


Acoustic radiation force impulse (ARFI) shear wave elastography of the bowel wall in healthy volunteers and in ulcerative colitis

Acta Radiologica Open
8(4) 1–7
© The Foundation Acta
Radiologica 2019
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/2058460119840969
journals.sagepub.com/home/arr


Ruediger S Goertz , Christian Lueke, Barbara Schellhaas, Lukas Pfeifer, Dane Wildner , Markus F Neurath and Deike Strobel

Abstract

Background: Acoustic radiation force impulse (ARFI) elastography is a non-invasive, ultrasound-based approach of evaluation of tissue elasticity. It has not yet been systematically applied to the bowel wall.

Purpose: To perform ARFI elastography of the bowel wall in healthy volunteers and patients with ulcerative colitis (UC).

Material and Methods: A high-frequency ultrasound (with bowel wall thickness and vascularization score) and an ARFI elastography of the bowel wall were performed in 20 patients with UC and 13 healthy volunteers. At least 10 ARFI measurements were obtained within the terminal ileum and the ascending, transverse, descending, and sigmoid colon and correlated with results of high-frequency ultrasound.

Results: The UC group had mostly moderate disease activity. All patients had signs of inflammation upon B-mode ultrasound. Eight patients showed an ulcerative (ileo)pancolitis. Overall, ARFI elastography values and wall thickness were higher in the UC group than in the group of healthy volunteers ($P = 0.021$ and $P < 0.001$, respectively). ARFI velocities of the separate segments were significantly higher in the transverse ($P = 0.045$) and sigmoid colon ($P = 0.032$) in case of UC.

Conclusion: ARFI elastography of the bowel wall of the colonic frame and the terminal ileum is feasible but shows high standard deviation. ARFI shear wave velocities appear to be slightly higher in patients with UC than in healthy volunteers, particularly in the sigmoid and transverse colon. Further studies are needed.

Keywords

Ulcerative colitis, ARFI, elastography, ultrasonography, bowel wall

Received 25 January 2019; accepted 7 March 2019

Background

Elastography is a non-invasive, ultrasound-based technique for the evaluation of tissue elasticity and has emerged in recent years. Ultrasonic elastography comprises two different approaches, namely strain elastography and shear wave elastography (1). Strain elastography visualizes relative elasticity within a region of interest (ROI) as a color-coded elastogram. Recently, Ishikawa et al. (2) evaluated strain elastography in comparison to endoscopic findings in 37 patients with ulcerative colitis (UC). The classification by four

Department of Internal Medicine I, Friedrich-Alexander-University Erlangen-Nurnberg, Erlangen, Germany

Corresponding author:

Ruediger S Goertz, Department of Internal Medicine I, Friedrich-Alexander-University Erlangen-Nurnberg, Ulmenweg 18, 91054 Erlangen, Germany.

Email: ruediger.goertz@fau.de



elastographic patterns (normal, homogeneous, random, and hard) correlated significantly with quiescent disease, slight or moderate inflammation, or fulminant disease.

Acoustic radiation force impulse (ARFI) point shear wave elastography rapidly measures a regional average of shear wave velocity (m/s) as an objective quantitative marker of elasticity. It has mainly been used in liver disease to detect hepatic fibrosis or cirrhosis (3). Normal shear wave velocities can exclude hepatic cirrhosis with a negative predictive value of about 96% (4). Elastography was used to evaluate inflammation or fibrosis in Crohn's disease (5–7) but has not yet been systematically applied in the bowel wall of patients with UC.

Transabdominal high-frequency ultrasound is often initially performed in inflammatory bowel disease (8–11) to assess localization and extent of disease with its possible complications. An elastographic assessment by ARFI could easily complement disease evaluation within the same setting but has not yet been assessed in patients with UC.

In an animal model of UC, optical coherence elastography showed recently significant stiffness differences between a healthy colon and UC (12). Normal ARFI values for healthy gut segments are unknown. This study aimed at performing ARFI measurements within the bowel wall in healthy volunteers and in patients with UC. ARFI shear wave velocities of the terminal ileum and the colonic frame segments were analyzed and correlated with findings of B-mode sonography of the bowel wall.

