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Harmonic US imaging of appendicitis in children

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Abstract *Background:* Harmonic imaging (HI), a relatively new ultrasound modality, was initially reported to be of use only in obese adult patients. HI increases the contrast and spatial resolution resulting in artefact-free images, and has been shown in adults to significantly improve abdominal sonography. Regarding its application in paediatric patients, just a handful reports exist and these do not encompass its use in intestinal sonography. *Objective:* To compare the sonomorphological image quality of HI and fundamental imaging (FI, conventional grey-scale imaging) in the diagnosis of histologically confirmed appendicitis in children. *Materials and methods:* For this prospective comparative study, 50 children (male/female 25/25; mean age 9.9 years) suspected of having appendicitis were recruited. In all patients US examination of the appendix and periappendiceal region was performed preoperatively and appendectomy carried out. The final diagnosis was based on histological examination of the appendix. Both FI and HI were used in the US examination (tissue harmonic imaging, THI; Sonoline Elegra, Siemens; 7.5 MHz linear transducer). A

detailed comparison of the images from FI and HI was performed using a scoring system. The parameters compared included delineation of the appendiceal contour, wall, mucosa, contents of the appendix and surrounding tissues. Furthermore, periappendiceal findings such as mesenteric echogenicity, free fluid, lymph nodes and adjacent bowel wall thickening were compared. *Results:* In 43 children (86%) acute appendicitis was histologically confirmed. The inflamed appendix could be depicted in the HI and FI modes in 93% and 86%, respectively. HI was found to be significantly better for the depiction of the outer contour, wall, mucosa and contents of the appendix ($P<0.01$). This was also true for the demonstration of free fluid, mesenteric lymph nodes, adjacent bowel walls and mesenteric echogenicity. *Conclusion:* HI should be the preferred modality for scanning the right lower abdomen in suspected acute appendicitis. The diagnosis of acute appendicitis can then be more definitely ascertained.

Keywords Appendicitis · Children ·
Harmonic US imaging · Sonomorphology

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Introduction

Appendicitis is the most common acute surgical emergency in childhood [1]. Conventional grey-scale US (fundamental imaging, FI) has proved to be a reliable aid in the preoperative diagnosis of this disease [2]. The accuracy of sonography is increased by the additional use of the graded compression technique and colour Doppler [3, 4]. CT, utilizing a variety of techniques, has also been shown to be very effective in the diagnosis of acute appendicitis [1, 5]. The main drawback of CT still remains its high radiation dose [6]. Thus further improvements in US image quality are desirable in order to reduce the use of CT in children for the diagnosis of appendicitis.

Harmonic imaging (HI) is a relatively new imaging modality that was first introduced to improve the diagnostic performance of sonography in adults, particularly obese

patients [7]. Meanwhile, its superiority in image quality compared with FI has also been shown in the paediatric age group [8–10]. However, no studies have yet been published on the implementation of HI in the sonographic imaging of acute appendicitis in childhood. The aim of our study was to evaluate the use of HI in comparison to FI in the diagnosis of histologically confirmed appendicitis.

Materials and methods

A total of 50 consecutive patients were recruited for this prospective study. Their mean age was 9.9 years (range 2–17 years) and there were equal numbers of girls and boys. All patients were referred to the Division of Paediatric Radiology, Institute of Diagnostic and Interventional Radiology, Klinikum Nuremberg Süd, with the clinical suspicion of acute appendicitis. Preoperative sonography of the whole abdomen and particularly of the right lower quadrant, focusing on the region of the appendix, was performed in all patients by an experienced paediatric radiologist. After sonography, all patients underwent appendectomy. The decision to operate was based on the history, clinical parameters and sonographic findings. In all patients histological examination of the surgical specimens was carried out. The local hospital ethics committee approved the study and informed consent was obtained from all enrolled patients' parents or depending on the age from the patient.

The US examinations were performed using a Sonoline Elegra (Siemens, Issaquah, Wash.) scanner encompassing the HI modality (tissue ensemble harmonic imaging, THI). This is a wide-band harmonic modality based on the phase inversion technique. A 7.5-MHz linear transducer was used with transmission frequency ranges for FI and THI of 7.2–8.0 and 3.4–4.0 MHz, respectively. The appendix was documented in longitudinal and transverse planes in both the FI and HI modalities. The examiner switched between FI and HI for each view while maintaining the US plane as constant as possible, each time optimizing the gain without changing other presets. The same procedure was also performed to document the surrounding structures of the appendix. The graded compression sonographic technique was used whenever the condition of the child permitted.

