DIGITAL COLPOSCOPY: READY FOR USE?
AN OVERVIEW OF LITERATURE

JA Louwers*, M Kocken*, WA ter Harmselb, RHM Verheijenc

*Department of Pathology, VU University Medical Center, Amsterdam, the Netherlands;
*bDepartment of Obstetrics and Gynaecology, Reinier de Graaf Gasthuis, Delft, the Netherlands;
cDepartment of Reproductive medicine and Gynaecology, University Medical Center Utrecht, Utrecht, the Netherlands
ABSTRACT

The aims of this review were to summarise the various methods of digital colposcopy and to provide an overview of their efficacy. We conducted a literature search and focused on papers that described a technique for colposcopy, other than conventional colposcopy and compared this with conventional colposcopy and/or histology and included digitalisation of the process. All papers have been classified in one of the following categories: digital imaging and telecolposcopy, spectroscopy, computerised colposcopy, optical coherence tomography and confocal microcolposcopy. Among the most promising developments is spectroscopy, allowing a more or less automated analysis and interpretation of the colposcopic image.
INTRODUCTION

In 1925, Dr. Hans Hinselmann(1) was the first to describe a colposcopic examination of the cervix uteri. Today, colposcopy is well established in the clinical gynaecological practice for defining cytologically or clinically detected lesions of the cervix. Visual examination of the cervix of a woman, performed by a gynaecologist, aims at the detection of macroscopic changes in tissue features such as colour and morphology. Comparison of these features with established patterns of lesions is the next step in order to classify the lesion. The diagnostic performance of the examiner depends heavily on his visual skills in detecting early signs of disease and therefore on his training, experience and competence in processing and comparing the perceived pattern with the established features of a premalignant lesion.(2) Although a high variation in colposcopic performance has been reported, the sensitivity of colposcopy to distinguish normal from abnormal tissue is relatively high, but to distinguish low-grade (LG) lesions from high-grade (HG) lesions and cancer, long-term studies have reported a sensitivity of colposcopy of approximately 56%. (3-5) This low sensitivity indicates that a substantial number of women are overtreated. Also, a substantial proportion of HG lesions fail to be identified at colposcopy. This has been confirmed in the ASCUS/LSIL Triage Study for Cervical Cancer (ALTS trial), where only half of the finally detected cases of cervical intraepithelial neoplasia grade 3 (CIN3) were identified in the immediate colposcopy arm of the trial.(6)

In addition, the low to average sensitivity and specificity of colposcopic examination are associated with a high degree of subjectivity and inter- and intra-observer variability. (7;8) These findings have also been supported by an additional study performed within the context of the ALTS trial in an attempt to assess the inter-observer agreement among the colposcopy quality control reviewers.(9) So, the establishment of a ‘baseline’ colposcopic assessment with the ability to minimise both the inter- and the intra-observer variability would constitute a major improvement in colposcopic practice.(2)

Since histology is the gold standard to detect HG lesions, the colposcopic impression is confirmed by biopsies. This sampling of the cervix is, however, often stressful and painful for the woman, and there is no immediate test result. Therefore, a colposcopic device with the possibility of ‘optical biopsy’, that is examination of the tissue with great accuracy without the need for actual sampling, would be a major improvement for both the patient and doctor.

Another issue of interest is the quantitative measurement of the size of a cervical lesion. For example, when studying the influence of the human papillomavirus (HPV), it would be interesting to know whether the size of the affected cervical area is related to the duration of an HPV infection. A correct and precise measurement by conventional colposcopy or by digital imaging alone is very difficult and hindered by the discrepancy between the three-dimensional round shape of the cervix and the two-dimensional image. Colposcopic devices with the ability of digital imaging, in combination with
advanced software, can overcome this discrepancy and are often used to quantitatively measure a cervical lesion.\(^{(10-12)}\)

To address these various issues, alternative methods for colposcopy have been developed, including adoption of digital techniques for colposcopy, in which ‘digital’ means every method of colposcopy using any form of image enhancement by a computer. New techniques that provide increased sensitivity and specificity and also allow instantaneous treatment without the need of biopsies will be described. The aims of this review is to summarise the various methods of digital colposcopy and to provide an overview of their efficacy.

