Summary

This thesis describes the results of several studies on two minimally-invasive modalities used to investigate the small intestine: magnetic resonance (MR) enteroclysis and video capsule endoscopy (VCE). Focus is on the use of these modalities in small-bowel neoplasms, refractory coeliac disease and midgastrointestinal bleeding. Additionally, this thesis highlights several aspects of quality in VCE, including safety and complication management, and assessment of bowel preparation.

Chapter 1 briefly summarizes the most important aspects of small-bowel anatomy and physiology. Additionally, the most important clinical conditions affecting the small bowel are introduced.

Part One: MR enteroclysis

Chapter 2 provides a review of radiological modalities that can be used to investigate the small intestine. These methods include more traditional methods, such as small-bowel follow through and conventional enteroclysis. These techniques are more and more being replaced by cross-sectional imaging techniques, such as computed tomography (CT) and MR imaging. The latter technique does not use ionizing radiation, which is an important advantage, especially when repeated examinations are needed. In order to achieve optimal imaging of both the small-bowel lumen and wall, luminal distension is a prerequisite. This can be achieved by oral contrast (enterography) or by contrast delivered through a nasojejunal catheter (enteroclysis). Although enteroclysis is a somewhat more invasive than enterography is, it allows better distension of especially the jejunum. The advantages and disadvantages of several radiological imaging methods for different small-bowel diseases are discussed and compared to VCE.


Chapter 3 describes the results of a study on the diagnostic accuracy of MR enteroclysis in the detection of small bowel neoplasms, with small-bowel endoscopy, surgery, histopathologic analysis and follow-up serving as standards of reference. Ninety-one MR enteroclysis studies performed to investigate or exclude the presence of small-bowel neoplasms were retrospectively evaluated by two radiologists. Imaging findings were compared with the results of invasive small-bowel tests or surgery, or with clinical follow-up for more than 18 months in case of normal imaging findings. Thirty-two patients had a small-bowel neoplasm. Eighty-six of 91 studies were correctly interpreted, resulting in an overall diagnostic accuracy of 0.95 for MR enteroclysis in the detection of small-bowel neoplasms. Sensitivity and specificity in the diagnosis of small-bowel neoplasms was 0.91 and 0.97, respectively, for the expert radiologist and 0.94 and 0.95, respectively, for the less experienced radiologist; the \( \kappa \) value was 0.95. Factors associated with malignancy were the presence of longer solitary nonpedunculated lesions, mesenteric fat infiltration, and the presence of enlarged mesenteric lymph nodes.

Chapter 12

Chapter 4 reports on the use of MR enteroclysis in patients suspected of having refractory coeliac disease. We aimed to determine MR enteroclysis findings in patients with uncomplicated coeliac disease (CD), refractory coeliac disease type I (RCD I) and refractory coeliac disease type II (RCD II). Especially the latter subset of patients is at increased risk of developing lymphoma. One radiologist blinded to clinical details retrospectively evaluated quantitative and qualitative criteria of 28 studies obtained in symptomatic patients with CD. We developed a scoring-system using parameters identified in multivariate analysis to be associated with RCD II. The presence of less than 10 folds per 5 cm jejunum, mesenteric fat infiltration and bowel wall thickening were associated with RCD II. We defined a positive MR score as the presence of two or more of these features. This scoring system was then used by two radiologists to evaluate a second group of 40 symptomatic patients with CD. In the validation group, the MR score was positive in 13 of 15 patients with RCD II (sensitivity 0.87) and negative in 24 of 25 patients without RCD II (specificity 0.96). The 5-year survival rate was 95% in patients with a negative MR score and 56% in patients with a positive MR score (p < 0.0001). MR enteroclysis helped to identify the presence of seven of eight malignancies and to diagnose absence of malignancy in 58 of 60 studies. It was concluded that MR enteroclysis can be used to investigate the presence of RCD II or malignancy in symptomatic patients with CD.


Part Two: Video capsule endoscopy

Chapter 5 is a short review aimed to provide the reader with some basic knowledge concerning the latest developments in small-bowel endoscopy. An emphasis is on the way radiology and endoscopy may interact.

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Chapter 6 concerns VCE findings in patients with CD and persisting or relapsing symptoms despite a gluten-free diet. Most of these patients with nonresponsive CD will have slow-responding, but otherwise uncomplicated, CD. A minority of patients will have true RCD, some of which may rapidly progress to lymphoma. Discrimination between these two extremes is difficult, especially because many abnormalities encountered in complicated CD are not within reach of conventional oesophagogastroduodenoscopy. We retrospectively analysed 48 VCE examinations performed in adult CD patients because of persisting or relapsing symptoms despite adherence to a gluten-free diet. Patients with either uncomplicated CD or RCD I were considered to have a good prognosis, whereas patients with RCD II or enteropathy-associated T-cell lymphoma were considered to have a poor prognosis. Multivariate analysis was performed to identify VCE findings independently associated with either good or poor prognosis. Proximal focal erythema (OR 6.7; 95% CI, 1.2–38.7; p = 0.033) and absence of progression of the capsule to the distal intestine (OR 16.5; 95% CI, 1.2–224.9; p = 0.035) were independently associated with poor prognosis. Of the 28 patients with none of these two features, none died during
follow-up, compared to 2 (13%) of the 15 patients with one of both features, and 4 (80%) of the 5 patients with both features. These results suggest that VCE could be of use in the identification of patients with nonresponsive CD who are at risk of poor prognosis.