The US images were documented on laser film. Two paediatric radiologists (from Nuremberg and Würzburg) and a paediatric surgeon, all experienced sonographers, analysed the quality of the images. For this purpose a conspicuity score (CS) was applied. The scoring was done by consensus on a scale from 0 to 3 (0 not visible, 1 poor, 2 good, 3 very good). The following parameters were evaluated:

- Appendix: outer contour, wall layers, signal of mucosa, content, appendicoliths.
- Periappendiceal structures: free fluid, mesenteric lymph nodes, adjacent intestinal walls, mesenteric fat echogenicity.

Table 1 Parameters of the appendix: visibility by HI and FI ($n=40$)

Parameter	Visibility	
	HI	FI
Outer contour	40 (100%)	37 (93%)
Wall layers	40 (100%)	36 (90%)
Mucosa signal	25 (63%)	16 (40%)
Contents	29 (73%)	24 (60%)
Appendicoliths	9 (23%)	9 (23%)

For each of these parameters the mean CS (MCS) for FI and HI was taken for the purpose of comparison.

The sonographic diagnosis of appendicitis was made based on one or more of the following criteria:

- AP diameter of the appendix exceeding 6 mm in one or more segments (base, mid-portion, tip).
- Blurring or interruption of the outer contour.
- Loss of typical layering of the appendiceal wall, alteration in echogenicity of wall components, particularly the mucosa and muscularis signal, mural thickening and discontinuity.

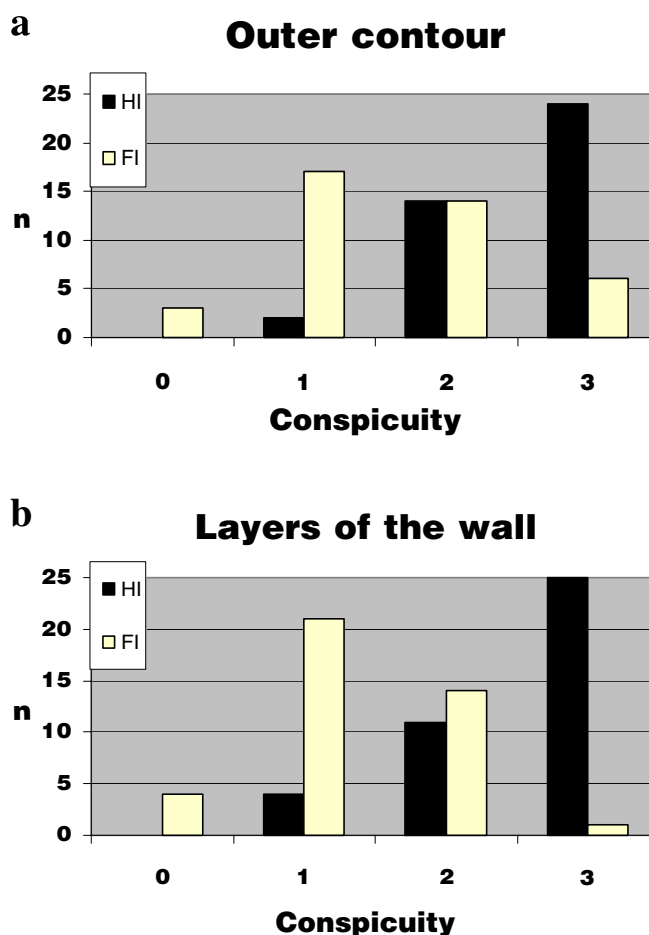


Fig. 1 Delineation of (a) outer contour and (b) layers of the appendiceal wall by FI and HI using a CS from 0 to 3 (0 not visible, 1 poor visibility, 2 good visibility, 3 excellent visibility; n number of patients)