**METHODS**

All relevant literature has been searched and reviewed for this paper. The period covered in this search is April 1985 until the end of search date, February 2008. Databases used are: Medline, Embase, the Cochrane Library, appropriate internet website and citation lists. Search terms employed were ‘colposcopy’ or ‘colposcopes’, ‘(digital) device’, ‘uterine cervical diseases’ or ‘cervix uteri’ or ‘cervical intraepithelial neoplasia’ and ‘sensitivity and specificity’. We focused on papers that described a technique for colposcopy, other than conventional colposcopy, and that compared a digitalised technique with conventional colposcopy or histology.

**RESULTS**

Using our search strings and criteria for inclusion, we were able to identify a total of 41 papers. According to the different types of digital colposcopy, all articles have been classified in one of the following categories: digital imaging and telecolposcopy, spectroscopy (including fluorescence, trimodal, contact probe and impedance spectroscopy), computerised colposcopy, optical coherence tomography (OCT) and confocal microcolposcopy (Table 1).

**Digital imaging and telecolposcopy**

The first steps on the path of digital colposcopy were taken by photographing the cervix during the colposcopic examination and subsequently digitalising the image. This combination of computerised image processing and colposcopy is called digital imaging colposcopy. Digital image processing techniques permit contrast enhancement of features, such as white epithelium and abnormal vasculature, and are in this way able to help the colposcopist to identify and grade a lesion.\(^{(13)}\) Current digital imaging and imaging techniques have evolved from, among others, the cervicoscope, introduced in 1981 by Stafl.\(^{(14)}\) The cervicoscope is a camera with a fixed telephoto lens that takes a photograph of the cervix, the so called cervicogram.\(^{(14-16)}\) The cervicogram may be projected onto a screen so that the image is approximately the equivalent of a colposcopic magnification of 16. The projected image is evaluated in a completely
<table>
<thead>
<tr>
<th>Colposcopic method</th>
<th>Features</th>
<th>Sensitivity (%) (LG vs HG)</th>
<th>Specificity (%) (LG vs HG)</th>
<th>Setting</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digital imaging and telecolposcopy</td>
<td>- Electronic transmission of digital cervical images</td>
<td>34.1 – 43.2</td>
<td>55.3 – 59.4</td>
<td>Secondary</td>
<td>Ferris et al.²⁶,²⁷ and Etherington et al.²⁹</td>
</tr>
<tr>
<td></td>
<td>- Image enhancement</td>
<td></td>
<td>93.3(^a)</td>
<td>Secondary</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- (Remote) Expert reviewing</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spectroscopy</td>
<td>- Non invasive method</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SpectRx</td>
<td>Fluorescence and reflectance spectra from the cervix \textit{in vivo}</td>
<td>95</td>
<td>55 - 83</td>
<td>Secondary</td>
<td>Ferris et al.³⁸ and DeSantis et al.³⁹</td>
</tr>
<tr>
<td>LUMA™</td>
<td>Combination of fluorescence, white light backscattered spectroscopy and video imaging</td>
<td>92</td>
<td>50</td>
<td>Secondary</td>
<td>Huh et al. ⁴²</td>
</tr>
<tr>
<td>DySIS™</td>
<td>Measures spectroscopically the acetowhitening effect</td>
<td>79</td>
<td>76</td>
<td>Secondary</td>
<td>Sutter et al.⁴¹</td>
</tr>
<tr>
<td>Trimodal</td>
<td>Combination of fluorescence, diffuse reflectance and light scattering spectroscopy</td>
<td>92(^b)</td>
<td>71(^b)</td>
<td>Secondary</td>
<td>Georgakoudi et al.⁴⁹</td>
</tr>
<tr>
<td>Truscreen*</td>
<td>A probe in contact with the cervix collects spectrometric data</td>
<td>70</td>
<td>-</td>
<td>Both</td>
<td>Singer et al.⁵¹</td>
</tr>
<tr>
<td>Impedance</td>
<td>Impedance spectrum is measured through a contact probe that uses electrical current</td>
<td>74</td>
<td>53</td>
<td>Secondary</td>
<td>Abdul et al.⁵³</td>
</tr>
<tr>
<td>Computerised colposcopy</td>
<td>- Analysis of digital cervical images for various characteristics.</td>
<td>91.2</td>
<td>94.8</td>
<td>Secondary</td>
<td>Cristoforoni et al.⁵⁶</td>
</tr>
<tr>
<td></td>
<td>- Enhancement of the objectivity of the colposcopy.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Optical coherence tomography</td>
<td>- Non-invasive technique that uses infrared light.</td>
<td>56</td>
<td>59</td>
<td>Secondary (adjunct to colposcopy)</td>
<td>Escobar et al.⁶⁴</td>
</tr>
<tr>
<td></td>
<td>- Real-time, \textit{in vivo} images of the cervix with high resolution.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Confocal microcolposcopy</td>
<td>- Optical imaging technique with high contrast.</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Reconstruction of three-dimensional images, through point illumination and a pinhole conjugate plane in front of a detector.</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

