

Recto-sigmoid endoscopic-ultrasonography in the staging of deep infiltrating endometriosis

Gilles Roseau

Gilles Roseau, Department of Gastroenterology, Hôpital Cochin, 75014 Paris, France

Gilles Roseau, Clinique du Trocadero, 75116 Paris, France

Author contributions: Roseau G solely contributed to this paper. Correspondence to: Dr. Gilles Roseau, MD, Department of Gastroenterology, Hôpital Cochin, 27 rue du faubourg saint Jacques, 75014 Paris, France. gilles.roseau@free.fr

Telephone: +33-1-47421249 Fax: +33-1-42663681

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Abstract

Recto-sigmoid endoscopic ultrasonography (RS-EUS) has first been used in the staging of pelvic deep infiltrating endometriosis in the early 1990's. Since then, although publications have been sparse, RS-EUS is routinely used for this indication in few centers. In this paper, we focus on technical aspects and operating method of rectal and sigmoid endo-sonography, and describe the most characteristic echographic presentations of endometriosis of the lower digestive tract. Through a literature review, results obtained with different types of endo-rectal probes, either flexible endoscopic, or blind rigid, are presented and compared with those of other close imaging techniques: magnetic resonance imaging and the more recent trans-vaginal sonography. As well as these two latter techniques, RS-EUS appears as an interesting method in the staging of pelvic deep infiltrating endometriosis particularly to evaluate rectal and sigmoid infiltrations. However, more prospective studies are required, to correctly define respective indications for each exam, in the light of recent advancements in treating this frequent disease.

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Key words: Endometriosis; Rectum and sigmoid; Ultrasound; Endoscopic-ultrasonography; Surgical treatment; Magnetic resonance imaging

Core tip: Pelvic deep infiltrating endometriosis is a disabling disease of increasing rate. Today new medical and surgical therapies are proposed in the management of pain and infertility, and the choice of an optimal treatment strategy requires a precise anatomic evaluation. Several imaging techniques are available, either additive or competitive, in this staging. Rectosigmoid endoscopic-ultrasonography (RS-EUS), is routinely used in the field of gastroenterology, mostly for staging of rectal cancer. Few studies have demonstrated it could also be of interest to image endometriotic recto-sigmoid infiltrations. In this review, we tried to assess indications and results of RS-EUS, compared to those of magnetic resonance imaging and transvaginal sonography.

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INTRODUCTION

Pelvic deep infiltrating endometriosis affects 5% to 15% of women of reproductive age, and may hence impair quality of life of many young women suffering from pain and/or infertility^[1,2]. When originating from recto-vaginal septum or retro-cervical areas, it has the potential to infiltrate the muscularis propria of rectum and sigmoid, characteristic locations of the so-called digestive tract endometriosis^[3-5]. Diagnosis of this contingent infiltration is mandatory in order to correctly interpret clinical symptoms, either digestive or gynecologic, and to optimize treatment. Indeed management of pelvic deep infiltrating endometriosis relies on medical therapies or surgical interventions, and as far as recto-sigmoid locations are concerned, surgical laparoscopy is the reference

