Deep learning for real time histologic differentiation

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Conflict of Interest/disclosures

• Satis Operations Inc (partner in “ai4gi” venture)----CEO and shareholder
• Co-development agreement between ai4gi and Olympus
Attempts to improve optical biopsy—Image Enhanced Endoscopy (IEE)

• Chromoendoscopy
• Virtual chromoendoscopy
  - NBI, iScan, FICE, Spies, BLI, LCI
• Magnification endoscopy
• Confocal laser endoscopy
  - probe based (Mauna Kea “Cellvizio”)
  - or scope based (Pentax)
• Endocytoscopy (EC)
• HD scopes
• OCT/VLE
• Molecular Imaging
• Human eye training
# Optical Biopsy

## NBI International Colorectal Endoscopic (NICE) Classification

<table>
<thead>
<tr>
<th>Type</th>
<th>Color</th>
<th>Vessels</th>
<th>Surface Pattern</th>
<th>Most Likely Pathology</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1</td>
<td>Same or lighter than background</td>
<td>None, or isolated lacy vessels</td>
<td>Dark or white spots of uniform size, or homogeneous absence of pattern</td>
<td>Hyperplastic</td>
<td><img src="image1" alt="Hyperplastic Example" /></td>
</tr>
<tr>
<td>Type 2</td>
<td>Brown to dark brown relative to background (verify color arises from vessels)</td>
<td>Brown vessels surrounding white structure**</td>
<td>Oval, tubular or branched white structure surrounded by brown vessels**</td>
<td>Adenoma***</td>
<td><img src="image2" alt="Adenoma Example" /></td>
</tr>
<tr>
<td>Type 3</td>
<td>Brown to dark brown relative to background; sometimes pachy white areas</td>
<td>Has area(s) of disrupted or missing vessels</td>
<td>Amorphous or absent surface pattern</td>
<td>Deep submucosal invasive cancer</td>
<td><img src="image3" alt="Invasive Cancer Example" /></td>
</tr>
</tbody>
</table>

* Can be applied using colonoscopes with or without optical (zoom) magnification
** These structures (regular or irregular) may represent the pits and the epithelium of the crypt opening.
*** Type 2 consists of Vienna classification types 3 and superficial 5 (all adenomas with either low or high grade dysplasia, or with superficial submucosal carcinoma). The presence of high grade dysplasia or superficial submucosal carcinoma may be suggested by an irregular vessel or surface pattern, and is often associated with atypical morphology (e.g., depressed area).

## JNET classification

- **1**: NBI magnification (IEE)
- **2A**: 2B-low
- **2B**: NBI: narrow-band imaging, IEE: image enhanced endoscopy, SSP: sessile serrated polyp, WLI: white-light imaging, EUS: endoscopic ultrasonography
- **2B-high**: pit pattern diagnosis (magnifying chemoendoscopy)
- **3**: Surgery (does not require chemoendoscopy)

- **Follow-up** (does not require chemoendoscopy)
  - **Endoscopic treatment** (does not require chemoendoscopy)
    - **Surgery** (does not require chemoendoscopy)

※ Indigo carmine dye spraying is essential for some cases.

※ SSP needs removal in some cases.

※ WLI observation and EUS are useful for making the final diagnosis.
The Problem

Improving real-time detection and diagnosis of GI cancer and related diseases

Doctors need help with real-time cancer detection and diagnosis
The human (doctor) eye is not accurate enough
Current solutions focus on better resolution, improved lighting technology, and so forth, and yet doctors’ performance does not radically improve
Endomicroscopy (CEM)

- Endomicroscopy is born—do we still need the pathologist?

Gastrointestinal Endoscopy, Volume 66, Issue 1, July 2007, Pages 150-153
Ralf Kiesslich et al.

Figure 4: Intraepithelial Neoplasia – Confocal Endomicroscopy, Kiesslich et al., Mainz
Challenges in Modern Endoscopy

Ways to help endoscopist with new technology implementation

Cost
Difficult/impossible interpretation
Lack of Widespread Expertise
Deep learning allows computational models that are composed of multiple processing layers to learn representations of data with multiple levels of abstraction. These methods have dramatically improved the state-of-the-art in speech recognition, visual object recognition, object detection and many other domains such as drug discovery and genomics. Deep learning discovers intricate structure in large data sets by using the backpropagation algorithm to indicate how a machine should change its internal parameters that are used to compute the representation in each layer from the representation in the previous layer. Deep convolutional nets have brought about breakthroughs in processing images, video, speech and audio, whereas recurrent nets have shone light on sequential data such as text and speech.

