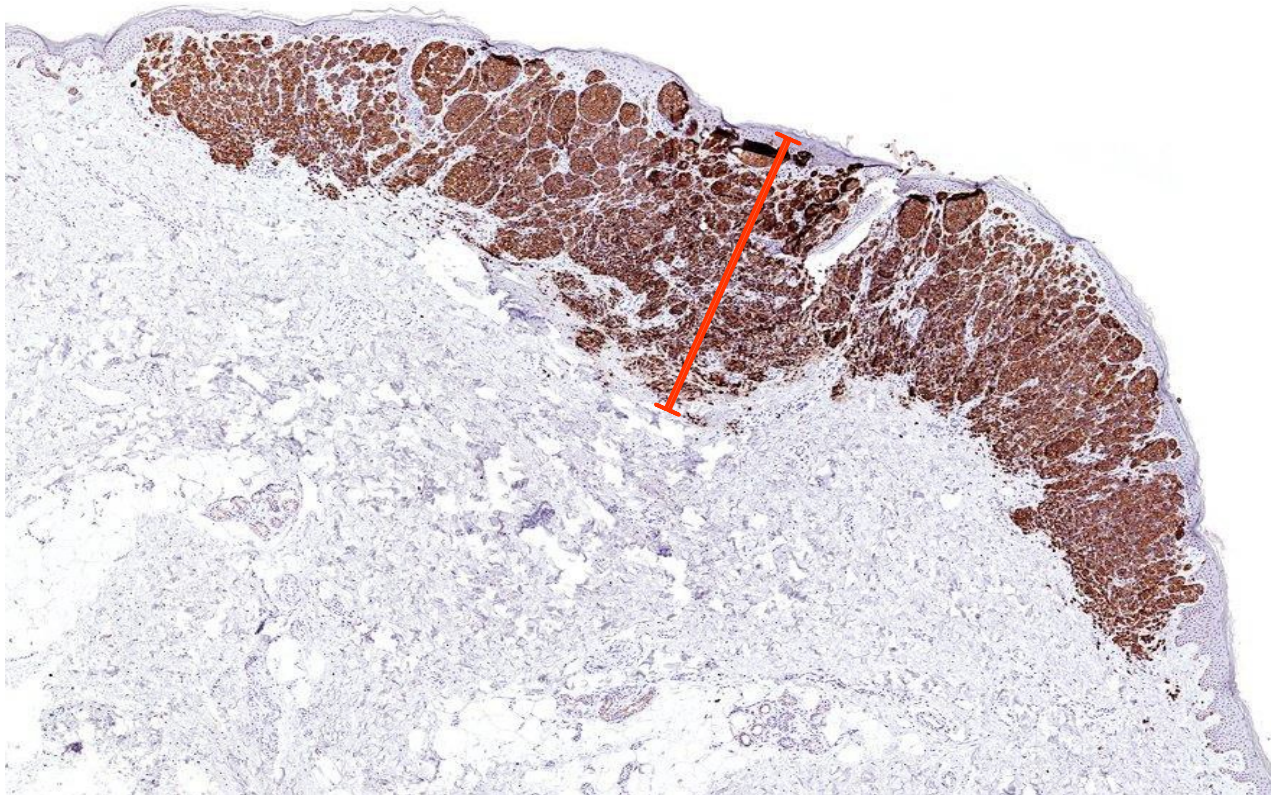
# Non invasive diagnosis



# Breslow scale

Breslow thickness is the measurement of the depth of the melanoma from the surface of the skin down through to the deepest point of the tumour.

Stratum granulosum





# Clark scale

- I. Only epidermis (Carcinoma in situ)
- II. down to papillary dermis
- III. papillary dermis involvement without reticular dermis invasion
- IV. reticular dermis involvement without subcutis invasion
- V. Da full monty

**TABLE 1**

**STAGES OF MELANOMA**

Stage	T	N	M
<b>0</b>	Tis	N0	M0
<b>IA</b>	T1a	N0	M0
<b>IB</b>	T1b T2a	N0 N0	M0 M0
<b>IIA</b>	T2b T3a	N0 N0	M0 M0
<b>IIB</b>	T3b T4a	N0 N0	M0 M0
<b>IIC</b>	T4b	N0	M0
<b>IIIA</b>	T1-T4a T1-T4a	N1a N2a	M0 M0
<b>IIIB</b>	T1-T4b T1-T4b T1-T4a T1-T4a T1-T4a	N1a N2a N1b N2b N2c	M0 M0 M0 M0 M0
<b>IIIC</b>	T1-T4b T1-T4b T1-T4b Any T	N1b N2b N2c N3	M0 M0 M0 M0
<b>IV</b>	Any T	Any N	M1

