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Title: Combined Transvaginal/Transabdominal Pelvic Ultrasonography Accurately Predicts the 3 Dimensions of Deep Infiltrating Bowel Endometriosis Measured after Surgery: a Prospective Study in a Specialized Center.: Diagnostic Value of TV/TA-US for Bowel DIE

Author: Alessandra Di Giovanni, Lucia Casarella, Marina Coppola, Domenico Iuzzolino, Marianna Rasile, Mario Malzoni

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1 **Original article**

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3 **Combined transvaginal/transabdominal pelvic ultrasonography accurately predicts**
4 **the 3 dimensions of deep infiltrating bowel endometriosis measured after surgery: a**
5 **prospective study in a specialized center.**

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8 Diagnostic value of TV/TA-US for Bowel DIE

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11 Alessandra Di Giovanni, MD; Lucia Casarella, MD; Marina Coppola, MD; Domenico

12 Iuzzolino, MD ; Marianna Rasile, MD; Mario Malzoni, MD

13

14 Endoscopica Malzoni, Center for Advanced Endoscopic Gynecologic Surgery, Avellino, Italy.

15

16

17 **Corresponding author**

18 Alessandra Di Giovanni, MD

19 Endoscopica Malzoni, Center for Advanced Endoscopic Gynecological Surgery

20 Via C. Errico 2

21 Avellino

22 Italy

23 E-mail: dott.a.digiovanni@gmail.com

24 Tel. +39 3337663219

25

26

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30 nothing to disclose

31 **PRECIS**

32 Ultrasonography can be considered an accurate diagnostic technique for the evaluation of
33 deep infiltrating bowel endometriosis when performed by a dedicated experienced
34 sonographer in the setting of a specialized center .

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37 **ABSTRACT**

38 **Study objective:** To assess sensitivity and accuracy of combined
39 transvaginal/transabdominal ultrasonography for evaluation of deep infiltrating bowel
40 endometriosis nodules measured after surgery.

41 **Design:** A prospective study (Canadian Task Force classification II.1).

42 **Setting:** A Center for Advanced Endoscopic Gynecologic Surgery from January 2014 to
43 December 2016.

44 **Patients:** All women undergoing laparoscopic surgery and scheduled for segmental
45 resection for clinically suspected bowel endometriosis.

46 **Interventions:** In all women clinically suspected for bowel endometriosis, an ultrasound
47 scan was performed before surgery to detect and measure the 3 diameters of bowel
48 endometriotic lesions. These diameters were compared with those obtained by direct
49 measurement on the fresh specimen. Sensitivity and specificity values of ultrasound
50 evaluation were calculated, with 95% confidence intervals (CIs).

51 **Measurements and Main Results:** The sensitivity and specificity of
52 transvaginal/transabdominal ultrasound , in the 328 patients of this study were 100% when
53 rectal endometriotic lesions were investigated. The specificity was 100% while the sensitivity
54 decreased to 91.4% when sigmoid lesions were investigated. Bowel muscularis infiltration
55 was histologically confirmed in all cases (284/284; 100%) where endometriotic lesions were
56 sonographically detected. All missed sigmoid lesions (12/296) were at a distance of >25 cm
57 from the anal verge. Mean diameters of endometriotic nodules calculated by ultrasound
58 evaluation and by direct measurement on fresh specimen were 43.19×19.87×10.79 mm and

59 42.76×19.64×10.62 mm respectively, without statistically significant differences between
60 methods used.

61 **Conclusion:** In conclusion, we believe that ultrasonography can be considered an accurate
62 diagnostic technique for the evaluation of deep infiltrating bowel endometriosis when
63 performed by a dedicated experienced sonographer in the setting of a specialized center .

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68 INTRODUCTION

69 Deep infiltrating endometriosis (DIE) is defined as an endometriotic lesion infiltrating the
70 peritoneum and penetrating into the retroperitoneal space or the wall of the pelvic organs to
71 a depth of at least 5 mm [1]. Many of the anterior and posterior compartment of the pelvis
72 can be involved [2–4]. The most common site of extragenital endometriosis is the intestinal
73 tract, which is involved in 3-37% of cases of DIE [5–7]. Bowel infiltration is defined as
74 endometriosis invading the muscularis, lesions limited to the serosa are superficial disease
75 [2,8]. Bowel endometriosis is most frequently found in the rectosigmoid junction and rectum
76 (65.7%), the sigmoid colon (17.4%), the caecum and ileo-caecal junction (4.1%), the
77 appendix (6.4%) and the small bowel (4.7%) [9].

