Louwers *et al.*, 2011[6]

Study details and design	Participant details	Intervention/comparators	Outcomes/analyses	Results
Linked references: Zaal *et al.*, unpublished **Type of report:** Full publication **Funding:** The VU University Medical Centre, Amsterdam and Forth Photonics Ltd, UK. Forth Photonics had a role in the study design and critically appraised the manuscript, but they had no role in data collection or final data analysis **Study design:** Diagnostic cohort study **Setting:** Outpatient colposcopy clinics at the VU University Medical Centre, Amsterdam, the Reinier de Graaf Hospital, Voorburg, and the Sint Antonius Hospital, Nieuwegein, the Netherlands **Duration of recruitment:** 1 July 2008 to 1 September 2009	**Inclusion/exclusion criteria:** Women aged ≥18 years referred for colposcopy with abnormal cervical cytology (at least borderline nuclear abnormalities) or for follow-up of a CIN1 or CIN2 lesion Exclusion criteria were previous surgery on the cervix, pelvic radiotherapy, current pregnancy or pregnancy in the last 3 months Substudy by Zaal *et al.*, unpublished: Women from the ATP cohort who had an adequate HPV test result were included **Number recruited:** 275 consecutive women were recruited, of which 36 (13.1%) were excluded owing to unsaved examination data (9), no colour-coded map available (9), DSI colposcope did not start (7), no available histology (5), no abnormal referral cytology (3), no DSI colposcopy after signing informed consent (3)	**Intervention:** DSI colposcope – DySIS v2.1. Digital video camera resolution 1024 × 768 pixels; white bright LED illumination; field of view (approx.) 25 × 35 mm; ×10 to ×27 magnification; polarised glare-free images; green and blue digital filter Additionally, there is the option to measure and map the dynamics (i.e. rise time, intensity and persistence) of the acetowhitening effect, for every point of the cervix. Modelling of the measured dynamic curves provides a per-point analysis of the acetowhitening effect. Once acetic acid has been applied, DySIS starts automatically with the measurement of the acetowhitening effect; this data acquisition phase lasts approximately 3 minutes. At the end of the examination the DySIS information is concisely presented in the form of a colour-coded map, which can be overlaid on to the colour image of the tissue. DySIS and the measurement principles and procedures have been described previously (including study by Soutter *et al.*)[17]	**Outcome measures:** The primary outcome was histologically confirmed high-grade cervical disease (CIN2+) Patients were also given a questionnaire to evaluate patient satisfaction **Details of assessment:** All clinical data were analysed using 2 × 2 tables, chi-squared tests, asymptotic McNemar's tests and 95% CIs Substudy by Zaal *et al.*, unpublished: Difference in colposcopic impression and histological outcome in women positive for HPV16 (HPV16+) vs women negative for HPV16 but positive for at least one hrHPV type (non-16 hrHPV+) was calculated using two-sided Fisher's exact test The MWW test was performed to assess whether the number of high-grade pixels in the DSI map (a reflection of lesion size) was related to the HPV16 status and the ability to correctly classify a lesion as high grade	**Analyses presented:** per patient **ITT cohort – DySIS** Sensitivity = 65% (95% CI 56% to 74%), specificity = 70% (95% CI 62% to 78%), PPV = 64% (95% CI 55% to 73%), NPV = 71% (95% CI 63% to 79%) ***Calculated by EAG*:** *Sensitivity = 64.8% (95% CI 55.4% to 73.2%), specificity = 70.2% (95% CI 61.9% to 77.4%), PPV = 64.2% (95% CI 54.9% to 72.6%), NPV = 70.8% (95% CI 62.4% to 77.9%), accuracy = 67.8%, LR+ = 2.18 (95% CI 1.62 to 2.93), LR− = 0.50 (95% CI 0.38 to 0.66), prevalence = 45.2%* **ITT cohort – conventional colposcopy (using DSI colposcope)** Sensitivity = 52% (95% CI 42% to 61%), specificity = 82% (95% CI 75% to 88%), PPV = 70% (95% CI 60% to 80%), NPV = 67% (95% CI 60% to 75%)