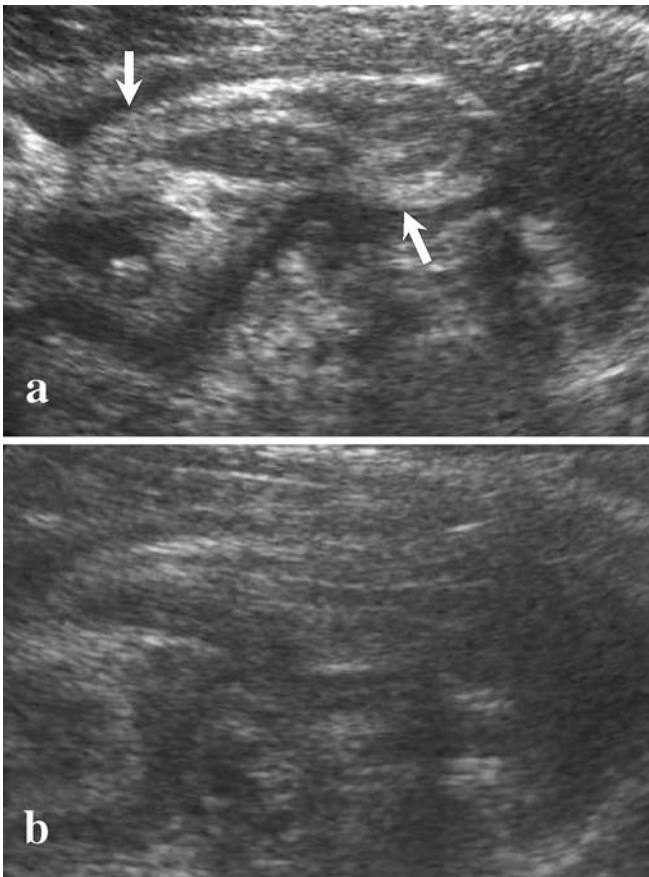
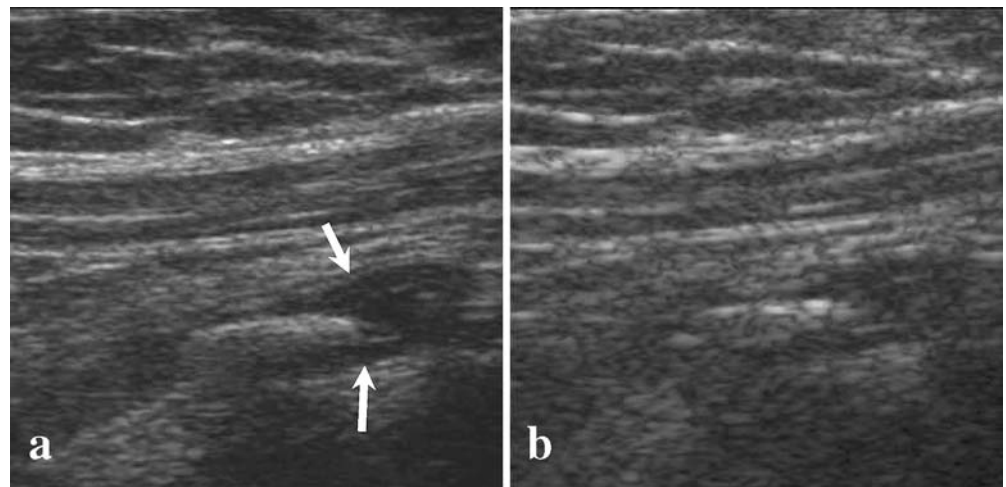


Fig. 2 Outer contour. Comparison of (a) HI and (b) FI. Longitudinal section of the appendix in an 8-year-old girl with suppurative appendicitis. In contrast to FI, where the outer contour was not really demarcated from the surrounding soft tissue, there was complete delineation with high image quality with HI (arrows; CS: HI 3, FI 0)

- Contents with distension of the appendiceal lumen such as hypoechoic material, suggesting seropurulent fluid, or appendicoliths, the latter causing incarceration, wall necrosis or retention of endoluminal pus collections.
- Surrounding free fluid, especially if localized directly around the appendix.

Fig. 3 Outer contour. Comparison of (a) HI and (b) FI. Longitudinal section of the appendix in an obese 12-year-old girl showing phlegmonous appendicitis with an endoluminal faecolith. On switching from HI to FI the demarcation of the outer contour (arrows) of the inflamed organ became much poorer (CS: HI 3, FI 1)



- Periappendiceal abscess.
- Enlarged lymph nodes in the right lower abdomen and small bowel mesentery, with a short-axis diameter exceeding 8 mm.
- Thickening, blurring and pathological layering of adjacent intestinal walls, indicating spread of inflammation to the neighbouring intestine.
- Increased echogenicity and volume of inflamed adjacent mesenteric fat.

Excel (Microsoft Office XP) and SPSS 11.5 (Windows NT 4.0) software packages were used for data documentation and statistical analysis. The *t*-test and Wilcoxon signed rank test were performed. *P* values <0.05 were considered statistically significant.

Results

In 43 (86%) of 50 children who underwent appendectomy, histological examination revealed acute appendicitis. In 7 patients there was no histological evidence of acute appendicitis, i.e. a negative appendectomy rate of 14%. The perforation rate was 12% (6 of 50). In 42 of 43 patients with histologically confirmed appendicitis the correct diagnosis was made preoperatively by sonography. In 6 of 7 patients with negative appendectomy, the US scan had been normal. The resulting overall sensitivity of our US examinations was 98% and the specificity 86%.