**TABLE 2**

**TNM SYSTEM FOR CLASSIFYING MELANOMA**

Stage	Description
<b>Tumor (T)</b>	
<b>Tx</b>	Primary tumor cannot be assessed.
<b>T0</b>	No evidence of primary tumor.
<b>Tis</b>	Also known as "melanoma in situ," melanoma cells are found only between the outer layer (epidermis) and the inner layer (dermis) of skin and have not yet invaded these layers. This lesion is considered precancerous.
<b>T1</b>	Melanoma is no more than 1 millimeter (mm) thick (about the thickness of a credit card).
<b>T1a</b>	Melanoma is no more than 1 mm thick, without ulceration and a mitotic rate of less than 1/mm <sup>2</sup> .
<b>T1b</b>	Melanoma is no more than 1 mm thick, either with ulceration or a mitotic rate of 1/mm <sup>2</sup> or greater.
<b>T2</b>	Melanoma is thicker than 1 mm but not more than 2 mm thick.
<b>T2a</b>	Melanoma is thicker than 1 mm but not more than 2 mm thick, without ulceration.
<b>T2b</b>	Melanoma is thicker than 1 mm but not more than 2 mm thick, with ulceration.
<b>T3</b>	Melanoma is thicker than 2 mm but not more than 4 mm (about one-tenth of an inch) thick.
<b>T3a</b>	Melanoma is thicker than 2 mm but not more than 4 mm, without ulceration.
<b>T3b</b>	Melanoma is thicker than 2 mm but not more than 4 mm, with ulceration.
<b>T4</b>	Melanoma is thicker than 4 mm.
<b>T4a</b>	Melanoma is thicker than 4 mm, without ulceration.
<b>T4b</b>	Melanoma is thicker than 4 mm, with ulceration.
<b>Node (N)</b>	
<b>Nx</b>	Regional lymph nodes cannot be assessed.
<b>N0</b>	No melanoma found in regional lymph nodes.
<b>N1</b>	Melanoma found in one lymph node.
<b>N1a</b>	Microscopic metastasis found in one lymph node.
<b>N1b</b>	Macroscopic metastasis found in one lymph node.
<b>N2</b>	Melanoma found in two to three lymph nodes.
<b>N2a</b>	Microscopic metastasis found in two to three lymph nodes.
<b>N2b</b>	Macroscopic metastasis found in two to three lymph nodes.
<b>N2c</b>	In-transit melanoma or satellite lesions are found, without metastasis to lymph nodes.
<b>N3</b>	Melanoma is found in four or more lymph nodes, or in two or more lymph nodes that appear to be joined together (known as matted lymph nodes). Or, melanoma is found as in-transit lesions or as satellite lesions that have spread to the lymph nodes.
<b>Metastasis (M)</b>	
<b>Mx</b>	Metastasis cannot be assessed.
<b>M0</b>	No metastasis.
<b>M1a</b>	Metastasis to skin, subcutaneous tissues or distant lymph nodes.
<b>M1b</b>	Metastasis to lung.
<b>M1c</b>	Metastasis to any other distant organs.

# Metastasis

- Lymphogenic a hematogenic spread
- Most often lungs, liver, brain, bones
  
- Satellites (2 cm from tumor)
- Intransit (more then 2 cm from tumor)
- Nodal (regional lymph nodes)
  
- Melanosis cutis diffusa

# Metastasis



# Primary therapy

- Wide excision (safety margin)
  - MM in situ – 0.5 cm
  - MM up to Breslow 2 mm – 1 cm
  - MM over Breslow 2 mm – 2 cm
- Excision and sentinel lymph node extraction
  - Breslow over 1 mm
  - Breslow 0.8 mm and ulcerations

# Adjuvant therapy

- Chemotherapy (Dacarbazine, Cisplatina)
- Interferon (Intron, Roferon)
- Cryosurgery (skin metastasis)
- Radiotherapy
- Targeted therapy (BRAF, MEK inhibitory)
- Immunotherapy (check point inhibition)
- Combination anti CTLA-4 + anti PD-1
- Therapy till progression or toxicity



# SKIN CANCER

Nature's way of killing retards

There's no  
stronger sunscreen  
than sitting in a bar.



someecards