Material and Methods

Thirteen healthy volunteers and 20 patients suffering from clinically active, histologically proven UC in a follow-up were enrolled in a prospective study between January 2014 and March 2015. Demographic data such as age, gender, and body mass index (BMI) were recorded. The patient cohort contained data of C-reactive protein (CRP < 5 mg/L) and the clinical MAYO-Subscore to evaluate disease activity of UC. The local ethics committee approved the study that complied with the ethics guidelines of the Helsinki Declaration. Informed consent was obtained from each study participant.

In patients with UC, the clinical Mayo-Subscore was assessed (13), which contains the mean daily stool frequency over the past three days (0–3 points), rectal bleeding (0–3 points), and subjective appraisal of disease activity by the physician (0–3 points). The clinical subscore can amount to a maximum of 9 points. A sum of 0–1 point indicates clinical remission, 2–4 points

mild disease, 5–7 points moderate, and >7 points severe activity.

Both, high-frequency ultrasound and ARFI point shear wave elastography of the bowel were carried out using an Acuson S2000 ultrasound device (Siemens Medical Solution, software version VB21A, Erlangen, Germany) with the linear transducer 9L4. All study participants were in a supine position with a relaxed breath-hold during ARFI measuring. The healthy volunteers had fasted for >8 h. One senior physician with >6 years of experience (DEGUM qualification level 2) performed the examinations. The targeted locations were the terminal ileum and ascending, transverse, descending, and sigmoid colon. Relevant bowel wall movements possibly affecting elastography were excluded visually. Contact pressure of the transducer was just as high as to visualize the destined locations. During gray-scale ultrasound, the bowel wall thickness (mm) and intramural semi-quantitative vascularization (grade 0–4) were evaluated. Vascularization was semi-quantitatively scaled according to Limberg et al. (14) (0 = normal bowel wall, 1 = thickened bowel wall without color Doppler signal, 2 = with few, short signals, 3 = with long intramural perfusion signals, and 4 = with intramural and mesentery signals). According to pathologic bowel wall thickening (≥ 3 mm) or pathologic semi-quantitative color Doppler vascularization score, the bowel segment was classified as inflamed (ileitis or sigmoiditis) or normal (ileum or sigmoid). Presence of mesenteric inflammation, inflammatory lymph nodes, or ascites was documented.

The Virtual Touch Tissue Quantification mode was used to perform ARFI measurements. The resulting shear wave velocity is proportional to the square root of tissue elasticity. Results are expressed in meters per second (m/s). A 6×5 mm region of interest (ROI) was centered within the bowel walls including the whole collapsed bowel section in healthy or mainly the anterior wall in diseased bowel during real-time B-mode imaging (Fig. 1). During a relaxed pause in breathing, measurements were conducted in a longitudinal section of the dedicated bowel segment. A least 10 measurements and the measurement depth were recorded.

ARFI shear wave velocities as well as clinical and laboratory characteristics were shown as mean \pm standard deviation (SD) together with the range. The Spearman's correlation coefficient (r) was used to analyze relationships between variables. The two-sided t -test was used for comparison of means. Tables or typical box plots illustrate the results. The circle and star mark outliers. A P value < 0.05 was considered a significant difference or analysis. The Statistical Package for the Social Sciences (version 19.0.0.1,