A: Normal versus abnormal cervix. Gold standard: Colposcopist’s opinion who examined the women in the hospital colposcopy clinic.
The advantage of the cervicogram is its simplicity, for instance, nurses can perform the procedure and the expert saves time because he is only needed for evaluation of the image. Also, this method is suitable for developing countries, where expert colposcopists may be scarce. Currently, most cervicograms are made with digital cameras and even remote cervicogram reviewing services are possible. Many studies about the efficacy of cervicograms have been published with varying outcomes. The sensitivity of cervicography is in general lower than the sensitivity of cytology (the pap smear), and the specificity is in general higher.

Progressively, the traditional binocular colposcopes are replaced by digital (video) colposcopes (Figure 1A). The need for projecting images thus disappears since a reviewer can easily enlarge the image on his computer. The reliability of cervical examinations with digital colposcopy compared with conventional colposcopy is good. Schädel et al. found no significant difference in terms of underrating or overrating of lesions when reviewing the images made by a digital colposcope. Furthermore, the compliance of women for follow up after colposcopy seems to be slightly better when they can follow the colposcopic examination and are able to see their own cervix. Finally, digital image storage created opportunities for further digital analyses of the image.

The introduction of internet and email has facilitated the review of digital colposcopic images outside the examination room. Therefore, digital colposcopy can take a central role in telemedicine, the electronic transmission of information for the delivery of quality clinical health care from a distance. A difference can be made between two types of ‘telecolposcopy’: network- and computer-based telecolposcopy. Network-based telecolposcopy uses an existing infrastructure of technologically advanced hardware, rapid telecommunication lines and trained support personnel. Most provide a real-time or television like video interface at both sites. In computer-based colposcopy, the (video) images are first stored on a computer using customised software and then forwarded. Both these systems may be limited by the provision of only static video images. Although the initial cervicogram had been developed as a mean of primary screening and an adjunct to cervix cytology, digital imaging is now also used for evaluation of woman referred with an abnormal smear or complaints.

Ferris et al. conducted several studies to evaluate the usefulness and efficacy of both types of telecolposcopy. The sensitivity for the detection of HG lesions (≥ CIN2) in a population referred to a colposcopy clinic because of an abnormal pap smear or symptoms ranges from 40.9 to 43.2% for network-based colposcopy and from 34.1 to 40.9% for computer-based colposcopy compared with a sensitivity of approximately 48% for on-site colposcopy. The specificity for the detection of lesions ≥ CIN2 ranges from 55.3 to 58.1% and from 58.9 to 59.4% for network- and computer-based colposcopy, respectively, compared with a specificity of approximately 59% for on-site colposcopy.
Figure 1: Examples of digital colposcopy devices. (A) Videocolposcope (Olympus, Tokyo, Japan). (B) Multimodal Hyperspectral Imaging Device (Guided Therapeutics (SpectRx)). (C) DySIS (Forth Photonics). (D) Truscreen (Polartechniques).

Etherington conducted another feasibility study in which a videocolposcope was used to record video clips, which were subsequently transmitted to an expert colposcopist for interpretation. The opinion of the colposcopist in the hospital colposcopy clinic, not the histology of the biopsies, was considered the gold standard.
In this setting, telecolposcopy had a very high sensitivity and specificity of 88.9 and 93.3%, respectively, in discriminating between a normal and abnormal cervix.