78 Although clinical suspicion increases with experience and awareness, the vast majority of
79 deep endometriotic lesions cannot be diagnosed by clinical examination alone [10]. Deep
80 endometriosis should be suspected in all women complaining of dysmenorrhea, deep
81 dyspareunia, severe chronic pain, dyschezia and bowel symptoms as constipation/diarrhea,
82 which is the most important sign of deep infiltrating bowel endometriosis. Some women,
83 however, are asymptomatic. In women suspected of having bowel endometriosis imaging
84 can confirm the presence and extent of the disease [11–13]. The reported sensitivities and
85 specificities of transvaginal ultrasonography to diagnose deep bowel endometriosis are
86 variable, between higher than 85% and up to 100% . [13–15].

87 The accuracy of US in predicting diameters of bowel endometriosis is not known.

88 The aim of this study therefore was to assess the accuracy of the dimensions of bowel
89 endometriosis predicted by ultrasound in comparison with those measured after surgery.

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92 **METHODS**

93 STUDY DESIGN - All women aged between 18 and 45 years undergoing laparoscopic
94 surgery and scheduled for segmental bowel resection in Malzoni Clinic, Center for
95 Advanced Endoscopic Gynecological Surgery (Avellino, Italy) between January 2014 and
96 December 2016 with an ultrasound evaluation performed by ADG less than 1 month before
97 surgery were included in this study.

98 Women were clinically suspected of having bowel endometriosis, based on their history of
99 cyclic and/or chronic pelvic pain and/or bowel symptoms and/or clinical examination (DIE
100 bowel nodule suspicion at pelvic manual exploration). When not responsive or with
101 contraindications to long term hormonal medical therapy, they were scheduled for
102 laparoscopic surgery with bowel segmental resection if needed.

103 Surgeon's decision to do a bowel segmental resection was based on the intraoperative
104 detection of the bowel infiltrating lesion(s) and upon estimated difficulty of shaving or
105 performing nodulectomy due to diameters of the nodule(s) itself.

106 As preoperative exams they underwent a transvaginal/ transabdominal US scan and some
107 of them an MRI (in case multifocal/multicentric bowel involvement at US evaluation);
108 patients complaining of rectal bleeding underwent colonoscopy in order to exclude bowel
109 malignancies and/or primitive inflammatory bowel diseases.

110 Symptoms were recorded on a 1-10 degrees Visual Analogic Scale (VAS) with value of 1
111 corresponding to minimal pain and 10 to very severe pain.

112 Exclusion criteria were: a past and/or current gynaecological malignancy; the absence of
113 symptoms and/or non-surgical management; a duration between ultrasound evaluation and
114 surgery greater than one month; US scans performed by operators other than
115 ADG or diagnosis exclusively performed by other imaging techniques (MRI).

116 The study was approved by our Institutional Review Board and all patients signed an
117 informed consent upon inclusion, confirming that the results of examination and/or biological
118 material could be used for research purposes.

119 ULTRASOUND SCANNING TECHNIQUE- Ultrasound evaluations in this study were
120 performed by one investigator (A.D.G.), with extensive experience in gynaecological US
121 scanning , especially for deep infiltrating endometriosis (>2000 scans only in this specific
122 field prior to the onset of the study)

123 The scans were performed with a GE E6 ultrasound machine (GE Healthcare, Zipf, Austria),
124 using a wideband 5–9 MHz endovaginal and 4–8 MHz abdominal transducers. A glycerol
125 micro enema (6,75 g glycerol solution for rectal administration) was given a few hours
126 before sonographic evaluation without other bowel preparation.

127 The ultrasound examination was performed irrespective of the phase of the menstrual cycle
128 or the intake of hormonal medical therapy.

129 Uterus, adnexa and all potential locations for DIE in the anterior (bladder) or posterior
130 compartment (vagina, recto-vaginal septum, torus and uterosacral ligaments, parametria and
131 ureters, rectum and recto-sigmoid junction) were examined. Ultrasound examination was
132 always completed with transabdominal evaluation for kidneys, diaphragm and bilateral iliac
133 fossa (in order to explore caecum/appendix/terminal ileum and descending colon). Trans-
134 rectal evaluation was occasionally performed only when vaginal endometriotic lesions were
135 suspected. In addition to bowel infiltrating lesions, all locations of pelvic endometriosis were
136 systematically evaluated and recorded but were beyond the scope of this study.

137 The standard ultrasound technique for the assessment of deep infiltrating bowel
138 endometriosis used in our institution was performed as follows: with the tip introduced into
139 the posterior vaginal fornix, the probe was moved upwards to achieve full visualization of the
140 rectosigmoid wall layers. Bowel muscular layer was identified as a hypoechogenic thin line in
141 the midsagittal plane adjacent to a hyperechogenic layer representing the rectosigmoid
142 submucosa (Fig.1)[16].

