Proposal of guidelines for the use of Video Capsule Endoscopy (VCE) in Europe

ESGE
Interest Group on the Video Capsule Endoscopy

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Madrid, November 2003
INTRODUCTION (1)

- Justification of the guidelines process
  - Country-specific environment
  - Adaptation to evolution of knowledge

- Methodology to define the guidelines:
  - Analysis of randomized controlled trials
  - Analysis of clinical experience in prospective studies
  - Summary of experiences in retrospective studies
  - Opinion of experts consensus groups
Small bowel remains:

- the « black box » of endoscopy
  
  *JD WAYE Endoscopy 2001; 33: 24-30*

- the « ultimate frontier »
  
  *B KREVSKY Gastroenterology 1991; 160: 838-839*

⇒ This is the context of use of VCE
BACKGROUND FOR THE USE OF VCE (2)

Difficulty to completely explore the small bowel:
1 - limits of radiological investigations

- intestinal tumours:
  SBFT < CT < Intestinal CT

- vascular lesions:
  Radionuclide scan < arteriography

2 - limits of endoscopic investigations of the small bowel
- sonde enteroscopy: fragile and tedious
- intraoperative videoenteroscopy: invasive, morbidity ++
- videopushenteroscopy limited to proximal jejunum and distal ileum
BACKGROUND FOR THE USE OF VCE (3)

Infectious risk and safety in Endoscopy
- endoscopes disinfection, AIDS, HCV
- trend toward the use of single use material

Social security politics in Europe
- financial resources
- quality assurance, appropriateness…

Increased demand
- Increase of aged population
- Need for savier investigations
The Technique (1)

**Inside the M2A™ Capsule**

1. Optical dome
2. Lens holder
3. Lens
4. Illuminating LEDs (Light Emitting Diodes)
5. CMOS (Complementary Metal Oxide Semiconductor) imager
6. Battery
7. ASK (Application Specific Integrated Circuit) transmitter
8. Antenna
The Technique (2)

- After completion of the recording, images are downloaded from the portable hard drive to a PC workstation (2 to 3 hours).

- A software is then used to review the images in an adjustable, rapid scan mode that can display between 1 and 25 frames per second.

- Thumbnails of images of interest, videoclips of segments incorporating 50 images can be annotated and stored.

- Interpretation requires 30 to 40 minutes
  - It needs good knowledge of digestive pathology\(^1\)
  - It needs an experience in interpretation of endoscopic images\(^2\)

\(^1\) BREITINGER et Al Am J Gastroenterol 2002 ; 97 : 85 (Abstract)
\(^2\) JACOB et Al Gastrointest Endosc 2002 ; 55 : 135 (Abstract)
The Technique (3)
Additional software features (1)

- Dynamic location utility:
  - Based on the strength of the signal received from the M2A capsule by the 8 sensors on the abdominal wall
  - The location is calculated from the position of these sensors and projected as a 2-D image.
  - Cleared by the FDA.
The Technique (4)
Additional software features (2)

- Multi-viewing of video stream
  - Utility to speed up the video replay
  - Dual display of the endoscopic image does not impair the usual assessment by observer.  

- Blood indicator function
  - Detects area with red colour
  - Good sensitivity and positive predictive value for actively bleeding lesions.  

1 SHREIBER et al. Gastrointest Endosc 2003; 57: 1864 (abstract)

2 LIANGPUNSAKUL et al. Gastrointest Endosc 2003; 57: 164 (abstract)
Undertaking of the examination (1)

- **The certainties:**
  * Patients are instructed to fast overnight
  * Water intake is allowed 2 hours after capsule ingestion
  * Food is allowed after 4 hours
  * Patients are asked to record abdominal symptoms on a diary
  * Patients are requested to intermittently check the blinking light on the belt pack for confirmation of signal reception.

*LEWIS et al. Gastrointest Endosc 2002; 56: 349-53*
Undertaking of the examination (2)

**Unfixed Issues**: Measures to improve detection of intestinal lesion and possibly allow the examination of the right colon and caecum:

- Use of prokinetics to promote progression of the capsule?
- Bowel cleansing similar to colonoscopy?
Undertaking of the examination (3)

- **Erythromycin** 200 mg IV or oral, 1 hour before capsule ingestion seems effective¹

- Controversy on usefulness of bowel cleansing²
  (2 l PEG, 2 hours before capsule ingestion)

- **Experts consensus:**
  These two methods can be used but are not systematically recommended.