Study details and design	Participant details	Intervention/comparators	Outcomes/analyses	Results
	Number analysed: 239 women were included in the ITT cohort 183 women were included in the ATP cohort, as the management of 56 women did not strictly adhere to the protocol: the transformation zone was not completely visible with DSI (19), no biopsy was taken from the DSI colposcope high-grade location (14), image quality was unsatisfactory (7), hardware failed (6), DSI colposcope started too late (2), too much blood (3) or miscellaneous (5) Substudy by Zaal *et al.*, unpublished: 177 **Mean age (range):** ITT cohort = 36.7 (18.7–62.6) years ATP cohort = 36.6 (18.7–62.6) years Substudy by Zaal *et al.*, unpublished: median age 33.6 (18.7–62.6) years	After DySIS had been used as a regular video colposcope, the colour-coded map was then revealed and overlaid on the image of the cervix, but not before the entry of the colposcopist's final predictions. Using the same thresholds as the study by Soutter *et al.*,[17] the colour-coded map provided a prediction for the presence and grade of neoplasia, and indication of the most atypical site for biopsy sampling accordingly **Type of speculum:** NR **Comparator:** Colposcopic examination using DySIS as a regular video colposcope. The colposcopic impression was then digitally recorded by the colposcopist with annotation of the most atypical location and predicted severity of the lesion. Up to this point, the colposcopist was blinded to the DySIS analysis of the images **Type of speculum:** NR		***Calculated by EAG*:** *Sensitivity = 51.9% (95% CI 42.5% to 61.0%), specificity = 81.7% (95% CI 74.2% to 87.4%), PPV = 70% (95% CI 59.2% to 78.9%), NPV = 67.3% (95% CI 59.7% to 74.1%), accuracy = 68.2%, LR+ = 2.83 (95% CI 1.89 to 4.24), LR– = 0.59 (95% CI 0.48 to 0.73), prevalence = 45.2%* The difference between sensitivity of 65% and 52% is statistically significant ($p = 0.039$). The difference between specificity of 70% and 82% is statistically significant ($p = 0.011$) **ITT cohort – DySIS and conventional colposcopy combined** Sensitivity = 80% (95% CI 72% to 87%), specificity = 63% (95% CI 54% to 71%), PPV = 64% (95% CI 56% to 72%), NPV = 79% (95% CI 71% to 87%). ***Calculated by EAG*:** *Sensitivity = 79.6% (95% CI 71.1% to 86.1%), specificity = 62.6% (95% CI 54.1% to 70.4%), PPV = 63.7% (95% CI 55.3% to 71.3%), NPV = 78.8% (95% CI 70.0% to 85.6%), accuracy = 70.3%, LR+ = 2.13 (95% CI 1.67 to 2.71), LR– = 0.33 (95% CI 0.22 to 0.48), prevalence = 45.2%*

Study details and design	Participant details	Intervention/comparators	Outcomes/analyses	Results
	Indication for colposcopy: ITT cohort = 219 (91.6%) abnormal cytology; 20 (8.4%) follow-up CIN1–2 ATP cohort = 166 (90.7%) abnormal cytology; 17 (9.3%) follow-up CIN1–2 Substudy by Zaal *et al*., unpublished: 129 (72.9%) abnormal cytology; 31 (17.5%) abnormal cytology and HPV+; 15 (8.5%) follow-up CIN1; 2 (1.1%) follow-up CIN2 **Other relevant participant information:** Substudy by Zaal *et al*., unpublished: 152 (85.9%) patients were premenopausal/ perimenopausal, 13 (7.3%) were postmenopausal and 12 (6.8%) had unknown menopausal status **Result of last smear:** ITT cohort: normal = 5 (2.1%), borderline or mild dyskaryosis = 153 (64.0%), worse than borderline/mild dyskaryosis = 81 (33.9%) ATP cohort: normal = 4 (2.2%), borderline or mild dyskaryosis = 118 (64.5%), worse than borderline/mild dyskaryosis = 61 (33.3%) Substudy by Zaal *et al*., unpublished: normal = 4 (2.3%), borderline or mild dyskaryosis = 113 (63.8%), worse than borderline/mild dyskaryosis = 60 (33.9%)	**Reference standard:** Histology result. The colour-coded map produced by DySIS was compared with the colposcopist's own impression (when using DySIS as a regular video colposcope) and punch biopsies were taken from all identified suspicious areas, including those indicated by the colposcopist, DySIS and one additional control biopsy of apparently normal cervical tissue on the opposite side of the lesion(s). If the colposcopist and DySIS evaluated the cervix as normal, one biopsy was taken from the transformation zone at the 12 o'clock position. For patients having a 'see and treat' loop electrosurgical excision procedure, no punch biopsies were taken. The biopsy sampling procedure was recorded on video and later reviewed to check whether the tissue sample was collected from the annotated area All histology was independently reviewed by a pathologist specialising in gynaecological pathology. In case of disagreement between original assessment and review, a third expert reviewer graded the lesion (19% of all samples), blinded to all previous results, and final diagnosis was determined by the majority decision		**ATP cohort – DySIS** Sensitivity = 79% (95% CI 70% to 88%), specificity = 77% (95% CI 69% to 86%), PPV = 76% (95% CI 67% to 84%), NPV = 81% (95% CI 73% to 89%) ***Calculated by EAG*:** *Sensitivity = 79.1% (95% CI 69.3% to 86.3%), specificity = 77.3% (95% CI 68.0% to 84.5%), PPV = 75.6% (95% CI 65.8% to 83.3%), NPV = 80.6% (95% CI 71.5% to 87.4%), accuracy = 78.1%, LR+ = 3.49 (95% CI 2.38 to 5.11), LR– = 0.27 (95% CI 0.18 to 0.41), prevalence = 47.0%* **ATP cohort – conventional colposcopy (using DSI colposcope)** Sensitivity = 55% (95% CI 44% to 65%), specificity = 85% (95% CI 77% to 92%), PPV = 76% (95% CI 65% to 86%), NPV = 68% (95% CI 59% to 76%)