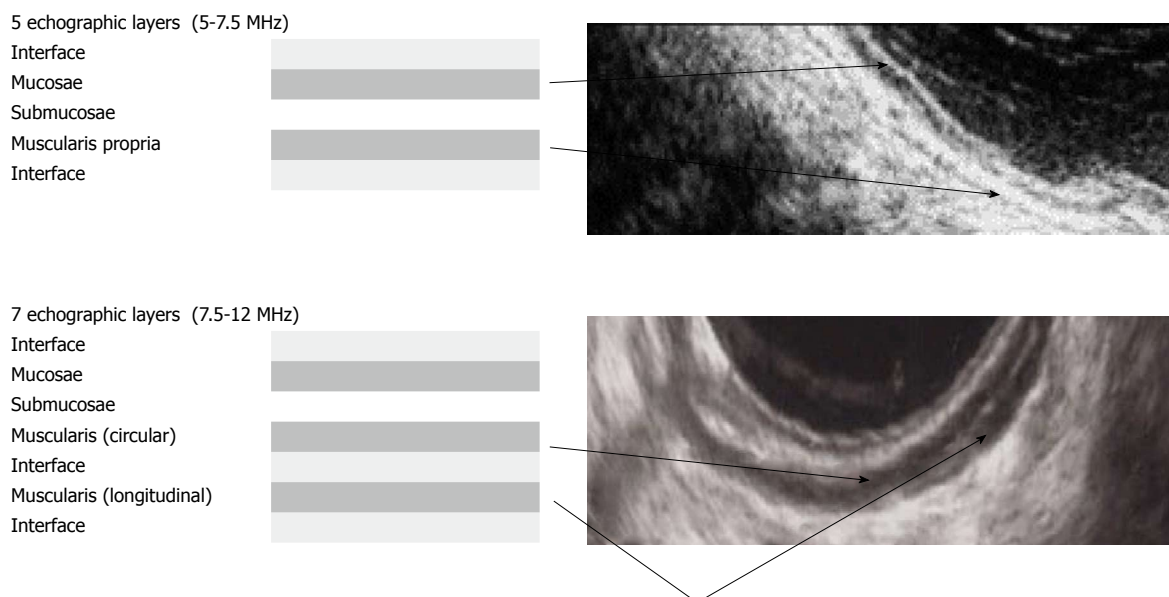


Figure 1 Digestive walls echoic stratifications depending on frequencies.

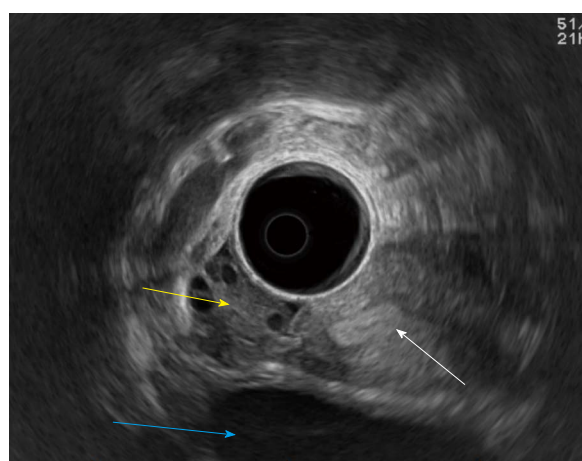


Figure 2 Normal peri-rectal anatomy. White arrow: Uterus; Yellow arrow: Right ovary; Blue arrow: Bladder.

technique for resection^[6,7]. The recent trend is to prefer nodule excision, when feasible, than radical digestive resection^[8,9], therefore it is of utmost importance to appreciate endometriotic rectal and sigmoid infiltration, in the pre-operative staging. Diagnosis of recto-sigmoid endometriosis definitely relies on imaging as clinical examination is not sufficient for the diagnosis of location of deeply infiltrating endometriosis^[10]. Since the early 1980's different techniques, from barium enema to the most recent magnetic resonance imaging (MRI), have been proposed and evaluated to achieve diagnosis of endometriosis^[3,11-13]. However these various imaging techniques have been used with variable results, equally to diagnose endometriosis and to evaluate its extension in pelvic locations such as uterosacral ligaments (USL), recto-sigmoid, recto-vaginal septum and bladder. Today, three endocavitary ultrasonic exams, transvaginal sonography (TVS),

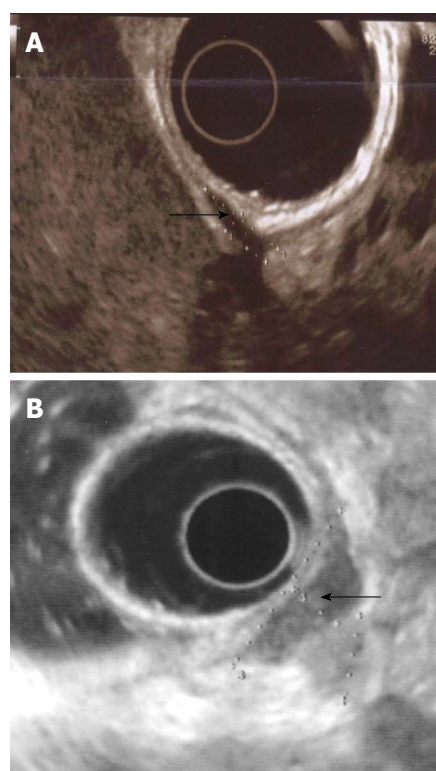


Figure 3 Different types of muscularis propria infiltration. A: Infiltration limited to external muscularis propria; B: Infiltration of the entire thickness of the muscularis propria.

