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Detection and characterization of colorectal polyps using high-definition white light and i-Scan: Evidence-based consensus recommendations using a modified Delphi process

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Abstract

Background: i-Scan is an image enhancement modality, which provides enhanced views of mucosal structures and vascular patterns.

Methods: A modified Delphi process was used to develop a series of evidence-based statements on the role of high-definition white light (HDWL) and i-Scan for the detection and diagnosis of colorectal neoplasms. Each statement was voted to achieve consensus (i.e. >80% agreement).

Results: Seven proposed statements achieved consensus: (1) HDWL is recommended rather than standard definition (SD) for detection and diagnosis of colorectal neoplasms; (2) HDWL colonoscopy with i-Scan improves polyp and adenoma detection rates when compared with SD colonoscopy; (3) HDWL + i-Scan is superior to HDWL alone for the optical diagnosis of colorectal neoplasms; (4) HDWL + i-Scan in expert hands meets American Society for Gastrointestinal Endoscopy (ASGE) in the Preservation and Incorporation of Valuable Endoscopic Innovations (PIVI) standards for optical diagnosis of diminutive neoplasms; (5) HDWL + i-Scan in non-expert hands does not meet ASGE PIVI standards for optical diagnosis of diminutive neoplasms; (6) optical diagnosis of polyps with i-Scan has a learning curve and needs systematic training; and (7) the performance of i-Scan for the in vivo diagnosis of colorectal neoplasms is similar to Narrow Band Imaging (NBI) and Fuji Intelligent Chromo Endoscopy (FICE).

Conclusions: Seven proposed statements on the use of HDWL and i-Scan for the detection and diagnosis of colorectal neoplasms achieved consensus.

Keywords

i-Scan, colonoscopy, colorectal neoplasm, colorectal polyp, image-enhanced endoscopy, colon, endoscopic diagnosis

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Key summary

- i-Scan is a type of image enhancement technology that can assist the in vivo distinction between hyperplastic and adenomatous polyps and reduce the need for unnecessary polypectomy.
- It has largely been used in expert settings, and because it is used so freely, it is unlikely that large multicentred randomized controlled trials will be carried out.
- The consensus statements were developed to provide clinically useful practical guidelines to endoscopists.
- Seven proposed statements achieved consensus.

Introduction

Colorectal cancer is one of the most common cancers. Colorectal cancer screening has been shown to reduce mortality by detecting cancers at an early stage through the diagnosis and removal of adenomas.[1–3] The National Polyp Study showed that colonoscopic polypectomy reduced the incidence of colorectal cancer.[4]

Accurate in vivo distinction between hyperplastic and adenomatous polyps would reduce unnecessary polypectomy. Image enhancement techniques can assist with the in vivo detection and characterization of lesions as proposed by the American Society for Gastrointestinal Endoscopy (ASGE) in the Preservation and Incorporation of Valuable Endoscopic Innovations (PIVI) statement for colorectal polyps.[5] The incorporation of a 'resect and discard' policy would be encouraged so that small adenomas are resected without histological analysis, whilst hyperplastic polyps in the recto-sigmoid are left without removal.[6,7]

i-Scan (Pentax, Tokyo, Japan) is a digital contrast system that uses post-processing computer algorithms combined with a standard high-definition (HD) processor to enhance visualization of the mucosal epithelial surface pattern and vascular pattern that forms the basis for in vivo diagnosis of lesions.[8]

Most studies published on the use of i-Scan during colonoscopy have been single centred. Robust data from large multi-centre randomised controlled trials are lacking. The aim of this study was to perform a comprehensive review of the available literature and develop evidence-based clinical guidelines using a modified Delphi process.

Methods

International key opinion leaders in the field of optical diagnosis and i-Scan formed the i-Scan consensus group. Their recommendations were made on the basis of literature searches and therefore did not require ethical review or patient consent. Literature searches were performed using Medline, Cochrane Central Register of Controlled Trials; conference abstracts. The following search terminologies were used: i-Scan; colon; colo-rectum; polyps; adenoma; hyperplastic polyps; colitis. Original studies were retrieved by title and full text was reviewed to filter out publications deemed irrelevant.