**Spectroscopy**

Spectroscopy is a noninvasive method in which, for example, light or electric current is used to study the biochemical composition as well as the metabolic and structural features of tissue. Components of the electromagnetic spectrum relevant to diagnostic spectroscopy include the ultraviolet A range (315-400 nm), the visible light range (400-700 nm) and the near infrared range (700-900 nm). When light strikes tissue, it will be absorbed with or without re-emission of the light or will be scattered by (sub) surface interactions.

With autofluorescence spectroscopy, it is possible to measure a wide range of optical characteristics of cervical tissue, sensitive to structural and molecular changes that accompany dysplastic progression. For example, nicotinamide adenine dinucleotide (NADH) and flavin adenine dinucleotide (FAD) are two autofluorescent molecules in the mitochondria of human cells that play an important role in the cellular metabolism. An increase in NADH and FAD fluorescence in dysplastic tissue is correlated with increased cellular metabolic activity.

In 1999, Mitchell *et al.* presented a review concluding that to diagnose squamous intraepithelial lesions, fluorescence spectroscopy outperforms not only colposcopy alone but also has better results compared with cervicography, speculoscopy, cytology and HPV testing. More recently, two reviews were published about point probe versus multispectral fluorescence and reflectance spectroscopy. Their conclusions were that optical spectroscopy has a similar performance to colposcopy and may help localise lesions and therefore might be an effective adjunct to colposcopy.

A study with a Multimodal Hyperspectral Imaging device, (Guided Therapeutics (SpectRx), Inc., Norcross, GA, USA) has been published in 2001 (Figure 1B). This device non-invasively collects and analyses fluorescence and reflectance spectra from the cervix in vivo. Data of 111 enrolled women who were referred for colposcopy were included for analysis. With the use of receiver operating characteristic curve analysis, the optimal sensitivity for the detection of HG lesions was found to be 95%, with a specificity of 83%.

More recently, DeSantis *et al.* published the results of a prospective multicenter study to evaluate the safety and effectiveness of tissue spectroscopy for the diagnosis of cervical cancer with a device, also developed by Guided Therapeutics. This study was designed to evaluate the sensitivity and specificity of fluorescence reflectance spectroscopy also in women scheduled for colposcopy. Data of 572 women were evaluated. A sensitivity of 95% (95% CI 92-99) for the detection of \( \geq \) CIN 2 was calculated, with a specificity of 55% (95% CI 69-81). One of the
disadvantages of this study, as in many others, is that no biopsy has been taken from colposcopically normal women, resulting in no available histology for 149 (60%) of the 250 women with a final diagnosis of no CIN. (39;40)

In July 2006, the Food and Drug Administration approved the LUMA™ Cervical Imaging System (MediSpectra Inc., Lexington, MA, USA). (41) This optical detection system (ODS) combines fluorescence, white light backscattered spectroscopy and video imaging by shining a light on the cervix and analysing how different areas of the cervix respond to this light. The ODS divides the cervix in four hundred and ninety-nine 1 mm² spots and assigns a score to all the different areas. This score corresponds with different colours on a colour map that indicate which areas might contain a HG lesion. (41;42)

It is intended to be used in addition to visual colposcopy. (42-45) In two prospective, randomised controlled trials (with a combined total of more than 2900 subjects), the addition of this ODS to colposcopy in comparison with colposcopy alone displayed an increase of at least 25% in the true-positive biopsy rate for women with a cervical cytology as a result of borderline or mild dyskaryosis, at the cost of a 4% increase in the false-positive rate. (42;43) One study describes the development of a classification algorithm, with a calculated sensitivity for HG lesions of 92% and a specificity of 50%. (42) In another study with 193 evaluable subjects, the ODS increased the detection of HG lesions by 22% for all abnormal pap smear referrals and the detection of HG lesions by 25% in the group with borderline and mild dyskaryosis. (44)

The Dynamic Spectral Imaging System (DySIS™; Forth Photonics, Athens, Greece) is a colposcope that measures the acetowhitenmg effect of every image pixel of the cervix after the application of acetic acid (Figure 1C). (46;47) It is meant to replace conventional colposcopy. To maintain approximately the same field-of-view throughout the entire colposcopic examination, the optical imaging head is connected to the speculum. The sensor used has such a spatial resolution that the backscattered light intensity recorded by a given pixel corresponds approximately to the area occupied by one single cell (35 μm). A phase II clinical trial has been performed in 447 women who were referred for colposcopy. The quantitative assessment of the acetowhitenmg effect succeeded in discriminating objectively LG from HG lesions, with a sensitivity and specificity of 79 and 76%, respectively, while in the same study, conventional colposcopy had a sensitivity and specificity of 49 and 89%, respectively. (47;48)