Study details and design	Participant details	Intervention/comparators	Outcomes/analyses	Results
	hrHPV test: ITT cohort: negative = 73 (30.5%), positive = 158 (66.1%), not performed = 8 (3.3%) ATP cohort: negative 54 (29.5%), positive = 123 (67.2%), not performed = 6 (3.3%) Substudy by Zaal *et al*., unpublished: HPV test was positive in 133 women; 10 lrHPV+, 80 non-16 hrHPV+, 42 hrHPV16+, in one case the typing was inconclusive	High-risk HPV and viral load were also tested in the cervical sample		***Calculated by EAG*:** *Sensitivity = 54.7% (95% CI 44.2% to 64.7%), specificity = 84.5% (95% CI 76.0% to 90.4%), PPV = 75.8% (95% CI 63.8% to 84.8%), NPV = 67.8% (95% CI 59.0% to 75.4%), accuracy = 70.5%, LR+ = 3.53 (95% CI 2.14 to 5.85), LR– = 0.54 (95% CI 0.42 to 0.69), prevalence = 47.0%* The difference between sensitivity of 79% and 55% is statistically significant ($p = 0.0006$). The difference between specificity of 77% and 85% is not statistically significant ($p = 0.144$) **ATP cohort – DySIS and conventional colposcopy combined** Sensitivity = 88% (95% CI 82% to 95%), specificity = 69% (95% CI 60% to 78%), PPV = 72% (95% CI 63% to 80%), NPV = 87% (95% CI 80% to 95%) ***Calculated by EAG*:** *Sensitivity = 88.4% (95% CI 79.9% to 93.6%), specificity = 69.1% (95% CI 59.3% to 77.4%), PPV = 71.7% (95% CI 62.5% to 79.4%), NPV = 87.0% (95% CI 77.7% to 92.8%), accuracy = 78.1%, LR+ = 2.86 (95% CI 2.10 to 3.89), LR– = 0.17 (95% CI 0.09 to 0.31), prevalence = 47.0%* **Adverse events** No adverse events were reported during the study period

Study details and design	Participant details	Intervention/comparators	Outcomes/analyses	Results
				Patient satisfaction 178/183 (97.3%) women in the ATP cohort completed the patient satisfaction questionnaire; the main result was that DSI colposcopy was no extra burden for the majority of women, compared with conventional colposcopy Substudy by Zaal *et al.*, unpublished: Final histology was normal or low grade in 92 (52%) and high grade in 85 (48%) women Among all women, DySIS indicated a higher percentage of lesions as being severe in HPV16+ women than among non-16 hrHPV+ women (73.8% vs 52.5%, $p = 0.032$). CIN2+ threshold: Total population: *DySIS*: sensitivity = 80% (95% CI 70% to 88%), specificity = 77% (95% CI 67% to 85%) *Conventional colposcopy*: sensitivity = 55% (95% CI 44% to 66%), specificity = 85% (95% CI 76% to 91%). Non-16 hrHPV+ population: *DySIS*: Sensitivity = 74% (95% CI 57% to 87%), specificity = 67% (95% CI 50% to 80%) *Conventional colposcopy*: Sensitivity = 61% (95% CI 43% to 76%), specificity = 83% (95% CI 69% to 93%). HPV16+ population: *DySIS*: Sensitivity = 97% (95% CI 84% to 100%), specificity = 100% (95% CI 69% to 100%);

Study details and design	Participant details	Intervention/comparators	Outcomes/analyses	Results
				Conventional colposcopy: Sensitivity = 53% (95% CI 35% to 71%), specificity = 90% (95% CI 55% to 100%) The sensitivity of DySIS to detect CIN2+ lesions was better among HPV16+ women than among non-16 hrHPV+ women (97% vs 74%; $p = 0.009$). The sensitivity of DySIS to detect CIN3+ lesions was better among HPV16+ women than among non-16 hrHPV+ women (96% vs 79%, p = not significant). No significant differences were observed in the visual impression of the colposcopist between HPV16+ and non-16 hrHPV+ women There were no differences in the mean number of high-grade pixels according to HPV16 status. However, among the CIN2+ lesions that were appointed as high grade by DySIS, those lesions that were also appointed as high grade by the colposcopist were significantly larger than those that were appointed as negative/low grade by the colposcopist (mean rank 35.74 vs 21.02, $p = 0.001$)

lrHPV, low-risk human papillomavirus; MWW, Mann–Whitney–Wilcoxon.

Soutter *et al.*, 2009[17]

