



## The American Society for Gastrointestinal Endoscopy PIVI (Preservation and Incorporation of Valuable Endoscopic Innovations) on imaging in Barrett's Esophagus

*The PIVI (Preservation and Incorporation of Valuable endoscopic Innovations) initiative is an ASGE program whose objectives are to identify important clinical questions related to endoscopy and to establish a priori diagnostic and/or therapeutic thresholds for endoscopic technologies designed to resolve these clinical questions. Additionally, PIVIs may also outline the data and or the research study design required for proving an established threshold is met. Once endoscopic technologies meet an established PIVI threshold, those technologies are appropriate to incorporate into clinical practice presuming the appropriate training in that endoscopic technology has been achieved. The ASGE encourages and supports the appropriate use of technologies that meet its established PIVI thresholds.*

*The PIVI initiative was developed primarily to direct endoscopic technology development toward resolving important clinical issues in endoscopy. The PIVI initiative is also designed to minimize the possibility that potentially valuable innovations are prematurely abandoned due to lack of utilization and to avoid widespread use of an endoscopic technology before clinical studies documenting their effectiveness have been performed. The following document, or PIVI, is one of a series of statements defining the diagnostic or therapeutic threshold that must be met for a technique or device to become considered appropriate for incorporation into clinical practice. It is also meant to serve as a guide for researchers or those seeking to develop technologies that are designed to improve digestive health outcomes.*

*An ad hoc committee under the auspices of the existing ASGE Technology and Standards of Practice Committees Chairs develops PIVIs. An expert in the subject area chairs the PIVI, with additional committee members chosen for their individual expertise. In preparing this document, evidence-based methodology was employed, using a MEDLINE and PubMed literature search to identify pertinent clinical studies on the topic. PIVIs are ultimately submitted to the ASGE Governing Board for approval, as is done for all Technology and Standards of Practice documents.*

*This document is provided solely for educational and informational purposes and to support incorporating these*

*endoscopic technologies into clinical practice. It should not be construed as establishing a legal standard of care.*

### GENERAL CLINICAL AREA OF THIS PIVI AND BRIEF SUMMARY OF BACKGROUND/ CLINICAL RELEVANCE

This PIVI addresses the issue of real-time imaging of Barrett's esophagus.

The clinical problems addressed by the PIVI are the effectiveness, cost, and compliance of current surveillance protocols. Endoscopic surveillance of Barrett's esophagus, as currently practiced, has numerous shortcomings. Dysplasia and early adenocarcinoma may be endoscopically indistinguishable from nondysplastic tissue. The distribution of dysplasia and cancer is highly variable, and even the most thorough biopsy surveillance program has the potential for sampling error. Current surveillance programs are expensive and time-consuming. Survey data indicate that although surveillance is widely practiced, there is marked variability in the technique and interval of surveillance because practice guidelines are not widely followed.<sup>1-4</sup>

### THRESHOLDS RECOMMENDED FOR THIS PIVI

To eliminate the need for random mucosal biopsies during the endoscopic surveillance of patients with nondysplastic Barrett's esophagus, an imaging technology with targeted biopsies should have a per-patient sensitivity of 90% or greater and a negative predictive value (NPV) of 98% or greater for detecting high-grade dysplasia (HGD) or early esophageal adenocarcinoma (EAC) compared with the current standard protocol (white-light endoscopy and targeted and random 4-quadrant biopsies every 2 cm). In addition, the new imaging technology should have a specificity that is sufficiently high (80%) to allow a reduction in the number of biopsies (compared with random biopsies).

