

Contrast Harmonic-Enhanced Endoscopic Ultrasound (EUS) Is the Perfect Companion of EUS-Guided Tumor Ablation

Gianmarco Marocchi, Andrea Lisotti, and Pietro Fusaroli

Gastrointestinal Unit, Department of Medical and Surgical Sciences, Hospital of Imola, University of Bologna, Imola, Italy

To the Editor:

We read with great interest the article by Choi *et al.*,¹ published online in February 2020, describing the use of contrast-enhanced harmonic endoscopic ultrasound (CH-EUS) for guidance and monitoring of EUS-guided radiofrequency ablation (RFA) of solid abdominal tumors. The authors reported good results using CH-EUS in guiding the treatment of 19 patients with pancreatic neuroendocrine tumors (n=13), pancreatic solid pseudopapillary neoplasm (n=2), pancreatic insulinoma (n=1), adrenal adenomas (n=2) and adrenal metastasis from hepatocellular carcinoma (n=1). At the 1-year follow-up, a complete response was achieved in 68.4% of cases, with a moderate complication rate (two cases of acute pancreatitis, one mild and one moderate). In particular, CH-EUS proved useful in assessing early therapeutic responses and in targeting residual viable lesions susceptible to additional RFA sessions.

In our experience, CH-EUS was successfully used to guide ablation with ethanol injection of a 14-mm hepatocellular carcinoma.² The lesion was located in the deep subcapsular portion of hepatic segment 2 in a 76-year-old female patient with contraindications to surgery, in whom percutaneous ablation was considered unfeasible due to the interposition of vascular structures. The procedure was well tolerated without adverse events. Forty days later, follow-up with CH-EUS showed a tiny 3 mm residual vascularization component at the periphery of the previously treated area. In the same session, it was possible to ablate the residual area with an additional ethanol injection under CH-EUS guidance. Follow-up at 20 months with computed tomography showed neither local nor distant recurrence.

Recently, Jiang and Chai³ reported EUS-guided laser ablation of adrenal metastasis from pancreatic cancer, and Mangiavillano *et al.*⁴ reported EUS-guided RFA for colon cancer recurrence around the anastomotic site. In both cases, CH-EUS was used

for identifying remnant tumor after ablation.

CH-EUS has also been used to guide EUS tissue acquisition. A large retrospective study showed that adequate specimens in the CH-EUS-guided fine needle aspiration group (96.6%) was greater than that in the conventional EUS group (97% vs 87%, respectively).⁵ Kamata *et al.*⁶ demonstrated that avascular areas seen by CH-EUS were a predictor of inadequate specimens after EUS-fine needle acquisition in up to 27% of cases. Additionally, Yamashita *et al.*⁷ found that CH-EUS could be used for predicting the efficacy of chemotherapy in patients with advanced pancreatic cancer. The patients were divided into two groups according to the intratumoral vessel flow observed with CH-EUS, showing that the greater the vascularization of the tumors, the better were the response to chemotherapy and overall survival.

CH-EUS has increasingly gained acceptance in clinical practice,⁸ ranging from the diagnosis of pancreatic cancer⁹⁻¹² to the differential diagnosis of lymphadenopathy^{13,14} and gastric subepithelial tumors.¹⁵⁻²¹ As far as EUS-guided tumor treatment is concerned,^{22,23} we believe that CH-EUS offers a unique advantage by allowing for the analysis of intratumoral vessels that are not detected with B-mode. In this respect, the arterial phase is crucial for evaluation, as viable tumor tissue will be visible a few seconds after contrast agent injection. When CH-EUS is performed after EUS-guided ablation, it may show either complete absence of vascular areas, compatible with effective treatment, or residual enhanced areas suggestive of persistent tumor that needs further ablation.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

Correspondence to: Gianmarco Marocchi

Gastrointestinal Unit, Department of Medical and Surgical Sciences, Hospital of Imola, University of Bologna, Ospedale di Imola, Via Montericco 4, 40026 Imola, Italy

Tel: +39-542-662407, Fax: +39-542-662409, E-mail: gianmarco.marocchi@libero.it

Received on March 2, 2020. Revised on March 31, 2020. Accepted on April 4, 2020.

pISSN 1976-2283 eISSN 2005-1212 <https://doi.org/10.5009/gnl20077>

© This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ORCID

Gianmarco Marocchi <https://orcid.org/0000-0001-9925-3486>
Andrea Lisotti <https://orcid.org/0000-0002-7724-7402>
Pietro Fusaroli <https://orcid.org/0000-0002-4397-9314>

