

## Clinical and Economic Evaluation of the Diagnostic Method of Capsule Endoscopy for Examination of the Small Intestine.

Capsule endoscopy is an endoscopic method for the examination of the small intestine. It enables a non-invasive, pain free visualisation of the whole of the small intestine and provides high quality pictures, even of areas of the small intestine which are not accessible by other conventional methods.

The most common methods used at present for the evaluation of the small intestine are either endoscopic (enteroscopy, intraoperative enteroscopy) or radiographic procedures (small bowel follow through, enteroclysis, angiography, computed tomography) as well as sonography and magnetic resonance imaging. All these methods have certain restrictions with respect to their diagnostic capabilities.

Important applications of these methods are the evaluation of gastrointestinal bleeding and inflammatory bowel disease of the small intestine.

Currently, the source of the gastrointestinal bleeding remains undiagnosed in 5 % of patients in spite of repeated examinations. This suggests that it is localised in the small intestine, which can now be viewed in its entirety with the help of capsule endoscopy. This is also the case for inflammatory bowel disease. 40 % of patients have an exclusive involvement of the small intestine. The time span from the first symptoms to the diagnosis ranges from a few months to several years.

Currently capsule endoscopy is reimbursed by many (> 120) health insurances in the USA. The main indication is the clarification of unknown causes of bleeding. Numerous insurance companies also reimburse the use in cases of suspected Crohn's disease. In Europe capsule endoscopy is currently reimbursed in Austria, Portugal, Sweden, Denmark and Switzerland, sometimes without restrictions, in some cases without restriction regarding the gastrointestinal diseases.

The diagnostic yield of capsule endoscopy compared to other methods of diagnosis (enteroscopy, small bowel follow through) has been ascertained by Given Imaging (the producer) in clinical studies in various countries. For gastrointestinal bleeding 50 to 87.5 % (median 73.3 %, average 73 %) of cases were able to be diagnosed. In comparison only 15 to 50 % (median 40 %, average 31.7 %) of the cases were able to be diagnosed with enteroscopy. In the diagnosis of chronic inflammatory bowel disease the relevant rates of diagnosis using capsule endoscopy were between 66.7 and 100 % (median 89.9 %, average 85.2 %) and using small bowel follow through between 14.8 and 48.1 % (median 28.4 %, average 30.5 %).

Published peer reviewed studies reported a diagnostic yield of capsule endoscopy ranging from 20 to 81 %. When capsule endoscopy was compared with another diagnostic procedure, it had a higher diagnostic yield than the comparator.

In an article of Pennazio et al.<sup>1</sup>, sensitivity and specificity of capsule endoscopy were 89 % and 95 % respectively. These values correspond with the independently determined values from studies described above. They were used for the economic analyses described in this dossier. The diagnostic yield of capsule endoscopy according to scientific publications also corresponds with the described data from the clinical studies.

Authors of scientific reviews conclude that capsule endoscopy will become the method of choice in the diagnosis of diseases of the small intestine after negative gastroscopy and colonoscopy. It is expected that the diagnosis and therapy of diseases of the small intestine will be improved by capsule endoscopy.

Since the introduction of capsule endoscopy in 2001 the number of examinations using capsule endoscopy has risen worldwide from 3.600 (4<sup>th</sup> quarter of 2001) to 19.000 (1<sup>st</sup> quarter of 2004). Up to now in Germany more than 8.800 capsule endoscopy examinations were performed until July 2004 in 183 centers. In Germany the future overall need depends largely on the application of the method in the evaluation of various gastrointestinal diseases. Therefore the yearly total demand of capsule endoscopy in Germany can be estimated only for specific indications. For the indication obscure gastrointestinal bleeding 4.500 examinations and for the indication suspected inflammatory bowel disease 3.500 examinations have been estimated on the basis of German disease incidences.

The health economic analysis described here from the perspective of the public health insurance concentrates on the diagnosis of obscure gastrointestinal bleeding and of suspected inflammatory diseases located in the small intestine. On the basis of a decision analytic model the cost and usefulness expected of capsule endoscopy for examining obscure gastrointestinal bleeding has been compared to enteroscopy as well as to small bowel follow through for the examination of suspected inflammatory bowel disease.

Repeated examinations which are not only expensive but which have a negative influence on the quality of life of a patient can be avoided by earlier diagnosis. At the same time unnecessary therapies can also be avoided. These potential savings are part of the economic analysis. The analysis is based on the modelling of a hypothetical cohort of 10.000 patients in various scenarios. The average expected cost effectiveness rate is given for each scenario.