Study details and design	Participant details	Intervention/comparators	Outcomes/analyses	Results
Linked references: Soutter *et al.*, conference abstract[18] **Type of report:** Full publication **Funding:** UK SMART program LOT/031/428 and Forth Photonics **Study design:** Diagnostic cohort study **Setting:** Outpatient colposcopy clinics at Hammersmith Hospital and St Mary's Hospital, London, and the Alexandra Hospital, Athens, Greece **Duration of recruitment:** May 2004 to July 2005	**Inclusion/exclusion criteria:** Women with abnormal cervical cytology (showing squamous or glandular cell dyskaryosis or borderline nuclear change) or symptoms suggesting the possibility of cervical neoplasia (postcoital bleeding, postmenopausal bleeding or intermenstrual bleeding) Exclusion criteria were self-referring women without an abnormal cervical cytology result, an inadequate or inflammatory cytology result, any other clinical indication for referral for colposcopy, pregnancy, previous pelvic radiotherapy or any woman for whom any prolongation of the examination was thought to be inadvisable **Number recruited:** 529 consecutive women were recruited; 82 women were recruited to the training group (May to July 2004) and 447 women were recruited to the test group (August 2004 to July 2005), of which 139 were excluded owing to software problems (15), no biopsy taken (23), unsatisfactory view of the cervix owing to the size and design of the speculum (45), problems with the application of acetic acid (37) owing to a batch of faulty disposable nozzles, other reasons (19)	**Intervention:** Precommercial DySIS model (FPC-03) 1024 × 768, 8-bit/channel digital colour CCD camera. The optical head captures images from a 23 mm × 20 mm area, including the transformation zone of the cervix. In this precommercial version, the optical head was mounted on a mechanical arm to position and stabilise it, and locked on to an extension shaft attached to the speculum, to ensure a stable field of view during image acquisition. A syringe was used to spray 2 ml of 3% acetic acid on to the cervix through a nozzle mounted on the extension shaft. After application of the acetic acid, a series of images is captured automatically every 5 seconds for 240 seconds and stored in the computer. Changes in the diffuse reflectance vs time integral are calculated through curve modelling and fitting (CB parameter – diffuse reflectance vs time curves and their interval value) and their spatial distribution is displayed as a PCM	**Outcome measures:** The primary outcome was the incremental DySIS test characteristics over conventional colposcopy, using histology as a reference **Details of assessment:** A ROC curve analysis of the training group data was used to choose an appropriate cut-off value to identify high-grade disease in the test group (553 CB units) A ROC curve analysis was used to evaluate the overall performance of DySIS in the test group. Fisher's exact test with two-sided *p*-values was used to evaluate the differences in the number of cases correctly identified by the different tests *Subgroup assessment by Soutter et al., conference abstract*:[18] For 299 patients the grade of the abnormal smear was known. The sensitivities and specificities of DySIS and conventional colposcopy were calculated separately for patients referred with low-grade smears and patients referred with high-grade smears	**Analyses presented:** per patient 72/308 (23.4%) women had high-grade disease or worse, of which 43 had CIN3, one had adenocarcinoma in situ, two had microinvasive squamous cell carcinoma **DySIS** Sensitivity = 79% (68% to 88%), specificity = 76% (70% to 81%) ***Calculated by EAG*:** *Sensitivity = 79.2% (95% CI 68.4% to 86.9%), specificity = 75.8% (95% CI 70.0% to 80.9%), PPV = 50.0% (95% CI 41.0% to 59.0%), NPV = 92.3% (95% CI 87.6% to 95.3%), accuracy = 76.6%, LR+ = 3.28 (95% CI 2.54 to 4.23), LR– = 0.28 (95% CI 0.17 to 0.43), prevalence = 23.4%*

Study details and design	Participant details	Intervention/comparators	Outcomes/analyses	Results
	Number analysed: 308 women (the test group). 603 punch biopsies were suitable for comparison with the DySIS data, of which 102 (in 72 women) were high-grade disease or worse. Treatment biopsies from 86 women and follow-up biopsies from 15 women were included, two review visit biopsies and three treatment biopsies were excluded because they were not reviewed **Median age (upper and lower quartiles):** 37 (29–46) years 28 women were >50 years, of which nine were >60 years **Indication for colposcopy:** 296 had abnormal cytology; 12 had symptoms **Other relevant participant information:** No women with clinically apparent cancer were included Four women were referred with AGUS cervical cytology result	The DySIS user was guided by the PCM and marked the areas with the highest CB values with a coloured circle **Type of speculum:** NR **Comparator:** While the DySIS examination was being conducted by one colposcopist, a second colposcopist did a colposcopic assessment using a separate video monitor displaying the images of the cervix captured by DySIS. The second colposcopist completed a colposcopy form and indicated on a diagram the areas for biopsy **Type of speculum:** NR		**Conventional colposcopy** Sensitivity = 49% (37% to 61%), specificity = 89% (85% to 93%) ***Calculated by EAG*:** *Sensitivity = 48.6% (95% CI 37.4% to 59.9%), specificity = 89.4% (95% CI 84.8% to 92.7%), PPV = 58.3% (95% CI 45.7% to 69.9%), NPV = 85.1% (95% CI 80.1% to 89.0%), accuracy = 79.9%, LR+ = 4.59 (95% CI 2.96 to 7.13), LR– = 0.58 (95% CI 0.46 to 0.72), prevalence = 23.4%* **ROC curve analysis:** Area under the curve = 0.844 (95% CI 0.797 to 0.892) Subgroup results: Of the four women who were referred with AGUS cervical cytology result, one had adenocarcinoma in situ and one CIN3; both of these had abnormal DySIS. The remaining two had CIN1, neither had abnormal DySIS results Of the 28 women who were aged >50 years, eight had high-grade disease, seven of which were detected by DySIS. Of the 20 without high-grade disease, 16 were correctly categorised by DySIS