REFERENCES

1. Choi JH, Seo DW, Song TJ, et al. Utility of contrast-enhanced harmonic endoscopic ultrasound for the guidance and monitoring of endoscopic radiofrequency ablation. *Gut Liver*. Epub 2020 Feb 3. <https://doi.org/10.5009/gnl19123>.
2. Lisotti A, Piscaglia F, Fusaroli P. Contrast-enhanced harmonic endoscopic ultrasound-guided ethanol injection for a small hepatocellular carcinoma. *Endoscopy* 2019;51:E317-E318.
3. Jiang T, Chai W. Endoscopic ultrasonography (EUS)-guided laser ablation (LA) of adrenal metastasis from pancreatic adenocarcinoma. *Lasers Med Sci* 2018;33:1613-1616.
4. Mangiavillano B, Auriemma F, Scaltrini F, et al. Endoscopic ultrasonography-guided radiofrequency ablation for a perianastomotic neoplastic colorectal recurrence. *Am J Gastroenterol* 2019;114:1709.
5. Hou X, Jin Z, Xu C, et al. Contrast-enhanced harmonic endoscopic ultrasound-guided fine-needle aspiration in the diagnosis of solid pancreatic lesions: a retrospective study. *PLoS One* 2015;10:e0121236.
6. Kamata K, Takenaka M, Omoto S, et al. Impact of avascular areas, as measured by contrast-enhanced harmonic EUS, on the accuracy of FNA for pancreatic adenocarcinoma. *Gastrointest Endosc* 2018;87:158-163.
7. Yamashita Y, Ueda K, Itonaga M, et al. Tumor vessel depiction with contrast-enhanced endoscopic ultrasonography predicts efficacy of chemotherapy in pancreatic cancer. *Pancreas* 2013;42:990-995.
8. Fusaroli P, Napoleon B, Gincul R, et al. The clinical impact of ultrasound contrast agents in EUS: a systematic review according to the levels of evidence. *Gastrointest Endosc* 2016;84:587-596.
9. Yamashita Y, Shimokawa T, Napoléon B, et al. Value of contrast-enhanced harmonic endoscopic ultrasonography with enhancement pattern for diagnosis of pancreatic cancer: a meta-analysis. *Dig Endosc* 2019;31:125-133.
10. Fusaroli P, Eloubeidi MA. Diagnosis of pancreatic cancer by contrast-harmonic endoscopic ultrasound (EUS): complementary and not competitive with EUS-guided fine-needle aspiration. *Endoscopy* 2014;46:380-381.
11. Fusaroli P, D'Ercole MC, De Giorgio R, Serrani M, Caletti G. Contrast harmonic endoscopic ultrasonography in the characterization of pancreatic metastases (with video). *Pancreas* 2014;43:584-587.
12. Li Y, Jin H, Liao D, et al. Contrast-enhanced harmonic endoscopic ultrasonography for the differential diagnosis of pancreatic masses: a systematic review and meta-analysis. *Mol Clin Oncol* 2019;11:425-433.
13. Lisotti A, Fusaroli P. Contrast-enhanced EUS for the differential diagnosis of lymphadenopathy: technical improvement with defined indications. *Gastrointest Endosc* 2019;90:995-996.
14. Lisotti A, Ricci C, Serrani M, et al. Contrast-enhanced endoscopic ultrasound for the differential diagnosis between benign and malignant lymph nodes: a meta-analysis. *Endosc Int Open* 2019;7:E504-E513.
15. Kamata K, Takenaka M, Kitano M, et al. Contrast-enhanced harmonic endoscopic ultrasonography for differential diagnosis of submucosal tumors of the upper gastrointestinal tract. *J Gastroenterol Hepatol* 2017;32:1686-1692.
16. Tamura T, Kitano M. Contrast enhanced endoscopic ultrasound imaging for gastrointestinal subepithelial tumors. *Clin Endosc* 2019;52:306-313.
17. Pantaleo MA, Lolli C, Nannini M, et al. Good survival outcome of metastatic SDH-deficient gastrointestinal stromal tumors harboring SDHA mutations. *Genet Med* 2015;17:391-395.
18. Catena F, Di Battista M, Ansaloni L, et al. Microscopic margins of resection influence primary gastrointestinal stromal tumor survival. *Onkologie* 2012;35:645-648.
19. Pantaleo MA, Nannini M, Saponara M, et al. Impressive long-term disease stabilization by nilotinib in two pretreated patients with KIT/PDGFRα wild-type metastatic gastrointestinal stromal tumours. *Anticancer Drugs* 2012;23:567-572.
20. Fusaroli P, Kypreos D, Alma Petrini CA, Caletti G. Scientific publications in endoscopic ultrasonography: changing trends in the third millennium. *J Clin Gastroenterol* 2011;45:400-404.
21. Fusaroli P, Kypraios D, Eloubeidi MA, Caletti G. Levels of evidence in endoscopic ultrasonography: a systematic review. *Dig Dis Sci* 2012;57:602-609.
22. Fabbri C, Luigiano C, Lisotti A, et al. Endoscopic ultrasound-guided treatments: are we getting evidence based: a systematic review. *World J Gastroenterol* 2014;20:8424-8448.
23. Fusaroli P, Jenssen C, Hocke M, et al. EFSUMB guidelines on interventional ultrasound (INVUS), Part V - EUS-guided therapeutic interventions (short version). *Ultraschall Med* 2016;37:412-420.