143 Rotation of the probe and up and down movements were necessary to extend the
144 visualization of the rectosigmoid as far as technically feasible. We usually started from the
145 caudal part of the rectum, at the level of the posterior vaginal fornix, proceeding upwards
146 and following rectosigmoid curves, up to recto-sigmoid junction and proximal sigmoid,

147 approximately at the level of uterine fundus and above the left adnexa (25-30 cm from the
148 anal verge).

149 Bowel endometriotic infiltrating nodule was identifiable as the presence of a regular or
150 irregular hypoechogenic mass, with poor or no vascularization, distorting and replacing the
151 normal appearance of the muscular layer of the recto-sigmoid wall [16,17].

152 The hypoechogenic area represents infiltration and hypertrophy of the rectosigmoid muscle
153 (normal thickness 1.5-2.5 mm) (Fig.2a).

154 According to recent published criteria, each bowel infiltrating lesion (as all other pelvic DIE
155 lesions) was measured systematically in three orthogonal planes, to obtain the length (mid-
156 sagittal measurement), thickness (anteroposterior -AP measurement) and transverse
157 diameter [17] (Fig 2b and 3a).

158 In our experience, mid-sagittal and transversal diameter are measured with curved lines
159 following infiltrated muscular layer axis in order to avoid underestimation of the lesion (Fig 2b
160 and 3a).

161 Moreover, in transversal section the percentage of circumference involved was calculated
162 automatically (Fig 3b).

163 Nodule infiltration depth at the level of the muscular layer was measured as anteroposterior
164 diameter on the mid sagittal plane (Fig 4). Often bowel nodules are contiguous to infiltrating
165 lesion of adjacent structures (retro-cervical area, vagina, RVS) but they appear slightly more
166 hypoechoic than the latter. It is important to exclude from the AP diameter of the bowel
167 nodule any extra-intestinal component in order to avoid overestimation of the true thickness
168 of the muscularis lesion itself (Fig 5).

169 Moreover, stenosis can be evaluated comparing lumen width at the level of deepest
170 infiltration with adjacent segment free of disease.

171 The distance between the lowest limit of the bowel nodule and the anal verge was always
172 evaluated by retracting the probe down to the perineal plane and measuring the resulting
173 distance (splitting in dual image for nodules not so low as to be included in a single

174 screenshot). Endometriotic nodules are considered as rectal when detected within 12 cm
175 from the anal verge, otherwise as sigmoid if over 12 cm from the anal verge.

176 In cases of nodules infiltrating the rectum-sigmoidal junction, the lesion was considered
177 rectum or sigmoid according to localization of the largest part of the nodule itself.

178 In cases of multicentric/multifocal bowel involvement (multiple nodules, 12% of cases) only
179 the biggest nodule was considered for analysis.

180 Often the bowel is so retracted that even the upper segments can adhere to the posterior
181 wall of the uterus, with complete disruption of normal anatomy. Clear identification of normal,
182 thin muscular layer allows measurement of mid sagittal diameter (length) of healthy/normal
183 bowel segment below the infiltrating nodule with a curved line following muscular layer axis
184 and its distance from the anal verge (Fig 6).

185 It is important to be aware that sometimes the retraction within rectosigmoid DIE lesions can
186 result in an underestimation of the true length of the lesion. This has been described as the
187 'mushroom cap' sign on MRI and can also be noted on TVS[17].

188 Special attention was given to the pain felt by the patient when evaluating all painful sites
189 evoked by a gentle pressure of the probe ("tenderness-guided" ultrasonography) [18,19]

190 SURGICAL PROCEDURES AND SPECIMEN EVALUATION- Surgical procedures, when
191 severe endometriosis with bowel and/or ureteral involvement is suspected, are performed by
192 an expert surgeon (M.M.) with extensive experience in laparoscopic pelvic surgery. All
193 procedures, including colorectal and urological ones were performed by him and his surgical
194 team, with no need for further multidisciplinary approach; surgical techniques were
195 extensively described previously [20].

196 After surgery, all measurements were performed on the fresh specimen by the surgeon
197 (M.M.) using a flexible ruler. The length of the resected bowel segment, the diameters of the
198 nodule and its thickness of infiltration in the muscular layer were assessed.

199 Deep endometriosis was confirmed in all women by the presence of endometrial glands and
200 stroma at histopathological examination of resected bowel segments.

201 STATISTIC DATA ANALYSIS- According surgical confirmation of presence/absence of
202 sonographically identified bowel nodules, sensitivity and specificity were calculated with
203 95% confidence intervals (CIs).

