Innovative Medical Technology Overview: Number 005/2015

This IMTO review document describes an impartial review of the strengths and weaknesses of the submission by DySIS Medical Limited regarding the following medical technology.

DySIS\textsuperscript{®} colposcope

Overview of technology

The DySIS\textsuperscript{®} colposcope is a class IIa\textsuperscript{i} medical device indicated for the colposcopic evaluation of the cervix on patients that are referred to colposcopy following an abnormal smear result, and/or a positive human papillomavirus (HPV) deoxyribonucleic acid (DNA) test. DySIS\textsuperscript{®} is a digital video colposcope that uses dynamic spectral imaging (DSI) to quantify the aceto-whitening effect across the cervix during conventional colposcopy and displays the results in the form of a colour-coded map superimposed on the cervical image (DySISmap). DySIS\textsuperscript{®} differs from conventional colposcopes by measuring aceto-whitening automatically, producing a clear map.

Comparator(s) and use in pathway of care

The DySIS\textsuperscript{®} colposcope is positioned for use as an alternative to conventional optical colposcopes, used during conventional colposcopy and the associated methods of cervical lesion identification. A conventional colposcope is a binocular field microscope that offers optical examination under illumination and magnification only, ie visual documentation is not produced automatically. Using conventional colposcopes requires clinicians to view the cervix to manually assess the aceto-whitening process. As such, assessment is very subjective - the results from the same patient may vary when assessed by different colposcopists.

There is anticipated to be no change to the current pathway of care or the general practice of colposcopy.

Product performance

The evidence relating to product performance comprised of two main studies. A prospective, multi-centre, non-randomised, paired clinical study undertaken in the United Kingdom (UK) and Greece compared DySIS\textsuperscript{®} colposcopy with traditional colposcopy to identify high-grade cervical lesions in women referred to colposcopy clinics\textsuperscript{1}. In this study, 308 women referred to colposcopy clinics because of an abnormal smear or symptoms suggesting the possibility of cervical neoplasia were examined simultaneously with conventional colposcopy and DySIS\textsuperscript{®} colposcopy using a precommercial DySIS\textsuperscript{®} model (FPC-03). The primary outcomes included the diagnostic accuracy measures: sensitivity\textsuperscript{ii}, specificity\textsuperscript{iii}, and the area under the

\textsuperscript{i} Class IIa – a medium risk medical device, which requires a conformity assessment from a notified body – eg quality assurance audit or examination.

\textsuperscript{ii} Sensitivity: the probability that a person having a disease will be correctly identified by a clinical test, ie the number of true positive results divided by the total number with the disease.

\textsuperscript{iii} Specificity: the probability that a person not having a disease will be correctly identified by a clinical test, ie the number of true negative results divided by the total number of those without the disease.
receiver operating characteristic curve (AUC). The study reported that DySIS® colposcopy detected 62.9% more high-grade cases than conventional colposcopy (57 versus 35; p=0.0001). The sensitivities of DySIS® colposcopy and conventional colposcopy were 79.2% (95% confidence interval (CI) 68.4 to 86.9) and 48.6% (95% CI 37.4 to 59.9) respectively. The specificities were 75.8% (95% CI 70.0 to 80.9) for DySIS® colposcopy and 89.4% (95% CI 84.8 to 92.7) for conventional colposcopy. The AUC was 0.844 (95% CI 0.797 to 0.892), suggesting high diagnostic accuracy of DySIS® colposcopy. The authors concluded that DySIS® colposcopy is more sensitive than conventional colposcopy in detecting high-grade lesions and can provide improved guidance for biopsy.

A prospective, multi-centre comparative Dutch clinical study compared DySIS® colposcopy with conventional colposcopy to detect high grade lesions in 275 women referred for colposcopy. In this study, colposcopy was performed using the DSI colposcope as a regular video colposcope during the 3-minute data acquisition phase. Following on from this, the colposcopic impression was 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 DSI analysis of the images. The images collected were then digitally analysed by the DSI colposcope, and the resulting quantitative colour-coded map of the aceto-whitening effect was revealed and overlaid on the image of the cervix, after the colposcopist’s final predictions had been entered. The colour-coded map was then compared with the colposcopist’s own impression.

The primary outcome measures were the sensitivity and specificity to detect high-grade CIN2+ lesions. The results were analysed for two cohorts: the according-to-protocol (ATP) and intention-to-treat (ITT). The study reported that in the ATP cohort, DySIS® colposcopy detected 76 of the 86 women with histologically confirmed high-grade disease, compared with 47 of the 86 women using conventional colposcopy. This resulted in sensitivities of 88% (95% CI 82 to 95) for DySIS® colposcopy compared to a sensitivity of 55% for conventional colposcopy (95% CI 44 to 65). With regards to specificity, these were reported to be 69% (95% CI 60 to 78) for DySIS® and 85% (95% CI 77 to 92) for conventional colposcopy.

In the ITT cohort DySIS® colposcopy correctly identified 86 of the 108 women with histologically confirmed high-grade disease compared with 56 of the 108 detected by the conventional colposcopy. This resulted in sensitivities of 80% (95% CI 72 to 87) for DySIS® colposcopy and 52% (95% CI 42 to 61) for conventional colposcopy. In terms of specificity, the results showed the specificity of DySIS® was 63% (95% CI 54 to 71) compared with 82% for conventional colposcopy (95% CI 75 to 88).

The National Institute for Health and Care Excellence (NICE) published guidance* in August 2012 stating that DySIS® colposcopy is clinically and cost effective compared with conventional colposcopy, for examining the uterine cervix in women referred for colposcopy. These recommendations were based on the results of the two main studies referred to above.

*NICE have initiated a review of this guidance which is set to begin in October 2015.