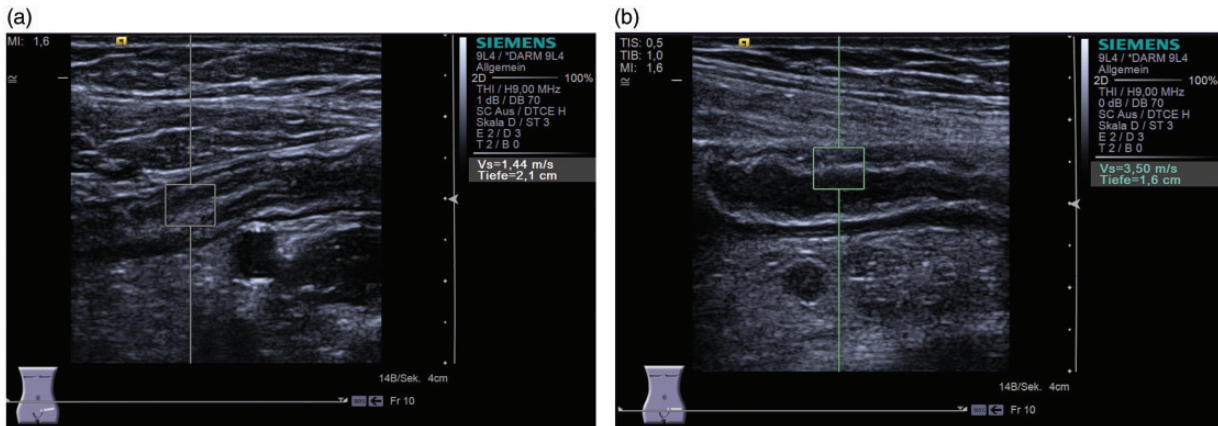


Fig. 1. Differences of ARFI elastography in UC: (a) a slight 3.8-mm sigmoid thickening with low-grade hypervascularization; and (b) high active ulcerative sigmoiditis.

Table 1. Overall characteristics of the healthy group and 20 patients with ulcerative colitis (UC).

	Healthy	UC	P value
Sex (M/F)	7/6	10/10	
Age (years)	26.4 ± 4.9 (18–34)	33 ± 10.8 (18–51)	0.048
BMI (kg/m ²)	22.5 ± 3.9 (17.7–32.1)	24.8 ± 4.3 (18.8–32.5)	n.s.
CRP (<5 mg/L)	–	39 ± 42 (1.7–137.5)	–
Mayo-Subscore (points)	–	6.6 ± 1.7 (3–9)	–
Overall wall thickness (mm)	1.55 ± 0.42 (0.6–2.9)	3.38 ± 1.36 (0.6–7.5)	<0.001
ARFI of all bowel segments (m/s)	1.75 ± 0.51 (0.92–3.29)	1.97 ± 0.64 (0.85–4.12)	0.021
Measurement depth (cm)	2.4 ± 0.8 (1–4)	2.7 ± 0.7 (1–4)	0.284

Table 2. ARFI shear wave velocities of different bowel segments of 13 healthy volunteers and 20 patients with ulcerative colitis (UC).

	ARFI (m/s)		P value	Bowel wall thickness (mm)		P value
	Healthy	UC		Healthy	UC	
Terminal ileum	1.6 ± 0.35 (1.08–2.27)	1.62 ± 0.53 (0.85–2.89)	n.s.	1.4 ± 0.3 (0.7–1.9)	2.2 ± 1.1 (1.1–5.0)	0.024
Ascending colon	1.96 ± 0.57 (1.36–3.29)	2.10 ± 0.84 (1.29–4.12)	n.s.	1.6 ± 0.5 (0.8–2.3)	2.5 ± 1.5 (0.6–5.8)	0.046
Transverse colon	1.55 ± 0.37 (1.11–2.29)	1.94 ± 0.60 (0.94–3.61)	0.045	1.3 ± 0.5 (0.6–2.1)	3.4 ± 1.3 (1.4–5.7)	<0.001
Descending colon	1.90 ± 0.71 (0.92–3.23)	2.03 ± 0.71 (1.02–3.46)	n.s.	1.7 ± 0.5 (1.2–2.9)	4.0 ± 1.3 (1.9–6.3)	<0.001
Sigmoid colon	1.76 ± 0.55 (1.01–2.80)	2.18 ± 0.51 (1.42–3.12)	0.032	1.8 ± 0.4 (1.3–2.7)	4.8 ± 1.6 (2.1–7.5)	<0.001

IBM SPSS Statistics, Armonk, NY, USA) was used for statistical analyses.