Study details and design	Participant details	Intervention/comparators	Outcomes/analyses	Results
		Reference standard: Histology result. Both colposcopists selected areas for biopsy and also selected sites that did not seem to contain CIN in order to reduce verification bias. The DySIS user took biopsies from all the points identified by both colposcopists (a single biopsy was taken when selected sites coincided) The initial histological report was provided by institutional pathologists. All diagnostic biopsies and any subsequent treatment or follow-up biopsies were evaluated independently by two accredited histopathologists not associated with the hospital in which the biopsies were taken or originally assessed. Disagreements were resolved by a third histopathologist; 16.5% biopsies needed to be sent for a third opinion. Histopathologists were unaware of the DySIS result and the histopathology reports of the other pathologists. The final diagnosis was determined by the majority opinion		Although women with only inflammatory changes on cervical cytology were excluded, many had inflammatory changes on the cervix but a more marked cytological picture. Cervicitis did not affect the interpretation as areas of high-grade CIN were clearly seen as distinct areas with high CB values **Unsatisfactory examination:** Colposcopy was described as unsatisfactory in 65 cases because the squamocolumnar junction was not clearly visible; however, these women were not excluded from the study **Adverse events:** No adverse events were reported **Subgroup assessment by grade of referral smear:** Subgroup assessment by Soutter *et al*., conference abstract:[18] Among 224 women referred with a low-grade smear, 31 (13.8%) had a high-grade or invasive lesion, whereas in 75 women referred with a high-grade smear, 40 (53.3%) had a high-grade or invasive lesion *Patients referred for a low-grade smear*: DySIS: Sensitivity: 77.4%, specificity: 77.2% Colposcopy: Sensitivity: 19.4%, specificity: 93.3% *Patients referred for a high-grade smear*: DySIS: Sensitivity: 80.0%, specificity: 74.3% Colposcopy: Sensitivity: 72.5%, specificity: 68.6% The difference in DySIS sensitivity between low- and high-grade smear referrals was 2.6% (95% CI –22.9% to 16.5%; $p > 0.999$) The difference in DySIS specificity between low-grade and high-grade smear referrals was 2.9% (95% CI –10.5% to 20.2%; $p = 0.532$) The difference in colposcopy sensitivity between low- and high-grade smear referrals was 53.1% (95% CI 30.8% to 69.8%; $p < 0.0001$) The difference in colposcopy specificity between low- and high-grade smear referrals was 24.7% (95% CI 11.1% to 41.6%; $p < 0.0001$)

AGUS, atypical glandular cells of undetermined significance; CCD, charged, coupled device; NR, not reported; PCM, pseudocolour map; ROC, receiver operator characteristic.

Flowers *et al.*, unpublished

Study details and design	Participant details	Intervention/comparators	Outcomes/analyses	Results
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Gallwas *et al.*, 2011[32]

Study details and design	Participant details	Intervention/comparators	Outcomes/analyses	Results
Linked papers: Gallwas *et al.*, 2010[34] **Type of report:** Full publication **Funding:** Grants from Friedrich-Baur-Stiftung and Muenchener Medizinische Wochenschrift. A Niris Imaging System was loaned by Imalux **Study design:** Diagnostic cohort study **Setting:** Outpatient Munich, Germany **Duration of recruitment:** July 2008 to May 2010	**Inclusion/exclusion criteria:** All women were referred for colposcopy. Women aged <18 years, and pregnant women, were excluded **Number recruited:** Unclear, although 1375 images were taken from 120 women (1165 images were from unsuspicious areas, and 210 were compared with histology) **Number analysed:** 210 images (number of women unknown) **Mean age (range):** 31.1 years (18–46) **Indication for colposcopy:** All women had abnormal cytology **Other relevant participant information:** All participants were pre-menopausal **Result of last smear:** PAP II, 19; PAP IIW, 14; PAP III, 5; PAP IIID, 44; PAP IVA, 32; PAP IVB, 5; PAP V, 1 hrHPV test: 93 women tested positive	**Intervention:** Colposcopy-guided OCT using the Niris Imaging system (consisting of an imaging console, a keyboard, a touchpad for data entry, and a detachable fibre optic probe). The console produces near-infrared light ($\lambda = 1310$ nm) through a 2.7-mm diameter probe. Light is back-scattered from the patient's tissue, collected by the probe and combined with an internal reference signal to produce a high-spatial resolution image of the superficial tissue microstructure with a depth scanning range of 1–2 mm (10-to 20-μm resolution) a lateral scanning range of approximately 2 mm at (approximately 25-μm resolution) acquiring a 200×200 pixel image in 1.5 seconds Images were evaluated by two investigators, blinded to colposcopic and histological findings, as being normal, inflammation, CIN1, CIN2, CIN3 or squamous carcinoma **Type of speculum:** NR **Details of cleaning/sheath:** Niris probe sheath was used **Comparator:** Conventional colposcopy **Type of speculum:** NR **Details of cleaning/sheath:** NR	**Outcome measures:** CIN using cut offs at CIN1+, CIN2+ and CIN3+ **Details of assessment:** Clinical data were analysed using 2×2 tables with 95% CIs reported	In this paper, similar results were presented separately for two investigators. Presented here are the results for the first investigator: **Analyses presented:** per image Nine images were confirmed by histology to be cancerous (no details on grade were reported) **Colposcopy-guided Niris Imaging system: CIN1+ threshold:** Sensitivity = 98% (95% CI 96% to 100%), specificity = 39% (95% CI 27% to 51%), PPV = 79% (95% CI 73% to 85%), NPV = 89% (95% CI 78% to 101*%), LR+ = 1.61 (95% CI 1.31 to 2.05), LR– = 0.05 (95% CI 0.00 to 0.16) **sic* ***Calculated by EAG*:** *Sensitivity = 97.9% (95% CI 94.1% to 99.3%), specificity = 39.1% (95% CI 28.1% to 51.3%), PPV = 78.6% (95% CI 72.1% to 83.9%), NPV = 89.3% (95% CI 72.8% to 96.3%), accuracy = 80.0%, LR+ = 1.61 (95% CI 1.32 to 1.96), LR– = 0.05 (95% CI 0.02 to 0.17), prevalence = 69.5%*

