

**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

# BACKGROUND (1)

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...

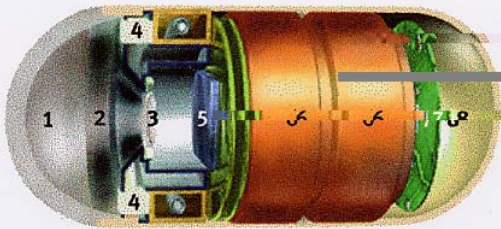
## **Increased demand**

- Increase of aged population
- Need for savier investigations

# The Technique (1)

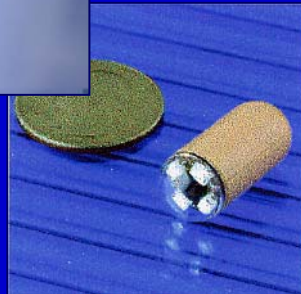
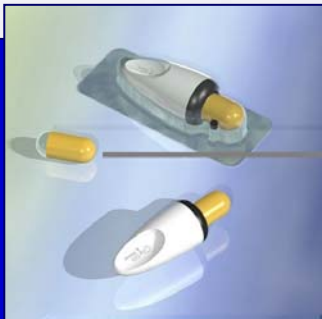


Actual size



## INSIDE THE M2A™ CAPSULE

1. Optical dome
2. Lens holder
3. Lens
4. Illuminating LEDs (Light Emitting Diode)
5. CMOS (Complementary Metal Oxide Semiconductor) imager
6. Battery
7. ASIC (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<sup>1</sup>
  - ⇒ It needs an experience in interpretation of endoscopic images<sup>2</sup>

<sup>1</sup> BREITINGER et al *Am J Gastroenterol* 2002 ; 97 : 85 (Abstract)

<sup>2</sup> 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 impaire the usual assessement by observer. <sup>1</sup>
- Blood indicator function
  - Detects area with red colour
  - Good sensitivy and positive predictive value for actively bleeding lesions.<sup>2</sup>

<sup>1</sup> SHREIBER et Al *Gastrointestendosc* 2003 ; 57 : 1864 (abstract)

<sup>2</sup> LIANGPUNSAKUL et Al *Gastrointestendosc* 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.

## 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 effective<sup>1</sup>
- **Controversy on usefulness of bowel cleansing**<sup>2</sup>  
(2 l PEG, 2 hours before capsule ingestion)
- **Experts consensus:**  
These two methods can be used but are not systematically recommended.

<sup>1</sup> FIREMAN et al *Gastrointest Endosc* 2003; 57: 163 (abstract)

<sup>2</sup> 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

# INDICATIONS (1)

***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**

Saurin JC, Delvaux M, Gay G, Gastrointest Endosc 2002; 55 :88 (abstract)  
Endoscopy 2003: 35, 569-575