blind endo-rectal sonography (ERS), and recto-sigmoid endoscopic ultrasonography (RS-EUS), are also available^[14-16], the latter, although slowly developing, appears as an interesting technique. In this review we will first consider technical aspects and operative method of RS-EUS, and describe echographic presentations of recto-

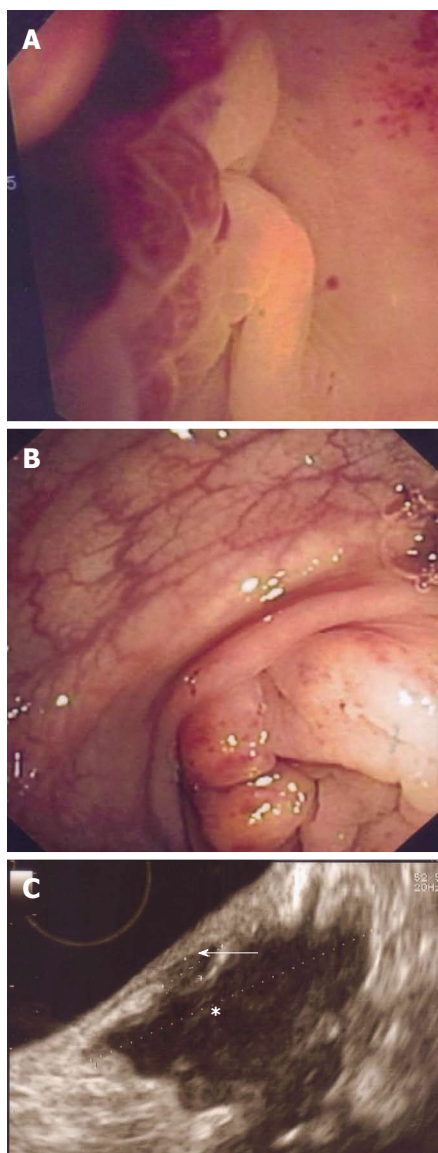


Figure 4 Endoscopic and echographic presentations of recto-sigmoid endometriosis. A: Mucosae infiltration; B: Sigmoid stenosis; C: Sub-mucosae (white arrow) and muscularis (white star) infiltrations.

sigmoid, either normal or infiltrated by endometriosis. Then, performances of recent imaging in the staging of deep infiltrating endometriosis will be discussed, with a special focus on results of RS-EUS in staging of recto-sigmoid endometriosis infiltration.

RS-EUS, TECHNICAL CONSIDERATIONS AND ECHOGRAPHIC PRESENTATION OF NORMAL RECTO-SIGMOID PARIETAL WALLS AND SURROUNDINGS

Initially proposed in the early 1980's mostly for rectal cancer staging^[17,18], RS-EUS was first described in the evaluation of recto-sigmoid endometriosis in 1993^[19]. In this early work, a radial RS-EUS (GF UM2), from Olympus was used, allowing circular images of 360°.

This device was a flexible optical scope equipped with an echographic probe of 7.5 MHz frequency. Ever since then, many other radial scopes with a mechanical transducer (GF UM3, GF UM20, and GF UM 160) have been used to stage patients with pelvic deep infiltrating endometriosis. These scopes have diameters and frequencies respectively varying from 10.4 to 11.5 mm and 5 to 20 MHz. In 2008 the electronic probe (GF-UM160, 13.8 mm diameter and variable frequencies from 5 to 10 MHz) became available. To date, this video-echoendoscope is used connected to alpha 5 or alpha 10 dedicated central ultrasound unit device allowing doppler function. Other similar devices from Pentax (reference EG 3630 UR) and Fujinon (reference EG-530 UR with SU-7000 ultrasound system) have also been used with similar efficiency. On the other hand, the use of linear scopes, probably less suitable in this indication has never been reported. RS-EUS is usually performed without the recourse to general anesthesia, after one or two rectal Normacol[®] enemas, the patient lying on the lithotomy position. Progression of the endoscope is initiated under endoscopic and ultrasonic control up to the recto-sigmoid junction, and above, in the distal sigmoid when possible. Most part of the endoscopic exploration is done while progressing (looking for stenosis, extrinsic compressions, relief and mucosal coloration abnormalities ...), while ultrasonic exam is performed when slowly withdrawing the probe^[20]. Rectal and sigmoid parietal walls are explored, and semiology interpreted according to the well-known 5 or 7 layers description of the digestive tract (Figure 1), while anatomical structures around the digestive tract are simultaneously imaged (Figure 2).