The statements were originally defined using a PICO (population/intervention/outcome/comparator) format. Two investigators developed the statements after the available literature was searched and reviewed. A modified Delphi process was then used to develop consensus statements for the use of i-Scan during colonoscopy. With this approach a systematic literature review is combined with repeated anonymous voting. The software program permitted the inclusion of anonymized individual feedback, along with changes of opinion throughout the process.[9–11]

The key steps in the process were: (1) selection of the consensus group; (2) systematic literature reviews; (3) development of draft statements; (4) rounds of repeated anonymous voting on statements with feedback at each round, until consensus agreed or statement rejected; and (5) grading of the strength and quality of the evidence and strength of the recommendations using the **well accepted GRADE system.**[12–14] The respondents were asked to choose one of the following for each statement: (A+) strongly agree; (A) agree with reservation; (N) neutral; (D) slightly disagree; (D+) strongly disagree.

The level of agreement increased with each round of voting. Statements were accepted if $> 80\%$ of the panel members strongly agreed or agreed with the statement. If the statement received $< 80\%$ agreement, then the panel members made modifications, which were then put forward again for re-voting. If $> 80\%$ agreement was not achieved after four rounds of voting, then the statement was rejected.

Recommendations and statements

Statement 1

When performing routine colonoscopy, HD white light (HDWL) is recommended rather than standard definition (SD) for the detection and diagnosis of colorectal polyps.

64% (A+), 36% (A), 0% (N), 0% (D), 0% (D+)

Grade of recommendation: Strong; level of evidence: Moderate

Summary of evidence. A meta-analysis including five studies and 4422 patients showed a small difference between the detection of colonic polyps and adenomas when using HD colonoscopy vs. standard video endoscopy. For polyp detection, the incremental yield was 3.8% (95% CI 1–6.7%), with a number needed to treat (NNT) of 26. For adenomatous polyps, the incremental yield was 3.5% (95% CI 0.9–6.1%) with an NNT of 28. There was no difference in the detection rate of high-risk adenomas.[15]

A retrospective study by Buchner et al. demonstrated an improvement in polyp detection when using HDWL, compared with SD colonoscopy (42.2% vs 37.8%).[16]

The grade of recommendation for this statement was strong, although the data to support it are limited and of a moderate level. This recommendation is based more on the experts' own clinical experience and because the meta-analysis was more powered to detect any differences between both technologies as opposed to individual studies.

Statement 2

HD Colonoscopy with i-Scan improves polyp and adenoma detection rates when compared with SD colonoscopy without i-Scan.

36% (A+), 64% (A), 0% (N), 0% (D), 0% (D+)

Grade of recommendation: Strong; level of evidence: Moderate

Summary of evidence. Overall, more studies found an improvement in adenoma detection with HD + i-Scan versus SD. Testoni's retrospective analysis of 1101 colonoscopies concluded that HD + i-Scan found significantly higher detection rates of polyps < 10 mm (67.9%) vs. SD 48.1%, $P < 0.0001$, as well as a significantly higher number of flat polyps HD + i-Scan 27.8% vs. SD 9.9%, $P = 0.04$.[17]

Hoffman's study examining the distal 30 cm of the colon concluded that the detection rate of small circumscribed lesions (<5 mm) was 2.48 using HDWL, 4.7 for HDWL + i-Scan and 9.1 for dye-based chromoendoscopy. A sensitivity of 82% and a specificity of 96% in the last 30 cm of the colon when using i-Scan was shown.[18] Another randomized study by Hoffman et al. found that HD + i-Scan detected significantly more adenomatous and cancerous lesions than SD endoscopy (38% vs. 13%, $P < 0.0001$).[19]

Lee et al. showed encouraging results of up to 90% diagnostic accuracy with the use of i-Scan.[20]

In Bowman et al.'s prospective study 1936 patients underwent colonoscopy in an ambulatory care centre; 618 adenomas were detected in the i-Scan group compared with 402 in the HDWL group ($P < 0.01$).[21]

Other trials by Chan et al. and Hong et al. found no difference in adenoma detection when using HD colonoscopy with i-Scan versus SD colonoscopy without i-Scan.[8,22] Chan et al.'s study had the following limitations: small sample size (43 patients); no standardized training programme; and one of the two endoscopists had a high baseline sensitivity and specificity of 88.9% and 100% for HDWL, making any additional gain with i-Scan minimal.[8] In Hong et al.'s study the endoscopists involved had varying levels of experience and were from a single institution, which may explain their findings.[22] All experts agreed with the above statement as overall, larger, better designed studies show that i-Scan has the potential to improve polyp detection rates.