Study details and design	Participant details	Intervention/comparators	Outcomes/analyses	Results
		Reference standard: Histology result. Biopsies taken from suspicious areas identified using OCT. Details of when biopsies were taken as a result of colposcopic examination were not reported		**Colposcopy-guided Niris Imaging system: CIN2+ threshold:** Sensitivity = 86% (95% CI 80% to 93%), specificity = 64% (95% CI 54% to 73%), PPV = 73% (95% CI 65% to 80%), NPV = 81% (95% CI 72% to 90%), LR+ = 2.38 (95% CI 1.75 to 3.45), LR– = 0.21 (95% CI 0.10 to 0.37) ***Calculated by EAG*:** *Sensitivity = 86.5% (95% CI 78.9% to 91.6%), specificity = 63.6% (95% CI 53.8% to 72.4%), PPV = 72.7% (95% CI 64.6% to 79.6%), NPV = 80.8% (95% CI 70.7% to 88.0%), accuracy = 75.7%, LR+ = 2.38 (95% CI 1.81 to 3.12), LR– = 0.21 (95% CI 0.13 to 0.35), prevalence = 52.9%*

Study details and design	Participant details	Intervention/comparators	Outcomes/analyses	Results
				Colposcopy-guided Niris Imaging system: CIN3+ threshold: Sensitivity = 87% (95% CI 80% to 95%, specificity = 81% (95% CI 74% to 88%), PPV = 73% (95% CI 64% to 82%), NPV = 91% (95% CI 86% to 97%), LR+ = 4.60 (95% CI 3.11 to 7.72), LR– = 0.16 (95% CI 0.06 to 0.27) ***Calculated by EAG*:** *Sensitivity = 87.2% (95% CI 78.0% to 92.9%), specificity = 81.1% (95% CI 73.5% to 86.8%), PPV = 73.1% (95% CI 63.3% to 81.1%), NPV = 91.5% (95% CI 85.0% to 95.3%), accuracy = 83.3%, LR+ = 4.60 (95% CI 3.20 to 6.62), LR– = 0.16 (95% CI 0.09 to 0.28), prevalence = 37.1%* **Colposcopy alone:** Sensitivity: CIN1+ = 99%, CIN2+ = 99%, CIN3+ = 78% Specificity:CIN1+ = 19%, CIN2+ = 61%, CIN3+ = 74% **Adverse events:** NR as an outcome

NR, not reported.

Liu *et al.*, 2010[32]

Study details and design	Participant details	Intervention/comparators	Outcomes/analyses	Results
Linked references: Wulan *et al.*,[35] Liu *et al.*,[32] Rasool[36] **Type of report:** Full publication **Funding:** NR **Study design:** Diagnostic cohort study **Setting:** Outpatient, Peking University Shenzhen Hospital, Shenzhen, China **Duration of recruitment:** NR	**Inclusion/exclusion criteria:** Non-pregnant women aged ≥ 18 years referred for colposcopy Participants had to have abnormal cervical cytological findings or a positive test for one of the high-risk types of HPV **Number recruited:** Unclear Number analysed: 299 women (1237 paired diagnoses) **Median age (range):** 36.7 (19.2–67.9) years **Indication for colposcopy:** NR Other relevant participant information: 10% of women were menopausal **Result of last smear:** NR **hrHPV test:** NR	**Intervention:** Niris Imaging System (consisting of an imaging console, a keyboard, a touchpad for data entry, and a detachable fibre optic probe). The console produces near-infrared light ($\lambda = 1310$ nm) directed through a 2.7-mm diameter probe. Light is back-scattered from the patient's tissue, collected by the probe and combined with an internal reference signal to produce a high-spatial resolution image of the superficial tissue microstructure with a 10- to 20-μm depth resolution and 15- to 25-μm lateral resolution, acquiring a 200×200 pixel image in 1.5 seconds Niris images were read at the time of image capture by the operator and impressions were rated as being normal, indeterminate or abnormal **Type of speculum:** NR Details of cleaning/sheath: Disposable OCT probe sheath Comparator: Conventional colposcopy. The cervix was divided into quadrants for examination. Impressions were rated as being normal, low grade, high grade, or cancer. Type of speculum: NR Details of cleaning/sheath: NR	**Outcome measures:** CIN using cut-offs at indeterminate or abnormal **Details of assessment:** Sensitivities and specificities were presented with 95% CI	**Analyses presented:** By lesion, by woman, and by a woman's worst quadrant biopsy result 53 women (18%) had CIN2+, 28 (9%) had CIN3+ **Colposcopy-directed Niris Imaging System** Sensitivity and specificity results were also reported in the paper using the proportion of patients with a histology result of CIN3+

