

PillCam Colon 2[®] capsule endoscopy versus standard colonoscopy:

Results of studies in Europe and the United States

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“The colon capsule, PillCam Colon2[®], has been in development since 2009. As compared with the previous capsule, it incorporates technical advances that improve the quality of the images obtained and the frequency of image capture during sequences in which the capsule is propelled rapidly through a colonic segment. Studies comparing this capsule with colonoscopy have shown a sensitivity of 87% and a specificity of 79% for polyps ≥ 6 mm, with values of 89% and 92% for polyps ≥ 10 mm. These results provide ground to consider Pill-Cam Colon 2[®] for use in colorectal cancer screening. Studies will be required to assess its effectiveness and its impact on healthcare costs, particularly in comparison with immunological tests in the investigation of blood in the stools. Other indications are also being evaluated, notably in the context of inflammatory bowel disease.”

Initially developed for the examination of the small intestine, capsule endoscopy has undergone technical developments that have enabled its use for the examination of the colon. The PillCam Colon 2[®] capsule (Given Imaging Covidien GI Solutions) represents the latest generation in capsule endoscopy for the examination of the colonic mucosa. The aim of this overview is to summarize and to discuss studies comparing PillCam Colon 2[®] with colonoscopy.

Technical specifications of the PillCam Colon 2[®] capsule

The PillCam Colon 2[®] capsule has been in development since 2009. As for the previous version, PillCam Colon 1[®], it differs from the capsule used for exploration of the small intestine by the presence of two optical systems, each capturing 4 images per second. The technical improvements to PillCam Colon 2[®] include an angle of view of 172 ° instead of 156 °, which allows a better examination of the colonic mucosa, and a capture frequency that can vary between 4 and 35 frames per second, providing a better visualization in colonic segments where the capsule progresses rapidly, in particular in the transverse colon. The recorder worn by the patient on his/her belt has also been improved, allowing real time visualization of the images obtained by the capsule, and including algorithms for detecting the presence of the capsule in the small intestine that inform patients of the different stages of the colonic preparation protocol.

In parallel with these technical advances in the capsule, the reading software provided by Given Imaging (Rapid Access 8[®]) has also been improved and includes a function to facilitate the estimation of polyp size as well as the possibility of FICE-type electronic coloration (Fujifilm Inc. Omiya, Japan), which highlights polyp structure and the changes in vasculature, as in conventional colonoscopy.

Comparative studies of the PillCam Colon 2[®] capsule and colonoscopy

Since 2009, several studies have been conducted comparing PillCam Colon 2 with colonoscopy, primarily for the detection of colorectal polyps, with a view to assessing the effectiveness of the capsule in colorectal cancer screening. More recently, several comparative studies

have also been performed in patients with ulcerative colitis.

Comparative studies of colorectal polyp detection

The first comparative study of PillCam Colon 2[®] was carried out by Eliakim et al. [1] and indicated a sensitivity of 89% and a specificity of 76% for the detection of polyps ≥ 6 mm in diameter. The results for the PillCam Colon 2 capsule were considered to be better than those of the Colon 1 capsule reported in several previous studies [2-4]. It should be noted that in this study the discordant cases between capsule endoscopy and colonoscopy were reassessed retrospectively by a panel of experts. This may have contributed to the improvement in results between the two studies carried out by same group – one with the Colon 1[®] capsule [2] and the other with the Colon 2[®] capsule [1]. Furthermore, the specificity reported by these authors reflected a large number of PillCam Colon 2[®] capsule false positives for polyps ≥ 6 mm that were not identified during colonoscopy.

A multicenter European study was subsequently carried out, including 117 patients with an average age of 60 years [5]. In this study, examination of the colonic mucosa involved the entire colon and rectum in 88% of patients. This rate of “complete” examination was comparable to that previously reported with the Colon 1 capsule [2-4,6]. The per-patient analysis showed, for PillCam Colon 2[®], a sensitivity of 84% for polyps ≥ 6 mm and 88% for polyps ≥ 10 mm. Specificities were, respectively, 64% and 95% for the detection of these polyps. Three cancers were discovered during this study, all detected by PillCam Colon 2[®]. During the analysis of the results, half of the false negatives for PillCam Colon 2[®] were in fact errors in estimation of the size of polyps with a diameter close to 6 mm, which had been noted as < 6 mm from the capsule reading. More recently, a North American study was published as an abstract [7]; this included 884 patients at average risk for colorectal neoplasia. The sensitivity of PillCam Colon 2[®] was 88% for adenomas ≥ 6 mm and 92% for adenomas ≥ 10 mm, with specificities of 82% and 95%, respectively. When the analysis was based on all polyps, including hyperplastic polyps and serrated polyps, the sensitivity was 81% for polyps ≥ 6 mm and 80% for polyps ≥ 10 mm, with specificities of 93% and 97%, respectively. This observation may reflect the difficulty for the capsule to identify flat lesions such as serrated adenomas.

