So-called ‘early melanoma’
Popular subject, impopular questions

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‘Early’ (i.e., small) melanoma

F, 50 yrs, pigmented lesion, skin of calf
PubMed Interest Index

![Graph showing PubMed search interest by year for early cancer and uncertain malignant potential.](graph.png)

* Nr of hits in PubMed search per year
PubMed Interest Index

* Nr of hits in PubMed search per year
Donald Rumsfeld’s most famous quote

There are known knowns; there are things we know that we know.

There are known unknowns; that is to say, there are things that we know we don't know.

But there are also unknown unknowns; there are things we do not know we don’t know.
The pathologist cannot arrive at a diagnosis. What may be the cause?
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- Inadequate or traumatized biopsy
- Insufficient clinical information
- Suboptimal dissection and processing of specimen
- Insufficient experience and knowledge of the pathologist
- Equivocal histological findings
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## Clinical information and histological findings

<table>
<thead>
<tr>
<th>Parameter</th>
<th>In naevi</th>
<th>In melanomas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Growth, pruritus, burning sensation; change after period of stability</td>
<td>Sutton naevus</td>
<td>Sometimes</td>
</tr>
<tr>
<td></td>
<td>Naevus with folliculitis</td>
<td></td>
</tr>
<tr>
<td>Irregular contour, ‘asymmetry’</td>
<td>Recurrent naevus</td>
<td>Often, but by no means always (nodular melanoma, spitzoid melanoma)</td>
</tr>
<tr>
<td></td>
<td>Acral naevus</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Traumatized naevus</td>
<td></td>
</tr>
<tr>
<td>Several colours</td>
<td>Combined (‘true &amp; blue’) naevus</td>
<td>Sometimes / often, by no means always</td>
</tr>
<tr>
<td></td>
<td>Traumatized naevus</td>
<td></td>
</tr>
<tr>
<td>Large</td>
<td>Congenital naevus</td>
<td>Sometimes</td>
</tr>
<tr>
<td></td>
<td>Cellular blue naevus ( &amp; variants)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Some acral, genital and mucosal naevi</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Recurrent naevus, naevus in bullous dermatoses</td>
<td></td>
</tr>
</tbody>
</table>
The Influence of Clinical Information in the Histopathologic Diagnosis of Melanocytic Skin Neoplasms

Gerardo Ferrara¹, Zsolt Argenyi², Giuseppe Argenziano³, Rino Cerio⁴, Lorenzo Cerroni⁵, Arturo Di Blasi¹, Elisa A. A. Feudale⁶, Caterina M. Giorgio³, Cesare Massone⁵, Oscar Nappi⁷, Carlo Tomasinii⁸, Carmelo Urso⁹, Iris Zalaudek⁵, Harald Kittler¹⁰, H. Peter Soyer¹¹*

Table 2. Change of diagnosis following provision of clinical information.

<table>
<thead>
<tr>
<th>Diagnostic change</th>
<th>Diagnostic information</th>
<th>D2</th>
<th>D3</th>
<th>D4</th>
<th>D5</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Into benign</td>
<td>Unknown to naevus</td>
<td>14</td>
<td>1</td>
<td>3</td>
<td>2</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>Melanoma to naevus</td>
<td>12</td>
<td>4</td>
<td>4</td>
<td>3</td>
<td>23</td>
</tr>
<tr>
<td>Into malignant</td>
<td>Unknown to melanoma</td>
<td>11</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>Naevus to melanoma</td>
<td>11</td>
<td>3</td>
<td>11</td>
<td>6</td>
<td>31</td>
</tr>
<tr>
<td>Into unknown</td>
<td>Nevus to unknown</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Melanoma to unknown</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>49</td>
<td>8</td>
<td>19</td>
<td>11</td>
<td>87</td>
</tr>
</tbody>
</table>

D1: Diagnosis with no information available.
D2: Diagnosis with knowledge of age and sex of patient, as well as location of the lesion.
D3: Diagnosis with knowledge of the clinical diagnosis, as made in agreement by two of us (GA and IZ).
D4: Diagnosis with the clinical image available.
D5: Diagnosis with the dermoscopic image available.