204 Statistical evaluation was performed with SPSS version 19.0 (SPSS, Inc., Chicago, Illinois).
205 A p-value of <0.05 was considered statistically significant.

206 The 3 diameters of each nodule, measured by ultrasound and following surgery, were
207 evaluated by Pearson regression analysis. Mean diameters , expressed as mean \pm
208 standard deviation (SD), were evaluated with Student t-test.

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211 **RESULTS**

212 Deep infiltrating bowel endometriosis was suspected in 1,005 patients during the observation
213 period. Bowel nodule resection by shaving was performed in 633 patients. Bowel segmental
214 resection was scheduled in 372 patients of whom 328 met inclusion criteria. Bowel
215 segmental resection was performed in 296 patients, who met inclusion criteria. Clinical
216 features of patients enrolled in the present study are reported in Table 1.

217 Ultrasound pelvic investigation took between 30 and 45 minutes. All 3 diameters, -
218 longitudinal, antero-posterior and transverse-, of endometriotic nodules measured by
219 ultrasound, accurately predicted diameters measured on the fresh specimen (Table 2, Fig
220 7). This is obvious from their correlations and the narrow 95% confidence limits .

221 All rectal nodules had been diagnosed by ultrasound which is a sensitivity of 100% ;sigmoid
222 lesions were diagnosed in 128/140 cases which is a sensitivity of 91.4 %. Results are
223 reported in table 3. The accuracy of the US evaluation was 0.93.

224 All undetected sigmoid lesions (12/296) were at a distance >25 cm from the anal verge; all of
225 them were associated with at least one other bowel deep endometriotic lesion detected
226 preoperatively.

227 Among all 328 patients scheduled for bowel resection and undergoing LPS surgery, 32
228 were intraoperatively judged negative for bowel infiltration, thus not resected (other non-
229 intestinal deep endometriotic lesions were removed, but out of the aims of this study); all
230 these patients were negative for bowel infiltrating lesions at the time of US preoperative
231 evaluation.

232 Muscularis infiltration was predicted by ultrasound in 284/296 women and was histologically
233 confirmed in all of them (100%) after surgery.

234 For mucosal involvement sensitivity was 50% while specificity was 100%.

235

236

237 **DISCUSSION**

238 The main challenges of imaging for endometriosis are the detection of non-ovarian disease
239 and the evaluation of the extension of the disease into pelvic structures[1].

240 Systematic evaluation of DIE abdomino-pelvic extension includes details of the anatomical
241 localizations, size and number of DIE nodules and, concerning bowel lesions, depth of
242 infiltration of nodules with opportunity to estimate wall deformation/degree of stenosis of the
243 bowel lumen and the distance from the anal verge (lower lesions are associated with higher
244 risk of complications, [19]).

245 This information is important to plan surgical procedures, to choose the appropriate
246 multidisciplinary surgical team if not available a pelvic surgeon (who is able to perform
247 colorectal/urologic/neuropelvicologic procedures alone) and to accurately counsel the
248 patient[1].

249 Because of its high diffusion and relatively low cost and discomfort, transvaginal
250 ultrasonography is considered as the first line procedure, even if controversial results
251 regarding sensitivity and specificity in the diagnosis of deep bowel endometriosis are
252 recognized[13].

253 The present study shows that high specificity and sensitivity can be obtained when a skilled
254 ultrasonographer performs the scans. The lack of a difference between the direct
255 measurement on fresh specimen and the ultrasound evaluation showed that the latter
256 method is extremely accurate for quantifying features of bowel endometriotic nodules.

257 The main strengths of the present study were that we included a large number of patients,
258 that all ultrasound scans were performed in the same center by the same sonographer and
259 all suspicious ultrasound lesions were confirmed on the surgical specimen by histologic
260 examination. However, this study was limited by the fact that both surgeons and the
261 sonographer knew the history and clinical symptoms of the patient.

262 Moreover, up to our knowledge, this is the first study assessing predictivity of non-contrast
263 enhanced US evaluation on all bowel nodules diameters (evaluated on the standard three
264 orthogonal planes).

265 To reach this level, a dedicated specialist training seems to be an essential step.

266 The main strengths of the present study were that we included a large number of patients,
267 that all ultrasound scans were performed in the same center by the same sonographer and
268 all suspicious ultrasound lesions were confirmed on the surgical specimen by histologic
269 examination. However, this study was limited by the fact that both surgeons and the
270 sonographer knew the history and clinical symptoms of the patient.