The inflamed appendix was visible with HI in 93% (40 of 43) and with FI in 86% (37 of 43). In three patients with an abscess in the right lower quadrant, and thus in the US examination suspected appendicitis, the appendix as such could not be directly depicted by either method. The sonographic diagnosis was confirmed by histology. The mean AP diameter of the 37 inflamed appendices, which could be detected by both modalities, was 6.4 mm by HI and 6.6 mm by FI. In serous appendicitis, with lack of endoluminal pus and histologically proven infiltration only of the paraluminal wall layers (mostly solely the tunica mucosa), only 33% of the measured diameters were larger

Table 2 Comparison of HI and FI (MCS mean conspicuity score)

Parameter	Comparison of HI and FI			MCS		P-value
	HI>FI	HI=FI	HI<FI	HI	FI	
Outer contour	32 (80%)	6 (15%)	2 (5%)	2.6	1.6	<0.01
Wall layers	35 (88%)	4 (10%)	1 (2%)	2.5	1.3	<0.01
Mucosa signal	20 (80%)	4 (16%)	1 (4%)	2.0	1.0	<0.01
Contents	21 (72%)	7 (24%)	1 (4%)	2.1	1.3	<0.01
Appendicoliths	8 (89%)	1 (11%)	0	2.9	1.9	<0.01
Surrounding free fluid	11 (85%)	2 (15%)	0	2.5	1.3	<0.01
Enlarged lymph nodes	13 (87%)	2 (13%)	0	2.6	1.4	<0.01
Thickened intestinal walls	11 (69%)	5 (31%)	0	2.8	1.9	<0.01
Increased fat echogenicity	30 (86%)	5 (14%)	0	2.5	1.4	<0.01

than 6 mm. This was true for 100% of the patients with suppurative appendicitis.

The US images of 40 patients with a visible appendix on at least one examination modality were included in the evaluation of the different comparative parameters (Table 1). The MCS were used for comparison. The outer contour of the appendix was more clearly visible with HI. In most cases (32 of 40) the image quality with HI was superior to that with FI (Figs. 1, 2 and 3). Only in 2 of 40 patients was FI better. The MCS was 2.6 for HI and 1.6 for FI ($P<0.01$; Table 2). Evaluation of the layers of the appendiceal wall led to similar results (Figs. 1 and 4). In 36 of 40 patients conspicuity of the wall was described as “very good” or “good” with HI, whereas demarcation of the wall was “poor” in most cases with FI (MCS: HI 2.5, FI 1.3; $P<0.01$). The mucosa signal was distinguishable from the wall signal in 25 of 40 patients with HI and in 16 of 40 patients with FI (MCS: HI 2.0, FI 1.0; $P<0.01$; Fig. 4). The contents of the appendiceal lumen were visible in 29 and 24 patients with HI and FI, respectively (Fig. 5). There was also a statistically significant difference in the MCS with 2.1 for HI and 1.3 for FI ($P<0.01$). Although appendicoliths were detected equally by both methods in nine patients (Figs. 5 and 6), the conspicuity was significantly increased when the HI mode was switched on (MCS: HI 2.9, FI 1.9; $P<0.01$).

This was also true for parameters concerning the periappendiceal tissues. In this evaluation, all 43 patients with histologically proven appendicitis were included, even if the appendix was not directly visible with one or both methods (Table 3). Surrounding free fluid was visualized in nearly the same number of patients (HI 13, FI 11), but particularly small amounts of fluid collections could be visualized much more easily using HI (MCS: HI 2.5, FI 1.3; $P<0.01$; Fig. 7). Significantly superior depiction of enlarged mesenteric lymph nodes was also apparent (MCS: HI 2.6, FI 1.4; $P<0.01$; Fig. 8) and wall thickening of adjacent intestinal segments (MCS: HI 2.8, FI 1.9; $P<0.01$; Fig. 7), although the total number of detected pathologies was nearly the same with both modalities.

An increase in echogenicity of the surrounding fat was apparent in 81% of patients examined by HI and in 67% of

patients examined by FI. This finding was definitively more evident with HI (MCS: HI 2.5, FI 1.4; $P<0.01$; Fig. 9).

Discussion

Appendicitis occurs in approximately 2–4 per 1,000 children and is still the most common cause of acute abdominal pain that necessitates surgical intervention [11].