Three different spectroscopic techniques (intrinsic fluorescence, diffuse reflectance and light scattering: trimodal spectroscopy) have been combined in a study published by Georgakoudi et al. in 2002. (49) Sensitivity and specificity values were determined by comparison of the spectroscopic classification with that of histopathology of 44 women referred for colposcopy. In this study, the sensitivity for trimodal spectroscopy in the detection of abnormal (both HG and LG) versus histopathologically proven normal cervices was 92% with a specificity of 71%. (49)

Another type of spectroscopic examination of the cervix is spectroscopy with a contact probe. A real-time device, intended to be used as a screening tool, has
been developed and marketed under the name of Truscreen® (previously known as Truscan® and Polarprobe®; Polartechnics, Sydney, Australia) (Figure 1D). This contact probe uses a combination of biosensors, including directly reflected light, backscattered light and electrical decay curves to classify cervical tissue. The device consists of a portable console connected to a probe-shaped handpiece. The distal tip of this handpiece is covered with a 5-mm-diameter single use sensor element, which comes into contact with the cervix. A multicentre study of 651 evaluable subjects revealed a sensitivity for this device of 70% (95% CI 67-74) and a sensitivity for the device and pap smear combined of 93% (95% CI 91-95) in the detection of HG lesions. In this study, 75% of the subjects were healthy volunteers and 25% were colposcopy clinic patients. No biopsy was taken from women with normal colposcopy, so histopathology was available for only 18% of women evaluated.

Impedance spectroscopy is another type of contact probe spectroscopy. The Royal Hallamshire Hospital in Sheffield, UK, has developed a four-electrode impedance probe, 5.5 mm in diameter, with two electrodes injecting a current of 20 μA peak-to-peak and the other two electrodes measuring the impedance spectrum. When an electrical current is applied to human tissue, the pattern of the resulting current flow is determined by the shapes, arrangements and internal structure of the tissue cells. A higher frequency current is able to penetrate the cell membranes and so passes through both intracellular and extracellular spaces. The current will thus be determined by intracellular volume and, as is hypothesised, the size of the nucleus. When the electrical current patterns over a range of frequencies is measured, electrical variables describing the tissue structure can be calculated. In two prospective trials of 176 and 87 women referred for colposcopy because of an abnormal pap smear, the sensitivity for ≥CIN1 for this device ranged between 75 and 89% and the specificity between 15 and 43%. The sensitivity and specificity for the detection of ≥CIN2 was calculated as 74 and 53%, respectively.

In addition to aforementioned techniques for spectroscopic colposcopy, many more are subject to research. Spectroscopy as an adjunct to and maybe even as a replacement for conventional colposcopy could be very likely in the near future.

**Computerised colposcopy**

Digital images of the cervix can be analysed by a computer for characteristic features and colour patterns, which may enhance the objectivity of the colposcopic examination. This process is known as computerised colposcopy and should be considered an adjunct to conventional colposcopy. Cristoforoni et al. have developed computer software that assigns nine-digit numeric values based on internationally recognised colposcopic criteria to a digital image of a cervix. Subsequently, the computer compares each numeric value to those memorised during a learning phase, in which scores of 70 women have been linked to the histological outcome. Images from 188 evaluable women were analysed and scored by the software. The results were compared with
conventional colposcopy and histology. A sensitivity of 91.2% in detecting HG lesions was reported for the computerised colposcopy compared with 61.8% for traditional colposcopy. The specificity was similar for the computerised and traditional colposcopy (94.8 and 92.2%, respectively).(56) So, this computerised colposcopy technique has an exceptional high sensitivity and specificity. Mikhail et al.(57) found statistically significant differences in intercapillary distances between CIN2 and CIN3 lesions when measuring this by computer. In general, the mean intercapillary distance in CIN3 lesions appears larger than in CIN2 lesions.