Safety

No procedure-related adverse events were reported in any of the studies. The manufacturer stated that approximately 40,000 DySIS® examinations have been performed to date and no procedure-related adverse events have been reported.
Strengths and limitations of the evidence

The product performance evidence comes from two studies that show that the sensitivity of DySIS® colposcopy is higher than conventional colposcopy for the detection of high grade cervical lesions. However, with reference to Fryback and Thornbury\(^4\), whilst the above studies demonstrate the diagnostic efficacy of DySIS\(^\circledR\), an improvement in patient outcomes will only follow if the increased diagnostic accuracy leads to changes in patient management decision making.

The current DySIS\(^\circledR\) colposcopy v3.2 was not used within any of the studies. The study undertaken in the UK and Greece used a pre-commercial DySIS\(^\circledR\) model, whilst the Dutch study used DySIS\(^\circledR\) v2.1. It is worth noting that a number of drop-outs were reported owing to software issues with the pre-commercial model. However, it is reasonable to expect that the current commercial version of DySIS\(^\circledR\) would perform better than the pre-commercial version used in the study. The manufacturer noted that, owing to a system redesign to improve ergonomics and stability, there have been no reported reliability issues with the current version.

The evidence presented here indicates that use of DySIS\(^\circledR\) has not led to any procedure-related adverse events. However, notwithstanding the limited description surrounding the reporting of adverse events within the studies, it is worth noting the following in relation to adverse events. Both studies reported that DySIS\(^\circledR\) was associated with a lower specificity than conventional colposcopy, i.e. an increase in the false positive rate. Such results may lead to additional unnecessary biopsy procedures for healthy women. However, given the nature of how the technology is used in practice, this is not considered to be a major concern.

There was some heterogeneity between the two main studies in terms of patient characteristics, with the prevalence of CIN2+ higher in the Dutch study (45%) than the study undertaken in the UK and Greece (23%). However, both studies demonstrated higher sensitivity regardless of the difference in patient characteristics between the studies. Within the studies, assessment using DySIS\(^\circledR\) or conventional colposcopy was not undertaken by multiple colposcopists. The subjective nature of conventional colposcopy lesion detection means that the results – even from the same patient – may vary when assessed by different colposcopists.

Conventional colposcopy within the studies consisted of video colposcopy using the DySIS\(^\circledR\) colposcope, rather than the conventional colposcopy methods and equipment used within NHSScotland. As such the accuracy of conventional colposcopy may not entirely reflect that of current practice. However, as it is likely that the accuracy of conventional colposcopy within the studies would be no worse than that of the conventional colposcopy methods within NHSScotland, the study results can be considered conservative.

Following on from the above, concern has been raised surrounding the generalisability of the studies – particularly the comparator arm – to clinical practice in Scotland. For example, if the conventional colposcopy methods described in the studies are not as accurate as those used in Scotland, then the benefits of DySIS\(^\circledR\) colposcopy will have been overestimated for Scottish decision-making. However, clinical experts consulted by NICE advised that colposcopy practice in the Netherlands resembles that in the UK, and therefore these results should be generalisable to the UK.
Economic considerations

With regards to the cost effectiveness of the DySIS® colposcope, the manufacturer presented a cost-utility analysis commissioned by NICE. The analysis compared DySIS® colposcopy with conventional colposcopy for examination of the uterine cervix to detect cancerous and pre-cancerous cervical tissue in women referred for colposcopy through the NHS Cervical Screening Programme. The results showed that DySIS® colposcopy costs less and is more accurate than conventional colposcopy, based on throughput of 1,229 women examined per device per year. A scenario analysis showed that DySIS® remained cost effective when the number of women examined per device per year was reduced to 250. Based on this analysis, NICE considered DySIS® colposcopy to be cost-effective. It is worth noting that the cost-utility analysis was based upon the cited studies, and therefore concerns surrounding these translate to the economic model.

A new cost analysis submitted by the manufacturer estimated the relative treatment costs, the relative number of recalls and the relative number of biopsy volumes, based on the sensitivities observed in the clinical studies. This showed that the adoption of DySIS® colposcopy into the cervical screening programme at Ninewells Hospital could produce potential non-cash releasing savings of approximately £50,000 over a 5 year period, based on 160 women examined per annum. These cost savings may generalise to other hospitals within NHSScotland, should similar numbers of colposcopies be undertaken. However, as the cost savings are sensitive to the volume of colposcopy patients seen per annum, these savings will be much lower in hospitals undertaking fewer colposcopies. In order for DySIS® colposcopy to be cost saving, the minimum volume of colposcopy patients required to be seen per hospital per annum is 67.

Organisational and patient issues

Colposcopy is only performed by trained professionals (either British Society for Colposcopy and Cervical Pathology qualified nurse colposcopists or gynaecologists). Both NICE and one SHTG clinical expert indicated that up to 4 hours training may be required for new staff to use the DySIS® colposcope.

Based on clinical expert feedback, consideration should be given to the space requirements of the DySIS technology in relation to some existing NHS facilities.

The average length of use per examination is reported to be less than 15 minutes. Currently, a NHS-funded evaluation is being carried out on one DySIS® colposcope in NHS Tayside but, as yet, DySIS is not in routine clinical use.

A patient satisfaction survey completed during one of the studies reported that the DySIS® colposcopy was no extra burden for the majority of the participating women, compared with conventional colposcopy.

Summary

In summary, the DySIS® colposcope appears to be a clinically and cost-effective device for the colposcopic evaluation of the cervix on patients that are referred to colposcopy following an abnormal smear result, and/or a positive HPV DNA test.

Adoption of DySIS® colposcopy into NHSScotland may represent a cost saving relative to conventional optical colposcopy.
References