271 Moreover, up to our knowledge, this is the first study assessing predictivity of non-contrast
272 enhanced US evaluation on all bowel nodules diameters (evaluated on the standard three
273 orthogonal planes).

274 Sensitivity and specificity in this study refer to nodules detected or undetected at LPS
275 evaluation and scheduled for bowel resection, thus being for sure larger nodules.

276 Our main aim was to evaluate the accuracy of us evaluation on nodules' diameters more
277 than the detection rate of all bowel nodules, for this reason we didn't include all the small
278 nodules undergoing nodulectomy procedures : there our detection rate it's the same (data
279 not shown), but not specified because out of the aims of the present study.

280 We only included patients scheduled for bowel resection because we wanted an entire
281 surgical specimen to be compared with US findings. We couldn't do it on shaved nodules
282 because, for the technique itself , the specimen would be necessarily smaller than
283 sonographically measured (a minimal fibrosis is always left in place in that cases), and
284 sometimes fragmented at histopathological evaluation; it could have be done on specimens
285 from discoid resection, but we didn't performed any of such procedure in that period: we
286 usually only do it for nodules less than 2/2.5 cm in length but with deep infiltration of the
287 muscularis, quite rare in our experience, and we didn't found such lesions in our case series
288 .

289 Close cooperation and dialogue between the surgeon and imaging specialist are crucial. At
290 the time of surgery the verification of the sonographically suspected lesions is a key stage to
291 improve detection and definition of deep infiltrating bowel endometriosis. We would like to

292 emphasize that all missed sigmoid lesions (12/296) were at a considerable distance from the
293 anal verge (>25 cm), not presumably within the ultrasound field.

294 Findings observed in the present study have been corroborated by recent studies. In a
295 recent meta-analysis, TVS, either with or without bowel preparation, was found to be an
296 accurate predictor of rectosigmoid DIE[14]. Variation and controversy regarding results from
297 undertaking this first-line procedure may be attributed to the different levels of expertise of
298 sonographers.

299 TVS was observed to be a highly accurate and reproducible method for non-invasive
300 diagnosis of DIE in well-trained staff[12,13]. Furthermore, Ros and colleagues demonstrated
301 that transvaginal ultrasound (TVUS) with bowel preparation has a higher accuracy than
302 TVUS without bowel preparation[15]. However, this study was limited by the small sample
303 size (N=40) and tissue specimens were not compared to US measurements. Other
304 procedures are often employed in other centers for the detection of deep infiltrating bowel
305 endometriosis. Magnetic resonance imaging may be considered technically less operator
306 dependent and can also provide information about lesions at the level of the sigmoid, but
307 specific expertise of radiologists in the evaluation/interpretation of resulting images is crucial;
308 the conclusions reached are similar to those of ultrasonographic examination [20–24].

309 In our institute, MRI is recommended as a second-line integrative procedure in the following
310 cases: multicentric endometriotic infiltration of the rectosigmoid segment evaluable by TVS
311 (≥ 2 detectable nodules in the bowel tract up to 25-30 cm from the anal verge); strong
312 clinical suspicion of bowel endometriotic infiltration with completely negative TVS evaluation
313 of the rectosigmoid segment indicated above; clinical and/or TVS suspicion of right colon
314 segments (caecum, appendix, ileo-cecal valve) not completely evaluable by
315 ultrasonographic combined TV/TA approach.

316 Our data suggest that transvaginal ultrasonography has good sensitivity and high specificity
317 in the evaluation of bowel endometriotic nodules when performed by a dedicated
318 sonographer with extensive training and expertise. According to some authors, in cases of

319 suspected bowel stenosis based on symptoms and on TVS findings, a barium enema could
320 be useful to decide for segmental resection[1].

321 Colonoscopy is almost invariably negative. Only in rare cases of very large nodules with a
322 severe bowel stenosis and/or mucosal/submucosal infiltration colonoscopy may be judged
323 positive. The prevalence is estimated to be <5 in 1,000 cases[1]. In our practice, we
324 abandoned colonoscopy and barium enema, because these procedures were not
325 considered to provide additional information that could influence the decision of whether to
326 perform surgery. However, we believe that colonoscopy is always indicated in patients with
327 rectal bleeding and/or lesion with atypical morphology/vascularization (e.g. atypical grey
328 scale features different from the usual ones previously described and extensive infiltration of
329 mucosal layer and/or increased Doppler vascularization) requiring differential diagnosis with
330 bowel cancer.

331 According to available data, TVS has low accuracy in diagnosing the infiltration of the
332 mucosal layer[10]. Transrectal ultrasound, which is a valuable tool for detecting rectal
333 endometriosis as endometriotic infiltration of the muscularis layer, is less accurate in
334 assessing submucosal/mucosal layer involvement[25–27]. In contrast, our data showed high
335 specificity and high positive predictive value in excluding the involvement of the mucosal
336 layer. However, this assessment has little significance because it is a very rare event.