¹ FIREMAN et al Gastrointest Endosc 2003; 57: 163 (abstract)
² STOPMAN Gastrointest Endosc 2003; 57: 165 (abstract)
- Today, only the Given Imaging Ltd device is commercially available

- Approved by FDA in 2001, in USA

- CE mark obtained in 2002, in Europe
Validated Indications (1) = Accepted and recommended indications

Patients with obscure digestive bleeding:
- Overt bleeding: Recurrent episodes of bleeding
- Occult bleeding: positive FOBT, iron deficiency with or without anaemia

All these patients have previously been investigated with normal EGD and colonoscopy.
INDICATIONS (2)

- Obscure bleeding: controlled prospective studies

Endoscopy 2003: 35, 569-575

Ell C et all Endoscopy 2002; 34, 686-689
INDICATIONS (3)

60 patients
27 males, 33 females
Mean age: 58 ± 18 years

32 patients
With Occult digestive bleeding

28 patients
With Overt digestive bleeding

Haemoglobin: 9.4 ± 2.5 g/dL
Number of patients having received blood transfusion: 24
Mean number of blood units: 2.3 ± 3.8
INDICATIONS (4)

58 patients

15 patients with negative PE and negative capsule

- PE + Capsule + N = 20
- PE - Capsule + N = 15
- PE + Capsule - N = 8

43 patients with lesion at PE or capsule
INDICATIONS (5)

Follow-up study at 12 months

44 patients (20 men – 63 ± 17 years
Obscure digestive bleeding
Normal EGD + colonoscopy

23 patients
with Overt bleeding
Hb = 9.3 ± 2.9 g/dl

21 patients
with Occult bleeding
Hb = 9.6 ± 2.0 g/dl

Delvaux, Fassler, Gay, AGA 2003
INDICATIONS (6)

Outcome of the patients at 12 months

<table>
<thead>
<tr>
<th>Patients with Positive Capsule recording</th>
<th>N = 18 (41.9%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapeutic enteroscopy</td>
<td>8</td>
</tr>
<tr>
<td>Surgery</td>
<td>4</td>
</tr>
<tr>
<td>Medical treatment</td>
<td>2</td>
</tr>
<tr>
<td>Stop NSAIDS</td>
<td>4</td>
</tr>
</tbody>
</table>

15 OK
1 recurrence, same lesion
1 patient died after surgery
1 was diagnosed with an other intestinal lesion
INDICATIONS (7)

Other digestive lesion
N = 9 (20.4 %)

Upper GI lesion 4
Blood in Stomach 2
Blood in colon 3

Negative
N = 17 (39.5 %)

10 Patients with an other digestive source of bleeding demonstrated
ENT 1
Upper gut 5
Colon 4

7 Patients with an anaemia of other origin
Haematological origin 3
Insufficient iron intake 4

No patient diagnosed with an intestinal lesion during the follow-up
### INDICATIONS (8)

**Obscure bleeding: Controlled Studies**

<table>
<thead>
<tr>
<th>Study</th>
<th>Journal/Publication</th>
<th>N</th>
<th>Controlled Study</th>
<th>% Diagn. CE</th>
<th>% Diagn. PVE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lewis</td>
<td>GI Endos</td>
<td>21</td>
<td>Yes</td>
<td>55.0</td>
<td>30.0</td>
</tr>
<tr>
<td>Delvaux et al</td>
<td>AGA 2002</td>
<td>58</td>
<td>Yes</td>
<td>68.9</td>
<td>37.9</td>
</tr>
<tr>
<td>Janowski/Cave</td>
<td>AGA 2002</td>
<td>39</td>
<td>No</td>
<td>74.3</td>
<td></td>
</tr>
<tr>
<td>Chutkan</td>
<td>AGA 2002</td>
<td>20</td>
<td>No</td>
<td>70.0</td>
<td></td>
</tr>
<tr>
<td>Yousfi</td>
<td>AGA 2002</td>
<td>12</td>
<td>Yes</td>
<td>83.3</td>
<td>41.6</td>
</tr>
<tr>
<td>Remke</td>
<td>AGA 2002</td>
<td>32</td>
<td>Yes</td>
<td>62.5 (84.4)</td>
<td>21.9 (31.3)</td>
</tr>
<tr>
<td>Pennazio</td>
<td>AGA 2002</td>
<td>60</td>
<td>Yes N = 29</td>
<td>48.3 58.6</td>
<td>27.6</td>
</tr>
<tr>
<td>Demets</td>
<td>AGA 2002</td>
<td>10</td>
<td>Yes</td>
<td>70.0</td>
<td>50.0</td>
</tr>
<tr>
<td>Van Gossum</td>
<td>AGA 2002</td>
<td>21</td>
<td>Yes</td>
<td>55.0</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>10 lesions in the range of upper GI</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Controlled Studies**

