

Wireless Capsule Colonoscopy versus colonoscopy in patients at average or increased risk for Colorectal Cancer.

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Introduction

- Colorectal cancer (CRC) is a major cause of mortality and morbidity worldwide
- Screening and surveillance of patients at average or increased risks for CRC are based on detection and removal of adenomatous polyps
- In many countries, Colonoscopy is considered the standard procedure for screening and surveillance
- However Colonoscopy has some limitations (e.g. invasiveness, discomfort, cost...)

“average risk” = asymptomatic, 50-74 years old

“increased risk” = asymptomatic, with personal or family history of colonic neoplasia (polyps or cancer)

Wireless Colon Capsule (WCC)



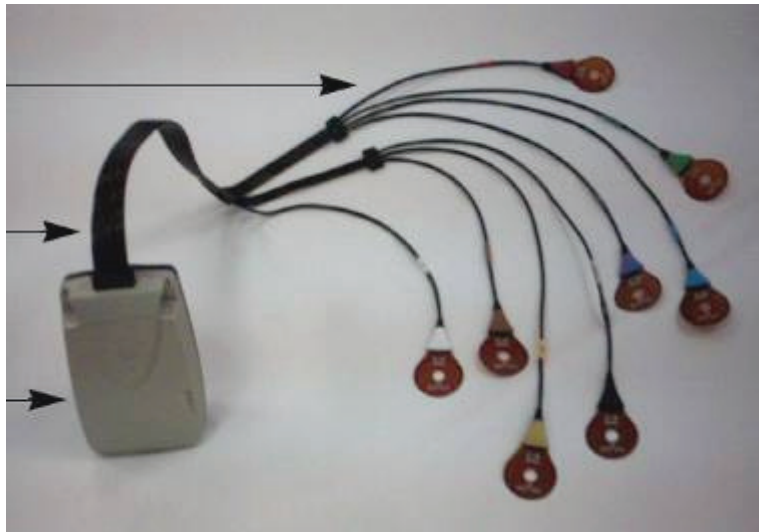
31 mm X 11 mm

2 video cameras with optimized optics

4 images per second

Battery (8 to 10 h autonomy)

Sensors array



Specific software RAPID 5



Primary Objective

- Assess the diagnostic yield (especially Negative Predictive Value and sensitivity) of Wireless Capsule Colonoscopy (WCC) compared to conventional colonoscopy (CC) for **screening and surveillance** in subjects at average or increased risks for Colorectal Cancer .
- Main criterion of judgment: proportion of patients with **polyps \geq 6mm or cancer detected.**

Exclusion Criteria

- **Existence of GI symptoms**
- Any suspicion of occlusive bowel disease
- Recently complicated colonic diverticulosis (< 3 months ago)
- Absence of written informed consent
- Pregnant women or women who can become pregnant or breast-feeding mothers
- Patient with a pacemaker
- Patient with advanced heart or kidney failure

Study protocol

Time	Procedures
Day -3 → -2	Low residue diet
Day -1	Low residue breakfast & lunch Liquid snack (yogurt, cream)
16 ⁰⁰	3 Liters <i>Colopeg</i> [®]
18 ⁰⁰ – 21 ⁰⁰	
8 ⁰⁰ – 9 ⁰⁰	1 Liter <i>Colopeg</i> [®]
9 ⁴⁵ – 10 ⁰⁰	20mg <i>Domperidone</i> & PillCam
Day 0	
12 ⁰⁰	Booster I (45ml NaP)*
15 ³⁰	Booster II (30ml NaP)**
18 ⁰⁰	10mg Bisacodyl suppository**
18 ³⁰	Low-fiber snack
Day +1	
6 ⁰⁰ – 7 ⁰⁰	1 Liter <i>Colopeg</i> [®]
After 10 ⁰⁰	Conventional colonoscopy