doi:10.1371/journal.pone.0005375.t002
The most serious problem in melanoma underdiagnosis: split-second erroneous diagnosis
The most serious problem in melanoma underdiagnosis: split-second erroneous diagnosis

- Female, 43 years.
- Skin lesion, back.
- Five years later: local recurrent lesion.
Local recurrence
Melanoma: rise in incidence, but more or less stable mortality
Risk of second primary *in situ* and invasive melanoma in a Dutch population-based cohort: 1989–2008

R.J.T. van der Leest,¹ L. Liu,² J.W.W. Coebergh,²,³ H.A.M. Neumann,¹ W.J. Mooi,⁴ T. Nijsten¹ and E. de Vries¹,²
Development of multiple primary melanomas is a rare but well recognized disease, with an estimated incidence ranging from 1.75% to 8.5% in several series. The clinical, histological and epidemiological characteristics of 49 patients, identified from 2470 with histologically confirmed melanoma, are described in this study. Thirty-five of these patients had two primary melanomas, 11 had three melanomas and three had four, five and six melanomas, respectively. Diagnosis was concurrent in 22 patients (45%); in the remaining cases the median time interval between the first and second melanoma was 22.6 months and the longest interval was 21.5 years. The mean Breslow’s thickness decreased significantly ($P < 0.001$) from the first melanoma to the second and third lesion. The multiple melanoma patients had a higher percentage of subjects over 70 years of age or with lentigo maligna melanoma than single melanoma patients. The mean follow-up time was 12 years (range 4–23 years). The 5-year survival rate from first melanoma excision (83%) does not differ from that of patients with a single melanoma. In conclusion, the presence of multiple primary melanomas does not appear to be a negative prognostic factor; our data show the importance of close follow-up in melanoma patients in order to detect not only metastases, but also subsequent primaries in their earliest phases. © 1998 Lippincott Williams & Wilkins
**Figure 1.** Mean Breslow’s thickness in metachronous melanomas. The mean Breslow’s thickness decreased significantly from the first melanoma to the second and third lesion.
Risk of second primary *in situ* and invasive melanoma in a Dutch population-based cohort: 1989–2008

R.J.T. van der Leest,¹ L. Liu,² J.W.W. Coebergh,²,³ H.A.M. Neumann,¹ W.J. Mooi,⁴ T. Nijsten¹ and E. de Vries¹,²

<table>
<thead>
<tr>
<th></th>
<th>1st melanoma</th>
<th>2nd melanoma</th>
<th>P-value^b (degrees of freedom)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n)^a</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>1st melanoma</td>
<td>2nd melanoma</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(n)</td>
<td>(n)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>%</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>Breslow thickness</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 1 mm</td>
<td>21 276</td>
<td>836</td>
<td>68.3</td>
</tr>
<tr>
<td>1.01–2.0 mm</td>
<td>7952</td>
<td>202</td>
<td>16.5</td>
</tr>
<tr>
<td>2.01–4.0 mm</td>
<td>5061</td>
<td>89</td>
<td>7.3</td>
</tr>
<tr>
<td>&gt; 4 mm</td>
<td>3111</td>
<td>48</td>
<td>3.9</td>
</tr>
<tr>
<td>Unknown</td>
<td>1384</td>
<td>49</td>
<td>4.0</td>
</tr>
</tbody>
</table>
There are precious few ‘events’ in follow-up of thin melanoma

How many melanocytic lesions with an average thickness of 1 mm should not have recurred after 5 years in order to reach a significant (p<0.05) difference with a similar series of melanomas?
How many melanocytic lesions with an average thickness of 1 mm should not have recurred after 5 years in order to reach a significant (p<0.05) difference with a similar series of melanomas?

www.melanomaprognosis.org: The number is: about 100 cases
There are precious few ‘events’ in follow-up of thin melanoma

Absence of recurrence after short follow-up periods are reported, therefore are apparently considered to be worth reporting.
There are precious few ‘events’ in follow-up of thin melanoma

Absence of recurrence after short follow-up periods are reported, therefore are apparently considered to be worth reporting.

