seen on capsule enteroscopy or CT or seen on BAE without having been identified on previous investigations. Results: A total of 580 double-balloon enteroscopy procedures were carried out. Anterograde (oral) and retrograde (anal) route double-balloon enteroscopies were performed in 359 and 221 patients, respectively. A total of 48 patients were found to have neoplastic disease/masses. Thirty-five tumours were detected prior to DBE (33 by capsule enteroscopy and 2 by Computer tomography), 9 were suspected by CE but found only at DBE and 2 cases were missed by CE altogether. Twenty-one tumours were found at retrograde DBE, whilst 27 were found at antegrade DBE. 46 patients presented with OGIB, where 2 presented with abdominal pain. The distribution of lesions was duodenum 5, jejunum 22, mid small bowel 16 and ileum 5. Morphologically, 2 were infiltrative, 7 were pedunculated, and the remainder were sub mucosal. At DBE 13 were inspected only, 25 were biopsied, 6 were tattooed for potential surgery and 4 were resected endoscopically. The final pathology was: 9 small sub mucosal lesions with normal biopsy (normal histology), 4 adenomas , 3 lymphomas , 3 lymphangitic cysts, 2 adenocarcinomas , 1 Meckels diverticulum, 1 hamartoma, 1 lymphoid hyperplasia, 1 lipoma, and 1 metastatic melanoma. Eighteen patients avoided surgery (diagnosis made and observation only), 4 resected by endoscopy, 3 underwent surgery (adenocarcinoma with invasive infiltration), and 3 underwent chemotherapy for lymphoma. Conclusions: Our analysis shows that small bowel tumours are a significant finding at double-balloon enteroscopy and that this procedure has a therapeutic impact on the management of suspected or documented small bowel neoplasia.

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Improved Video Quality and Reliability With Self-Stabilizing Colon Capsule Endoscopy: Pilot Study in Acute Canine Models

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Background: Video capsule endoscopy (VCE) is a non-invasive method for examining the gastrointestinal tract which has been successful in studies of the small intestine. Recently VCE has been attempted in the colon as well. However, the capsule often tumbles in the wider lumen of this organ, resulting in missed regions when traveling too fast or closely facing the colonic wall. Self-stabilizing VCE is a novel method to visualize the colon without tumbling. Aim: To comparatively evaluate the effect of stabilization of a commercially available VCE (MiroCam®; IntroMedic Co. Ltd., Seoul, Korea) in acute canine experiments. Methods: Two MiroCam® VCEs were modified by attaching to them a custom-made, biocompatible stabilizing component designed from a knitted, liquid-permeable polyglicolic acid sac filled with granules of superabsorbent polymer (FAVOR PAC, Evonik Industries, Stockhausen, Germany). Two additional MiroCam® VCEs were left non-modified. Four anesthetized mongrel dogs (2M, 2F, 25.3+/-4.5 kg) underwent laparotomy followed by exposure of part of the proximal left colon, where a 0.5-cm incision was made. A single VCE capsule (self-stabilizing, or non-modified) was inserted through the incision, which was immediately closed. 200 ml saline was injected locally, followed by 0.04 mg/kg IV Neostigmine (APP Pharmaceuticals, Schaumburg, Illinois, USA). The inserted capsule was propelled through the colon due to the Neostigmine-induced colonic peristalsis. Upon the expulsion of the capsule through the anus, collected video data were stored for further image processing. After the clearance of Neostigmine, another capsule was administered in a similar fashion. Four such administrations were sequentially performed on each dog at random, two with the non-stabilized and two with the stabilized capsule. A novel signal processing method was developed to quantify the video stabilization based on optical flow analysis using a commercially-available video tracking software (Syntheyes, Andersson Technologies LLC, Malvern, PA, USA). Results: The average optical flow trajectory for the stabilized capsule was statistically significantly lower at 4,066.21±186.64 pixels vs. 30,434.48±687.98 pixels for the non-stabilized ($p<0.05$). The stabilized capsule did not lose visual contact with the centroid of the colon during the transit. The maximum rate of change for sequential images was measured to be 43.72±12.04 pixels/sec for the stabilized case, while for the non-stabilized it was statistically significantly higher at 445.98±71.23 pixels/sec ($p<0.05$). The average radius movement of the VCE relative to the centroid of the colon was 63.48±27.59 pixels for the stabilized capsule and 100.38±46.68 pixels for the non-stabilized ($p<0.05$). Conclusion: The feasibility of self-stabilized colon capsule endoscopy has been demonstrated in acute canine experiments.

