Computer aided diagnosis of early GI neoplasia: hope or hype?

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**Institute of Science and Technology, Klosterneuburg, Austria  
***Moscow Medical University
Scientific interest in computer-aided decision support systems in endoscopy (CADSSs): the number of publications is rising

Number of publications between 1988 and 2014 found on PubMed and ScienceDirect (publications dealing with CADSS or supportive systems for endoscopy)

Based on M. Liedlgruber, A. Uhl. Endoscopic image processing - an overview ISPA’2009, PubMed, ScienceDirect Search
It requires a support system for gastroenterologist in making clinical decision

Exers III images with near focus (~80 degree magnification)
Computer-aided decision support systems (CADSSs): systems designed to detect and/or classify abnormalities and thus to assist a medical expert in improving the accuracy of medical diagnosis

**Expected Aims:**

- Saving time and reducing cost of procedures
- Enhancing accuracy of diagnosis
- Training of non-experts to new endoscopic imaging modalities

**Focus on:**

- **Flexible magnification endoscopy**
- Capsule endoscopy
- Confocal laser endomicroscopy
CADSSs are based on images acquired with high-magnification endoscopes (Olympus GIF Q 160Z, GIF HQ 260Z, GIF H190).

x 115 magnification (160 & 260 scopes)  X 70-80 magnification (Exera III)
Organ specific approach in high-magnification GI endoscopy

**Esophagus**
- **V** Intrapapillary capillary loop (IPCL-classification)
- **S**

**Colon**
- **V** Pit patterns (Kudo’s classification)
- **S**

**Stomach**
- **V** Microvessel pattern (regular/irregular)
- **S** Microsurface pattern (regular/irregular/absent)

**Stomach is the most difficult part of GI tract for magnification diagnosis**

K Kaise M., Kato M., Tajiri H. High-Definition Endoscopy and Magnifying Endoscopy Combined with Narrow Band Imaging in Gastric Cancer In book New Challenges in Gastrointestinal Endoscopy, Springer 2008;177-190
High-magnification endoscopy in stomach

Non-cancer

<table>
<thead>
<tr>
<th>Regular</th>
<th>Irregular</th>
<th>Absent (disappearance)</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="V.png" alt="Image" /></td>
<td><img src="V.png" alt="Image" /></td>
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</table>

Dysplasia / Cancer

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<th>Irregular</th>
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MS disappearance, MV dilation, and MV heterogeneity appeared to be the best combination for diagnosis of gastric cancer with sensitivity and specificity 92.9% and 94.7% respectively.

In spite of high sensitivity and accuracy for predicting gastric neoplasia the studies showed moderate inter- and intra-observer agreement for magnifying endoscopy with NBI

- The mean $K$ for intra-observer agreement was 0.69 (experts, 0.74; trainees, 0.64), the mean $K$ for inter-observer agreement was 0.42 (experts, 0.49; trainees, 0.40)*
- Evaluation of depressed gastric lesions by the ME-NBI:
  - inter-observer reproducibility of the ME-NBI microvascular findings ($K$ value 0.49–0.60) and the ME-NBI final diagnosis ($K$ value 0.50) showed fair agreement;
  - intra-observer reproducibility of the ME-NBI microvascular findings ($K$ value 0.61–0.78) and the ME-NBI final diagnosis ($K$ value 0.77) exhibited a moderate agreement.**
- value of inter-observer concordance for an ME-NBI diagnosis was 0.47 in the evaluation of depressed gastric lesions based on the ME-NBI features of combined irregular microvascular and microstructural patterns.***


***Yoo CH., Observer Variability in Gastric Neoplasm Assessment Using the Vessel Plus Surface Classification for MEwith NBI et al. Clin Endosc 2014;47:74-78
Number of early gastric cancer cases referred annually to the expert’s units

- Naohisa Yahagi: ~150 cases
- Toru Ito: ~100 cases
- Takuji Gotoda: ~100 cases
- Haruhiro Inoue: ~150 cases
- Mario Ribeiro: ~50 cases
- Horst Neuhaus & Sergey Kashin: ~50 cases
- Stefan Seewald: 15 cases
- Michael Hafner: <15 cases
- Lars Aabakken: <5 cases
The work of our team is focused on computer-aided decision support system for differentiating gastric superficial lesions.
Simplified NBI classification of gastric Mucosal and Vessels Patterns for histology prediction

