

Dear Sir,

Thank you very much for reviewing for the World Journal of Gastroenterology our review entitled “Maximising the endosonography- the role of contrast harmonics, elastography and confocal endomicroscopy”.

Answer to the reviewer 1.

Thank you very much for your observations. The conclusion section was modified as :” The new derivative modalities described above represent a step forward in maximizing the results of endoscopic ultrasonography procedures. Their additional role became more and more visible, and elastography and harmonic contrast enhanced EUS found their place for routinely use in the future. However, none of them is yet able to replace EUS-FNA. “

The language was revised.

Answer to the reviewer 2.

Thank you very much for your observations.

The introductory part of the needle confocal endomicroscopy was changed as follows>

“The standard confocal laser endomicroscopy (CLE) allows the real time visualization of cellular and subcellular structures with up to 1000 times magnification and penetration of 100 micrometers below the mucosal surface [错误!未找到引用源。]¹. The tissue is illuminated with a low-power laser with subsequent detection of the fluorescence of light reflected from the tissue through a pinhole [错误!未找到引用源。]¹. The returned light is reflected by the same lens and reach the detector of the confocal system. The illumination and detection systems are “confocal” meaning they are aligned in the same focal plane [错误!未找到引用源。]¹. A contrast agent administered intravenously (fluorescein) or topically (acriflavine and cresyl violet) emphasizes the cellular, subcellular and vasculature elements.

In the clinical practice there were used two CLE systems: an endoscope integrated CLE and a probe-based CLE(p-CLE), the latter being the widest system used for the assessment of colonic polyps, neoplastic lesions in the inflammatory bowel diseases or Barrett esophagus^[99-102]

Needle confocal endomicroscopy (nCLE) represents an improved version of CLE and it is performed during EUS, assessing the organs within or adjacent to the GI tract using a miniprobe passed through an endoscopic needle. nCLE allows an *in vivo*, real time histological diagnosis, thus enhancing the EUS performance mainly in the setting of pancreatic and lymph node lesions. The inconclusive diagnostic procedures could be decreased by using this technique, considered as “ optical needle biopsy”^[95] .”

We do not have our own data of nCLE, but we added images of contrast enhanced and elastography.

Language revise was done.

Answer to the reviewer 3.

Thank you very much for your review. Images on contrast enhanced EUS and elastography were added.

Yours respectfully,

Andrada Seicean

The manuscript provides an interesting and critical review of the literature on the application of contrast-enhanced harmonic endoscopic ultrasound, elastography and needle confocal laser endomicroscopy, in the diagnosis pancreatic lesions. Each technique is thoroughly described and critically assessed in the light of the existing literature. The reference list consists of 114 carefully selected citations. However, the style of the presentation (language and style) is somewhat choppy and dry, and hence requires your additional attention. Also, there are sections difficult to comprehend, i.e., second sentence in the “conclusions”.

This is a well conceived and timely article summarizing recent progress in endosonography. the role of contrast harmonics, elastography and in confocal endomicroscopy. Comments: 1)In regard to: #3. Needle-based confocal endomicroscopy (nCLE), the authors should first explain to the readers what a standard confocal endomicroscopy is (e.g, allows a real time in vivo visualization of mucosal structures under 1000X magnification) and its application to colon cancer and Barret’s esophagus. Then they should mention limited depth of tissue penetration (about 100 microns) by luminal CLE probe and on this background discuss advantage of nCLE. They should also point out that nCLE requires simultaneous use of EUS to localize needle probe within tissue, e.g. muscularis propria, pancreas etc. 2)If the authors have their own data or images they would be nice addition to this paper and welcome by the readers. 3)Paper is overall well written but requires minor linguistic polishing.