Statement 3

HDWL + i-Scan is superior to HDWL alone for the optical diagnosis of colorectal polyps.

36% (A+), 55% (A), 9% (N), 0% (D), 0% (D+)

Grade of recommendation: Strong; level of evidence: Low

Summary of evidence. Two studies by Hoffman's group showed that HDWL + i-Scan provided better accuracy for in vivo polyp characterization than HDWL alone.[18,19] One small study of 69 patients found that HDWL + i-Scan had a greater detection rate of diminutive colon polyps than HDWL alone: 2.48 and 4.7, respectively.[18]

The other study of 220 patients demonstrated that HDWL + i-Scan found more colorectal neoplasia (38%) compared with SD colonoscopy (13%). However, the comparison was between HDWL + i-Scan versus SD colonoscopy without i-Scan.[19]

A study by Lee at al. evaluated 296 diminutive colon polyps using HDWL colonoscopy followed by either NBI or i-Scan without optical magnification. They found that both NBI and i-Scan demonstrated a significantly greater sensitivity and accuracy compared with HDWL alone for the prediction of histology ($P < 0.05$).[20]

This statement is more applicable to diminutive polyps < 5 mm in size.

Statement 4

HDWL + i-Scan in expert hands meets ASGE PIVI standards for optical diagnosis of diminutive polyps.

27% (A+), 64% (A), 0% (N), 9% (D), 0% (D+)

Grade of recommendation: Strong; level of evidence: Moderate.

Summary of evidence. The PIVI document on the Real-Time Endoscopic Assessment of the Histology of Diminutive Colorectal Polyps histology highlights two technology performance thresholds:

1. A 90% or greater negative predictive value (NPV) for adenomatous histology;
2. A 90% or greater agreement in assigning post-polypectomy surveillance intervals.[5]

Pigo et al.'s single endoscopist study used HDWL + i-Scan for the real-time histology prediction of 150 polyps. The calculated NPV was 93%, so it met the first PIVI standard for not resecting suspected hyperplastic polyps (<5 mm) in the recto-sigmoid area. No conclusions could be drawn about the second PIVI standard as no data were collected on the prediction of surveillance intervals.[23]

In Hoffman's first study expert endoscopists evaluated diminutive polyps in the distal 30 cm of the colon and reported a NPV of 96.5%.[18] In the second study an NPV of 97% was found.[19]

Finally, Basford et al.'s single centre, single endoscopist study is the only study to have reported on both PIVI standards. A sensitivity of 97.1%, specificity of 90.7% and accuracy of 94.7% for the in vivo characterization of 209 diminutive polyps were found. An NPV of 100% was found for adenomatous histology of diminutive recto-sigmoid polyps with both HDWL and i-Scan. This study showed that HDWL alone and HDWL + i-Scan meet both PIVI standards. The second PIVI criterion was also met as the i-Scan predicted surveillance recommendations were met in > 90% of the cases.[24]

The above studies demonstrate that i-Scan use in expert hands meet PIVI standards, but more information on surveillance intervals is needed for them to meet the second PIVI recommendation, as only one study addressed this.

Statement 5

HDWL + i-Scan in non-expert hands does not meet ASGE PIVI standards for optical diagnosis of diminutive polyps.

27% (A+), 73% (A), 0% (N), 0% (D), 0% (D+)

Grade of recommendation: Strong; level of evidence: Moderate.