<table>
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<tr>
<th>Proposed classification</th>
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<tbody>
<tr>
<td>A</td>
</tr>
<tr>
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<tr>
<td>Mucosal pattern</td>
</tr>
<tr>
<td>Vascular pattern</td>
</tr>
<tr>
<td>Expected outcome</td>
</tr>
</tbody>
</table>

- “Circular Mucosa with regular Vessels” was associated with normal histology (accuracy 83%)
- “Tubulo-villous Mucosa with regular Vessels” was associated with intestinal metaplasia (accuracy 84%)
- “Irregular Mucosa and irregular Vessels” was associated with dysplasia or cancer (accuracy 95%)

Three types of gastric mucosal Surface and Vessels patterns combinations in correspondence to histology prediction and clinical management

- **Surface& Vessels patterns combinations**
  - Circular regular Surface with regular Vessels patterns
  - Tubular Surface with regular Vessels patterns
  - Irregular/Absent Surface with irregular Vessels patterns

- **Expected histological changes**
  - Non-metaplastic non-neoplastic lesion
  - Metaplastic non-neoplastic lesion
  - Neoplastic lesion

- **Management (clinical decision)**
  - Medication treatment if necessary
  - Treatment and endoscopic surveillance if necessary
  - Endoscopic resection/surgery

Main steps of computer-aided decision support system for stomach

Image acquisition

Endoscopy

Zoom

Input image

Pre-processing

Feature extraction

Post-processing

Medical Expert

Decision support

Biopsy/No EMR/ESD

No cancer risk

No biopsy

Image classifier

Computer-aided image analysis and pathology prediction system
Algorithm for the computer-aided image analysis and pathology prediction

**Pre-processing**
- Preparation the image for further analysis:
  - Exclusion of reflections
  - Gray scale image
  - Brightness adjustment
  - Binarization

**Processing**
- Feature extraction:
  - Geometrical features
  - Topological features

**Image classifier**
- Post-processing:
  - Endoscopic Database
  - Classification:
    - 3 types of gastric mucosal Surface and Vessels patterns
  - Testing Protocol
Classification of the image with unknown pathology

Irregular type

Tubulo-villous type

Regular type

Computing of geometrical and topological features.....
Classification of the image with unknown pathology

Irregular type

Tubulo-villous type

Regular type

Classification.....
Results of classification

For visualisation of classifier results we painted the points of image in a color of the corresponding class.

Brown area indicates destroyed structure with vessel network (neoplastic lesion), blue color of background indicates tubular structure (metaplastic mucosa).
Preliminary clinical trial

Tokyo Medical University

Yaroslavl Regional Cancer Hospital

Endoscopy images

The results of classification

Blinded for the results of classification

Blinded for histology
Preliminary clinical trial: Case 1

Endoscopic and histological images were provided by Takuji Gotoda (Tokyo Medical University)
Well-differentiated adenocarcinoma

Endoscopic and histological images were provided by Takuji Gotoda (Tokyo Medical University)
Preliminary clinical trial: Case 2

Endoscopic and histological images were provided by Takuji Gotoda (Tokyo Medical University)
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Well-differentiated adenocarcinoma
Case 1
Early gastric body cancer (type IIa)
Off-Line System Testing Results

<table>
<thead>
<tr>
<th>Indicators / Type of lesions</th>
<th>Sensitivity (95 %CI)</th>
<th>Specificity (95 %CI)</th>
<th>Positive predictive value (95 %CI)</th>
<th>Negative predictive value (95 %CI)</th>
<th>Kappa value (95 %CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-metaplastic non-neoplastic</td>
<td>0.928 (0.926–0.93)</td>
<td>0.982 (0.98–0.983)</td>
<td>0.97 (0.968–0.972)</td>
<td>0.955 (0.954–0.957)</td>
<td>0.917 (0.913–0.92)</td>
</tr>
<tr>
<td>Metaplastic</td>
<td>0.928 (0.925–0.93)</td>
<td>0.945 (0.944–0.947)</td>
<td>0.90 (0.898–0.903)</td>
<td>0.961 (0.96–0.962)</td>
<td>0.867 (0.863–0.871)</td>
</tr>
<tr>
<td>Neoplastic</td>
<td>0.893 (0.89–0.897)</td>
<td>0.954 (0.953–0.955)</td>
<td>0.872 (0.868–0.875)</td>
<td>0.962 (0.961–0.964)</td>
<td>0.84 (0.835–0.845)</td>
</tr>
</tbody>
</table>