Study details and design	Participant details	Intervention/comparators	Outcomes/analyses	Results
		Reference standard: Histology result from a team of pathologists. One gynaecologic pathologist served as the final reference and quality control All patients had a minimum of 5 biopsies, one in each quadrant, and endocervical curettage. In normal quadrants biopsies were taken at the 2, 4, 8 and 10 o'clock positions at the squamocolumnar junction		***Selected 2 × 2 data provided following personal correspondence with an author*:** **Colposcopy-directed Niris Imaging System, by woman** Histology Device / CIN2+ / <CIN2 / Total Colposcopy-directed Niris — Indeterminate/abnormal: 24 / 34 / 58 Colposcopy-directed Niris — Normal: 29 / 211 / 240 Total: 53 / 245 / 298 ***Calculated by EAG*:** *Sensitivity = 45.3% (95% CI 32.7% to 58.5%), specificity = 86.1% (95% CI 81.2% to 89.9%), PPV = 41.4% (95% CI 29.6% to 54.2%), NPV = 87.9% (95% CI 83.2% to 91.5%), accuracy = 78.9%, LR+ = 3.26 (95% CI 2.12 to 5.02), LR– = 0.64 (95% CI 0.50 to 0.82), prevalence = 17.8%* **Colposcopy-directed Niris Imaging System, by woman** Histology Device / CIN2+ / <CIN2 / Total Colposcopy-directed Niris — Abnormal: 17 / 17 / 34 Colposcopy-directed Niris — Normal/indeterminate: 36 / 228 / 264 Total: 53 / 245 / 298 *Calculated by EAG*: *Sensitivity = 32.1% (95% CI 21.1% to 45.5%), specificity = 93.1% (95% CI 89.2% to 95.6%), PPV = 50.0% (95% CI 34.1% to 65.9%), NPV = 86.4% (95% CI 81.7% to 90.0%), accuracy = 82.2%, LR+ = 4.62 (95% CI 2.53 to 8.45), LR– = 0.73 (95% CI 0.61 to 0.88), prevalence = 17.8%*

Study details and design	Participant details	Intervention/comparators	Outcomes/analyses	Results

Colposcopy alone

Type of analysis	Sensitivity (95% CI)	Specificity (95% CI)
By lesion		
Colpo low grade pos	60 (48 to 72)	83 (86 to 80)
Colpo high grade pos	NR in paper *Calculated by EAG*: *29 (21 to 39)*	98 (97 to 99)
By woman		
Colpo low grade pos	74 (60 to 84)	67 (73 to 61)
Colpo high grade pos	23 (13 to 36)	96 (91 to 93[a])
By worst quadrant biopsy		
Colpo low grade pos	58 (45 to 71)	81 (76 to 86)
Colpo high grade pos	19 (10 to 32)	99 (96 to 100)

Colpo, colposcopy; pos, positive.
a *sic* (EAG calculation below).

Sensitivity and specificity results were also reported in the paper using the proportion of patients with a histology result of CIN3+

Study details and design	Participant details	Intervention/comparators	Outcomes/analyses	Results

***Selected 2 × 2 data provided following personal correspondence with an author*:**

Colposcopy alone, by woman

Device		Histology		
		CIN2+	<CIN2	Total
Colposcopy	High grade	12	9	21
	Normal/low grade	41	237	278
Total		53	246	299

Calculated by EAG:

Sensitivity = 22.6% (95% CI 13.5% to 35.5%), specificity = 96.3% (95% CI 93.2% to 98.1%), PPV = 57.1% (95% CI 36.5% to 75.5%), NPV = 85.3% (95% CI 80.6% to 88.9%), accuracy = 83.3%, LR+ = 6.19 (95% CI 2.75 to 13.94), LR– = 0.80 (95% CI 0.69 to 0.93), prevalence = 17.7%

Adverse events:

NR as an outcome

NR, not reported.

Escobar *et al.*, 2006[31]