ECHOGRAPHIC PRESENTATIONS OF RECTO-SIGMOID ENDOMETRIOSIS AND OF SOME OF THE CLOSE PELVIC LOCATIONS

Endometriotic infiltration of the muscularis-propria defines endometriosis of the digestive tract^[21]. Rectum and sigmoid are the most frequent locations representing 90% of cases^[3,4], and infiltration is imaged, by endorectal ultrasound using 5 or 7 MHz frequencies, as a hypoechoic thickening of the muscularis-propria corresponding to the fourth layer, from superficial to deep part of the parietal wall (Figure 3). Instead with 10 to 12 MHz frequencies, lesions infiltrating the entire muscularis-propria or solely the external longitudinal layer can be differentiated. Depending on their origin (torus uterinus or USL), these thickenings respectively stand on the median line or on the lateral surfaces of the rectum and/or sigmoid. In 15% of cases separated locations can also be found in the sigmoid^[3,5].

In all cases, measurements should be imperatively performed either in depth, width, and height. Complete evaluation by using figures in degrees of the circumference, and specification of distance in centimeters, be-

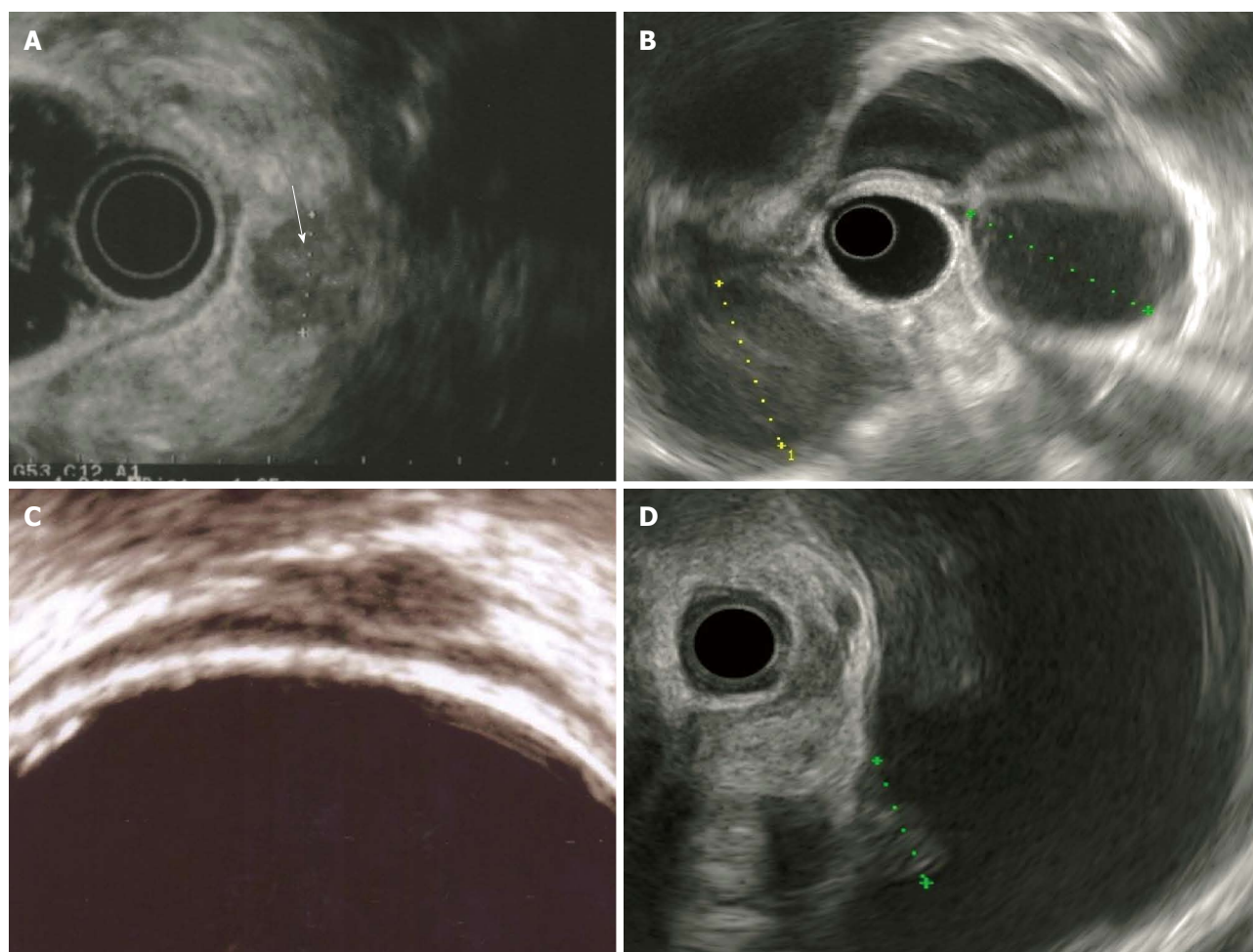


Figure 5 Other pelvic endometriosis locations. A: Infiltrated Torus; B: Bilateral Ovarian endometriomas; C: Infiltrated utero-sacral ligament; D: Bladder nodule.

Table 1 Main “exclusive” blind endo-rectal or endoscopic ultrasonography¹ in deep infiltrating endometriosis

Author	Ref.	Year	No.	Type	se%	sp%	ppv%	npv%
Roseau ¹	[19]	1993	(11)		Descriptive rectal endometriosis			