* Pending verification that PillCam left stomach with RAPID **real-time viewer**

** If PillCam was not expelled from anus

WCC and colonoscopy performed by endoscopists blind to each other

Assessment of Colon Cleanliness

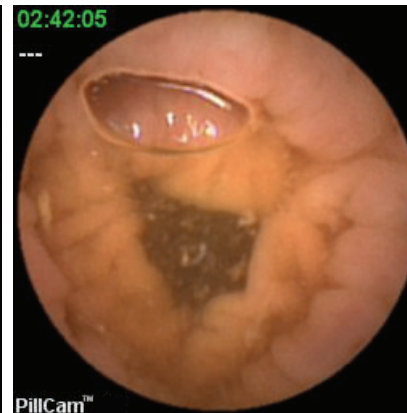
Poor



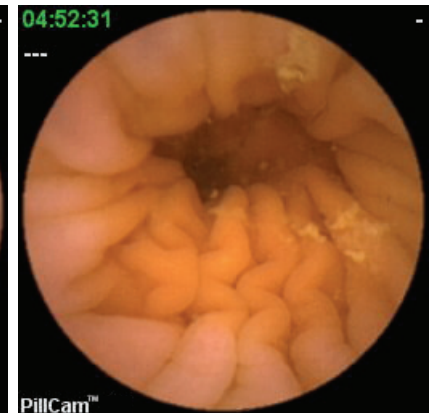
Fair



Good



Excellent



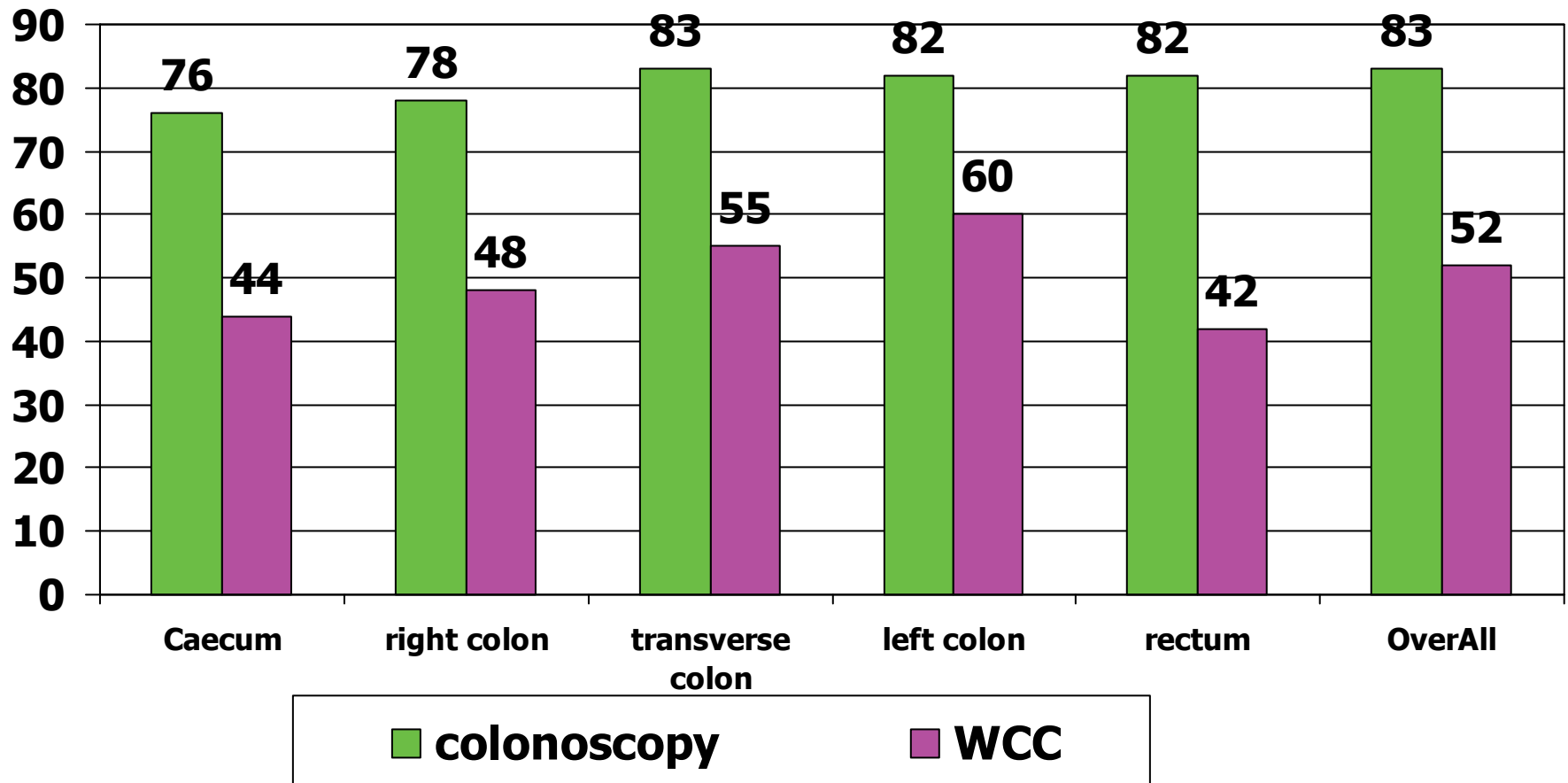
Poor	Large amount of fecal residue
Fair	Enough feces or dark fluid present to preclude a completely reliable examination
Good	Small amount of feces or dark fluid, but not enough to interfere with examination
Excellent	No more than small bits of adherent feces