337 Some authors reported that the mean time for the performance of the ultrasound technique
338 was 20 minutes in cases where the presence of deep endometriosis was suspected, less if
339 not suspected[28]. Furthermore, standardized evaluation of painful symptoms is useful for
340 screening women who may require a more detailed examination[29]. In our experience, all
341 patients with clinical suspicion of endometriosis undergo systematic ultrasound evaluation of
342 all pelvic compartments and not just those suspected for DIE, in order to obtain a complete
343 mapping of all affected areas.

344 In conclusion, we believe that ultrasonography can be considered an accurate diagnostic
345 technique for the evaluation of deep infiltrating bowel endometriosis when performed by a
346 dedicated experienced sonographer in the setting of a specialized center .

347 Moreover, surgery is not indicated in all patients with deep endometriosis but when surgery
348 is chosen, the most appropriate surgical procedure should be performed with the goal to
349 achieve the best patient outcome. Concerning bowel infiltrating nodules, when to perform
350 segmental bowel resection instead of nodulectomy is still a matter of debate. It has been
351 debated too whether and when imaging can predict whether a bowel resection has to be
352 performed or whether the decision should be taken during surgery.

353 According a recent experts' consensus paper [30] some criteria for bowel segmental
354 resection were highlighted: large nodules (>3 cm) and/or involvement of inner layer of the
355 muscularis or deeper and/or multiple nodules.

356 Our high accuracy of the ultrasonographic measurement of the diameters of a deep
357 endometriosis nodule infiltrating the bowel before surgery strongly suggests that these
358 measurements can be used to decide about the most appropriate surgical procedure.

359

360

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367 **CONFLICT OF INTEREST**

368 All authors declare no conflicts of interest.

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477 **FIGURE LEGENDS**

478 Figure 1. Normal rectosigmoid wall layers: M , muscularis (hypoechoic); SM , submucosa
479 (hyperechoic); m, mucosa (hyperechoic); the thin hypoechoic layer between submucosa
480 and mucosa can be identified as the muscularis mucosae.

481

482 Figure 2. A) Normal muscular (white arrow); endometriotic infiltration with resulting thickened
483 muscular layer (yellow arrow) hyperechoic submucosal layer (red arrow) with signs of
484 infiltration (hypoechoic spots). B) mid-sagittal nodule diameter (length) measured with a
485 curved line (yellow) following muscular layer axis; hyperechoic submucosal layer (white
486 arrows) with signs of infiltration (hypoechoic spots).

487

488 Figure 3. a) transversal nodule diameter measured with a curved line (yellow) following
489 muscular layer axis; b) percentage of involved circumference.

490

491 Figure 4. Nodule infiltration depth at level of muscular layer measured as anteroposterior
492 diameter of the lesion on the mid sagittal plane.

493

494 Figure 5. Correct measurement of bowel lesion depth of infiltration with exclusion of less
495 hypoechoic outer endometriotic infiltrating tissue (RVS nodule in the image shown).

496

497 Figure 6. Mid sagittal diameter (length) of healthy/normal muscular layer below the
498 infiltrating nodule measured with a curvy line (yellow) following muscular layer axis

499

500 Figure 7. Distribution of nodules according to longitudinal (a), AP (b) and transverse (c)
501 diameter. The association between US and specimen nodule diameter is represented by
502 scatter plots (d-f ; please note: the software automatically couples very close values so on
503 the grid only less than one third of dots are shown even if all the 284 coupled values are
504 included in the data sets). Regression coefficient and p-values are indicated. Data presented

505 as mm and %. Confidence intervals (CI) indicated by dashed lines (---), for transversal
506 diameters (fig. 7f so narrow to be not shown).

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509 **Table 1. Anamnestic and clinical features of patients.**

Anamnestic Data	Mean±SD	
Age (years)	35.5±4.7	
BMI (Kg/M ²)	21.9±3.0	
Symptoms	Number (%) of 296 patients with Bowel DIE	VAS Score Mean±SD
Dysmenorrhea	281 (95)	8.8±1.6
Dyspareunia	225 (76)	7.0±3.0
Dyschezia	240 (81)	7.7±2.6
Constipation	219 (74)	
Bowel Occlusion	18 (6)	
Diarrhea	53 (18)	
Rectal Bleeding	62 (21)	
Infertility	Number (%) of 296 patients with bowel DIE	
Primary	71 (24)	
Secondary	15 (5)	
Previous Surgery for endometriosis	Number (%) of 296 patients with bowel DIE	
Total	249 (84)	
≥2 surgery	124 (42)	