The majority of the Barrett's patients encountered in clinical practice are those with nondysplastic Barrett's esophagus. These patients have a very low incidence of HGD and EAC development; therefore, the vast majority of patients undergoing surveillance have multiple biopsy specimens obtained that show no evidence of HGD/EAC. For populations with a low prevalence of disease, the most important metrics for a diagnostic test are the sensitivity and NPV. Previous clinical trials have reported that

this biopsy protocol has a sensitivity ranging from 28% to 85% for the detection of patients with HGD/EAC.<sup>5-9</sup> Analyses that have demonstrated the cost-effectiveness of Barrett's esophagus surveillance have assumed that surveillance programs in Barrett's esophagus patients would have a sensitivity of 85% to 90%.<sup>10,11</sup> Therefore, for endoscopic imaging-based surveillance to replace the current biopsy protocol, it should have a sensitivity of 90% or greater. The second issue to consider for any new diagnostic test is the specificity; new diagnostic tests should have a substantially higher specificity than random biopsies, but the exact value required for the new modality to be cost-effective depends on the cost of the test. Because abnormal imaging requires biopsies for confirmation, new imaging methods should not result in more biopsy specimens being obtained than would a random biopsy protocol. Based on the published literature, the specificity of biopsy protocols in patients with Barrett's esophagus has ranged from 56% to 100%<sup>9,12-27</sup>; therefore, we propose that any new technology should have a specificity that is at least 80%.

## LITERATURE REVIEW SUMMARY

Despite the alarming increase in the incidence of EAC, the precise incidence of cancer in patients with Barrett's esophagus is uncertain, with rates varying from approximately 1/52 to 1/694 years of follow-up.<sup>28</sup> However, the cancer risk for a given patient with nondysplastic Barrett's esophagus is quite low. The most recent meta-analysis of cancer risk in Barrett's esophagus patients produced a pooled estimate of 0.6% per year.<sup>29</sup> Thus, the majority of patients encountered in clinical practice are those without dysplasia.

The operating characteristics of the various currently available imaging modalities for the diagnosis of HGD/cancer were determined by performing a systematic review. Overall, the NPV for current advanced imaging methods ranged from 79% to 100%, with a mean NPV of 97%. The per-patient sensitivity and specificity of new imaging techniques have ranged from 33% to 100% and 56% to 100%, respectively.<sup>7,9,14,16-18,21,24,30-35</sup>

Finally, the primary costs associated with surveillance include physician time, nursing time, facility utilization (procedure rooms, time, and equipment for patient scheduling, reminders, and patient preparation), sedation expenses, equipment outlays (endoscopes, biopsy forceps, imaging devices), pathology processing, pathologist charges, time lost from work for the patient, and time lost from work for persons accompanying the patient. Adoption of imaging could conceivably affect all of these except the last 2 (time lost from work).

## AREAS FOR RESEARCH

There are several research areas relevant to this PIVI. Having a better estimate of which patients are at greatest risk of the development of esophageal cancer is important because screening and surveillance efforts should be focused more on these patients, with perhaps less frequent or no surveillance in those

patients at extremely low risk. New imaging techniques would need to be compared with the "current standard" available endoscope, which could change in the future as the next-generation endoscopes will continue to have improved imaging. Future studies will need to compare the new imaging technology with the standard 4-quadrant biopsy protocol in the same patient population to determine whether the PIVI thresholds are met. Additionally, cost-effectiveness studies will need to be performed related to the operating characteristics of any new imaging modality compared with standard biopsy protocol in the same population.

## TRAINING ISSUES/ESTABLISHMENT OF COMPETENCY

Training needs to be available to ensure the effectiveness of any new technology as it becomes used in nonresearch settings. Quality measures would need to be developed to ensure consistent, high confidence examinations. Gastroenterological societies, such as the American Society for Gastrointestinal Endoscopy, would develop position statements on minimum requirements for both trainees and practicing clinicians. There would need to be access to online materials/image libraries, hands-on workshops, and educational materials. There should be a way for individual practitioners to monitor their own accuracy as a performance quality measure (eg, prediction of neoplasia in lesions using white-light and/or enhanced imaging techniques, similar to detection of colonic adenomas).

## OTHER ISSUES CONSIDERED IN ESTABLISHING THE THRESHOLDS

1. Limitations of current methods for surveillance of patients with Barrett's esophagus
2. Low risk of HGD/EAC in patients with nondysplastic Barrett's esophagus
3. Costs of standard endoscopy and biopsy

## DISCLOSURE

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Abbreviations: EAC, early adenocarcinoma; HGD, high-grade dysplasia; NPV, negative predictive value.

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