Hypothesis and statistics

- **550 patients needed** to test non inferiority of WCC compared to CC in terms of **Negative Predictive Value** (maximal difference = 5%, Power=90% and alpha risk = 5%).
- Same estimation with an accepted loss of 20% **sensitivity** of WCC compared to CC for the detection of **polyps \geq 6mm.**
- Interim analysis planned after 1/5 of recruitment completed (data presented at last AGA meeting may 2009)

Colon Cleansing

% of Patients with Good-to-Excellent Colon Cleansing



Study protocol

Regimen I (n=232)		Regimen II (n=313)
Day -3 → -2	Low residue diet	Idem
Day -1	Low residue breakfast	Liquid diet
	Liquid snack (yogurt)	
Day 0	16 ⁰⁰ 18 ⁰⁰ – 21 ⁰⁰	3 Liters <i>Colopeg</i> [®]
	8 ⁰⁰ – 9 ⁰⁰	1 Liter <i>Colopeg</i> [®]
	9 ⁴⁵ – 10 ⁰⁰	20mg <i>Motilium</i> [®] & P
	12 ⁰⁰	Booster I (45ml NaF)
	15 ³⁰	Booster II (30ml NaF)
	18 ⁰⁰	10mg Bisacodyl sup
	18 ³⁰	Low-fiber snack
Day +1	6 ⁰⁰ – 7 ⁰⁰	1 Liter <i>Colopeg</i> [®]
	After 10 ⁰⁰	Traditional colonosc

* Pending verification that PillCam left stomach with RAPID **real-time viewer**

** If PillCam was not expelled from anus

Demographic characteristics

Patients	D545	
Gender	M: 305 (56%) F: 240 (44%)	
Age (years)	60 +/- 10	

	N	%
Increased risk	377	70
Family history of cancer	184	34
Personal history of cancer	18	3
Family history of polyps	63	12
Personal history of polyps	213	39
Average risk	163	30

Safety and tolerance

- Capsule easily ingested in all except one subject
 - Capsule excreted within 10 h in 91% of patients
 - 20 Adverse Events
 - 17 mild/moderate (haemorrhoid proctitis, fever, vomiting, bronchospasm...)
 - 3 severe (Perforation during colonoscopy, cardiac failure possibly related to colon preparation, bleeding after mucosectomy)
- 3 SAE due to Colonoscopy and/or preparation; none to capsule itself.