<table>
<thead>
<tr>
<th>Study</th>
<th>Journal/Publication</th>
<th>N</th>
<th>Controlled Study</th>
<th>% Diagn. CE</th>
<th>% Diagn. PVE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cave</td>
<td>AGA 2002</td>
<td>46</td>
<td>No</td>
<td>65.2</td>
<td></td>
</tr>
<tr>
<td>Demeds</td>
<td>UEGW 2002</td>
<td>18</td>
<td>Yes</td>
<td>77.7</td>
<td>30.0</td>
</tr>
<tr>
<td>Pennazio</td>
<td>UEGW 2002</td>
<td>89</td>
<td>Yes N = 45</td>
<td>47 73.3</td>
<td>37.9 42.2</td>
</tr>
<tr>
<td>Gonzales-Asansa</td>
<td>UEGW 2002</td>
<td>12</td>
<td>Yes</td>
<td>75.0</td>
<td>25.0</td>
</tr>
<tr>
<td>Mascarenhas</td>
<td>UEGW 2002</td>
<td>52</td>
<td>No</td>
<td>88.4</td>
<td></td>
</tr>
<tr>
<td>Fernandez Diez</td>
<td>UEGW 2002</td>
<td>22</td>
<td>No</td>
<td>68.2</td>
<td></td>
</tr>
<tr>
<td>Ell C</td>
<td>Endoscopy 2003</td>
<td>65</td>
<td>Yes N = 32</td>
<td>62.5 (84.4)</td>
<td>21.9 (31.3)</td>
</tr>
<tr>
<td>Saurin ... Gay</td>
<td>Endoscopy 2003</td>
<td>58</td>
<td>Yes</td>
<td>68.9</td>
<td>37.9</td>
</tr>
</tbody>
</table>
Validated Indications (1): Obscure Digestive Bleeding

Capsule endoscopy modifies the management of patients with obscure digestive bleeding.
Validated Indications (1): OBSCURE BLEEDING

- Obscure GI bleeding
- EGD and Colonoscopy NEGATIVE
- CT Scan
  - No tumors > 2 cm
  - No stenosis
- Capsule endoscopy
  - treat
  - EGD
  - VPE
  - Ileo-colonoscopy
- RBC scan
  - Angiography
  - Laparotomy and intraoperative enteroscopy

+ = treat
- = no treatment
Validated indications (2)

**Surveillance of Hereditary polyposis syndrome**

- FAP : Familial oedematous polyposis
- PJS : Peutz Jeghers syndrome
- FJP : Familial juvenile polyposis

Not yet validated:
- Screening of small bowel tumors in patients with hereditary colonic polyposis (Lynch)

*SCHULMAN K et al Gastrointest 2003 ; 57 : 550 (résumé)*
VALIDATED INDICATIONS (3)

Evaluation of side effects of NSAIDs on small bowel
- in the presence of chronic anaemia or,
- in the presence of unexplained abdominal pain,
- although NSAIDs-induced lesions may also be asymptomatic.
<table>
<thead>
<tr>
<th>First author</th>
<th>n</th>
<th>Crohn established</th>
<th>Crohn suspected</th>
<th>Coloileoscopy</th>
<th>Yield</th>
<th>Comparative test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lo</td>
<td>68</td>
<td>37</td>
<td>31</td>
<td>?</td>
<td>80-61%</td>
<td>Serology</td>
</tr>
<tr>
<td>Buchman</td>
<td>30</td>
<td>30 Recurrence suspected</td>
<td>-</td>
<td>?</td>
<td>87%</td>
<td>SBFT; 7 pts. Excluded due to strictures</td>
</tr>
<tr>
<td>Bloom</td>
<td>16</td>
<td>16 known or suspected</td>
<td>-</td>
<td>?</td>
<td>56%</td>
<td>Coloileoscopy 50%; SBFT 19%; Strictures on SBFT excluded</td>
</tr>
<tr>
<td>Vorderholzer</td>
<td>10</td>
<td>10 Follow up after clinical healing</td>
<td>-</td>
<td>+</td>
<td></td>
<td>CE endoscopy unchanged despite sonographic improvement</td>
</tr>
<tr>
<td>Heigh</td>
<td>8</td>
<td>8</td>
<td>-</td>
<td>?</td>
<td>88%</td>
<td>CT enteroclysis 88%; SFBT 14%</td>
</tr>
</tbody>
</table>
INDICATIONS CURRENTLY UNDER EVALUATION
CROHN’S DISEASE (2)