2015: Influential Deep Learning review paper in *Nature*
World Go Champion
Beaten by Machine
In the News
JANUARY 10, 2018

Artificial Intelligence Arrives in GI
“Siri, what is Deep Learning?”

tap to edit
Convolution Layer
(Variety of filters)

Subsampling Layer
(Pooling)

Convolution Layer

Subsampling Layer
(Pooling)

Fully Connected Layers

Model Prediction

Byrne et al, Gut, 2017-314547
Will Artificial Intelligence (AI) Revolutionize Colonoscopy?
Examples of the product development

= Seamless CAD system for colonoscopy

DETECTION

CHARACTERIZATION

Characterization by EC

Characterization by EC-NBI

CAD for cancer

CAD for SSA/P

UC MANAGEMENT

CAD for UC

Invasive Cancer

Healing: 6 %
Active: 94 %

Non-neoplastic: 0.7 %
Adenoma: 7 %
Invasive Cancer: 4 %
SSA/P: 89 %
DEEP LEARNING & OPTICAL 
BIOPSY

• **Unaltered** endoscopic video
• **Realtime** NICE Type 1&2 classification

PERFORMANCE

>94% accuracy

meeting PIVI guidelines

Preservation and Incorporation of Valuable endoscopic Innovations

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1. INVESTIGATIONAL & UNREGULATED. NOT AVAILABLE FOR COMMERCIAL SALE.

Byrne et al, Gut, 2017-314547
CLINICAL BENEFIT

Artificial Intelligence meets PIVI Guidelines
Figure 1. Full Colonoscopy Workflow Diagram
Computer-aided detection of early neoplastic lesions in Barrett's esophagus

van der Sommen et al. Endoscopy 2016
IBD and AI
Mucosal Healing and Dysplasia

Currently

Expanding portfolio in IBD.

New “gold standards” in assessment of treatment success in IBD are changing the field rapidly.

Problem

1. Significant variability in defining and assessing “mucosal healing” in IBD.
2. New “histological end points” in mucosal healing are costly, introduce some delay, and are still somewhat “subjective”.
3. New endoscopic imaging modalities and improvements are often difficult to utilize in routine clinical practice.
4. Evaluation of dysplasia/cancer risk in IBD is incredibly poor.

Solution

1. Provide a new “gold standard” to mucosal healing, namely AI-guided optical biopsy, which is real-time and objective.
2. Improve detection of dysplasia in live colonoscopy, even in community clinical practice.
3. Overhaul current methods of centralized reading of IBD disease activity for clinical trial inclusion by utilizing AI automated reading.

Alternatives?

Deep Learning lowers the time and cost of data acquisition for clinical outcome prediction & uses existing infrastructure to bridge the gap between in-vitro and in-vivo diagnostics.
Challenges for CAD

- Physician acceptance
- Patient acceptance
- Regulatory pathways
- Comparison against “imperfect” gold standard
- Quality data
- Widespread AI expertise
Validation for CAD

- Clinical trials in vivo, in real clinical scenarios
- At least equivalency to current gold standard (usually pathology)
- Replication with groups who are NOT optical biopsy experts---removing bias
- Applicable to technologies widely available
AI Clinical Evidence Network
AI-DRIVEN DISCOVERY ECOSYSTEM

Federating Data. Uniting Expertise.
New AI-centric classification systems?

- NICE has 3 features for the human eye
- Neural networks see over 1000 features in polyps
- Impossible for human eye to match the performance of machines
- Some technologies will struggle without some kind of “built in” machine intelligence
- There is a reason most endoscopists don’t use spray chromoendoscopy, or know how to really interpret virtual chromoendoscopy
- And even harder with CLE and OCT images
- We need to stop using scopes just as white-light instruments but we need help
Future of AI

• AI needs its own committees and groups to navigate this rapidly changing and quite different field for most doctors
• We need to be brave with AI
• Industry needs to embrace AI and bake it into their products
• Challenging but is already making huge strides in other industries, so will come to healthcare
• We need to embrace and prepare
Thank you

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