Chromoendoscopy or Narrow Band Imaging with Targeted biopsies Should be the Cancer Surveillance Endoscopy Procedure of Choice in Ulcerative Colitis

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Low-Grade Dysplasia in Flat Mucosa

- **Cohort study** - 46 UC pts with LGD in flat mucosa
- 11 pts - colectomy for LGD (2 cancer, 1 HGD).
- 14/35 (40%) progressed to more advanced neoplasia during intensive surveillance
  - 7 pts CRC (2 stage I, 2 stage II, 3 stage III)
- Rate of progression - 53% at 5 yrs, 80% at 10 yrs
- **Conclusion** - Colectomy for LGD in flat mucosa

Low-Grade Dysplasia in Flat Mucosa

Figure 5. Kaplan-Meier curve comparing the cumulative progression to advanced neoplasia in patients with any fLGd (solid line), unifocal fLGd (dashed line), and multifocal fLGd (dotted line). Cross-hatches (+) indicate censoring of patients for no further follow-up or colectomy without evidence of progression. Vertical lines (|) represent progression events.
Polyps or DALMs in UC

- 24 pts with DALMs – 14 (58%) developed polyps/DALMs over 3.5 years (no cancers)
- 48 pts with DALMs – 23 (48%) developed polyps/DALMs over 4.1 years (no cancers)
- Neither study stratified by age

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DALMs v. Adenomas in UC

Newer Endoscopic Techniques to Improve Sensitivity of Detecting Dysplasia

- Chromoendoscopy
- Narrow Band Imaging
- Autofluorescence
- Confocal endomicroscopy
Chromoendoscopy

- Absorptive stains
  - Methylene blue (with a mucolytic)
  - Lugol’s solution

- Reactive stains
  - Congo red
  - Phenol red

- Contrast stains
  - Indigo carmine
Chromoendoscopy

- RCT - 165 patients with UC > 8 years - conventional surveillance v. chromoendoscopy

- 0.1% methylene blue staining prior to biopsy - taken up by epithelial cells, stable staining pattern, pit pattern visible in polypoid lesions

- Dysplasia - 38% v. 12% (P=0.003)

## Findings

### Table 5. Intraepithelial Neoplasias and Cancers

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>( P^a )</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>84</td>
<td>81</td>
<td>—</td>
</tr>
<tr>
<td>Patients with INs</td>
<td>13</td>
<td>6</td>
<td>NS</td>
</tr>
<tr>
<td>Total no. of INs*</td>
<td>32</td>
<td>10</td>
<td>0.00315</td>
</tr>
<tr>
<td>Low-grade INs</td>
<td>24</td>
<td>8</td>
<td>—</td>
</tr>
<tr>
<td>High-grade INs</td>
<td>8</td>
<td>2</td>
<td>—</td>
</tr>
<tr>
<td>Invasive cancers</td>
<td>3</td>
<td>1</td>
<td>NS</td>
</tr>
<tr>
<td>Polypoid INs</td>
<td>8</td>
<td>6</td>
<td>NS</td>
</tr>
<tr>
<td>INs in “flat mucosa”(^a)</td>
<td>24</td>
<td>4</td>
<td>0.0007</td>
</tr>
</tbody>
</table>

*IN, intraepithelial neoplasia.  
*Fisher exact test.  

\(^a\)Group A - Chromoendoscopy
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Pit Patterns I & II

I

II

Same as surrounding epithelium

Stellate appearance
Low-grade Dysplasia
High-grade Dysplasia

Superficial Spreading Cancer
Chromoendoscopy for Mass Lesions

<table>
<thead>
<tr>
<th>Pit pattern III &amp; IV</th>
<th>Dysplasia</th>
<th>No Dysplasia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pit pattern I &amp; II</td>
<td>2</td>
<td>80</td>
</tr>
</tbody>
</table>

Sensitivity 94%, Specificity 93%
Targeted v. Non-Targeted Bxs

- Tandem colonoscopies, 100 UC pts, routine bxs then indigo carmine-directed biopsies
- Non-targeted bxs – 0/2904 with dysplasia
- Targeted biopsies – 157 in the population
  - No chromo – 2/20 pts with dysplasia
  - Chromo – 5/55 additional pts with dysplasia
  - 7/114 additional lesions had dysplasia

# Cleveland Clinic Experience

<table>
<thead>
<tr>
<th></th>
<th>UC</th>
<th>Crohn's Colitis</th>
<th>Indeterminate Colitis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N</strong></td>
<td>27</td>
<td>9</td>
<td>3</td>
</tr>
<tr>
<td>Mean age (range)</td>
<td>50 yrs (23-80)</td>
<td>50 yrs (33-65)</td>
<td>56 yrs (33-65)</td>
</tr>
<tr>
<td>Mean age with dysplasia (range)</td>
<td>46 yrs (25-66)</td>
<td>57 yrs (51-65)</td>
<td>-</td>
</tr>
<tr>
<td>Mean disease duration (range)</td>
<td>18 yrs (6-42)</td>
<td>17 yrs (9-29)</td>
<td>19 yrs (13-23)</td>
</tr>
<tr>
<td>Extensive Disease (%)</td>
<td>26 (96%)</td>
<td>-</td>
<td>3 (100%)</td>
</tr>
<tr>
<td>PSC (%)</td>
<td>2 (7%)</td>
<td>0</td>
<td>1 (33%)</td>
</tr>
<tr>
<td>Mean white light withdrawal time (range)</td>
<td>9 min (6-19)</td>
<td>-</td>
<td>6 min (6)</td>
</tr>
<tr>
<td>Mean chromo withdrawal time (range)</td>
<td>40 min (22-50)</td>
<td>-</td>
<td>43 min (36-50)</td>
</tr>
</tbody>
</table>