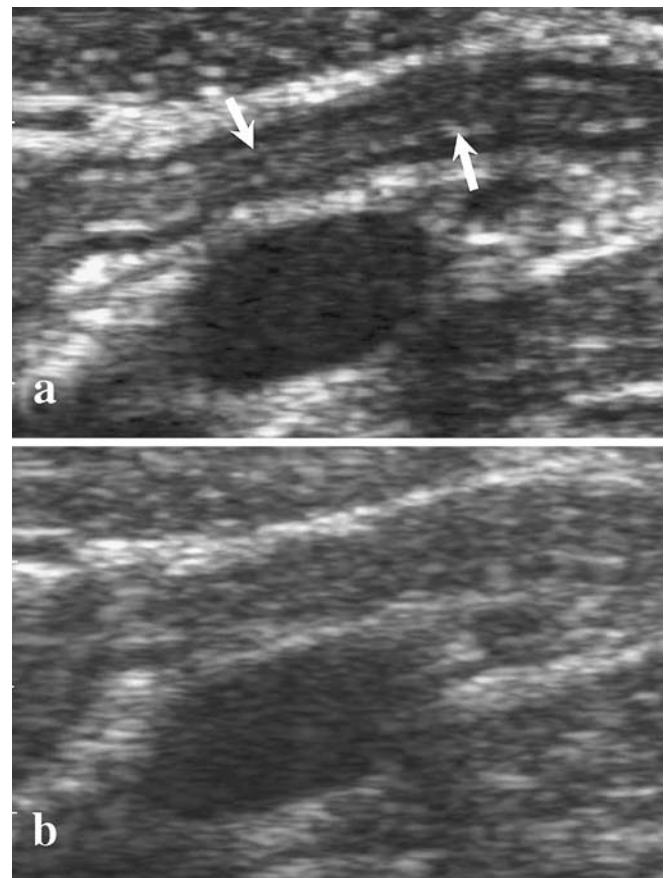


Fig. 4 Layers of the wall. Comparison of (a) HI and (b) FI. Longitudinal section of the inflamed appendix in an 11-year-old boy. Demarcation of the different layers of the appendiceal wall and especially the hyperechoic signal of the mucosa with partial discontinuity (arrows) was more obvious with HI (CS: HI 2, FI 1)

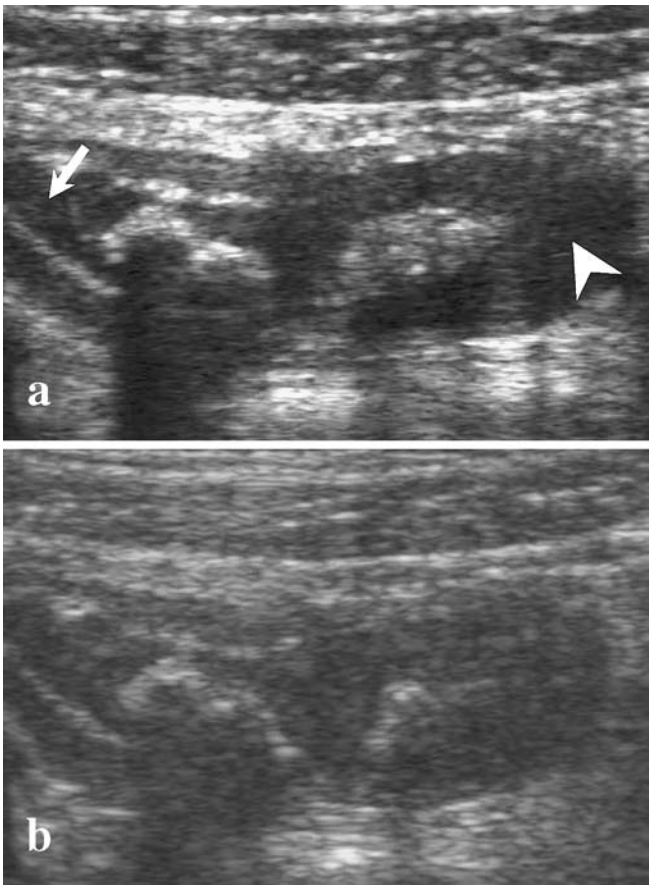


Fig. 5 Contents: appendicoliths. Comparison of (a) HI and (b) FI. Longitudinal section in a 5-year-old-boy with suppurative, perforated appendicitis with appendicoliths. Although the two concretions (the left one with a broad acoustic shadow) were visible by both modalities (CS: HI 3, FI 2), these and the hypoechoic endoluminal fluid collection (CS: HI 3, FI 1; *arrow*) and periappendiceal fluid collection (CS: HI 3, FI 0; *arrowhead*) as well as the mural discontinuity and loss of typical wall layering were more clearly depicted by HI than by FI

Diagnosis is based primarily on history, clinical symptoms, and physical and laboratory findings. According to Kosloske et al. [12] clinical examination by a paediatric surgeon is highly accurate when using a protocol based on clinical evaluation. Nevertheless, the initial presentation of the disease is often obscured. Classic clinical parameters are found in only 50–60% of patients [13]. This may often lead to delayed diagnosis and therapy. The risk of appendiceal perforation is highly dependent on the length of time between the first clinical symptoms and surgery. The perforation rate is 23–73% [1]. Moreover, acute appendicitis can be mimicked by many other diseases that can cause right lower quadrant pain. Up to 50% of children hospitalized for possible appendicitis do not actually have this disorder [14]. The literature indicates a negative appendectomy rate of about 15–20%, which has been generally considered acceptable [1, 15].