Study details and design	Participant details	Intervention/comparators	Outcomes/analyses	Results
Linked references: Kuznetsova *et al.*[39] (*AiC information has been removed*) Rojas-Espaillat *et al.*[38] Rasool *et al.*[36] Apisdorf *et al.*[37] **Type of report:** Full publication **Funding:** NR **Study design:** Diagnostic cohort study **Setting:** Outpatient. Cleveland Clinic Foundation, USA, and Hospital Maternidad Nuestra Senora de la Altagracia, Dominican Republic **Duration of recruitment:** June to November 2004	**Inclusion/exclusion criteria:** Women aged 18–80 years referred with abnormal cervical cytology (≥atypical squamous cells of undetermined significance) or with suspicious lesions of the uterine cervix were eligible **Exclusion criteria:** Previous hysterectomy, previous treatment for pre-invasive or invasive cervical cancer, pregnancy or being a prisoner **Number recruited:** 220 patients of which eight were excluded owing to age (1), heavy bleeding (2), normal Pap (1), recent cone biopsies (2), blank form (1) and unknown reason (1) **Number analysed:** 212 (1215 images) **Mean age (range):** 35.5 (18–80) years	**Intervention:** *Imalux OCT device*: Operating at a 980-nm wavelength, with a lateral resolution of 25 μm and in-depth resolution of 11 μm in tissue Three investigators independently interpreted the OCT images, which were graded as 'normal' if a well-organised, simple two-layer structure with a sharp interface between the surface epithelium and underlying stromal layer was seen, 'abnormal' if the tissue was unstructured with no apparent interface present, and 'indeterminate' if irregularities on the images suggested artefacts or physiological alterations and did not meet criteria for normal or abnormal Image readings were made three separate times (after the examination) for each patient: knowing only the patient's age; knowing the visual inspection results (including access to an image); and knowing referral Pap results, the colposcopic diagnosis by quadrant, and viewing the magnified digital photograph of the cervix **Type of speculum:** NR **Details of cleaning/sheath:** Disposable OCT probe sheath	**Outcome measures:** CIN using cut-offs at indeterminate or abnormal **Details of assessment:** Sensitivities and specificities were presented with 95% CI. ROC curves were also generated for the three sets of OCT readings	179 women had ≤CIN1 and 33 women had ≥CIN2 **Analyses per person:** *Colposcopy (and visual inspection) plus Niris, using abnormal as cut-off*: Sensitivity = 46% (95% CI 30% to 64%), specificity = 69% (95% CI 62% to 75%) *Colposcopy, using CIN2+as cut-off*: Sensitivity = 39% (95% CI 24% to 57%), specificity = 71% (95% CI 64% to 77%) *Analyses per lesion*: *Colposcopy (and visual inspection) plus Niris, cut-off not stated*: Sensitivity = 33% (95% CI 14% to 60%), specificity = 91% (95% CI 86% to 94%) ***2 × 2 data provided following personal correspondence with an author*:** **Analyses per person:** **Niris Imaging System alone** See table below *Calculated by EAG*: *Sensitivity = 93.8% (95% CI 79.9% to 98.3%), specificity = 10.7% (95% CI 7.0% to 16.2%), PPV = 16% (95% CI 11.4% to 21.9%), NPV = 90.5% (95% CI 71.1% to 97.3%), accuracy = 23.4%, LR+ = 1.05 (95% CI 0.95 to 1.16), LR– = 0.58 (95% CI 0.14 to 2.38), prevalence = 15.3%*

Device		Histology: CIN2+	Histology: <CIN2	Total
Niris alone	Indeterminate/abnormal	30	158	188
	Normal	2	19	21
Total		32	177	209

Study details and design	Participant details	Intervention/comparators	Outcomes/analyses	Results
	Other relevant participant information: 189 were premenopausal and 23 were postmenopausal. 89 (42%) had a symptomatic vaginal discharge at the time of the examination **Result of last smear:** 48 (23%) had ASCUS, 142 (67%) had LSIL, 22 (10%) had HSIL **hrHPV test:** NR	**Comparator:** Conventional colposcopy. The cervix was divided into quadrants for examination Unmagnified visual inspection with acetic acid (not a relevant comparator for this review) was also studied **Reference standard:** Histology result from one pathologist; a team served as consultants for problem cases. Biopsies were taken at all positive areas and at the 2, 4, 8 and 10 o'clock positions at the squamocolumnar junction. Biopsies were performed with a bronchoscopy biopsy instrument (with 2 mm jaws). Endocervical curettage was also performed on every patient		**Niris Imaging System alone** Histology Device / CIN2+ / <CIN2 / Total Niris alone – Abnormal: 18 / 72 / 90 Normal/indeterminate: 14 / 105 / 119 Total: 32 / 177 / 209 *Calculated by EAG*: *Sensitivity = 56.3% (95% CI 39.3% to 71.8%), specificity = 59.3% (95% CI 52.0% to 66.3%), PPV = 20.0% (95% CI 13.0% to 29.4%), NPV = 88.2% (95% CI 81.2% to 92.9%), accuracy = 58.9%, LR+ = 1.38 (95% CI 0.97 to 1.97), LR– = 0.74 (95% CI 0.49 to 1.11), prevalence = 15.3%* **Colposcopy alone** Histology Device / CIN2+ / <CIN2 / Total Colposcopy – High grade: 12 / 52 / 64 Normal/low grade: 20 / 125 / 145 Total: 32 / 177 / 209 *Calculated by EAG*: *Sensitivity = 37.5% (95% CI 22.9% to 54.7%), specificity = 70.6% (95% CI 63.5% to 76.8%), PPV = 18.8% (95% CI 11.1% to 30.0%), NPV = 86.2% (95% CI 79.7% to 90.9%), accuracy = 65.6%, LR+ = 1.28 (95% CI 0.77 to 2.11), LR– = 0.89 (95% CI 0.67 to 1.18), prevalence = 15.3%* **Adverse events:** NR as an outcome

ASCUS, atypical squamous cells with uncertain significance; NR, not reported; ROC, receiver operator characteristic.