Computer aided optical diagnosis of polyps

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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
Objectives

• Brief optical diagnosis overview
• Current state and future of machine learning/AI in endoscopic imaging
• Discuss barriers and opportunities to embrace new technologies into practice
Advanced Endoscopic Imaging

• Multi-modal in addition to white-light endoscopy
• Driven by need/desire to visually recognize pre-malignant lesions and early cancers in the GI tract
• “Optical biopsy” and “disease detection”
• Hopefully can influence/change the course of treatment with earlier identification
Electronic Based - IEE

<table>
<thead>
<tr>
<th>Olympus Narrow Band Imaging (NBI)</th>
<th>Fujinon Intelligence Color Enhancement (FICE)</th>
<th>Pentax Tone Enhancement (I-Scan)</th>
</tr>
</thead>
</table>

Principles of Tone Enhancement
LCI (Linked Color Imaging)

LCI expands close color letting us clearly see details that would otherwise be hidden within that color, yet it keeps the color natural and realistic.

White Light Image (H. pylori infection)

LCI Image (H. pylori infection)

Reallocating the crowded color

1. normal mucosa
2. reddish lesion
3. mucosal atrophy
4. Deep vessel
Autofluorescence imaging--AFI

Fig. 3  Endoscopic images of a laterally-spreading tumor (LST) with granular changes to the rectum (25 mm in size, white light endoscopy used) (a) and auto-fluorescence endoscopy (b)

The one-push button changes the light from white light endoscopy to auto-fluorescent endoscopy simply and easily. With auto-fluorescent endoscopy, the tumor margin can be seen clearly as magenta color. The lesion was diagnosed histologically as well differentiated adenocarcinoma after endoscopic mucosal resection (EMR).
Confocal Laser Endomicroscopy

Normal Endoscopy  Zoom Endoscopy  Confocal Endoscopy
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 1</th>
<th>Type 2</th>
<th>Type 3</th>
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</thead>
<tbody>
<tr>
<td><strong>Color</strong></td>
<td>Same or lighter than background</td>
<td>Brown to dark brown relative to background; sometimes patchy whiter areas</td>
</tr>
<tr>
<td><strong>Vessels</strong></td>
<td>None, or isolated lacy vessels</td>
<td>Brown vessels surrounding white structure**</td>
</tr>
<tr>
<td><strong>Surface Pattern</strong></td>
<td>Dark or white spots of uniform size, or homogeneous absence of pattern</td>
<td>Has area(s) of disrupted or missing vessels</td>
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<td><strong>Most likely pathology</strong></td>
<td>Hyperplastic</td>
<td>Adenoma***</td>
</tr>
<tr>
<td><strong>Examples</strong></td>
<td></td>
<td>Deep submucosal invasive cancer</td>
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</tbody>
</table>

*N Can be applied using colonoscopes with or without optical (zoom) magnification
** Some structures (regular or irregular) may represent the pits and the epithelium of the crypt opening.
*** Type 2 cancers of Vienna classification types 3, 4 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).

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## JNET classification

1. **Detection**
   - NBI magnification (IEE)
   - 2A
   - 2B-low
   - 2B-high

2. **Follow-up** (does not require chromoendoscopy)
   - SSP needs removal in some cases.

3. **Endoscopic treatment** (does not require chromoendoscopy)
   - Pit pattern diagnosis (magnifying chromoendoscopy)

4. **Surgery** (does not require chromoendoscopy)
   - WL: white-light imaging, EUS: endoscopic ultrasonography

※ Indigo carmine dye spraying is essential for some cases.
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

Yann LeCun, Yoshua Bengio & Geoffrey Hinton

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.
Cars are now driving themselves...
World Go Champion
Beaten by Machine
ImageNet Accuracy Still Improving

Top-5 Classification task

Use of Deep Learning over Conventional Computer Vision

74.2% 84.7% 88.3% 93.3% 96.4%


~ level of human accuracy

94.9%

Accuracy Still Improving
### Artificial Intelligence: Sub-Industry Heatmap

**2011-2016 (as of 6/15/2016)**

<table>
<thead>
<tr>
<th>Sub-Industry</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016(YTD)</th>
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<tbody>
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<td>Healthcare</td>
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<td>Advertising, Sales &amp; Marketing</td>
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*Min* | **No. of Deals** | *Max*

[CB INSIGHTS](http://www.cbinsights.com)
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 Fully Connected Layers Model Prediction

Byrne et al, Gut, 2017-314547
Will Artificial Intelligence (AI) Revolutionize Colonoscopy?
What is the role of CAD for colonoscopy?

Automated detection

Automated characterization (=pathological prediction)

*EC, endocytoscopy; pCLE, probe-based confocal endomicroscopy
Expert Endoscopists may **visually assess polyp histology** (optical biopsy) and accurately define future surveillance colonoscopy intervals, **forestalling lab analysis**.

However, this ability does not translate to non-experts in academic and community settings.
Examples of the product development

Seamless CAD system for colonoscopy

DETECTION

CHARACTERIZATION

Characterization by EC

Characterization by EC-NBI

CAD for cancer

Invasive Cancer

Probability: 60 %

CAD for SSA/P

Non-neoplastic: 0.7 %
Adenoma: 7 %
Invasive Cancer: 4 %
SSA/P: 89 %

UC MANAGEMENT

CAD for UC

Healing: 6 %
Active: 94 %
**RESECT & DISCARD STRATEGY**

Cost savings of discarding diminutive polyps resected during CRC after Optical Biopsy have been estimated to be >USD 1 Billion annually in the USA.

The subjectivity in Optical Biopsy assessment by endoscopists can be circumvented by computer based automated tools.

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A quantitative assessment of the risks and cost savings of forgoing histologic examination of diminutive polyps. Endoscopy 2011;43:683-691

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

Deep Learning Diagnosis Support

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
Tablet-based HRME with automated image interpretation for esophageal SCC

Quang et al, GIE, 84 (5), 2016
Artificial intelligence may help in predicting the need for additional surgery after endoscopic resection of T1 colorectal cancer.

**BACKGROUND AND STUDY AIMS:**

Decisions concerning additional surgery after endoscopic resection of T1 colorectal cancer (CRC) are difficult because preoperative prediction of lymph node metastasis (LNM) is problematic.

**CONCLUSIONS:**

Compared with current guidelines, artificial intelligence significantly reduced unnecessary additional surgery after endoscopic resection of T1 CRC without missing LNM positivity.

**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.

**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.

**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.
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.

HOSPITAL ADMINISTRATOR
REGULATOR
CLINICAL RESEARCHER
INDUSTRY
AI SCIENTIST
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
Summary

• White-light endoscopy still dominates a lot of practice
• Significant advances in quality of imaging, especially in last few years
• Real-time optical biopsy is feasible
• Barriers to adoption/implementation are many
• However, we owe it to ourselves and our patients to offer the best solutions available
• Multimodality will become the norm
• AI will play a significant role in near future and longer term
Thank you

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