Safety and tolerance

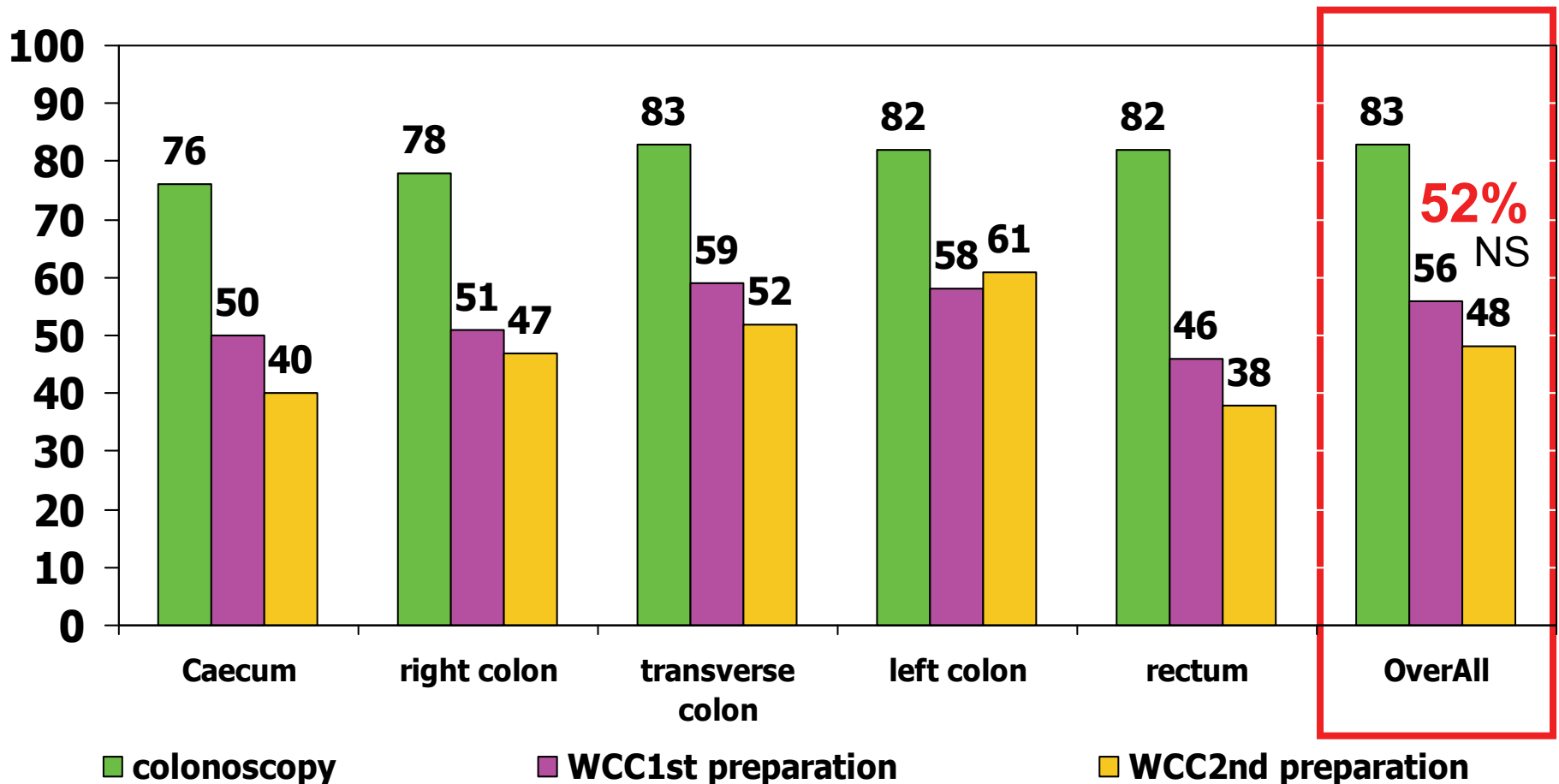
- Visual Analogic Scale from 0 to 10

	Mean	SD
Colonoscopy	8.25	2.00
WCC	8.74	1.56

* *P. value < 0.0001*

Colon Cleansing

% of Patients with Good-to-Excellent Colon Cleansing



Per-patient prevalence of polyps and cancer

	No. of Patients (%)		
	According to Colonoscopy	According to WCC	
Any size Polyp	311 (57)	249 (46)	P<0.0001
≥ 6mm	112 (21)	94 (17)	P = 0.097
≥ 10mm	43 (8)	29 (5)	P=0.03
Cancer	5 (0.9)	3 (0.6)	

The 118 (22%) discordant significant findings between CC and WCC were reviewed by a panel of 4 experts

Capsule Accuracy vs Colonoscopy

Intention-to-diagnose analysis

	Sens [%]	Spec [%]	PPV [%]	NPV [%]
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All patients, regardless of colon cleansing level (100% Pts)				
Any size Polyp	58	71	73	56
≥ 6 mm	39	88	47	85
≥ 10mm	35	97	52	95

Patients with good-to-excellent colon cleansing level (52%)				
Any size Polyp	66	63	69	59
≥ 6mm	53	84	46	88
≥ 10mm	60	97	56	98

Review of the videos of discordant cases between WCC and CC by the Expert Panel

(Main criterion i.e. polyps $\geq 6\text{mm}$)

	Sens [%]	Spec [%]	PPV [%]	NPV [%]
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All patients, regardless of colon cleansing					
Before review		39	88	47	85
After review		57	95	73	90

Patients with good-to-excellent cleansing					
Before review		53	84	46	88
After review		65	94	71	92

Capsule and Colonoscopy accuracies using a modified gold standard*

≥ 6mm

Sens [%]	Spec [%]	PPV [%]	NPV [%]
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All patients, regardless of colon cleansing level

WCC	51	94	72	85
Colonoscopy	83	100	100	95

Patients with good-to-excellent cleansing

WCC	65	91	69	89
Colonoscopy	79	100	100	94

* FP of WCC confirmed by expert panel are considered as TP of WCC and FN of colonoscopy