The results of the analysis prove that capsule endoscopy shows greater effectiveness in the diagnosis of the two indications examined; in other words is the better strategy with regard to effectiveness.

More patients can be correctly diagnosed using capsule endoscopy than using enteroscopy (gastrointestinal bleeding) or small bowel follow through (inflammatory bowel disease). As a result earlier treatment can be initiated with the correct and therefore effective therapy (patients diagnosed true positive) and further diagnostic methods (patients diagnosed true negative) can be reduced.

In the examination of obscure gastrointestinal bleeding capsule endoscopy is not only the more effective method compared to enteroscopy, it is also the less expensive alternative, in view of continued costs as a result of false positive or false negative diagnoses. The use of capsule endoscopy therefore has a cost saving potential which makes it the dominant strategy. The number of cases diagnosed false negative is much lower using this method as opposed to alternative methods.

Patients with non localised sources of bleeding of the gastro-intestinal tract find themselves subjected to a never ending round of gastroscopies, colonoscopies and x-rays using a contrast medium with very little probability of finding the source of the bleeding. This also causes high costs. According to the analyses presented here an average saving of € 318 per capsule endoscopy examination can be expected. On

average 40 extra correctly diagnosed cases for every 100 applications are to be expected. Capsule endoscopy is therefore more effective as well as being more economical than enteroscopy.

For the analysis concerning the diagnosis of suspected inflammatory bowel diseases, different scenarios were analysed based on great variances of the costs due to diagnostic failure (false negative and false positive costs). Those scenarios led to different model outcomes concerning the incremental cost-effectiveness of capsule endoscopy in comparison to small bowel follow through.

Whereas the minimal approach (worst-case) for the cost due to diagnostic failure, showed higher costs of capsule endoscopy in comparison to small bowel follow through amounting to € 361 per examination, the simulated median approach (base-case) and the maximum approach (best-case) for the cost incurred due to diagnostic failure evaluated capsule endoscopy to have a cost saving potential.

In the so-called best-case scenario capsule endoscopy shows median cost savings of € 565 per examination in comparison to small bowel follow through and the so-called base-case scenario evaluated mean cost savings of capsule endoscopy amounting to € 125 per examination. Those last named base-case scenario is assumed to be the most realistic approach for evaluating the costs due to diagnostic failure, based on the fact, that the real cost of diagnostic failure are most probably between the minimum and the maximum diagnostic failure costs, that were used for analysing the worst-case and the best-case scenario.

In each of these three analysis settings capsule endoscopy showed to be the more effective alternative in comparison to small bowel follow through. On average 47 extra correctly diagnosed cases for every 100 applications are to be expected.

Therefore capsule endoscopy shows also in diagnosing inflammatory bowel disease to be the more effective and the less costly (base-case and best-case) alternative in comparison to small bowel follow through and as a consequence of this capsule endoscopy was evaluated to be the dominant strategy.

Even in comparison to examinations that have a high significance for diagnosing suspected inflammatory bowel diseases in Germany (enteroclysis, computer tomography, magnet resonance imaging) capsule endoscopy showed to be dominant strategy that is not only more effective but also less expensive.

The examination cost of this method has been calculated for the consideration of reimbursement of capsule endoscopy by the public health insurance companies. The cost of the diagnostic method of capsule endoscopy, for which reimbursement is being applied, amounts according the suggested calculation to a total € 1.026.01 (physicians' costs = € 291.38, depreciation of equipment based on a utilisation ratio of 35 % = € 143.03 and materials for the endoscopic capsule = € 591.60).

The description of the payments being applied for is: „Capsule endoscopy for the diagnosis of diseases of the small intestine from the Ligament of Treitz to the ileocecal valve“. Capsule endoscopy is to be used to diagnose gastrointestinal bleeding as well as inflammatory bowel disease after previous negative gastroscopy and colonoscopy. This method is to be implemented by a specially trained gastroenterologist.

## Reference

- <sup>1</sup> Pennazio M, Santucci R, Rondonotti E, Abbiati C, Beccari G, Rossini FP et al. Outcome of patients with obscure gastrointestinal bleeding after capsule endoscopy: Report of 100 consecutive cases. *Gastroenterology* 2004; 126(3):643-653.