Ell C et al Endoscopy 2002; 34, 686-689

# INDICATIONS (3)

60 patients

27 males, 33 females

Mean age:  $58 \pm 18$  years

32 patients

With Occult digestive bleeding

28 patients

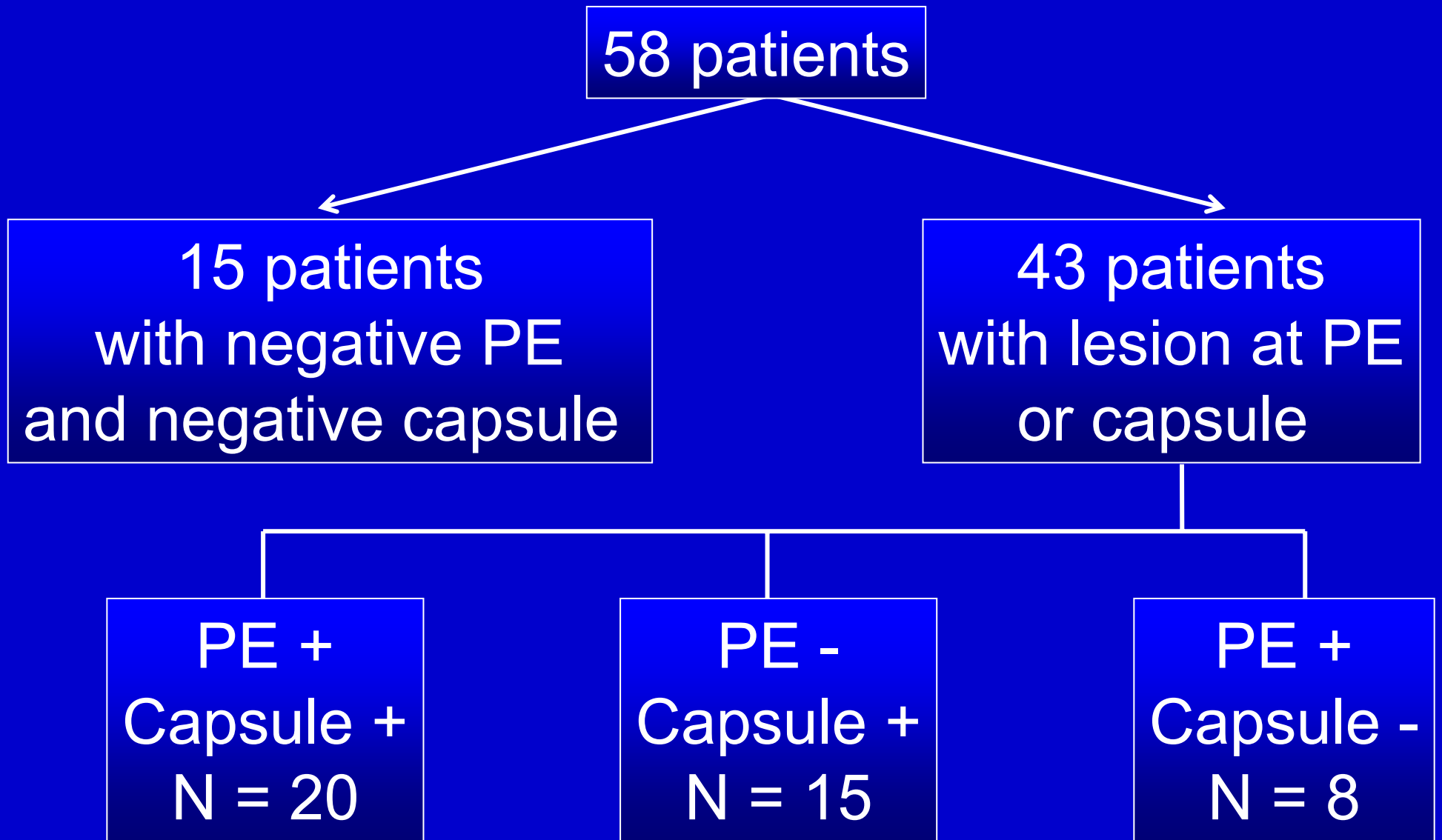
With Overt digestive bleeding

Haemoglobin :  $9.4 \pm 2.5$  g/dL

Number of patients having received blood transfusion : 24

Mean number of blood units :  $2.3 \pm 3.8$

# INDICATIONS (4)



# INDICATIONS (5)

## Follow-up study at 12 months

**44 patients (20 men –  $63 \pm 17$  years  
Obscure digestive bleeding  
Normal EGD + colonoscopy**

**23 patients  
with Overt bleeding**

**Hb =  $9.3 \pm 2.9$  g/dl**

**21 patients  
with Occult bleeding**

**Hb =  $9.6 \pm 2.0$  g/dl**

# INDICATIONS (6)

## Outcome of the patients at 12 months

Patients with Positive  
Capsule recording  
N = 18 (41.9 %)

Therapeutic enteroscopy 8  
Surgery 4  
Medical treatment 2  
Stop NSAIDS 4

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

Other digestive lesion  
N = 9 (20.4 %)

## INDICATIONS (7)

Negative  
N = 17 (39.5 %)