510

511

512

513 **Table 2. Similar (NS) diameters of endometriotic nodules as measured by Ultrasound**
514 **and on the surgical specimen. (Mean and SD).**

Measure	Ultrasound evaluation	Direct measurement on fresh specimen
Longitudinal Diameter (mm)	43.19±10.33	42.76±9.86
Transverse Diameter (mm)	19.87±6.51	19.64±6.39
Infiltration thickness (mm)	10.79±2.85	10.62±2.64

515

516

517 **Table 3. Diagnostic accuracy for deep infiltrating bowel endometriotic lesion.**

Location	TP	FP	TN	FN	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV % (95% CI)	NPV % (95% CI)
Sigmoid	128	0	24	12	91.4 (85.8–95.1)	100 (97.1–100)	100 (97.1–100)	66.7 (58.8–73.7)
Rectum	156	0	8	0	100 (97.1–100)	100 (97.1–100)	100 (97.1–100)	100 (97.1–100)
Bowel muscular layer infiltration >5 mm	284	0	0	0	100 (98.3–100)	-	100 (98.3–100)	-
Bowel mucosal layer involvement	2	0	280	2	50 (44.1–55.9)	100 (98.3–100)	100 (98.3–100)	99.3 (97.2–99.9)

518 TP= True Positive; FP = False Positive; TN = True Negative; FN = False Negative; CI = ConfidenceInterval; PPV = Positive Predictive Value;

519 NPV = Negative Predictive Value.

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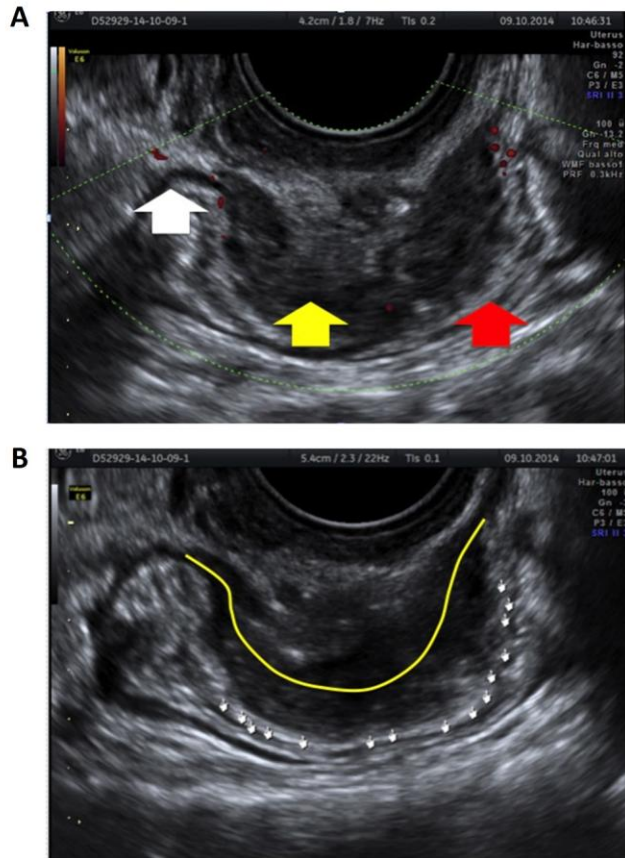


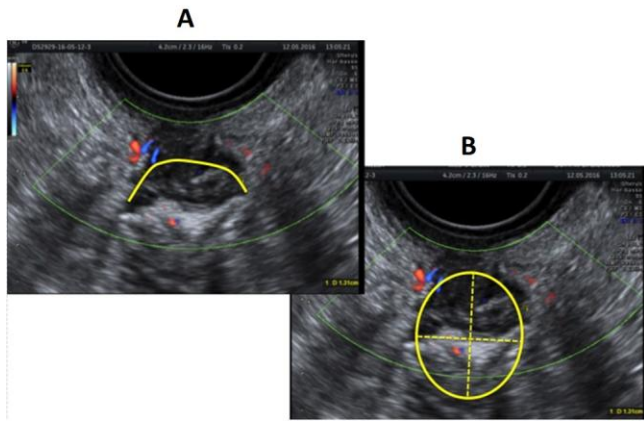
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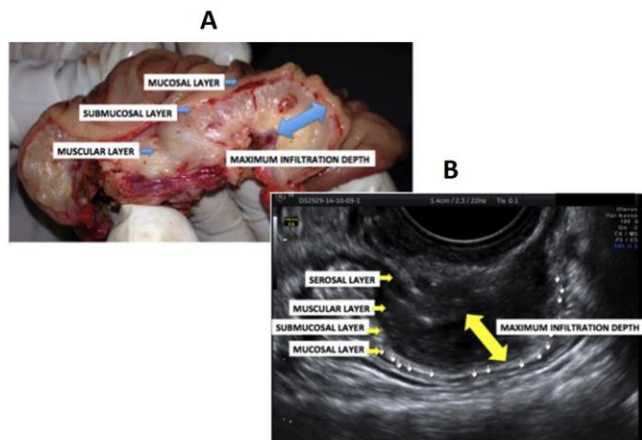