Summary of studies. In Schachschal et al.'s prospective study, in vivo diagnosis of 675 colorectal polyps using i-Scan was evaluated by comparing conventional high-resolution colonoscopes against HD. Ten experienced colonoscopists working in private practice with no expertise of in vivo diagnosis and no structured training were involved. They reported an accuracy, sensitivity and specificity of 76.6%, 78.1% and 73.4% with an NPV of 69%, therefore not meeting the PIVI 1 criteria. PIVI 2 criteria were also not met as the follow up recommendations were accurate in only 69.5%, falling well below the 90% agreement.[25]

A study by Hong et al. reported an NPV of 76.2% for the assessment of polyps using HDWL and i-Scan. This fell well below the PIVI standard. No description of any structured training with in vivo characterization was given in this study.[22]

Another study by Chan et al. included two experienced endoscopists without prior use of i-Scan, and 103 polyps were evaluated. The authors reported an NPV of 70%, which fell below the PIVI recommendations.[8]

In these studies, the endoscopists received no structured training on in vivo diagnosis of polyps. This explains the contrasting results from the expert centres. The consensus panel therefore recommends that only in expert hands is the ASGE PIVI criteria met for the optical diagnosis of diminutive polyps.

Statement 6

Optical diagnosis of polyps with i-Scan has a learning curve and needs systematic training.

36% (A+), 64% (A), 0% (N), 0% (D), 0% (D+)

Grade of recommendation: Strong; level of evidence: Moderate

Summary of evidence. Neumann et al. demonstrated in their ex-vivo study that image interpretation using i-Scan has a learning curve. Four endoscopists underwent a short online training session followed by a review of 110 polyp images. The accuracy level progressively improved from 73.9% to 94.3% as the endoscopists reviewed images from study set 1 to 5. Two out of four endoscopists achieved the first PIVI standard of NPV > 90% at the end of the study.[26]

An ex-vivo study by Bouwens et al. showed that after a short didactic training session on the use of i-Scan with HDWL, endoscopists could predict colorectal polyp histology with a mean accuracy of 84%.[27]

A distinct learning curve was again demonstrated in Basford et al.'s in vivo study of real-time histology prediction during colonoscopy. Accuracy of prediction gradually improved from 82% during the first 100 polyps to 97% during the last 100 polyps of the 400-polyp study. A PIVI standard of NPV > 90% was

achieved. The authors calculated that the NNT for in vivo, real-time prediction of histology is more than 200 polyps.[24]

All studies have clearly demonstrated a learning curve for i-Scan-assisted histological prediction. It is interesting to note that the endoscopists achieved a high level of accuracy very quickly in an ex-vivo setting but the third study demonstrated that in an in vivo setting, the real-time prediction of polyp histology takes much longer (200 polyps). The best strategy for future training would be a combination of both methods.

Statement 7

The performance of i-Scan for the real-time characterization of colorectal polyps is similar to NBI and FICE.

45% (A+), 55% (A), 0% (N), 0% (D), 0% (D+)

Grade of recommendation: Strong; level of evidence: Moderate

Summary of evidence:. A meta-analysis of 11 i-Scan studies, enrolling 1652 polyps demonstrated a summary sensitivity and specificity of 91.5% and 92.1%, respectively.[28] In another meta-analysis,[29] the pooled sensitivity and specificity of i-Scan was compared with NBI. The sensitivity of i-Scan (91.5%) was similar to that of NBI (91%) but specificity with i-Scan (92.1%) was higher than that of NBI (82.6%). The current data show that i-Scan is similar to NBI in making a correct diagnosis of adenoma, but that i-Scan is better than NBI in making a correct diagnosis of hyperplastic polyp.

Guo et al. in their meta-analysis compared the pooled sensitivity and specificity with i-Scan with similarly pooled sensitivity and specificity of FICE reported in another meta-analysis.[30] The sensitivity of i-Scan (91.5%) was similar to that of FICE (91.8%) but specificity with i-Scan (92.1%) was higher than that of FICE (83.5%). i-Scan is similar to FICE in making a correct diagnosis of adenoma but is better than FICE in making a correct diagnosis of hyperplastic polyps. However, it should be noted that there was no direct comparison between these technologies and going forward it will be important to see studies directly comparing these technologies.

Statement 8

The adenoma detection rate of HD + i-Scan is comparable to chromoendoscopy.

45% (A), 0% (A+), 36% (N), 9% (D), 9% (D+)

Statement rejected (45% acceptance)

Chromoendoscopy is associated with significantly prolonged withdrawal times, which limit its applicability in standard day-to-day colonoscopy. Techniques like i-Scan might be able to overcome the practical difficulties associated with chromoendoscopy.