Finally, a recent study assessed the diagnostic yield of PillCam Colon 2[®] and of virtual colonoscopy in patients who were positive for a fecal blood test [8]. Fifty patients with an average age of 59 years were evaluated by the following three methods: capsule endoscopy, virtual colonoscopy, and then conventional colonoscopy, considered as the gold standard. Sixteen patients (32%) had at least one polyp ≥ 6 mm. The sensitivity and specificity of PillCam Colon 2[®] were 88.2% and 87.8%, respectively, comparable to those of virtual colonoscopy: 88.2% sensitivity and 84.8% specificity. This study also included an assessment of patient preference for one examination or the other, indicating that 78% of patients preferred the capsule endoscopy to the virtual colonoscopy.

The colon capsule as a filter test before colonoscopy?

A first study with the Colon 1[®] capsule had tested this hypothesis [6], considering the healthcare costs of the large number of “negative” colonoscopies in everyday practice [9]. In this study, the indication for colonoscopy in light of the colon capsule results was defined as the presence of at least 1 polyp ≥ 5 mm, 3 polyps < 5 mm, or any other significant pathology: cancer, inflammatory bowel disease (IBD)... The positive predictive value of the colon capsule to indicate colonoscopy was 88% and the negative predictive value 76%, the latter being reduced by 8 false negatives with the capsule. Moreover, patient recruitment was not strictly that of a screening in the general population, as many patients with digestive symptoms or a high risk of polyps were included.

In a recent study, 62 patients with a positive immunoassay for detection of blood in the stool were examined by PillCam Colon 2[®], and then a conventional colonoscopy was performed the next day [10]. Colonoscopy, the reference examination, was completed in 94% of cases and the diagnostic yield was 58%, with 29 adenomas, 1 cancer, 2 cases of colitis, and 1 solitary rectal ulcer. The sensitivity of PillCam Colon 2[®] to detect all types of polyps was 95%, specificity 65%, positive predictive value 79%, and negative predictive value 90%. When only the 18 patients who had a significant lesion by colonoscopy were considered, the sensitivity of PillCam Colon 2[®] was 89%, specificity 96%, positive predictive value 89%, and negative predictive value 96%. The authors concluded that the colon capsule could be considered as

a filter test for the indication of colonoscopy.

Studies comparing colon capsule endoscopy and colonoscopy in ulcerative colitis (UC).

A few recent studies have evaluated the feasibility of examining the colon by colon capsule endoscopy in patients with UC. A first study in 100 patients using the Colon 1 capsule, carried out by Sung et al. [11], showed a rather high rate of incomplete examination, with 10% of patients not having expelled the capsule during the registration time period. Compared with colonoscopy performed on the same day, the capsule had a sensitivity of 89%, specificity 75%, positive predictive value 93%, and negative predictive value 63%, to detect the presence of inflammatory lesions of the colonic mucosa. A study that was also conducted in Asia, including 40 patients with UC and performed using PillCam Colon 2 ®, showed a high rate of capsule retention in the colon, as it was only expelled in 66% of cases [12]. The correlation between conventional colonoscopy and PillCam Colon 2 ® was good for the detection of inflammatory lesions of the colonic mucosa. A single-center Spanish study that included 42 patients also showed a good concordance ($k = 0.75$) for the endoscopic level of severity and the assessment of the extent of lesions ($k = 0.71$) [13]. Finally, a study of 26 patients found a similar concordance between capsule endoscopy and colonoscopy for the severity ($k = 0.75$; $P < 0.001$) and the extent ($k = 0.52$; $P < 0.001$) of lesions [14].