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Use of an External Real-Time Image Viewer Coupled With Prespecified Actions Enhanced the Complete Examinations for Capsule Endoscopy

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Background: The clinical utility of capsule endoscopy (CE) is often limited by delayed gastric emptying or prolonged small bowel transit which result in exhaustion of the battery before the capsule reaches the caecum. Aim: The aim was to determine whether the use of an external real-time viewer could reduce delays caused by delayed gastric emptying of the capsule or delayed intestinal transit and also improve the rate of positive findings. Methods: We compared the proportion of completed exams and positive results among a group of patients studied before introduction of real-time viewer and a group in which capsule transit through the esophagus, stomach, and small bowel was regularly monitored and actions (e.g., administration of water or intravenous metoclopramide) were taken if it was delayed. Results: One hundred procedures in the viewer group and 100 control procedures in the age-matched controls were analyzed. In the viewer group, additional water intake (22 cases) and/or administration of metoclopramide (26 cases) were required. Endoscopic-assisted duodenal placement of the capsule was required in 3 cases. Overall one-third (n=33) of cases required viewer-prompted interventions. The completion rate (86% vs. 66%, p=0.002) and the rate of positive findings (80% vs. 67%, p=0.04) were significantly higher in the viewer group compared to the no viewer group. Conclusions: Use of real-time viewer to monitor capsule location during the phases of the procedure where delayed transit is common, coupled with a prespecified response to delayed transit significantly enhanced completion rate and positive finding rate. Further improvements are needed ensure better completion rates and adequate visualization of distal part of small intestine.

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Accuracy of *In-Vivo* Optical Diagnosis of Colon Polyp Histology by Narrow Band Imaging (NBI) in Predicting Colonoscopy (CC) Surveillance Intervals (SI)

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Background: NBI has been shown to predict polyp histology with moderate to high accuracy. However, there is limited data assessing the accuracy of NBI in predicting SI. Aim: To determine accuracy of *In-Vivo* optical diagnosis of colon polyp histology with NBI for predicting SI Methods: Pts undergoing either screening or surveillance CC at 2 tertiary referral centers were prospectively enrolled by 6 endoscopists from Nov 2007 to Oct 2010 in one of 3 clinical trials investigating impact of novel imaging techniques on polyp detection and/or polyp histology prediction. Location, size, and morphology of each polyp detected was documented. Using a simple NBI surface mucosal/vascular pattern classification described earlier (standardized amongst all 6 endoscopists) an optical diagnosis of polyp histology was made in real-time. Each polyp was then resected, sent in a separate jar for histopathology. SI for future CC were calculated based on optical diagnosis and histopathological diagnosis (gold standard), and these were compared employing various hypothetical strategies using the US Multi-Society Task Force Guidelines on colorectal cancer screening and surveillance. Accuracy rates for each strategy were calculated. Results: 473 pts [294 (62.2%) pts with polyps] underwent CC with *In-Vivo* optical diagnosis of every polyp detected using NBI. Mean age 61.1 years (SD 8.3), 383 (81.0%)male, 354 (74.8%) Caucasian. 867 polyps were evaluated (558 adenoma, 224 hyperplastic, 50 no diagnostic abnormality, 35 other benign pathology). Overall sensitivity, specificity, and accuracy of NBI for predicting adenomas were 93.4% (95%CI 91.0 - 95.3), 86.1% (95%CI 81.7 - 89.7), and 90.8% (95%CI 88.6 - 92.6) respectively. If the practice is to perform repeat CC in 3 yrs for pts with ≥ 3 adenomas or with one or more advanced adenomas, and 5 yrs for pts with 1-2 small (<1cm) adenomas (Guideline A) - then using histopathological diagnosis 91 pts (19%) would undergo repeat CC in 3 yrs, 131 (28%) in 5 yrs, and 251 (53%) in 10 yrs. If the practice is to perform repeat CC in 3 yrs for pts with ≥ 3 adenomas or with one or more advanced adenomas, and 10 yrs for pts with 1-2 small adenomas (Guideline B) - then 91 pts (19%) would undergo repeat CC in 3 yrs and 382 (81%) in 10 yrs. Table 1 shows the accuracy of NBI in predicting SI and the number of polyps that would need to be sent for histopathological evaluation employing several hypothetical strategies listed for both guidelines A and B. Conclusion: Using NBI for *In-Vivo* optical diagnosis of colon polyps can achieve a high accuracy for predicting SI. This practice of predicting histology real time during CC, and then resecting and discarding polyps can significantly reduce the number of polyps sent for histopathological evaluation and may subsequently improve the cost-effectiveness of CC for colon cancer screening.