- FIREMAN et al, Gut 2003; 52: 390-392
  17 patients, only 10 had a CT scanner

- HEREIRAS et al, Endoscopy 2003; 35: 1-5
  21 patients VS SBFT

- COSTAMAGNA G et al, Gastroenterology 2002; 123:999-1005
  20 PATIENTS VS SBFT
INDICATIONS CURRENTLY UNDER EVALUATION
CROHN’S DISEASE (3)

1. The limits of the available studies:
   1. Evaluation of different clinical situations
   2. Limited number of patients
   3. Retrospective uncontrolled studies
   4. Comparison with SBFT but the gold standard is currently intestinal CT or MRI

2. One conclusion yet obtained: VCE detects more intestinal lesions than expected in patients with Crohn’s disease. Does this influence the management of these patients?
INDICATIONS CURRENTLY UNDER EVALUATION
CROHN’S DISEASE (4)

- Today statements:
  - VCE has no indication in patients with usual clinical presentation of the disease
  - VCE is useful in patients with suspected Crohn’s disease or with biological suspicion of relapse and normal endoscopic investigations.
  - VCE is useful to assess the response to an immunosuppressive therapy.
  - VCE seems useful to detect early lesions in case of intestinal recurrence (study in progress).
COELIAC DISEASE

- VCE not needed in typical cases,
- But possible interest in
  - patients with unexplained abdominal symptoms
  - in children with clinical or biological suspicion of coeliac disease
  - refractory sprue with ulcerative jejunitis: risk of T lymphoma
  - patients with microcytosis although they fully comply with the diet: risk of T lymphoma
INDICATIONS CURRENTLY UNDER EVALUATION

*Miscellaneous (2)*

**Interest in children**
- Capsule endoscopy is safe in children over the age of 9
- Potential use is under evaluation in:
  - Diagnosis of suspected coeliac disease
  - Detection the source of obscure bleeding
  - Suspision of Crohn’s disease of the small bowel
INDICATIONS CURRENTLY UNDER EVALUATION

Miscellaneous (3)

- Investigation of the colon
  - bowel cleansing needed, like for colonoscopy
  - possible interest for detection of angiodysplasia in the right colon
  - detection of a source of bleeding, in case of active bleeding

GAY et Al Gastrointest Endosc 2002; 56: 758-762
Main adverse event is the blockade of the capsule:
- anatomical stenosis
- impaired peristalsis
- impaired gastric emptying
- Endoscopic or surgical retrieval of entrapped capsules has been required in a few cases

No complication has been reported due to incidental leakage of the batteries or exposure to the ingested batteries
<table>
<thead>
<tr>
<th>Study</th>
<th>Mergener AGA 2003</th>
<th>Enns AGA 2003</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>197</td>
<td>272</td>
</tr>
<tr>
<td>Quality of the recording</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Technical failure</td>
<td>9.6%</td>
<td></td>
</tr>
<tr>
<td>- Partial examination</td>
<td>11.1%</td>
<td></td>
</tr>
<tr>
<td>- Presence of intraluminal content</td>
<td>5.6%</td>
<td></td>
</tr>
<tr>
<td>Complications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Capsule rétention</td>
<td>3.6% (7)</td>
<td>2.6% (7)</td>
</tr>
<tr>
<td>- Endoscopic retrieval</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>- Surgical retrieval</td>
<td>5</td>
<td>5</td>
</tr>
</tbody>
</table>
SAFETY (3)

Can we beforehand the risk of blockade the capsule?