Discussion

Comparison of the results obtained with PillCam Colon 1 ® and PillCam Colon 2 ® for the detection of colorectal polyps shows a better sensitivity of the second-generation capsule, but the number of studies available with the latter capsule is limited and there are differences in colonic preparation protocols between the different studies that may have influenced the results [1-8,15]. The quality of colonic preparation is an important factor that influences the diagnostic yield of the colon capsule as well as the rate of examinations completed (with expulsion of the capsule during the time of recording). A study comparing two preparation protocols [16] showed that the protocol used significantly influenced the rate of full examinations and the transit time of the cap-

sule through the colon, without affecting the diagnostic sensitivity and specificity of the capsule.

The capability of the endoscopic capsule to detect colorectal polyps also depends on the size and type of polyps. Table 1 summarizes the different comparative studies carried out with PillCam Colon 1[®] and PillCam Colon 2[®], separating polyps into ≥ 6 mm and ≥ 10 mm categories. The variability of the analysis criteria between the studies makes the comparison difficult, in particular for polyps ≥ 10 mm, which were only defined as a specific group in a small number of PillCam Colon 1[®] studies. Nevertheless, it can be noted that PillCam Colon 2[®] shows a better diagnostic yield that can be explained by the technical advances that improve the image quality of this capsule, and in addition by the growing experience of the readers who participated in most of the studies concerning the two types of capsule. Furthermore, the study presented by Rex et al. [7] analyzed polyps ≥ 6 mm, polyps ≥ 10 mm, and all polyps grouped together, regardless of their size and shape. It would seem that capsule endoscopy has a lower sensitivity in this latter category, notably by recognizing less easily flat or serrated polyps.

The colon capsule will find, primarily, a future clinical use in screening for colorectal cancer. Two studies have evaluated the colon capsule as a “filter test” for the indication of colonoscopy [6,10]. These have shown encouraging results, but it should be noted that one study was performed in a group of patients who were symptomatic or at high risk of colorectal cancer [6] and the other study involved patients who had a positive fecal blood test [10]. Nevertheless, in that study, the colonic capsule showed a very high negative predictive value, and therefore reliability for ruling out the indication of colonoscopy. This negative predictive value will increase even further when populations at medium or low risk of colorectal cancer are studied, as is the case in general population screening. Future studies conducted under strict screening conditions should demonstrate the advantages of this approach, in particular in reducing healthcare costs related to screening for colorectal cancer [19]. The effectiveness of the colon capsule in this screening strategy, and its impact on healthcare costs, should be evaluated against fecal blood immunoassays. Colon capsule endoscopy may in fact be proposed for ambulatory use, the recorder being able to warn the patient of the different times of the protocol of colonic washes [20].

Table 1. Detection of colorectal polyps by the PillCam Colon[®] capsule: comparison of the PillCam Colon 1 and PillCam Colon 2 capsules.

	Patients (n)	PillCam Colon 1				PillCam Colon 2			
		≥ 6mm		≥ 10mm		≥ 6mm		≥ 10mm	
		Sensitivity (%)	Specificity (%)						
Eliakim <i>et al.</i> [2]	91	56	69	-	-				
Schoofs <i>et al.</i> [3]	41	60	73	-	-				
Van Gossum <i>et al.</i> [4]	332	64	84	60	98				
Sieg <i>et al.</i> [17]	38	55	96						
Gay <i>et al.</i> [6]	128	76	76	80	100				
Pilz <i>et al.</i> [18]	62	79	55	-	-				
Sacher-Huvelin <i>et al.</i> [15]	545	39	88	-	-				
Eliakim <i>et al.</i> [1]	104					89	76	88	89
Spada <i>et al.</i> [5]	117					84	64	88	95
Rondonotti <i>et al.</i> [8]	50					88	84	88	87
Rex <i>et al.</i> [7]	884					88	93	92	97
Average		61	76	70	99	87	79	89	92

Conclusion

Studies conducted to date with PillCam Colon 2 ® have confirmed the results obtained with the previous version and shown a better diagnostic yield for the detection of colorectal polyps. Future studies should focus on demonstrating the effectiveness of PillCam Colon 2 ® in colorectal cancer screening and on evaluating its impact on the healthcare costs associated with this screening. Other indications, notably in patients with inflammatory bowel disease, are currently being evaluated.

Conflicts of interest

G rard Gay is a consultant for Given Imaging Covidien GI Solutions.

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