Hauge	[27]	1993	(1)		Descriptive, anal endometriosis			
Ohba	[26]	1996	64		Descriptive, correlation thickness USL and clinical symptoms			
Chapron ¹	[29]	1998	38 (17)	R preliminary results	Diagnosis accuracy: 100%			
Fedele	[28]	1998	140 (24)	R	97	96		
Roseau ¹	[16]	2000	46 (25)	R	100	100		
Doniec	[30]	2003	65 (32)	R	97	97		
Abrao ¹	[31]	2004	32 (6)	R	100	67		
Delpy ¹	[32]	2005	30 (17)	P	92	66	64	92
Bahr	[33]	2006	37 (8)	R	87.5	97	87.5	97
Roman ¹	[34]	2007	(16)		Kappa coeff: 0.22; limited accuracy to predict layer involvement			
Griffiths	[14]	2008	32		Likelihood ratio + : 10.89/-: 0.24; good results for recto-vaginal septum			
Mezzi ¹	[35]	2011	68 (34)					
Ferrari ¹	[36]	2012	(26)		Diagnosis accuracy: 100% with elastometry			
Rossi ¹	[22]	2013	(38)	R	89	26	55	71

¹Main “exclusive” blind endo-rectal or endoscopic ultrasonography. (): Patients with digestive infiltration/type; R: Retrospective; P: Prospective; se: Sensitivity; sp: Specificity; ppv: Positive predictive value; npv: Negative predictive value; USL: Utero-sacral ligament.

tween the lowest part of the digestive infiltration and the pubo-rectal muscle or the anal verge, provides precious informations in the pre-operative staging. In patients with advanced disease, superficial irregularities and abnormal

mucosal coloration or stenosis, can be encountered endoscopically, corresponding to entire muscularis-propria or even sub-mucosae infiltration. The latter can be certified either on endoscopy or ultrasonography when significant,

Table 2 Evaluation of magnetic resonance imaging in staging deep infiltrating endometriosis