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

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

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

		N	Controlled study	% Diagn. CE	% Diagn. PVE
Cave	AGA 2002	46	No	65.2	
Demeds	UEGW 2002	18	Yes	77.7	30.0
Pennazio	UEGW 2002	89	Yes N = 45	47 73.3	37.9 42.2
Gonzales-Asansa	UEGW 2002	12	Yes	75.0	25.0
Mascarenhas	UEGW 2002	52	No	88.4	
Fernandez Diez	UEGW 2002	22	No	68.2	
EII C	Endoscopy 2003	65	Yes N = 32	62.5 (84.4)	21.9 (31.3)
Saurin ...Gay	Endoscopy 2003	58	Yes	68.9	37.9

# INDICATIONS (9)

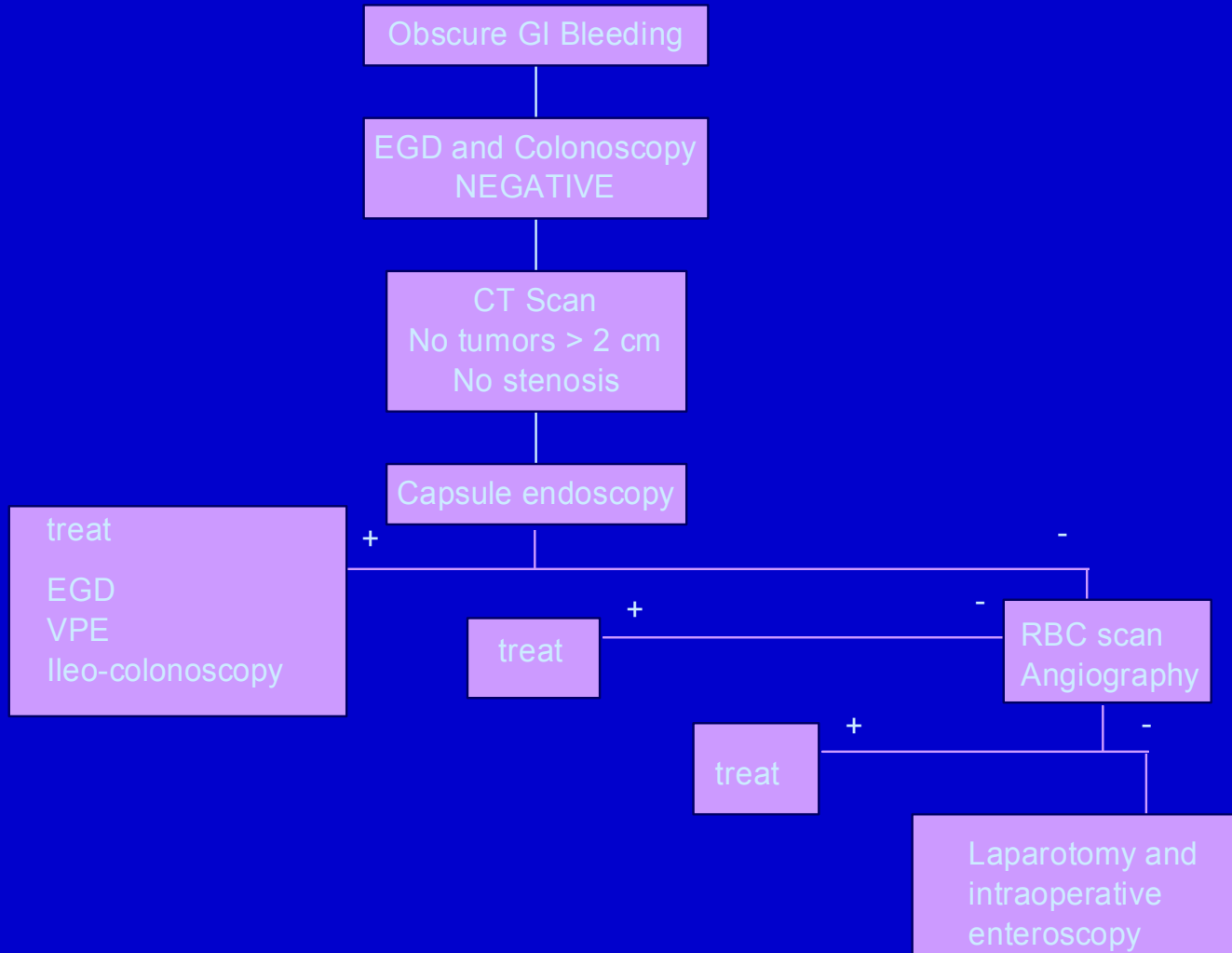
*Validated Indications (1): Obscure Digestive Bleeding*

Capsule endoscopy modifies the management of patients with obscure digestive bleeding.