In a study by Pogue et al.(58) images of the cervix from women with histologically confirmed HG CIN lesions are compared with those from women with histologically confirmed immature squamous metaplasia to determine optimal criteria for automated discrimination between these types of tissue. All cervical images were separated into the red, green and blue channels and a comparison was made between the different features. In this study, the computer-based processing of the images provides a discrimination of the features that are important for clinical evaluation, with the Euler number (a dimensionless value that may be used to calculate whether two surfaces are topologically distinct) being the most clinically useful to distinguish between normal and neoplastic cervical tissue.(58)

**Optical coherence tomography**

Optical coherence tomography (OCT) is a noninvasive technique that can be used to image tissue structures slice by slice with high, micrometer-scale resolution. The tissue is illuminated by low-power infrared light, and the backscattered light is collected. Subsequently, the optoelectronic processor and computer create a two- or three-dimensional map of the backscattered intensity. This map is a cross-sectional image similar to B-mode ultrasound but has much better spatial resolution for superficial layers.(59) It was initially developed for imaging the different structures of the eye, such as the macula and retina in which it appeared to be able to discriminate the cross-sectional morphologic features of the fovea and optic disc, the layered structure of the retina and retinal nerve fibre layer thicknesses.(60;61) Since OCT is capable of providing images of tissue structures at a cellular level with a resolution of 10-20 μm, this technique holds promise for diagnosing cervical lesions without having to take a biopsy (‘optical biopsy’).(59;62-65)

One study has been conducted to determine the sensitivity and specificity of OCT in which this technique is used as an adjunct to the traditional management of abnormal cytology with colposcopy and biopsy.(64) After completion of the examinations, all the OCT images were reviewed twice. The first review of the images was performed blind, and the second review was performed with knowledge of the outcome of cytology and colposcopy results and viewing the digital photograph of the cervix. Overall, the sensitivity and specificity of (traditional) colposcopy for lesions ≥CIN2 in this study are 39% (95%CI 24-57) and 71% (95%CI 64-77), respectively, while the sensitivity
and specificity of blinded OCT for this diagnosis are 56% (95% CI 39-72) and 59% (95% CI 52-66), respectively. The sensitivity and specificity of colposcopy and OCT together for diagnosing HG lesions are 46% (95% CI 30-64) and 69% (95% CI 62-75), respectively. So, this study suggests that OCT can improve the sensitivity of the colposcopic exam at a cost of a slightly lower specificity.

Confocal microcolposcopy

Confocal microscopy is an optical imaging technique used to increase contrast and to reconstruct three-dimensional images. It uses point illumination and a pinhole in an optically conjugate plane in front of a detector to eliminate out-of-focus light or light scattering. Only the light within the focal plane can be detected, so the image quality is much better than that of normal light microscopes. Although the use of confocal microscopy to examine the cervix uteri in vivo is a novelty, it has been used in the field of dermatology, ophthalmology and gastroenterology. Confocal optical imaging can detect superficial lesions and therefore seems to be suitable for the early detection of precancerous lesions.

In 2002, Collier et al. performed a study to determine the usefulness of confocal microscopy for the detection of dysplasia in ex vivo cervical biopsy tissue from 25 women. Three years later, Carlson et al. demonstrated that in vivo confocal images of the cervix have the potential to give clinicians real-time structural information about possible cervical lesions. She showed that the nuclear-to-cytoplasm ratio from the differentiated superficial epithelium to the dense basal epithelium is increased in normal epithelium, but the images of dysplastic epithelium show little change from the upper layer to the basal layer of the epithelium. Further research in this field is needed.

DISCUSSION

Colposcopy is a visual technique that requires extensive training and experience. Although the optical device in itself is quite simple and the examination does not have to take long, the sensitivity and specificity are average to low and it does not provide an immediate definitive (histology) test result. Cervical cytology is also hindered by a low to average sensitivity (30 – 87%). Technology that increases the sensitivity and specificity and reduces or eliminates the other problems would be a great improvement.