Results

Thirteen healthy volunteers were evaluated (6 women, 7 men; mean age = 26 years; BMI = 22.5 kg/m²). None of them had mesenteric inflammation, enlarged lymph nodes, or ascites. The group of healthy volunteers revealed a mean ARFI of all bowel segments of 1.75 ± 0.51 m/s (0.92–3.29) and a mean bowel wall thickness of 1.55 ± 0.42 mm (0.6–2.9) (Table 1). The specific

elastographic and thickness measurements of the separate bowel segments are shown in Table 2. No significant correlations between ARFI values and BMI, age, or bowel thickness in any of the bowel segments were observed.

A total of 20 patients with UC (10 women, 10 men; mean age = 33 years; BMI = 24.8 kg/m²) were evaluated. Three patients had only a therapy with aminosalicylates, six in addition with cortisone, three patients were on azathioprine, seven on infliximab or adalimumab, and one patient on vedolizumab. The mean Mayo-Subscore was 6.6 ± 1.7 points (range = 3–9).

CRP was 39 ± 42 mg/L (range = 1.7–137.5). Two patients had mild, ten moderate, and eight patients severe clinical activity. Sonographically, all patients had signs of inflammation: four patients had an ulcerative ileopanocolitis; four had pancolitis; four had enhanced left-sided colitis; five had left-sided colitis; and three had sigmoiditis. Sixteen patients had mesenteric fatty inflammation, nine had inflamed lymph nodes, and five had ascites. The patient group showed mean ARFI values of all bowel segments of 1.97 ± 0.64 m/s (range = 0.85–4.12) and a mean bowel wall thickness of 3.38 ± 1.4 mm (range = 0.6–7.5). Both were significantly higher than those of the healthy group ($P=0.021$ and $P<0.001$, respectively). Also, the ARFI elastography of the separate bowel segments showed higher shear wave velocities in UC than those of the healthy group, respectively (Fig. 2). A statistically significant difference was shown within the transverse and sigmoid colon (Table 2). The difference

of the bowel wall thickness between the healthy group and UC group was statistically significant in all segments (Fig. 3).

Neither Mayo-Subscore nor the CRP level correlated significantly with any of the ARFI measurements within the bowel segments. Only ARFI values of the sigmoid did correlate with wall thickness of the sigmoid ($r=0.491$; $P=0.028$), but not with the Limberg score. None of the other ARFI measurements correlated significantly with wall thickness or Limberg score within the corresponding bowel segment, respectively. ARFI elastography did not correlate with measurement depth in any of the bowel segments, neither in healthy volunteers nor in patients with UC. In the healthy group, the measurement depth of ARFI elastography in the descending colon (3.0 ± 0.8 cm) was significantly deeper than in the sigmoid (2.0 ± 0.7 cm; $P<0.01$), the transverse colon ($P=0.017$), the ascending colon ($P=0.049$), and the terminal ileum ($P=0.017$). In the