Take into account medical history of the patient:
- surgery, radiotional therapy, NSAIDs

Take into account contra-indications
- Known or suspected gut strictures
- Extensive Crohn Enteritis
- Presence of numerous intestinal diverticuli
## SAFETY (4)

<table>
<thead>
<tr>
<th>First author</th>
<th>n</th>
<th>Complication (n)</th>
<th>Entrapment</th>
<th>Type of complication surgical retrieval</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mixed series</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fleicher</td>
<td>AGA 2003</td>
<td>493</td>
<td>?</td>
<td>?</td>
<td></td>
</tr>
<tr>
<td>Enns</td>
<td>AGA 2003</td>
<td>272</td>
<td>7</td>
<td>7</td>
<td>5 (1 acute)</td>
</tr>
<tr>
<td>Fireman</td>
<td>AGA 2003</td>
<td>160</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Chutkan</td>
<td>AGA 2003</td>
<td>125</td>
<td></td>
<td>?</td>
<td>2</td>
</tr>
<tr>
<td>Willert</td>
<td>AGA 2003</td>
<td>33</td>
<td>2</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>Bolz</td>
<td>AGA 2003</td>
<td>33</td>
<td>0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Studies on bleeding</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adler</td>
<td>AGA 2003</td>
<td>267</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Cave</td>
<td>AGA 2003</td>
<td>137</td>
<td>5</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Bolz</td>
<td>AGA 2003</td>
<td>33</td>
<td>0</td>
<td>?</td>
<td></td>
</tr>
<tr>
<td>Buchman</td>
<td>AGA 2003</td>
<td>36</td>
<td>0</td>
<td>?</td>
<td></td>
</tr>
<tr>
<td><strong>Studies on crohn disease</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lo</td>
<td>AGA 2003</td>
<td>68</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Bushmann</td>
<td>AGA 2003</td>
<td>30</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Bloom</td>
<td>AGA 2003</td>
<td>16</td>
<td>1</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Heigh</td>
<td>AGA 2003</td>
<td>8</td>
<td>1</td>
<td>1</td>
<td>?</td>
</tr>
</tbody>
</table>

Rosch T, modified: Endoscopy 2003; 35:816-822
SAFETY (4)

Can we beforehand the risk of blockade the capsule?
- SBFT, CT and MRI do not fairly exclude the presence of an asymptomatic stenosis.
- So patient must be aware of the possibility of retention of the capsule and the need to remove it by an endoscopic or surgical procedure.
- In order to solve this problem, Given Imaging will propose the « PATENCY CAPSULE », in evaluation at the present time, to detect intestinal stenoses.
- Any investigation center performing capsule procedures MUST include a gastroenterologist trained in endoscopy and skilled to remove a stacked capsule, especially if blocked in the cricopharyngeal area.

- The ROTH NET retriever can be used for this purpose
SAFETY (6)
RELATIVE CONTRA-INDICATIONS

- Presence of a cardiac\(^1\) pacemaker is no longer regarded as a contra-indication

\(^1\) LEIGHTON et al. Gastroenterology 2003 ;
## FINANCIAL CONSIDERATIONS
### VCE: Reimbursement Status

<table>
<thead>
<tr>
<th>COUNTRY</th>
<th>Indications</th>
<th>Modalities of Reimbursement</th>
</tr>
</thead>
<tbody>
<tr>
<td>United States</td>
<td>CD – Obscure bleeding</td>
<td>National</td>
</tr>
<tr>
<td></td>
<td>Exclusion of small bowel tumor</td>
<td></td>
</tr>
<tr>
<td>Portugal</td>
<td>No restriction for indications</td>
<td>National</td>
</tr>
<tr>
<td>Sweden</td>
<td>No restriction for indications</td>
<td>National</td>
</tr>
<tr>
<td>Denmark</td>
<td>No restriction for indications</td>
<td>National</td>
</tr>
<tr>
<td>Austria</td>
<td>No restriction for indications</td>
<td>National (Public hospital)</td>
</tr>
<tr>
<td>Switzerland</td>
<td>Under evaluation</td>
<td></td>
</tr>
<tr>
<td>Netherlands</td>
<td>No restriction for indications</td>
<td>National (Public hospital)</td>
</tr>
<tr>
<td>France</td>
<td>No restriction for indications</td>
<td>No Reimbursement</td>
</tr>
<tr>
<td>Australia</td>
<td>Obscure gastrointestinal bleeding</td>
<td></td>
</tr>
</tbody>
</table>

Application for approval will be submitted in Germany, France, Italy and UK.
THE FUTURE

1. Definition of the role of VCE in the management of patients with IBD by comparing it fairly to other imaging techniques.
   - Need for larger controlled studies with more patients
2. Evaluation of the real clinical impact of VCE by follow-up and outcome studies
3. Development of devices for capsule retrieval
4. Development of devices to control the progression of the capsule
5. Standardize the language and the content of the capsule reports

1 DELVAUX et al Gastrointest Endosc 2003; 57: 1857 (Abstract)