CT has achieved an increasingly important role in the diagnostic imaging of suspected appendicitis. The use of CT in children has risen about sevenfold in the past 10 years [2]. In the same period, particularly in parts of the

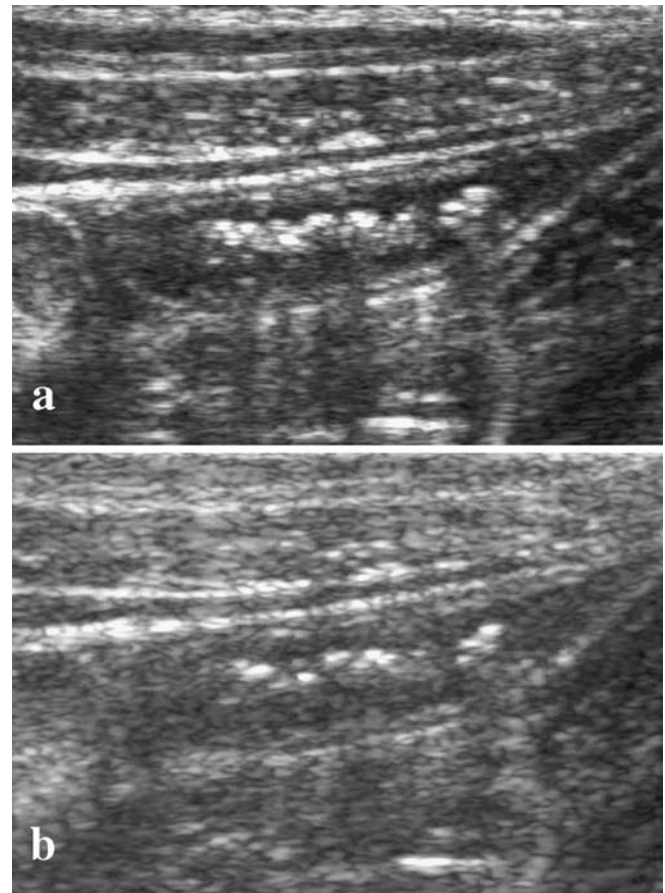


Fig. 6 Appendicoliths. Comparison of (a) HI and (b) FI. Longitudinal section of the appendix in a 4-year-old girl. Numerous small appendicoliths, some with posterior acoustic shadows, were detected by both modalities, but with HI producing a higher image quality (CS: HI 3, FI 2)

USA, the use of sonography for diagnosing appendicitis has decreased significantly [6]. Hagendorf et al. [16] describe the capacity of this modality to minimize perforation. In contrast to this opinion, Martin et al. [6] and Partrick et al. [17] emphasize that the liberal use of CT scans has not resulted in a decreased negative appendectomy rate. In their opinion the role of CT in the management of children with suspected appendicitis has to be critically reevaluated. This is particularly important with regard to the increased life-time risk of cancer in children undergoing CT. In our departments in Nuremberg and Würzburg, Germany, helical CT is not routinely employed; rather this method or MRI are reserved, for

Table 3 Parameters of the periappendiceal region: visibility with HI and FI ($n=43$)

Parameter	Visibility	
	HI	FI
Surrounding free fluid	13 (30%)	11 (26%)
Enlarged lymph nodes	15 (35%)	12 (28%)
Thickened intestinal walls	16 (37%)	16 (37%)
Increased fat echogenicity	35 (81%)	29 (67%)