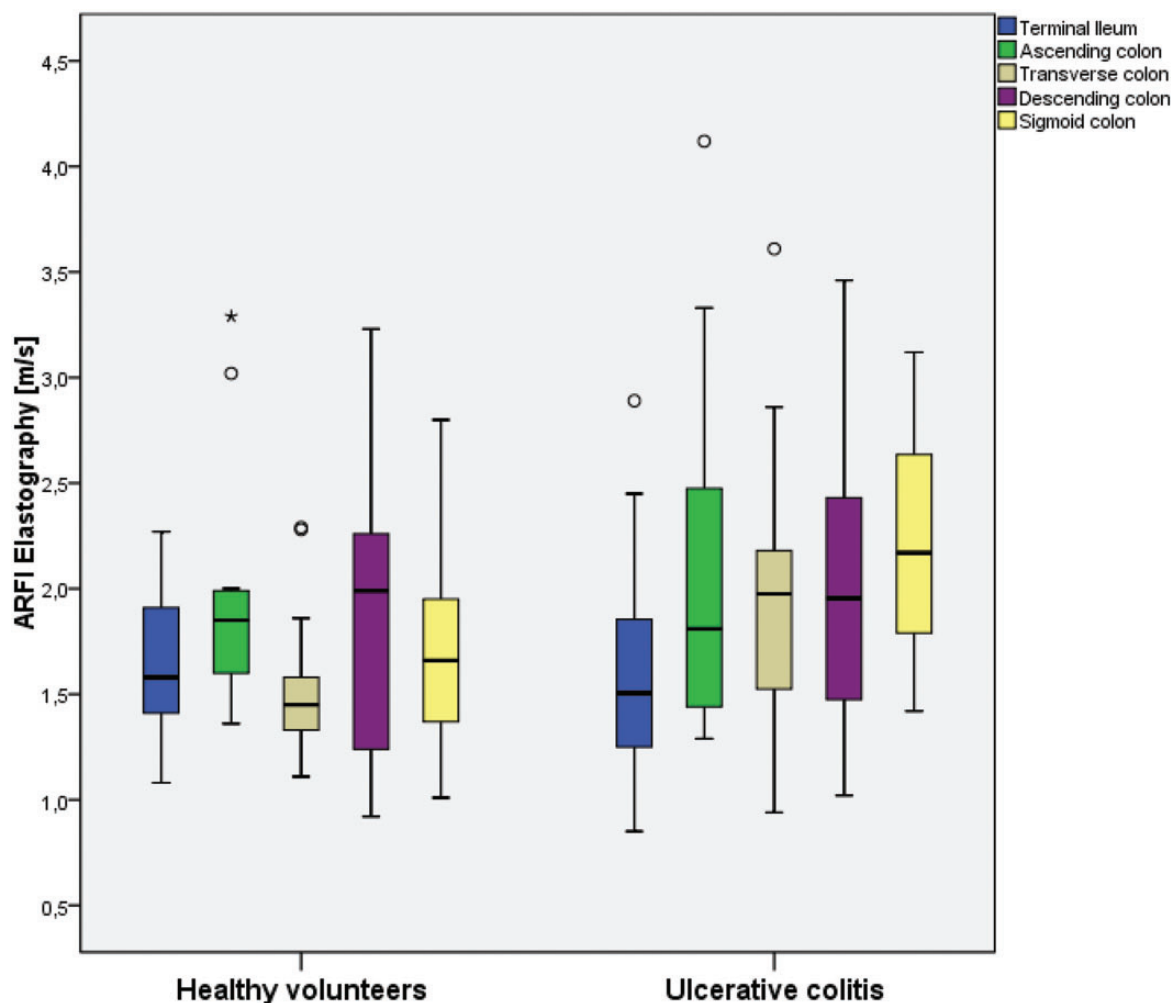


Fig. 2. Box plot of ARFI shear wave velocities of different bowel segments of 13 healthy volunteers and 20 patients with UC.