The reported adenoma detection rate with chromoendoscopy ranges from 60% to 65%.[31,32] Other studies with pan dye spray showed an increase in the detection of hyperplastic lesions only.[33,34] Hoffman's study examining the last 30 cm of the colon found that methylene blue had a greater detection rate of 9.1 for small < 5 mm lesions compared with other modalities of HDWL + i-Scan (4.7) and HDWL (2.48).[19] This study has limitations in that it was a small study (69 patients) and single-centred.

There is a need for high-quality data to compare i-Scan with chromoendoscopy before the recommendation that the adenoma detection rate of HD + i-Scan is comparable to chromoendoscopy can be adopted. This statement was therefore rejected by the consensus panel.

Statement 9

HDWL alone can be effective for the in vivo characterization of polyps in expert hands.

9% (A+), 45% (A), 27% (N), 9 %(D), 9 %(D+)

Statement rejected (54% acceptance)

This statement was primarily based on evidence from the prospective, single centre study (HISCOPE) which compared HDWL and HDWL + i-Scan for the assessment of 209 small colonic polyps < 10 mm in size. The overall diagnostic accuracy using HDWL alone was 93.3% with a sensitivity of 95.5% and a specificity of 89.3%. HDWL and HDWL + i-Scan both had a 100% NPV for adenomatous tissue for diminutive rectosigmoid polyps. Polyp surveillance intervals had an accuracy of 95.2% with HDWL and 97.2% with i-Scan.[24]

This was the first study to demonstrate a diagnostic accuracy greater than 90% for the in vivo characterization of diminutive colon polyps using HDWL. The authors attributed the differences to use of endoscopes with a 1.2-megapixel charge-coupled device with a very high definition. A strict protocol of cleaning all polyps with a mucolytic solution of water, simethicone and N-acetylcysteine before assessment was adhered to.[24]

In summary, the HISCOPE study demonstrated that the HDWL alone was found to have a similar efficacy to HDWL with i-Scan.[24] However, this statement was rejected as the data to support the statement were found in only one study from a single centre, carried out by a single experienced endoscopist, and needs further investigation before acceptance.

Discussion

The i-Scan consensus panel examined the clinical utility of i-Scan for the in vivo diagnosis of colorectal neoplasia, to produce a set of recommendations that could be adopted for use in clinical practice. Seven statements were selected to represent the following key relevant areas: use of HDWL alone or in combination with i-Scan, training in the use of i-Scan, whether PIVI standards were met and comparisons to NBI/FICE.

The statements were based on studies from both expert and non-expert settings. The consensus panel recommends that the use of optical enhancement technology such as i-Scan requires training and should only be used by endoscopists who have been through a formal training process.

A modified Delphi process was used to develop the statements. A literature search allowed the inclusion of additional articles throughout the consensus process, thereby including studies that might have been missed during the initial search. The included articles were reviewed by panel members and a chair, but a single senior author reviewed and graded each article to ensure consistency in the assessment of the evidence. A meta-analysis technique was not used to evaluate the literature due to the sparse evidence available.

The overall level of the evidence in relation to the recommendations was low to moderate. There was a high level of agreement for most statements, which would indicate that most of the recommendations are currently appropriate for clinical use. The recommendations were accepted if the level of agreement for them was $\geq 80\%$. The areas where the level of agreement was lower could guide future areas for research.

Areas were identified where the panel felt that future research was warranted: (1) post-EMR assessment of resection margins to reduce risk of recurrence; (2) i-Scan-assisted marking of lesion margins prior to resection of flat colonic neoplasia; (3) i-Scan-assisted assessment of large colonic polyps could potentially improve the prediction of invasive vs. non-invasive neoplasia; (4) to establish the role of HDWL and i-Scan during colitis surveillance; and (5) a validated and standard i-Scan classification for in vivo characterization of polyps is required.

Our work represents an informative evaluation of the available literature to develop the consensus guidelines and identify future research needs.

Declaration of conflicting interests

The authors have disclosed any conflicts of interest.

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Ethics approval

This study was a literature review. Therefore, ethics approval was not sought.

Informed consent

As the study was a literature review, informed consent was not sought.

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