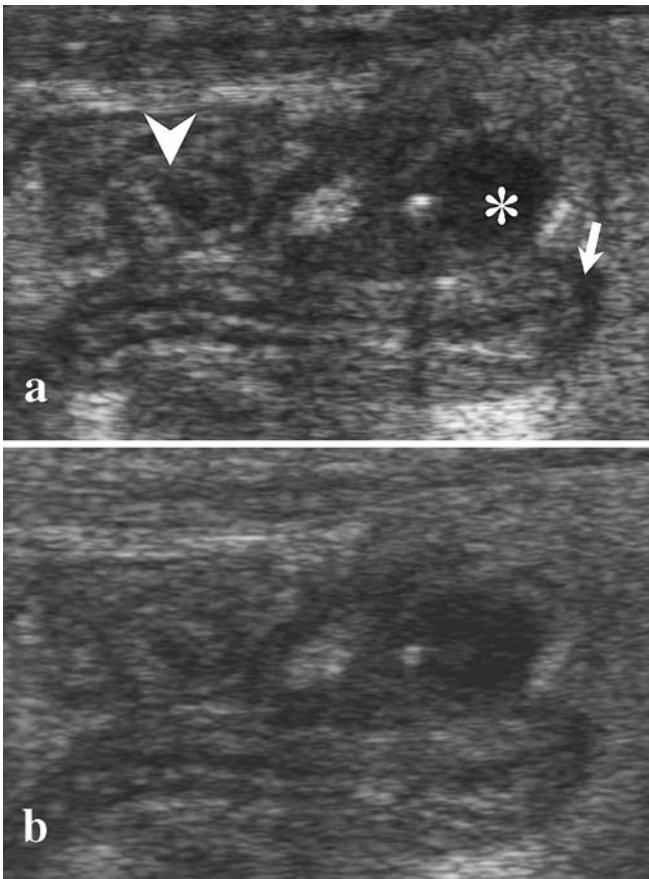


Fig. 7 Surrounding free fluid and adjacent intestinal walls. Comparison of (a) HI and (b) FI. Longitudinal section of the appendix in a 6-year-old boy with perforated appendicitis. Compared with FI, HI allowed superior detection of small amounts of free fluid next to the tip of the appendix (*arrow*) as well as wall thickening of the adjacent intestine (*arrowhead*) and a par-appendiceal abscess (*asterisk*). (CS for all: HI 3, FI 1)

example, for patients with repeated equivocal clinical and sonographic results.

Blab et al. [18] emphasize that high diagnostic accuracy can only be achieved by carefully combined evaluation of all individual diagnostic parameters and repeated investigations. In the diagnostic imaging algorithm of appendicitis the important role of sonography has been shown by many studies [19, 20]. In conformity with the results of other authors [18], the overall sensitivity of our US examinations was 98%. However, sonography is an operator-dependent modality, resulting in a wide range of diagnostic sensitivity and specificity. In this study, all examinations were conducted by the same experienced paediatric radiologist and this may partly explain the low rate of perforation (12%) and negative appendectomy (14%). The graded-compression sonographic technique described by Puylaert [3] in 1986 has proved to be very useful in the diagnosis of acute appendicitis. The additional use of the posterior manual compression technique or the use of power Doppler sonography and especially contrast-enhanced power Doppler sonography are also able to

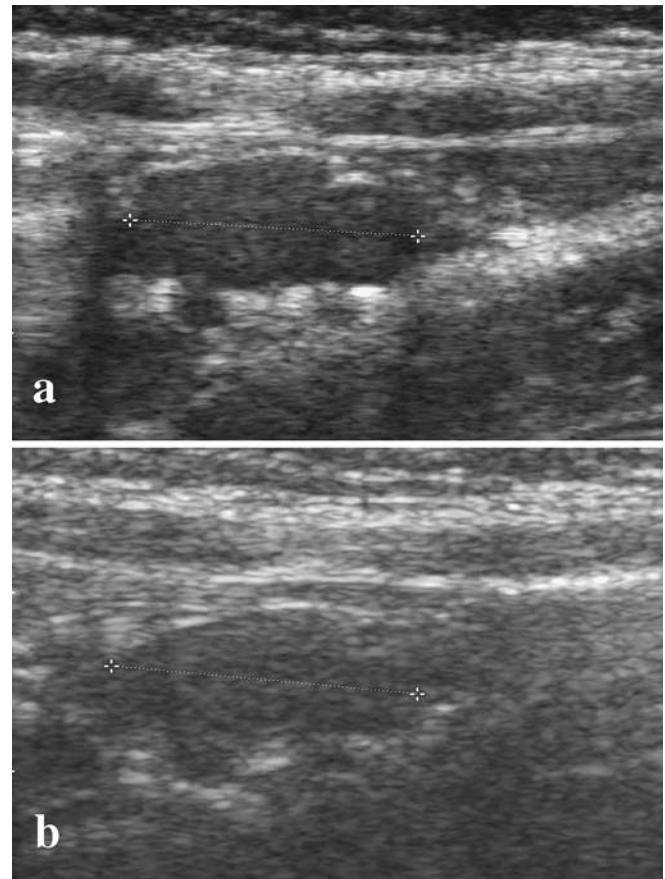


Fig. 8 Lymph nodes. Comparison of (a) HI and (b) FI. Oblique section of the right lower abdomen in a 9-year-old girl. The conspicuity of the enlarged lymph node was better with HI (CS: HI 3, FI 2)

improve the detectability of the inflamed appendix and thus raise the sensitivity of sonography [21, 22].