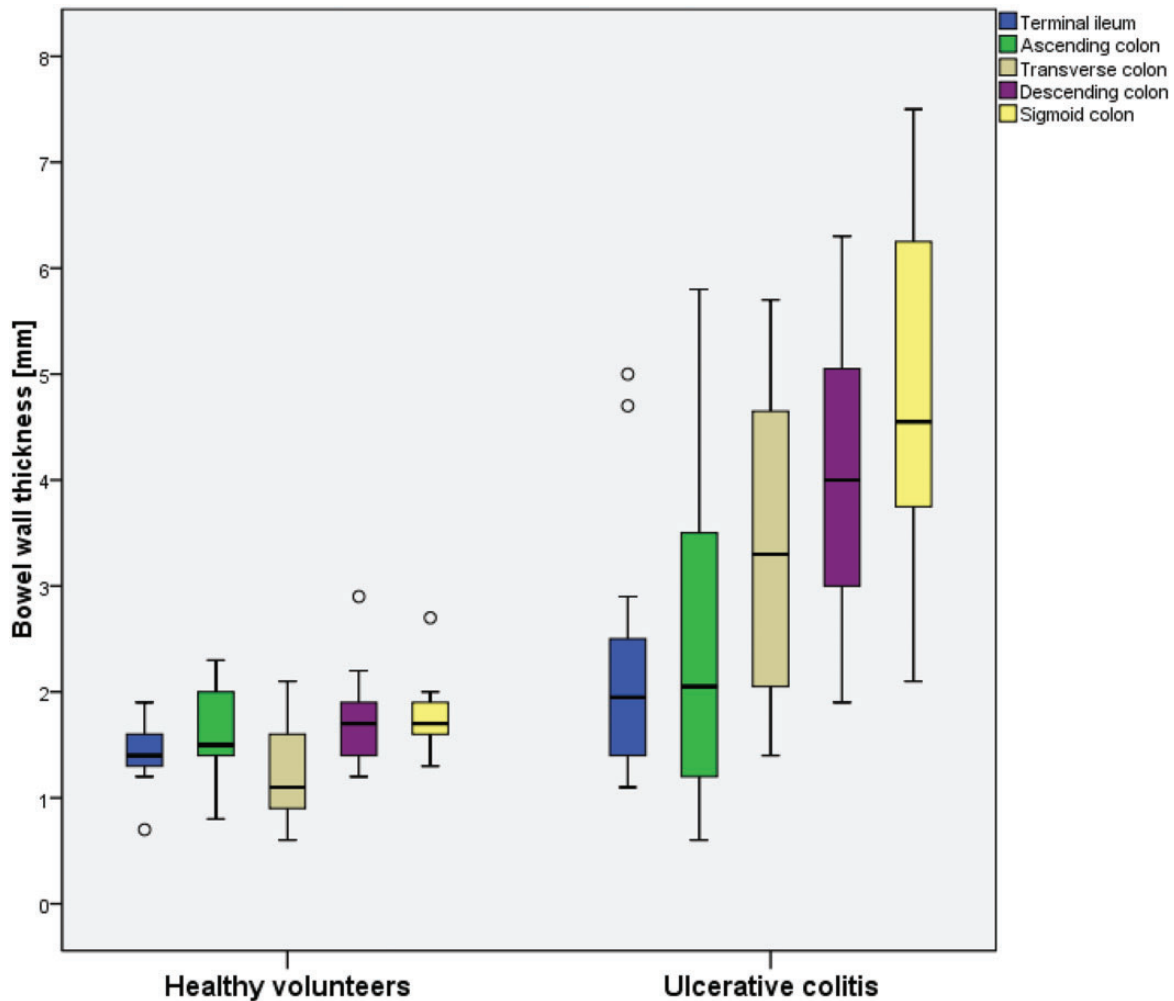


Fig. 3. Box plot of wall thickness of different bowel segments of 13 healthy volunteers and 20 patients with UC.

patient group, the measurement depth differed significantly ($P < 0.001$) between the sigmoid (2.3 ± 0.7 cm) and the descending colon only (3.1 ± 0.7 cm).

Discussion

High-frequency ultrasound of the bowel wall is used in patients with UC to reveal signs of inflammation such as bowel wall thickening, loss of wall stratification, or increased blood flow within the thickened wall (15,16). This inflammation may change elasticity of the bowel wall and might be depicted by ARFI point shear wave elastography.

In our study, the majority of patients with UC had moderate to severe activity and overall ARFI shear wave velocities of the bowel were significantly higher than in healthy volunteers. Also, within the separate colonic and ileal segments, ARFI mean values and the variability (standard deviation) were higher in case of UC. No correlations were found between

ARFI elastography and semi-quantitative vascularization score, clinical Mayo-Subscore or measurement depth.

