Dysplastic nevi with positive margins:
To re-excise or not to re-excise?

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F010, Practical Considerations for Patients with Melanoma or Dysplastic Nevi
Disclosures of Relevant Relationships

No relevant relationships
Overview:
Dysplastic nevi with positive biopsy margins

1. Synopsis of current clinical challenge
2. Review of data: management trends and outcomes of dysplastic nevi with positive margins
3. Future directions
Atypical Nevi

Significance:
Increased risk of developing MM

- General population: ~1.93% lifetime risk
- Atypical nevi: ~2-12 x risk
- Atypical Mole Syndrome:
  --10 yr cumulative risk for developing MM
  10.7% vs. 0.62% for controls


Dysplastic nevi and risk of melanoma

- 50-80% of melanomas arise *de novo*
- Similar rate may be observed of melanoma arising in association with dysplastic nevi (21-56%) vs. common nevi (44-79%)
- Actual transformation rate of dysplastic nevus cells into melanoma: ????
Atypical Nevi

When to biopsy?

--Diagnosis of atypical nevus can be made clinically

--Biopsy suspicious lesions concerning for melanoma

--Removal also option for nevi in areas difficult to monitor
Biopsy

Variable types of biopsies performed

- Incisional
- Excisional
- Shave
- Punch
- Elliptical
Biopsy
Variable types of biopsies performed
Guidelines of care for the management of primary cutaneous melanoma

Table IV. Recommendations for biopsy

Preferred biopsy technique is narrow excisional biopsy that encompasses entire breadth of lesion with clinically negative margins to depth sufficient to ensure that lesion is not transected, which may be accomplished by elliptical or punch excision with sutures, or shave removal to depth below anticipated plane of lesion. Partial sampling (incisional biopsy) is acceptable in select clinical circumstances such as facial or acral location, low clinical suspicion or uncertainty of diagnosis, or very large lesion. Repeat biopsy is recommended if initial biopsy specimen is inadequate for diagnosis or microstaging of primary lesion.
High suspicion for melanoma: narrow excisional biopsy preferred

1-3 mm margins

* Clear margins: no need to worry about + margin debate!
Partial biopsy: severely atypical melanocytic proliferation

Melanoma 3.3 mm/IV
Partial/incisional biopsy:

- Facial or acral areas
- Very large lesions
- Low suspicion
Atypical Nevi

Pathology result:
--grading system is variable
  dysplastic vs severely DN
  Mild, mod, severely DN
  Mild, mild-mod, mild-focal mod, mod-focal severe, mod-severe, severe

- Clinical term: Atypical mole
- Pathologic term: nevus with architectural disorder
- Recommended atypical moles be removed in total
- Recommended 2-5 mm margins for reexcisions of DN “if needed”

No guidelines on indications for re-excision
Management of Dysplastic Nevi with Positive Biopsy Margins: US
Atypical Nevi

Management in US: 2002

Questionnaire mailed to 1216 fellows of AAD: 456 responded

- 86% of respondents intend to do total removal when performing biopsy of an atypical nevus
- 75% use margins of 2mm or less
- 67% prefer to re-excise dysplastic nevus when margins positive, some use histologic atypia as criterion

## Comparison between Chicago dermatologist study and 2014 New England dermatologists survey

<table>
<thead>
<tr>
<th></th>
<th>Observe or other</th>
<th>Reexcise</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2009 Chicago</td>
<td>2014 New England</td>
<td>positive margins</td>
<td>positive margins</td>
</tr>
<tr>
<td>Mild</td>
<td>79%</td>
<td>95%</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>Mod</td>
<td>19%</td>
<td>39%</td>
<td>61%</td>
<td></td>
</tr>
<tr>
<td>Mod-Sev</td>
<td>19%</td>
<td>5%</td>
<td>95%</td>
<td>0%</td>
</tr>
<tr>
<td>Severe</td>
<td>5%</td>
<td>0%</td>
<td>100%</td>
<td></td>
</tr>
</tbody>
</table>

Tong L, Wu P and Kim CC (JAAD 2016)

No consensus
Outcomes of Dysplastic Nevi with Positive Histologic Margins
<table>
<thead>
<tr>
<th>Publication</th>
<th># DN with positive margins observed or re-excised</th>
<th>Distribution of atypia</th>
<th>Duration of follow up</th>
<th>#/% recurrence (AN)</th>
<th>#/% recurrence (MM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kmetz et al. 2009</td>
<td>26 observed</td>
<td>unstated</td>
<td>6.12 years</td>
<td>unstated</td>
<td>0</td>
</tr>
<tr>
<td>Goodson et al. 2009</td>
<td>69 observed</td>
<td>Mild: 65 Moderate: 4</td>
<td>At least 2 years</td>
<td>3-4 %</td>
<td>0</td>
</tr>
<tr>
<td>Hocker et al. 2013</td>
<td>115 observed</td>
<td>Mild: 66 Moderate: 42</td>
<td>17.4 years</td>
<td>unstated</td>
<td>0</td>
</tr>
<tr>
<td>Fleming et al. 2016</td>
<td>159 observed</td>
<td>Severe: 7</td>
<td>5.5 years</td>
<td>1 (AIMP favor early MMIS)</td>
<td>0</td>
</tr>
<tr>
<td>Reddy et al. 2013</td>
<td>127 re-excised</td>
<td>Mild: 2 Mild-moderate: 9 Moderate: 52 Moderate-Severe: 55 Severe: 9</td>
<td>unstated</td>
<td>N/A</td>
<td>2/127 (1.5%) (both from mod-severe DN biopsies)</td>
</tr>
<tr>
<td>Abello-Poble et al. 2013</td>
<td>91 re-excised</td>
<td>Mod: 75 Severe: 16</td>
<td>2-16 weeks, majority after 4 weeks</td>
<td>N/A</td>
<td>0</td>
</tr>
<tr>
<td>Strazzula et al. 2014</td>
<td>495 re-excised</td>
<td>Mild:16 Mild-mod: 137 Moderate: 342</td>
<td>Unstated</td>
<td>0.2% upgraded from Mod to Severe</td>
<td>0</td>
</tr>
</tbody>
</table>