HI is a relatively new US modality. Harmonic waves are generated from nonlinear distortion of US waves in tissue. These beams are integer multiples of the fundamental transmitted frequency and can be used for image formation. The fundamental beams are removed by either filters or the phase/pulse inversion technique. Advantages of HI include improved contrast and spatial resolution. Moreover, decreased noise from side lobes improves the signal-to-noise ratio and reduces artefacts. Deleterious effects of the body wall are also diminished [23–25]. HI was first introduced to improve grey-scale diagnosis in adults. Choudhry et al. [23] and Yücel et al. [26] have described improved visualization of lesions of the liver, pancreas, kidneys and other abdominal and pelvic organs using HI instead of FI. The lesions are clearer and better defined with HI, thereby improving the detection of subtle lesions. The use of higher effective frequencies yields improvement in axial resolution and thereby improves visualization of smaller objects; narrower beams lead to improved lateral resolution. Due to its better contrast-to-noise ratio, HI can improve the conspicuity of echogenic tissues as well as low-contrast lesions [8]. HI is especially helpful in obese patients because of the reduction in body wall artefacts. On

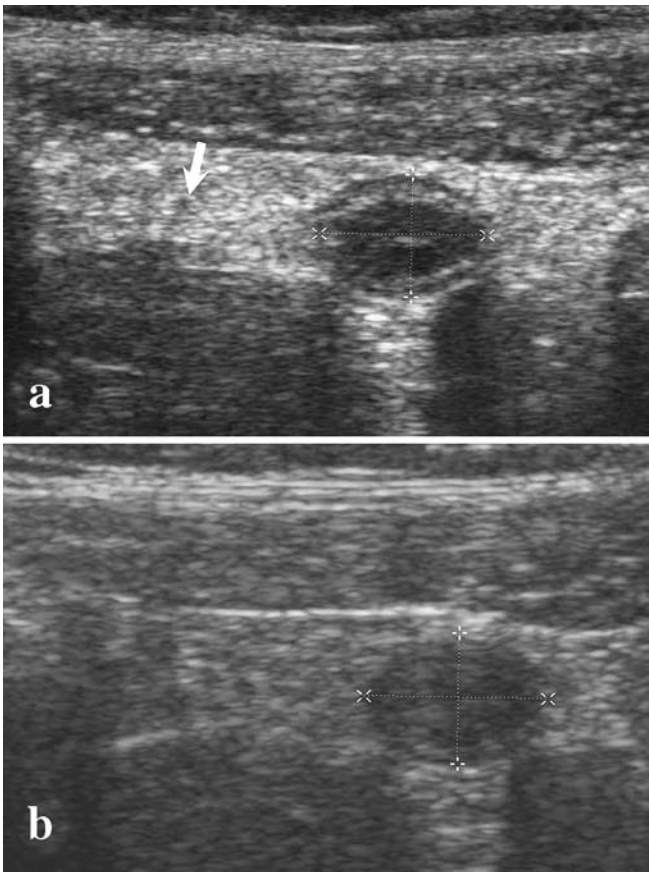


Fig. 9 Mesenteric fat echogenicity. Comparison of (a) HI and (b) FI. Transverse section of the appendix in a 5-year-old girl with suppurative appendicitis. The increase in echogenicity of the surrounding mesenteric fat (*arrow*) is clearly more evident with HI (CS: HI 3, FI 1)

the other hand, for patients with diffuse fatty infiltration of the liver, penetration of the US beam is better with FI [23]. Rosen and Soo [27] have described the superiority of HI in the detection and evaluation of breast lesions in adults.

In recent years, the usefulness of HI for fetal and paediatric imaging has been increasingly evaluated. Studies have shown higher image quality of HI in the examination of cardiac structures in children [9]. Bartram and Darge [8] demonstrated that HI also improves image quality of the urinary tract. Darge et al. [10, 28] reported the superiority of HI in contrast-enhanced voiding urosonography. HI resulted in more conspicuous microbubbles and increased the reflux detection rate.

In our study, image quality of the inflamed appendix was significantly higher with HI than with FI. In addition to increasing the global image quality, more details were visible for all analysed parameters of the appendix and its surrounding tissues. The layers of the wall were more distinctly visible, and the outer contour was better demarcated than with FI. HI led to a significant improvement in the detection of pus and detritus in the lumen, as well as free fluid in the tissues surrounding the appendix. The alteration in echogenicity of the mesenteric fat, a reliable finding of inflammation of the appendix or other

neighbouring tissues, was much better seen with HI. Enlarged mesenteric lymph nodes and thickened adjacent intestinal walls were also visualized better. In all patients the differences in MCS between HI and FI were statistically significant in favour of HI.

Consequently, HI should be the preferred modality for scanning the right lower abdomen in cases of suspected acute appendicitis. This imaging modality can routinely be combined with other sonographic techniques. The diagnosis of acute appendicitis can be more definitely ascertained, and thus clinical decisions regarding subsequent therapy made easier. With the improvement in sonographic diagnosis there is the potential to reduce the use of CT for routine imaging when appendicitis is suspected, leading to fewer children having to be exposed to ionizing radiation.

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