30 minutes after removal of the melanoma, the patient is free of local recurrence or metastasis.....
MELTUMP, STUMP, SAMPUS

- **All**: melanocytic proliferations of uncertain malignant potential
- **MELTUMP**: melanocytic *tumour* of uncertain malignant potential
  - Subgroup: Spitz tumour of uncertain malignant potential, STUMP
- **SAMPUS**: *Superficial* atypical melanocytic proliferation of uncertain significance
Superficial melanocytic proliferation of uncertain significance (SAMPUS) … are typically lesions in which the differential diagnosis lies between melanoma in situ or microinvasive radial growth phase melanoma and a benign simulant…. In these cases, tumorigenic proliferation in the dermis is not present, and the prognosis is very good, with a very low probability of metastatic disease as long as local control can be achieved…..

… Many observers sign out these lesions as ‘atypical intraepidermal or superficial melanocytic proliferation,’ however, in our opinion, this term does not adequately convey the potential significance of a differential diagnosis that may include a melanoma.
For such SAMPUS lesions, we typically recommend consideration of a reexcision, aiming at a minimum for a clear margin of normal skin around the scar of the biopsy and any residual portion of the lesion.

Many clinicians may choose to apply minimal treatment for melanoma in situ, i.e., a clinical measured margin of 3 to 5 mm, with clear margins histologically.
MELTUMP versus SAMPUS

**MELTUMP**: melanocytic *tumour* of uncertain malignant potential
- Subgroup: Spitz tumour of uncertain malignant potential

**SAMPUS**: *Superficial* atypical melanocytic proliferation of uncertain significance
- Proposed minor amendment of criteria: lesion must be < 1 mm in thickness and must lack intradermal mitotic activity, ulceration or obvious regression (the differential diagnosis being: naevus versus T1a melanoma)

David Elder
SAMPUS: the differential diagnosis
### Slide Set: Spitz Naevus and Variants

<table>
<thead>
<tr>
<th>Case 1A</th>
<th>Case 1B</th>
<th>Case 2</th>
<th>Case 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 4</td>
<td>Case 5A</td>
<td>Case 5B</td>
<td>Case 6</td>
</tr>
<tr>
<td>Case 7</td>
<td>Case 8</td>
<td>Case 9</td>
<td>Case 10</td>
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<tr>
<td>Case 11</td>
<td>Case 12</td>
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<td>Case 20</td>
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<td>Case 22</td>
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<td>Case 34</td>
</tr>
<tr>
<td>Case 35</td>
<td>Case 36</td>
<td>Case 37</td>
<td>Case 38</td>
</tr>
</tbody>
</table>
CLINICAL INFORMATION

CASE 7
Female, 5 years. Skin lesion, upper arm

Show diagnosis & comments

Previous case

Return to the "Spitz naevus and variants" slide set

TELL A FRIEND:
Send Email
CLINICAL INFORMATION

CASE 7
Female, 5 years. Skin lesion, upper arm

DIAGNOSIS
Spitz naevus, Kainno bodies.

COMMENTS
KAMINO BODIES are solitary rounded or confluent, amorphous, eosinophilic masses of basement membrane material, found at the dermoepidermal junction, most commonly at the tips of dermal papillae, in some Spitz naevi and, far less commonly, other benign and malignant melanocytic proliferations.

Clusters of Kainno bodies are so much more common in Spitz naevi than in other lesions, that they form an important diagnostic clue. However, their presence does not rule out melanoma completely, since a rare melanoma contains similar clustered Kainno bodies.

In H&E sections, Kainno bodies show some resemblance to Civatte bodies, as can be found in lichen planus, but the latter represent apoptotic cell remnants, whereas Kainno bodies consist of extracellular matrix components.
SEARCH RESULTS FOR: "Sutton naevus"

SUTTON NAEVUS
CASE 1 - COMMON ACQUIRED NAEVUS

SUTTON NAEVUS
CASE 21 - COMMON ACQUIRED NAEVUS

SUTTON NAEVUS
CASE 31 - COMMON ACQUIRED NAEVUS

SUTTON NAEVUS
CASE 39 - COMMON ACQUIRED NAEVUS

SUTTON NAEVUS
CASE 42 - COMMON ACQUIRED NAEVUS
Thank you