The average percentage of correctly recognized areas was **91.8±4.4%**

Kuvaev R., Edelsbrunner H., Kashin S. Nikonov E., DDW 2015
On-Line System Is Ready
And
Should Be Tested

Dr Sergey Kashin and Dr Roman Kuvaev are testing the on-line SYSTEM in Yaroslavl Regional Cancer Hospital
Conclusion
and
Future Perspectives

VS
## Missed gastric cancers within 3 years of gastroscopy

<table>
<thead>
<tr>
<th>Author</th>
<th>Study design</th>
<th>Time period</th>
<th>Population (n)</th>
<th>Country</th>
<th>&lt;3 year miss rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amin et al. (2002)</td>
<td>Surgical series, retrospective</td>
<td>1994–1999</td>
<td>-</td>
<td>UK</td>
<td>18/129 (13.9%)</td>
</tr>
<tr>
<td>Voutilainen et al.</td>
<td>Retrospective, link to cancer registry</td>
<td>1996–2001</td>
<td>-</td>
<td>Finland</td>
<td>13/284 (4.6%)*</td>
</tr>
<tr>
<td>Vradelis et al. (2011)</td>
<td>Retrospective</td>
<td>2005–2008</td>
<td>9,764</td>
<td>UK</td>
<td>6/74 (8.1%)</td>
</tr>
<tr>
<td>Menon et al. (2012)</td>
<td>Nested case control</td>
<td>Before 2012</td>
<td>5 million**</td>
<td>UK</td>
<td>128/5,473 (2.3%)</td>
</tr>
</tbody>
</table>

**Missed cancer rate in Western populations 2.3 – 13.9%** *(predominantly advanced cancers)*

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<tr>
<td>Hosokawa et al. (2007)</td>
<td>Retrospective, link to cancer registry</td>
<td>1990–1995</td>
<td>51,411</td>
<td>Japan</td>
<td>188/730 (25.8%)</td>
</tr>
<tr>
<td>Choi et al. (2011)</td>
<td>Screening programme</td>
<td>2002–2005</td>
<td>765,813</td>
<td>Korea</td>
<td>1083/3,498 (40.0%)</td>
</tr>
<tr>
<td>Ren et al. (2013)</td>
<td>Retrospective</td>
<td>2010–2011</td>
<td>44,500</td>
<td>China</td>
<td>23/103 (22.2%)</td>
</tr>
<tr>
<td>Cho et al. (2014)</td>
<td>Retrospective</td>
<td>2006–2013</td>
<td>-</td>
<td>Korea</td>
<td>52/284 (18.3%)</td>
</tr>
</tbody>
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**Missed cancer rate in Eastern populations 18.3 – 40%** *(include early gastric neoplasia)*
Miss rates for GI neoplasia are still high

**Esophagus**
- (early cancer)
  - 7.8% (UK)

**Stomach**
- (early cancer)
  - 19% (Japan)
  - 5-12% (China)
  - 22% (USA)

**Colon**
- (neoplasia)
  - 5-24% (USA)
  - 5.4-17% (China)

Chadwick G. Endoscopy 2014; 46: 553–559
Four D Protocol For Endoscopic Diagnosis of Early Gastric Neoplasia


Detection

Delineation

Differentiation

Depth of invasion assessment

The Role and Place of The Expert’s Eye and CADSS in Diagnostic Protocol
“Every new century brings new ideas and acquires new eyes”.

Heinrich Heine (1787–1856)

“At this time, there are no computers that can replace an experienced clinician’s intuition and eyes. Nonetheless, we are moving to the century of smart endoscopes which help the physician’s eyes to detect and differentiate the lesions”

Kazuhiro Gono (Olympus, Tokyo), YES 2014, Yaroslavl.
Welcome To Endoscopy Country

15th Live-Course on Advanced Digestive Endoscopy

June 30 - July 1, 2017, Yaroslavl
• There were around 7,100 new cases of stomach cancer in the UK in 2013, that’s 19 cases diagnosed every day.
• Stomach cancer is the 16th most common cancer in the UK (2013).
• Over the last decade, stomach cancer incidence rates have decreased by more than a quarter (27%) in the UK.
• Most stomach cancer cases are diagnosed at an late stage.
1 in 67 men and 1 in 135 women will be diagnosed with stomach cancer during their lifetime.
www.cancerresearchuk.org
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