Anatomical location	se%	sp%	acc%	ppv%	npv%
Global	90.3	91	90.8	92.3	89
USL	76	83.3	80.5	74	84.7
Vagina	76	95.4	93.3	67	97
Septum	80	97.8	96.9	67	98.7
Recto-sigmoid	88	97.8	94.9	95	95
Bladder	88	98.9	97.9	88	98

Bazot *et al*^[13], 2004: 195 patients treated by laparoscopy: $n = 136$ or laparotomy: $n = 59$; all specimens sent for histological examination as the gold standard. se: Sensitivity; sp: Specificity; ppv: Predictive positive value; npv: Negative predictive value; acc: Accuracy rate.

or only suspected in other cases (Figure 4). Indeed, to date, no imaging technique has been demonstrated as a reference in diagnosing mild sub-mucosae infiltration^[22,23]. Beside, other locations of pelvic deep infiltrating endometriosis can also be imaged with RS-EUS, either torus uterinus, USL and bladder (Figure 5). Ovarian endometriomas whatever their size are characterized by their “ground glass” echogenicity^[24].

RESULTS OF IMAGING (MRI AND ULTRASOUND), IN THE STAGING OF DEEP INFILTRATING ENDOMETRIOSIS; WHAT SHOULD BE THE PLACE OF RS-EUS?

For surgeons and gynecologists specialized in deep pelvic endometriosis, treatment decisions rely on several factors depending on the patient (age, intensity of the symptoms, and response to previous treatments), and the disease (loco-regional extension). Ureter dilatation and the risk of renal insufficiency must always be kept in mind and systematically searched on imaging^[25]. The other major question raised, concerns diagnosis of recto-sigmoid infiltration, either suspected on clinical signs (dyschesia, cyclic pains, transit time variations, or hematochezia), or systematically screened for, prior to surgical intervention. From a literature review using the key-words below (rectosigmoid endometriosis and ultrasound, endosonography, endoscopic ultrasonography, transvaginal sonography, and MRI) we tracked all “exclusive” RS-EUS and rectal endo-sonography studies, and searched for series, especially comparative with ultrasound, evaluating MRI in the loco-regional extension of pelvic endometriosis.

Exclusive endo-rectal ultrasound studies

There are only few exclusive studies evaluating the use of endo-rectal ultrasound in diagnosis and staging of recto-sigmoid endometriosis^[14,16,19,27-36]; they are presented in Table 1. Almost all are retrospective studies, and they have the limitation to be widely disparate in terms of purposes studied, and technical devices tested. Ohba *et al*^[26] are the only authors whose report had the aim to

demonstrate the usefulness of endo-rectal ultrasound in imaging USL. In this early paper, the type of probe used was a blind poly-plane probe (two dimensional mechanical sector probe); USL's description was performed in patients with or without endometriosis infiltration of these ligaments. Comparisons showed that patients with endometriosis had thickened and irregular ligaments, with correlation between the thickness and the intensity of pain. However, in no other study, whatever the probe used, normal USL has been correctly described. Actually, and this is consistent with most author's descriptions, endo-rectal ultrasound examination can localize USL clearly, only when it is already infiltrated by endometriosis.

Globally, when trying to answer to the question of the presence (or not) of endometriotic recto-sigmoid parietal infiltration, short series available, most of them published between 1998 and 2008^[14,22,28-34], show close sensitivities and negative predictive values, as well as with blind and endoscopic probes. Comparison of Delpy and Bahr's studies, clearly illustrates this conclusion^[32,33]. Sensitivity and specificity range respectively from 87% to 100% and 66% to 100% and the superiority of RS-EUS over blind rigid probes does not appear; this could be explained by the limited number of patients included, and the low prevalence of isolated upper sigmoid lesions already mentioned above^[3]. However, when looking at the 9 over 15 studies, in which the ultrasound device used was RS-EUS [Table 1, authors marked with (1)]; diagnosis accuracy may reach 100%, and in our own study published in 2000, we found the same high values of sensitivity and specificity. Furthermore, in their prospective study, Delpy *et al*^[32] have demonstrated high sensitivity (92%) and negative predictive values (92%) with RS-EUS.