Conclusions

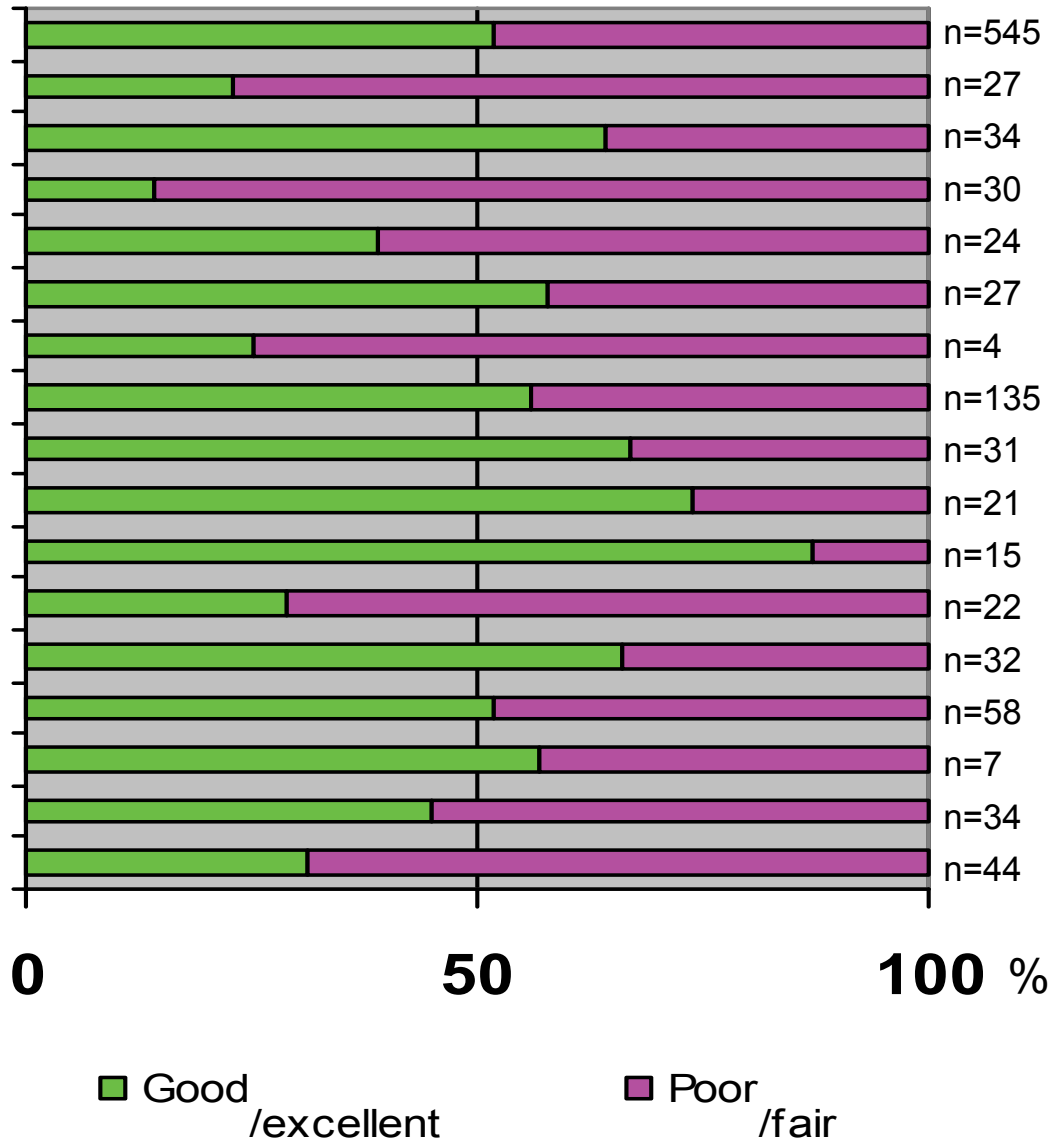
- Excellente faisabilité, sécurité et tolérance de la capsule colique
- La qualité de la préparation est insuffisante chez un malade sur deux dans les conditions réelles “ambulatoires” d’un dépistage ou d’une surveillance
- La VPN est élevée voir excellente (i.e. $\geq 95\%$) pour les polypes $\geq 10\text{mm}$
- La sensibilité demeure insuffisante pour remplacer la coloscopie à ce stade de développement (capsule C1)



Leçons du PHRC

- Nécessité d'essais sur des populations réelles de dépistage et de surveillance
- La préparation colique
 - Nature de la préparation mais surtout...
 - Motivation du malade
 - Informations délivrées
- Le contrôle qualité
 - Entraînement à la lecture
 - Indicateurs de qualité ?

Rate (%) of colon cleansing level for the WCC in every center



Rate (%) of misclassified WCC results (FN and FP) in every center