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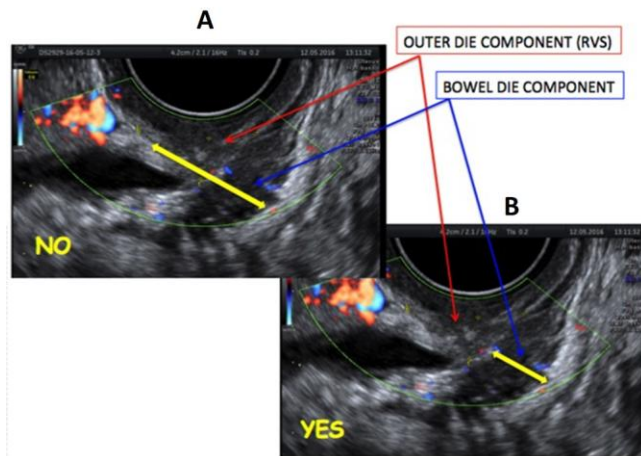


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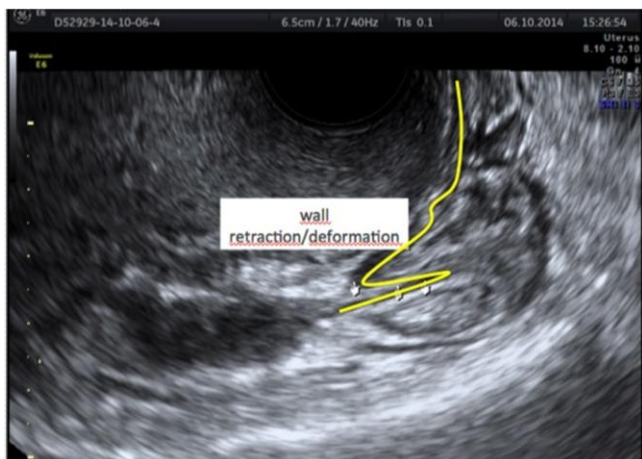


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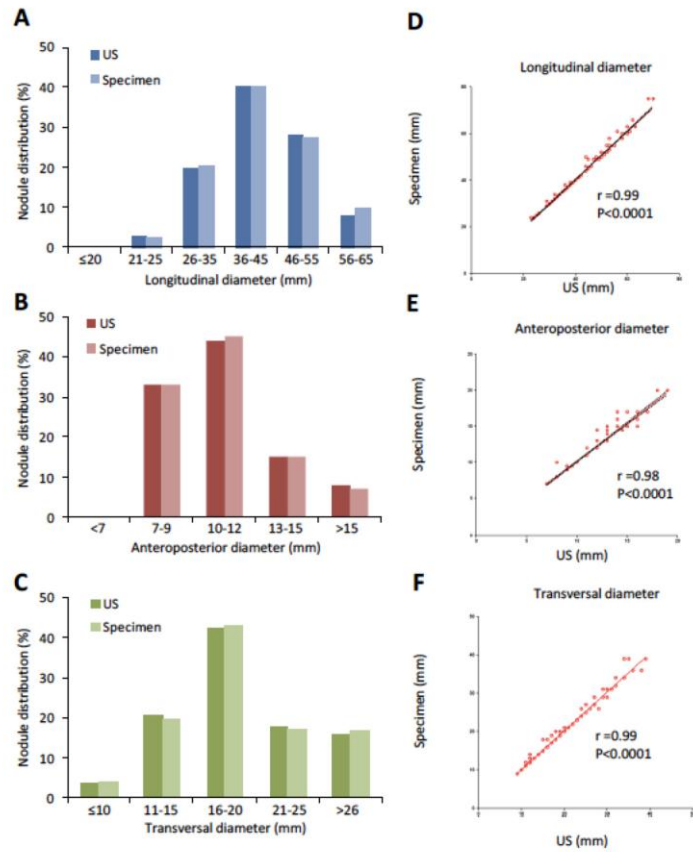


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543 FIG7.tiff