In the two studies from Rossi *et al*^[22] and Roman *et al*^[34], the aim was to evaluate precise parietal layer involvement. Compared to performances in the positive diagnosis of recto-sigmoid endometriosis, endo-rectal ultrasound is not as much demonstrative in this appreciation. Such results rely on incorrect sub-mucosal involvement's evaluation, and it is interesting to notice that the same limitation has also been recently reported by Busard *et al*^[23] with MRI. As for the interest of fine needle aspiration endoscopic ultra-sonography (FNA/EUS), it does not really concern the evaluation of parietal wall by endometriosis. Only mentioned in few papers, it can benefit to patients with para-rectal masses, the differential diagnosis of which can be resolved by puncturing under ultrasound control^[37-39].

Comparative studies between endorectal ultrasound and other imaging techniques

Other imaging techniques than endo-rectal ultrasound are also used to diagnose and stage pelvic deep infiltrating endometriosis. MRI has first been proposed in the late 1990s^[40-43]; both technical improvement and learning curves, have led to good results published first by Bazot *et al*^[13] in a prospective serie. In this work presented on Table 2, 195 patients were included, who all had surgical treatment (laparoscopy: $n = 136$, laparotomy: $n = 59$)

Table 3 Comparative studies magnetic resonance imaging *vs* recto-sigmoid endoscopic ultrasonography in staging deep infiltrating endometriosis

Author	Ref.	Year	No.	Type	se%		sp%		ppv%		npv%	
					MRI	RS-EUS	MRI	RS-EUS	MRI	RS-EUS	MRI	RS-EUS
Dumontier	[47]	2000	48 (16)	R	75	100	100	100				
Camagna	[48]	2004	50 (19)	R	53	100	82	71	69	81	19	100
Thomassin	[49]	2004	(27)	P	92	100			89	100		
Chapron	[50]	2004	81 (17)	R	76.5	97	98	89.4	96	87	85	98
Bazot	[51]	2007	88 (60)	P	88.3	90	92.8	89.3	96.4	94.7	78.8	80.6
Benbara	[52]	2008	50 (40)	R	55	100			Post operative follow up MRI contributive for torus, USL and bladder			
Gauche-cazalis	[53]	2012	25 (19)	R	89	94	50	66.7				

(): Number with digestive infiltration; R: Retrospective; P: Prospective; se: Sensitivity; sp: Specificity; ppv: Predictive positive value; npv: Negative predictive value; MRI: Magnetic resonance imaging; RS-EUS: Recto-sigmoid endoscopic ultrasonography; USL: Utero-sacral ligament.

Table 4 Comparative studies trans-vaginal sonography *vs* recto-sigmoid endoscopic ultrasonography in staging deep infiltrating endometriosis

Author	Ref.	Year	No.	Type	se%		sp%		ppv%		npv%	
					TVS	RS-EUS	TVS	RS-EUS	TVS	RS-EUS	TVS	RS-EUS
Bazot	[54]	2003	30	P	95	82	100	88	100	95	89	84
Bazot	[56]	2003	81	P	92	88.9	100	92.6	89	100	87	80.6
Piketti	[57]	2009	134	P	90.7	96	96	100	100	96	88.9	95.2
Gauche-cazalis	[53]	2011	25	R	73.7	94.7	66.7	66.7	RS-EUS : Appropriate for rectum and recto-vagina septum TVS: Good for ovarian endometriomas			

(): Number of patients with digestive infiltration; R: Retrospective; P: Prospective; se: Sensitivity; sp: Specificity; ppv: Positive predictive value; npv: Negative predictive value; RS-EUS: Recto-sigmoid endoscopic ultrasonography; TVS: Trans-vaginal sonography.