NBI Strategy	Guideline A Accuracy (95% CI)	Guideline B Accuracy (95% CI)	Total Polyps Sent to Pathology (% Reduction in polyps sent to pathology)
Prediction for all polyps (none sent to histopathology)	88.8 (85.6 - 91.5)	95.1 (92.8 - 96.9)	0 (100%)
Prediction for colon polyps < 1cm (and rest sent for histopathology)	89.8 (86.8 - 92.4)	96.2 (94.0 - 97.7)	87 (90%)
Prediction for colon polyps <= 5mm (and rest sent for histopathology)	90.9 (87.9 - 93.3	96.2 (94.0 - 97.7)	265 (69.4%)

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Epigenetic Control of Kit Expression in Murine Kit^{Low} Interstitial Cell of Cajal (ICC) Stem Cells and Gastrointestinal Stromal Tumors (GIST)

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Background & Aims: In the murine stomach, stem cells expressing low levels of Kit receptor tyrosine kinase (Kit^{low} ICC-SC) can give rise to Kit$^+$ ICC and, through oncogenic transformation, to GIST.[1] Dependence on Kit is a defining feature of both mature ICC and most GIST. Pharmacological inhibition of Kit e.g. with imatinib mesylate is the only treatment option for metastatic GIST. However, this treatment is not curative due in part to persistence of Kit^{low} ICC-SC which form a Kit-independent, therapy-resistant reservoir.[1] Previously we found that in ICC-SC, 12 polycomb group (PcG) members, key epigenetic regulators of gene expression and differentiation in stem cells, were overexpressed while 272 potential PcG target genes including *Kit* were downregulated. Therefore, we hypothesized that the Kit^{low} phenotype of ICC-SC is due to PcG-mediated repression of Kit transcription. Methods: Freshly isolated and cultured ICC-SC were studied. PcG members Ezh2, Suz12 and Eed were detected by RT-PCR and Western immunoblotting. PcG activity was reduced by RNAi-mediated knock-down of *Suz12* and by inhibiting Ezh2-mediated trimethylation of lysine 27 of histone 3 (H3K27me3) with adenosine dialdehyde (Adox; 2.5-10 μM; 3-5 days). Kit expression was studied by Western immunoblotting, RT-PCR and immunocytochemistry. PcG protein and H3K27me3 occupancy of the *Kit* promoter (-1 to -750 bp) was identified by chromatin immunoprecipitation. Cell proliferation was measured by MTS absorbance. Athymic NCr-*nu/nu* (nude) mice were injected s.c. with $5x10^6$ transformed ICC-SC and treated with 3 biweekly injections of Adox or vehicle. Tumors were resected after 9 weeks. Results: Both freshly isolated and cultured ICC-SC expressed mRNA and protein for PcG members Suz12, Ezh2 and Eed. Furthermore, Suz12, Ezh2 and H3K27me3 were found to occupy the *Kit* promoter, implying direct epigenetic control of *Kit* expression. RNAi-mediated knock-down of Suz12 significantly upregulated *Kit*. Inhibition of Ezh2 activity with Adox led to significantly reduced global H3K27me3 levels, reduced specific H3K27me3 occupancy of the Kit promoter, and upregulated Kit protein expression. Adox inhibited the proliferation of transformed ICC-SC and made them susceptible to further inhibition by imatinib. Adox also inhibited tumor growth from xenografts of transformed ICC-SC, revealing that its