UC as an ascending inflammation from the rectum shows not always a right-sided inflammation. Therefore, bowel wall thickness and ARFI elastography were more discriminative in the left-sided colon than in the right-sided colon. Both, bowel wall thickness and ARFI values may not exclude inflammation, as UC induces an inflammation confined to the mucosa and submucosal layers only being shown during endoscopy (17). An earlier study could show that elastograms generated by ARFI imaging can be used to visualize the normal anatomical planes of the intestinal bowel wall (18). Furthermore, the boundaries of colonic tumors could be delineated by ARFI imaging. These conclusions were drawn from an ex vivo evaluation of freshly excised surgical specimens using the high frequency linear transducer 75L40. An evaluation of strain elastography in UC then showed that a

normal/soft to an inhomogeneous/hard pattern corresponded to a higher endoscopic inflammatory activity (2). Rustemovic et al. used transrectal endoscopic ultrasound elastography in 28 healthy controls, 30 patients with Crohn's disease, and 25 patients with UC to assess disease activity in the rectum (19). There was no significant difference between UC and controls (strain ratio 0.65 vs. 0.68). In this study, 11 of 25 patients with UC had no signs of activity and none had high disease inflammation. To our knowledge, a study evaluating ARFI point shear wave elastography in UC does not exist. Normal ARFI values have not yet been presented.

Mean bowel wall thickness of the healthy group in our study was about 1.5 mm. The size of the ARFI ROI is not variable. Setting a fixed ROI with 6×5 mm might be disputed because, particularly in normal bowel wall thickness, obviously normal surrounding connective tissue lies within the ROI. Thus, the resulting shear wave velocity is a compound of elasticity of bowel wall, intestinal cavity, and surrounding tissue (possible mesenteric reaction). In this context, bowel wall thickening seems to be more helpful for distinguishing normal and inflamed bowel wall. In our study, bowel wall thickness differed statistically significant between the single bowel segments, whereas the differences between the ARFI values were not equally pronounced. Visualization of the sigmoid might be facilitated by its anatomic position being closer to the transducer than the other segments, particularly in comparison to the descending colon. This fact could have affected ARFI measurements. In this context, in an animal model of inflammatory bowel disease, ARFI shear wave velocities rose with increasing pressure induced by the linear transducer 9L4 (20). Thus, individually different pressures by the transducer during measurements might have affected the results. CRP as a systemic marker of inflammation and local blood flow seemed not to have any influence on ARFI bowel elastography.

Certain weaknesses might impair the interpretation of our results: possible reference standards such as imaging by magnetic resonance imaging (MRI) or such as endoscopic activity scoring by colonoscopy were not available; only correlation of ARFI elastography with ultrasonic and clinical parameters was performed. There exists no standardization of measuring bowel wall by ARFI. The significance of obesity, inter-/intra-observer reliability (depending on experience), and applicability of an ARFI quality parameter (interquartile range/median > 0.30) is unknown (21). A possible influence of disease duration (with unknown balance of normal, inflammatory, or even fibrotic components within the bowel wall) or concomitant medical drugs on ARFI elastography in UC is unclear. In the

prospective cohort, the sample size was quite small, but showed after all mainly higher (moderate to severe) activity. Inflammation of the bowel wall impairs peristalsis, thus inflamed colon or terminal ileum show regularly no relevant peristalsis during ultrasound. ARFI elastography in healthy volunteers was performed in apparently motionless walls, so we assume no relevant influence by possible bowel movements. Nevertheless, this prospective pilot study shows feasibility of bowel wall ARFI in UC and healthy volunteers.

In conclusion, ARFI elastography of the bowel wall of the colonic frame and the terminal ileum is feasible but shows high standard deviation. ARFI shear wave velocities appear to be slightly higher in patients with UC than in healthy volunteers, particularly in the sigmoid and transverse colon. Further studies are needed.



Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

ORCID iD

Ruediger S Goertz  <http://orcid.org/0000-0002-6998-6635>
Dane Wildner  <http://orcid.org/0000-0002-4916-6533>