# INDICATIONS (10)

## *Validated Indications (1):* OBSCURE BLEEDING

obscure GI bleeding



# 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.

# INDICATIONS CURRENTLY UNDER EVALUATION

## *CROHN'S DISEASE (1)*

Result of studies dealing with capsule endoscopy in crohn's disease

First author		n	Crohn established	Crohn suspected	Coloileoscopy	Yield	Comparative test
Lo	2003 DDW abstract	68	37	31	?	80-61%	Serology
Buchman	2003 DDW abstract	30	30 Recurrence suspected	-	?	87%	SBFT; 7 pts. Excluded due to strictures
Bloom	2003 DDW abstract	16	16 known or suspected		?	56%	Coloileoscopy 50%; SBFT 19%; Strictures on SBFT excluded
Vorderholzer	2003 DDW abstract	10	10 Follow up after clinical healing	-	+		CE endoscopy unchanged despite sonographic improvement
Heigh	2003 DDW abstract	8	8	-	?	88%	CT enteroclysis 88%; SFBT 14 %

# 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 All, 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).

# INDICATIONS CURRENTLY UNDER EVALUATION

## *Miscellaneous (1)*

### *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
  - Suspicion 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 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*

# SAFETY (1)

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

# SAFETY (2)

<b>Study</b>	<b>Mergener AGA 2003</b>	<b>Enns AGA 2003</b>
<b>Number of patients</b>	<b>197</b>	<b>272</b>
<b>Quality of the recording</b> <ul style="list-style-type: none"><li>- <b>Technical failure</b></li><li>- <b>Partial examination</b></li><li>- <b>Presence of intraluminal content</b></li></ul>	<b>9.6%</b> <b>11.1%</b> <b>5.6%</b>	
<b>Complications</b> <ul style="list-style-type: none"><li>- <b>Capsule rétention</b><ul style="list-style-type: none"><li>- <b>Endoscopic retrieval</b></li><li>- <b>Surgical retrieval</b></li></ul></li></ul>	<b>3,6% (7)</b> <b>2</b> <b>5</b>	<b>2,6% (7)</b> <b>2</b> <b>5</b>

# 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)

First author		n	Complication (n)	Entrapment	Type of complication surgical retrieval	Other
Mixed series						
Fleicher	AGA 2003	493	?			
Enns	AGA 2003	272	7	7	5 (1 acute)	2 endoscopic removals
Fireman	AGA 2003	160	2	2	2	
Chutkan	AGA 2003	125				2
Willert	AGA 2003	33	2	2	-	-
Bolz	AGA 2003	33	0	-	-	
Studies on bleeding						
Adler	AGA 2003	267	3	3	3	
Cave	AGA 2003	137	5	5	3	2 patients refuse, no symptoms
Bolz	AGA 2003	33	0			
Buchman	AGA 2003	36	0			
Studies on crohn disease						
Lo	AGA 2003	68	?	?	?	
Bushmann	AGA 2003	30	2	2	2	7 patients exluded
Bloom	AGA 2003	16	1	?	?	
Heigh	AGA 2003	8	1	1	?	

# 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.

# SAFETY (5)

- 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<sup>1</sup> pacemaker is no longer regarded as a contra-indication

<sup>1</sup> *LEIGHTON et Al Gastroenterology 2003 ;*

# FINANCIAL CONSIDERATIONS

## VCE : Reimbursement Status

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

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
3. Development of devices to control the progression of the capsule
4. Standardize the language and the content of the capsule reports <sup>1</sup>

<sup>1</sup> DELVAUX et al *Gastrointest Endosc* 2003 ; 57 : 1857 (Abstract)