Various innovative digital colposcopy techniques have been described in this review, and digital colposcopy as an adjunct to and perhaps as a replacement for traditional colposcopy seems very promising. Although some studies report (very) high sensitivities and specificities, until now, most digital colposcopy techniques have not been used on a large scale. There are a number of possible explanations for this discrepancy: one such explanation is the fact that digital colposcopy can take more time than an examination with a traditional colposcope. Furthermore, adjusting the
colposcope can be difficult in case of an abnormal position of the cervix or confounding factors as extreme obesity, especially when a colposcope is used in which the device is attached to the speculum or if the cervix needs to be immobilised for some time.

An explanation for colposcopists being hesitant about using a digital colposcope is the relatively high purchase and maintenance costs, an important factor especially in lower resource areas. It may also simply be a lack of knowledge of the possibilities that digital colposcopy provides and an unwillingness to abandon the well-established traditional colposcope.

However, the main drawback of the various techniques for digital colposcopy described is that only a few are extensively tested and validated in well-defined, sufficiently large patient populations. Some studies seem very promising, but after only one or perhaps a few publications, the publications cease. This may be because preliminary results may not have been validated in follow-up studies or simply that funds may be lacking for further research. The use of these techniques in the field of diagnosing cervical disease may also be considered a small niche since some techniques have been successfully implemented in other fields of medicine, for example ophthalmology.

A number of studies have been performed, which do not provide a histology reference in the case of a normal cervical image or digital test result. In these studies, no certainty can be obtained about the 'true negatives'. This is mainly a problem when calculating the specificity of the colposcopic examination since one cannot be sure that no undetected HG cases are represented in the numerator of the fraction. Also, when a colposcopy technique does not exceed a sensitivity of approximately 60-70%, there is no point in implementing the technique since this is similar to the sensitivity of cervical cytology. (76)

A potentially valuable use for digital colposcopy is the possibility of obtaining accurate and objective measurements of a number of cervical features. In this context, one can use the measurement of lesion size to study the possible correlation with high risk human papillomavirus infection. Perhaps, other independent features of HPV infection can also be established. Until now, precise measurements proved to be difficult, but with the development of new, advanced software techniques, the historical problems may be overcome.

Despite these considerations, there are many medical, technical and practical opportunities for digital colposcopes, which today are not used to their full extent. The question that needs to be answered is whether our clinics are ready for such a change. If prospective trials continue to demonstrate a good baseline sensitivity and specificity for digital colposcopes, then they could change the routine practice of colposcopy. Residents or even specialised nurses would be able to conduct a large part of the colposcopic examination, relying on the baseline performance of the device. Furthermore, tools such as video capturing of the colposcopy and biopsy taking can be used for educational purposes. If there is a steady baseline performance of the device,
it could be used in countries or areas where fewer expert colposcopists are available, achieving a sensitivity and specificity that could not be obtained with conventional techniques. However, that would mean that the new devices would need to be equipped for use in low-resource areas: at the moment, some of them do not appear to be suitable for that purpose.

Evidence for the use and experience with most of these techniques has been limited, and none of them should be considered to be an established procedure. However, some larger trials have been performed in the field of spectroscopy, which have demonstrated relatively high sensitivities. Therefore, we believe, of all currently available digital colposcopy devices available, that spectroscopy has the potential to emerge as the technique of choice and that one day it might become incorporated into routine clinical practice. We expect to see much progress and many great changes in the field of colposcopy in the near future.

DISCLOSURE OF INTERESTS

All authors are involved in a comparative clinical trial to validate the DySIS coloscope (Forth Photonics, Athens, Greece)

CONTRIBUTION TO AUTHORSHIP

R.V. and W. ter H. generated the concept for the manuscript. J.L. and M.K. performed the selection of papers and wrote the drafts of the manuscript. All authors took part in revision of the paper and have approved the final version.

FUNDING

No funding was received.

ACKNOWLEDGEMENTS

The authors would like to thank J.C.F. (Hans) Ket, medical information specialist of the VU Medical Centre, Amsterdam, the Netherlands for his search strategy advice.
REFERENCES


46. Balas C. A novel optical imaging method for the early detection, quantitative grading, and mapping of cancerous and precancerous lesions of cervix. *IEEE Transactions on Biomedical Engineering* 2001; 48(1), 96-104.


49. Georgakoudi I, Sheets EE, Muller MG, Backman V, Crum CP, Badizadehgan K et al. Trimodal spectroscopy for the detection and