References

1. Dietrich CF, Bamber J, Berzigotti A, et al. EFSUMB Guidelines and Recommendations on the Clinical Use of Liver Ultrasound Elastography, Update 2017 (Long Version). *Ultraschall Med* 2017;38:e16–e47.
2. Ishikawa D, Ando T, Watanabe O, et al. Images of colonic real-time tissue sonoelastography correlate with those of colonoscopy and may predict response to therapy in patients with ulcerative colitis. *BMC Gastroenterol* 2011;11:29.
3. Hu X, Qiu L, Liu D, et al. Acoustic Radiation Force Impulse (ARFI) Elastography for noninvasive evaluation of hepatic fibrosis in chronic hepatitis B and C patients: a systematic review and meta-analysis. *Med Ultrason* 2017;19:23–31.
4. Goertz RS, Sturm J, Pfeifer L, et al. ARFI cut-off values and significance of standard deviation for liver fibrosis staging in patients with chronic liver disease. *Ann Hepatol* 2013;12:935–941.
5. Giannetti A, Matergi M, Biscontri M, et al. Real-time elastography in Crohn's disease: feasibility in daily clinical practice. *J Ultrasound* 2017;20:147–155.
6. Baumgart DC, Muller HP, Grittner U, et al. US-based real-time elastography for the detection of fibrotic gut

- tissue in patients with stricturing Crohn disease. *Radiology* 2015;275:889–899.
7. Goertz RS, Lueke C, Wildner D, et al. Acoustic radiation force impulse (ARFI) elastography of the bowel wall as a possible marker of inflammatory activity in patients with Crohn's disease. *Clin Radiol* 2018;73:678.
 8. Bryant RV, Friedman A, Wright EK, et al. Gastrointestinal ultrasound in inflammatory bowel disease: an underused resource with potential paradigm-changing application. *Gut* 2018;67:973–985.
 9. Coelho R, Ribeiro H, Maconi G. Bowel thickening in Crohn's disease: fibrosis or inflammation? Diagnostic ultrasound imaging tools. *Inflamm Bowel Dis* 2017;23:23–34.
 10. Strobel D, Goertz RS, Bernatik T. Diagnostics in inflammatory bowel disease: ultrasound. *World J Gastroenterol* 2011;17:3192–3197.
 11. Nylund K, Maconi G, Hollerweger A, et al. EFSUMB Recommendations and Guidelines for Gastrointestinal Ultrasound. *Ultraschall Med* 2017;38:e1–e15.
 12. Nair A, Liu CH, Das S, et al. Detecting murine inflammatory bowel disease using optical coherence elastography. *Conf Proc IEEE Eng Med Biol Soc* 2018;2018:830–833.
 13. Schroeder KW, Tremaine WJ, Ilstrup DM. Coated oral 5-aminosalicylic acid therapy for mildly to moderately active ulcerative colitis. A randomized study. *N Engl J Med* 1987;317:1625–1629.
 14. Limberg B. [Diagnosis of chronic inflammatory bowel disease by ultrasonography]. *Z Gastroenterol* 1999;37:495–508.
 15. Ribaldone DG, Cammarota T, Resegotti A, et al. Power Doppler sonography to predict the risk of surgical recurrence of Crohn's disease. *J Ultrasound* 2015;18:51–55.
 16. Ripolles T, Martinez MJ, Barrachina MM. Crohn's disease and color Doppler sonography: response to treatment and its relationship with long-term prognosis. *J Clin Ultrasound* 2008;36:267–272.
 17. Waldner MJ, Rath T, Schurmann S, et al. Imaging of mucosal inflammation: current technological developments, clinical implications, and future perspectives. *Front Immunol* 2017;8:1256.
 18. Palmeri ML, Frinkley KD, Zhai L, et al. Acoustic radiation force impulse (ARFI) imaging of the gastrointestinal tract. *Ultrason Imaging* 2005;27:75–88.
 19. Rustemovic N, Cukovic-Cavka S, Brinar M, et al. A pilot study of transrectal endoscopic ultrasound elastography in inflammatory bowel disease. *BMC Gastroenterol* 2011;11:113.
 20. Dillman JR, Stidham RW, Higgins PD, et al. US elastography-derived shear wave velocity helps distinguish acutely inflamed from fibrotic bowel in a Crohn disease animal model. *Radiology* 2013;267:757–766.
 21. Lu C, Gui X, Chen W, et al. Ultrasound shear wave elastography and contrast enhancement: effective biomarkers in Crohn's disease strictures. *Inflamm Bowel Dis* 2017;23:421–430.