Chapter 7 describes the results of a study on VCE performed to evaluate midgastrointestinal bleeding in patients using anti-thrombotic drugs. We carried out a retrospective study of 56 patients who underwent VCE for evaluation of previous overt midgastrointestinal during anti-thrombotic therapy. VCE examinations were re-evaluated by a gastroenterologist blinded to clinical details. A probable cause for gastrointestinal bleeding was identified in 28 (50%) of the 56 studies. Angioectasia were found in 19 patients. Twenty-two studies showed a possible cause in the small bowel. Multivariate logistic regression analysis showed that reinstitution of anti-thrombotic therapy before VCE was carried out was the only independent predictor of positive VCE findings (OR 8.61; 95% CI, 1.20–60.42; \( p = 0.032 \)). These results suggest that in case of midgastrointestinal bleeding in patients using anti-thrombotic drugs, VCE should either be performed immediately, while the patients is still using these drugs, or at a later stage, but after these drugs have been restarted.


Chapter 8 shows the results of a study aimed to determine the incidence and causes of capsule retention, which is a known complication of small-bowel video capsule endoscopy. Surgery is the most frequently used method of capsule retrieval. We performed a retrospective analysis of 904 small-bowel video capsule examinations performed in our centre and evaluated the outcome of double-balloon endoscopy as the first method used to retrieve entrapped video capsules. Capsule retention occurred in eight patients (incidence: 0.88%; 95% CI, 0.41%–1.80%), and caused acute small-bowel obstruction in six patients. We were able to remove all retained capsules successfully during double-balloon endoscopy. Five patients underwent elective surgery to treat the underlying cause of capsule retention and one patient required emergency surgery because of multiple small-bowel perforations. These results show that in our series the incidence of capsule retention is low, and that double-balloon endoscopy is a reliable method to remove retained capsules which may prevent unnecessary surgery. If surgery is required, pre-operative capsule retrieval allows for pre-operative diagnosis, adequate staging in case of malignancy and optimal surgical planning.


Chapter 9 introduces a novel computed scoring system able to assess bowel cleansing during VCE examinations of the small intestine. A score derived directly from the VCE images could be a reliable and objective method to describe mucosal visibility, which is an important part of the endoscopy report, since inadequate bowel preparation negatively influences the reliability of endoscopic examinations. We designed a computed assessment of cleansing score based on colour intensities of the tissue colour bar of the VCE reading software. This score was retrospectively tested in 24 VCE studies, and prospectively
in 40 VCE segments from 10 consecutive VCE studies. The correlation between the computed score and three existing subjective scores was good. This computed scale could be integrated in VCE reading software. We have named this scoring system the Computed Assessment of Cleansing (CAC) score.


**Part Three: MR enteroclysis and video capsule endoscopy**

**Chapter 10** presents the results of a study performed to compare the diagnostic accuracy of MR enteroclysis and VCE. We retrospective analysed data from 77 patients who underwent both MR enteroclysis and VCE, and compared the findings of these examinations with the findings of enteroscopy, surgery, or with the results of clinical follow-up for more than 2 years. Specificity of MR enteroclysis was higher than that of VCE (0.97 vs 0.84, \( p = 0.047 \)), whereas sensitivity was similar (0.79 vs 0.74, \( p = 0.591 \)). In 2/32 (6.3%) patients with both negative VCE and negative MR enteroclysis a positive diagnosis was established, compared to 5/11 (45.5%) patients in whom VCE was positive and MR enteroclysis was negative (likelihood ratio 8.1; \( p = 0.004 \)), 9/11 (81.8%) patients in whom MR enteroclysis was positive and VCE was negative (likelihood ratio 23.5; \( p < 0.0001 \)), and all 23 patients in whom both VCE and MR enteroclysis showed abnormalities (likelihood ratio 60.8; \( p < 0.0001 \)). We concluded that VCE and MR enteroclysis are complementary modalities. In our study population, MR enteroclysis was more specific than VCE, while both produced the same sensitivity.


**Appendix A: Case reports**

**Appendices A1 to A5** show examples of the use of MR enteroclysis and VCE in patients with rare small-intestinal diseases. These examples provide an additional insight in the diagnostic possibilities of both modalities.

— *Clin Gastroenterol Hepatol* 2010;8:e123.
— *Dig Liver Dis* 2012;44:355.