Total 517

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Hiscox et al 147

Total 713

Mild: 131
Mod: 47
Severe: 7
?: 26
159

Fleming et al. 2016

1 (AIMP favor early MMIS)

Mild: 18
Mild-Mod: 146
Mod: 469
Mod-sev: 55
Sev: 25
Addressing the Knowledge Gap in Clinical Recommendations for Management and Complete Excision of Clinically Atypical Nevi/Dysplastic Nevi

Pigmented Lesion Subcommittee MPWG/ECOG/SWOG

- Mild + margins without pigment → Observation
- Moderate + margins without pigment → Observation may be reasonable, more data needed
- Severe + margins without pigment → Re-excision
- Monitor all biopsy sites for unusual regrowth

Pigmented Lesion Subcommittee MPWG/ECOG/SWOG
Management strategies of academic pigmented lesion clinic directors in the United States


- 38 of 40 identified PLC directors responded (95%) to REDcap survey 2015-6.

Table II. Recommended therapeutic clinical margins for various melanocytic diagnoses

<table>
<thead>
<tr>
<th>Scenario</th>
<th>No additional procedure</th>
<th>Clinical margin size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnoses with positive histologic margins and no clinical residuum, n %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nevus with mild atypia (n = 35)</td>
<td>32 (91)</td>
<td>2 (6)</td>
</tr>
<tr>
<td>Nevus with moderate atypia (n = 33)</td>
<td>17 (43)</td>
<td>9 (27)</td>
</tr>
<tr>
<td>Nevus with severe atypia (n = 35)</td>
<td>0</td>
<td>2 (6)</td>
</tr>
</tbody>
</table>
Need for large-scale data to further investigate role of observation vs. re-excision of dysplastic nevi

Pigmented Lesion Subcommittee
MPWG/ECOG/SWOG
Multi-center study
Risk of Subsequent Cutaneous Melanoma in Moderately Dysplastic Nevi Excisionally Biopsied but With Positive Histologic Margins

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Published online October 10, 2018.
Objective:

• To determine outcomes and risk for the development of subsequent cutaneous melanoma from moderately dysplastic nevi that had been excisionally biopsied with positive histologic margins observed for ≥ 3 years (January 1, 1990-August 31, 2014)

Design:

• Multicenter (9 US academic dermatology sites) retrospective cohort study
• Patients ≥ 18 years of age with a moderately DN excisionally biopsied with + histology margins with ≥ 3 years of clinical f/u
• Central dermatopathology review: 5 representative slide cases were reviewed per site to confirm histologic grading

Main outcomes and measures:

• Development of melanoma at 1) the same biopsy site or 2) elsewhere on the body
Results:

467 moderately DN + margins from 438 patients with a mean f/u time of 6.9 years.

- No biopsy-site melanomas developed
- 100 patients (22.8%) developed a cutaneous melanoma at a separate site
- Multivariable analysis revealed that history of cutaneous melanoma was significantly associated with the risk of subsequent melanoma at a separate site (OR 11.74; 95% CI: 5.71-24.15; p<0.001) as were 2 or more prior biopsied dysplastic nevi (OR 2.55; 95% CI, 1.23-5.28, p=0.1).

Central dermatopathology review:

- Agreement in 35 of 40 cases (87.5%)
- 3 of 40 cases upgraded in degree of atypia. Of these, 1 was interpreted as melanoma in situ. That patient remains without recurrence or evidence of melanoma after 5 years of follow-up.
Conclusions:

• Close observation with routine surveillance is a reasonable management approach for moderately dysplastic nevi (excisionally biopsied) with positive histologic margins.

• However, having 2 or more biopsies dysplastic nevi (1 of which is moderately dysplastic) appears to be associated with an increased risk for melanoma at a separate site—recommend continued surveillance.
Recurrent Pigmentation
Recurrent Pigmentation

- **Recurrent nevi**: tend to develop within 8 months with pigmentation confined to scar

- **Melanomas**: tend to recur more than 20 months after biopsy, in patients older than 30 years, and with pigmentation crossing into normal skin

Summary

Dysplastic nevi with positive biopsy margins:

- Excisional biopsy for highly suspicious lesions
- 1-3 mm clear clinical margins recommended for excisions
- Be aware of limitations of partial/incisional biopsies
- Recent outcomes data: observation of moderate dysplastic nevi that have been excisionally biopsied with + histologic margins may be reasonable; continued surveillance is important
- Future larger scale data: other subtypes of nevi, outcomes, margin types, patient populations
- If observing, clinician and patient should monitor biopsy sites for unusual regrowth
Dysplastic nevi with positive margins:  
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Thank you for your attention!  

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