All Detected Lesions

- 54 visible lesions with conventional white light colonoscopy
  - 7 (13%) low-grade dysplasia
- 28 additional lesions with chromoendoscopy
  - 2 (7%) low grade dysplasia
- Random biopsies of normal appearing mucosa
  - 1/39 patients had flat low-grade dysplasia with no visible lesions
- No high-grade dysplasia or cancer
### Polypoid Dysplastic Lesions

<table>
<thead>
<tr>
<th></th>
<th>UC Patients</th>
<th>Crohn’s Colitis Patients</th>
<th>Indeterminate Colitis Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N</strong></td>
<td>27</td>
<td>9</td>
<td>3</td>
</tr>
<tr>
<td>Polypoid dysplasia</td>
<td>3</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>white light alone</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Additional polypoid</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>dysplasia chromo</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total polypoid</td>
<td>5</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>dysplasia white light &amp;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>chromo</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>P value</strong></td>
<td>NS</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NS - Not Significant
## Flat Dysplastic Lesions

<table>
<thead>
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<th>UC Patients</th>
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<th>Indeterminate Colitis Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>27</td>
<td>9</td>
<td>3</td>
</tr>
<tr>
<td>Flat dysplasia white light alone</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Flat dysplasia chromo</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Flat dysplasia random biopsy</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Total flat dysplasia white light &amp; chromo &amp; random</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>
Mount Sinai Experience

- 102 patients with WLE (random biopsies) & methylene blue with targeted biopsies
- 17 pts with dysplasia (16 LGD, 1 HGD)
  - WLE – 9 pts detected with targeted bx
  - WLE – 3 pts detected with random bx
  - Chromo – 5 pts detected with targeted bx

Chromoendoscopy Conclusions

- Chromoendoscopy increases the sensitivity of detecting dysplastic lesions in ulcerative colitis pts by less than 2-fold.

- Chromoendoscopy with directed biopsies should be considered in all ulcerative colitis surveillance examinations, especially in pts at high risk for having dysplasia.

- Random biopsies of normal appearing mucosa may still be of benefit for dysplasia surveillance.
Narrow Band Imaging

- NBI employs a series of filters to project mostly blue light with shallow penetration into tissues.
- Vascular structures, like polyps and dysplasia, are darkly colored.
- Surrounding mucosa and residual stool are lightly colored.
- Convenient
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- 46 patients with ulcerative colitis, 5 dysplastic lesions were found in 276 areas of flat mucosa that were examined.
- “Tortuous” pattern - 4 cases of dysplasia
- “Villous” pattern – 1 case of dysplasia
- “Honeycomb-like” pattern – no dysplasia

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Tortuous Pattern - LGD
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Tortuous Pattern - HGD
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NBI

- 42 ulcerative colitis patients had surveillance colonoscopy with either NBI or WLE separated by 3 weeks.
- 11 patients with dysplasia were identified:
  - 4 pts - both WLE and NBI
  - 4 pts - NBI only
  - 3 pts - WLE only

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HGD

LGD
Autofluorescence

- Fluorophores – mitochondria, lysosomes, submucosal collagen – Red AF
- Chromophores – Hemoglobin – Purple AF
- Non-neoplastic mucosa – Green AF
Barrett’s Esophagus

- 20 pts with Barrett’s esophagus at high risk for dysplasia
- Autofluorescence - 28 dysplastic lesions
- NBI – 25 (89%) of those lesions detected
- WLE – 17 (61%) of those lesions detected
- Autofluorescence could be even more sensitive in detecting dysplastic lesions than NBI.

HGD in Barrett’s Esophagus
Sporadic Colonic Adenomas

- 107 Pts, 54 adenomas, 21 hyperplastic polyps

Differentiating adenomatous v. hyperplastic polyps with different Autofluorescence Intensity Ratio values

<table>
<thead>
<tr>
<th>AIR</th>
<th>% Sensitivity</th>
<th>% Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;2.0</td>
<td>91</td>
<td>57</td>
</tr>
<tr>
<td>&gt;2.3</td>
<td>85</td>
<td>81</td>
</tr>
<tr>
<td>&gt;2.5</td>
<td>78</td>
<td>86</td>
</tr>
<tr>
<td>&gt;3.0</td>
<td>69</td>
<td>95</td>
</tr>
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Adenomatous Polyps
Hyperplastic Polyps
Conclusions

- It is important to find dysplasia, if present, in ulcerative colitis pts having surveillance colonoscopy since the risk of progression is high.
- Chromoendoscopy, NBI, & AF with targeted biopsies all may increase the sensitivity of detecting dysplasia.
- Chromoendoscopy – widely available, inexpensive, data is promising, but random biopsies still needed
- NBI & AF – not widely available, little data