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Title: Advanced Imaging in surveillance of Barrett's Esophagus: Is the juice worth the squeeze?

Reviewer's code: 00182114

Reviewer's country: Japan

Science editor: Ruo-Yu Ma

Dear Ms. Ma,

Thank you for reviewing our paper entitled, Advanced Imaging in surveillance of Barrett's Esophagus. Is the juice worth the squeeze?"

We wanted to write to address the questions you asked in your peer-review report and indicate corresponding changes that have been made to our paper. We also reworded the text that was found to have minor overlapping in the published literature. Thank you for your time.

Sincerely,

Sara Cerrone and Arvind Trindade

1. Please tell me the benefit of VLE over ultrasound.

Endoscopic ultrasound technology provides detail of the esophageal wall and mucosal layers that allows for staging of esophageal tumors when they occur. VLE allows for high resolution detailed examination of microstructure of the esophageal mucosa prior to tumor development to identify potential areas of mucosal dysplasia.

2. What advantages and disadvantages are associated with VLE compared with other endoscopic techniques?

VLE allows for detailed examination of the microstructure of large segments of BE. Some disadvantages to VLE are the cost of this technology and the learning curve experienced by endoscopists prior to developing efficiency with this technology. VLE provides examination of a large field of BE that can be overwhelming to a novice user and lead to fatigue and potential for missed lesions.

(Section: Volumetric Laser Endomicroscopy paragraphs 1 and 2)

3. How safe is VLE compared with other imaging or endoscopic techniques, for example Confocal laser endomicroscopy?

VLE appears to be a safe form of advanced imaging. In a case series on 52 patients, the safety and feasibility of the Nvision VLE system was assessed. Of the 52 patients undergoing VLE, only 2 minor

adverse events were reported which includes mucosal lacerations that did not require therapy or intervention. VLE does not appear to significantly increase in endoscopic risk to patient but can lead to longer procedure times, estimated 22 minutes \pm 6 minutes standard deviation, which can be of anesthetic concern.

(Section: Volumetric laser endomicroscopy paragraph 1)

4. Which is most sensitive tool to detect dysplasia of Barrett esophagus, VLE or Confocal laser endomicroscopy, NBI and random biopsies.

We suspect VLE is the most sensitive tool for the detection of dysplasia in BE. Acetic acid chromoendoscopy, narrow band imaging and endoscopic CLE have been shown to have high sensitivity of close to 90% in various studies. The VLE scoring system is evolving as quickly as the technology is being developed. The traditional current VLE scoring system (OCT-SI) generates a dysplasia score after the combination of 2 independent criteria (surface to subsurface signal intensity and glandular architecture). The novel VLE diagnostic algorithm (VLE-DA) where a segment of BE is first characterized as having complete or partial effacement, then further categorized by subsurface intensity and number of atypical glands respectively. In a head to head comparison for the detection of dysplasia, probe-based CLE (pCLE), current VLE scoring index (OCT-SI) and novel VLE diagnostic algorithm (VLE-DA) were evaluated. The sensitivity for pCLE was 76% (95% CI, 59-88), for OCT-SI was 70% (95% CI, 52-84) and for VLE-DA was 86% (95% CI, 69-96).

(Section: Volumetric laser endomicroscopy paragraph 3)