and histological examination as a gold standard. MRI performances were evaluated for the main locations of pelvic deep infiltrating endometriosis, and results were given both globally, and for each of them. Since then, other studies evaluating MRI with a similar methodology have been published with same promising results^[44-46]. As for comparative studies, those concerning RS-EUS and MRI, have been published principally between 2000 and 2010^[47-53], whereas the first prospective one comparing performances of RS-EUS and TVS was published in 2003^[54], soon followed by other papers^[55-58]. Comparisons often rely on both recto-sigmoid parietal involvement, and also on other main locations of deep pelvic endometriosis (*i.e.*, Bladder, Recto-vaginal septum, Torus, USL), and on ovaries. Yet it is difficult to correctly appreciate specific results unless working on selected papers where distinction of each location would be correctly performed. We have reported these studies in the Tables 3 and 4. Comparisons of MRI and RS-EUS show improvements of MRI's results with time, and for RS-EUS fair results for specificity (66.7%-100%) and good ones both for sensitivity (90%-100%), predictive positive value (81%-100%), and negative predictive value (80.6%-100%). Two studies, from Thomassin *et al*^[49] and Bazot *et al*^[51], are prospective; the former shows better sensitivity and posi-

tive predictive values for RS-EUS whereas for Bazot *et al*^[51], the superiority of RS-EUS over MRI only concerns sensitivity and negative predictive value. For specificity and positive predictive value, MRI has a slight advantage although non statistically significant. As for the studies comparing RS-EUS and TVS, 3 of them are prospective; the first one from Bazot *et al*^[54], already mentioned, favors TVS, and the main ones from the same author^[56], and Piketti *et al*^[57] curiously demonstrates strictly inverse results with only slight differences. Both authors conclude that TVS is the perfect first line exam, and that RS-EUS may be useful as a second exam to certify the absence of parietal involvement if TVS is negative. It may also be used to provide an accurate description of parietal wall infiltration when surgery is mandatory, or as a baseline measurement for patients with continuous low doses oral contraceptive treatment^[56]. In the work of Huang (meta-analysis on ultrasound evaluating RS-EUS, blind ERS and TVS for deep infiltrating endometriosis, all locations combined), ERS had the highest performances (sensitivity and specificity of 92% and 98%), and areas under the curve of RS-EUS was 94%, and that of TVS was 92%^[58].

As MRI, RS-EUS and TVS are complementary imaging exams, it is important to determine in which locations

Table 5 Retrospective comparative study between trans-vaginal sonography, recto-sigmoid endoscopic ultrasonography, and magnetic resonance imaging for diagnosis of main locations of deep pelvic endometriosis

	OV			Torus			USL			RVS			RSJ			Bladder		
	TVS	RS-EUS	MRI	TVS	RS-EUS	MRI	TVS	RS-EUS	MRI	TVS	RS-EUS	MRI	TVS	RS-EUS	MRI	TVS	RS-EUS	MRI
se (%)	88	80	87	57	76	76	63	37	69	63	89	47	73	95	89	16	16	33
sp (%)	71	81	71	100	100	100	82	100	82	100	67	100	66	66	50	100	100	89

Gauche Cazalis *et al*^[53] 2012: 25 patients included. OV: Ovary; USL: Uterosacral ligament; RVS: Rectovaginal septum; RSJ: Rectosigmoid junction; se: Sensitivity; sp: Specificity are expressed in%.

each has the best diagnosis performances. This has been studied by Gauche Cazalis *et al*^[53] in a retrospective manner; results are presented in Table 5. In this work with 25 patients included, authors conclude that TVS is accurate for endometriomas, MRI for torus, USL, and small bladder lesions, while RS-EUS is particularly appropriate for recto-vaginal septum and recto-sigmoid parietal wall's involvement^[53]. Unfortunately this is a small retrospective study, and such results only could be confirmed by using prospectively such an "exhaustive staging methodology" through multi-centric studies.

CONCLUSION

RS-EUS is a promising tool for the diagnosis of digestive endometriosis. It has the advantage to combine endoscopic and ultrasonic evaluation of the rectum and the distal part of sigmoid where most cases of endometriosis of the digestive tract are localized. It allows a more complete exam than blind rigid rectal probe which can be deficient in diagnosing sigmoid lesions. Compare to other imaging exams appropriate for staging of pelvic deep infiltrating endometriosis, RS-EUS, is prone to diagnose parietal wall and recto-vaginal septum infiltrations, whereas MRI and TVS seem more appropriate in diagnosing ovarian endometriomas, and torus, USL or bladder infiltrations. However, precise performances for these three complementary explorations should be studied in prospective works, in order to exactly define which patients should really benefit from RS-EUS.

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