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Identification of inorganic particles resulting from degradation of ESSURE® implants: Study of 10 cases

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A B S T R A C T

Objective: Approximately 750,000 women worldwide have undergone ESSURE hysteroscopic sterilization since 2002. In 2015, an increase in adverse effects was noted, with gynaecological and systemic symptoms reported. Scanning electron microscopy (SEM) analysis of fallopian tube and uterine horn tissues and implants, after hysterectomy or salpingectomy, revealed the presence of inorganic particles resulting from implant degradation.

Study design: Ten patients (age 42–53 years) were included in this study. Of these, eight patients had undergone hysterectomy and two patients had undergone salpingectomy. Mean exposure time was 85.5 months (standard deviation 26.8 months, range 34–105 months). Mineralogical analyses were performed on 13 tissue biopsies and four implants by SEM coupled with energy dispersive x-ray spectrometry.

Results: In five of the 10 patients, tin particles were observed in fallopian tube or uterine horn tissues with inflammatory cell reactions. In the other five cases, iron, chromium, nickel or platinum particles were observed. For implants, major deterioration of the weld zone was observed with either destroyed appearance or the presence of an organic coating containing numerous particles.

Discussion and conclusion: Analysis of the preclinical studies performed by the manufacturer suggests that degradation of the tin weld plays a major role in these adverse events, with increasing leaching and corrosion between 3 and 6 months for an intratubal insert that si designed to remain in an woman's body for her entire life. For patients with gynaecological symptoms (e.g. pain, metrorragies) needing explantation, these findings raise the question of a causal relationship between tin particles from implant degradation and the inflammatory tissue response. For patients with systemic symptoms (e.g. blurred vision, headache, asthenia, myalgia), the hypothesis that these symptoms may be related to the formation of organotin (chemical compounds based on tin with hydrocarbon substituents) in the body has yet to be proven. Tin levels in blood have to be measured before and after explantation. To the authors' knowledge, this is the first study to report significant degradation of the ESSURE implant weld, evidenced by the detection of tin particles in the uterine tissue of patients and comparison of the welding zone between unused and used implants.

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Introduction

In 2002, a novel hysteroscopic sterilization device reached the market after review and premarketing approval by the US Food and Drug Administration (FDA): the ESSURE System (initially marketed by Conceptus, a start-up later bought by Bayer Healthcare, Whippany, NJ, USA, in 2013). With ESSURE, a coil designed to induce fibrosis and tubal occlusion is placed into each fallopian tube to prevent fertilization. Three months after placement of the coil, women undergo hysterosalpingography to confirm device placement and occlusion before discontinuing the use of other contraceptive methods.

The device offers clear advantages, namely the absence of incision and the ability to insert the device without general

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anaesthesia and in an ambulatory setting. The nickel/titanium-based ESSURE device is inserted transvaginally into the fallopian tubes to induce a moderate inflammatory response, resulting in fibrosis and subsequent tubal occlusion. The device consists of a stainless steel inner coil, and an outer coil made from Nitinol and polyethylene terephtalate (PET Dacron). PET fibres have been shown to produce an immediate inflammatory response characterized by macrophages, fibroblasts, foreign body giant cells and plasma cells, creating a chronic inflammatory response with extensive fibrosis and fallopian tube occlusion [1,2]. The outer coil and inner coil are linked by a tin solder.

Some cases of nickel allergy have been reported [3–5]. Pain [6–8], migration [9–11] and contraceptive failure [12] have also been noted, but studies comparing hysteroscopic sterilization with laparoscopic sterilization found in favour of micro-inserts [13–16].

In 2015, there was a sudden increase in the number of patient-reported adverse effects related to ESSURE [1,17]. The driving forces for the sudden increase in adverse event reporting remain unclear. The role of pharmacovigilance through online community outreach and mobile reporting applications may have played a role [18]. Submissions from 1349 women (average age 34 years) were analysed, and fatigue, back pain, pelvic pain, mental impairments, loss of libido, allergy to metals and alopecia were among the most common complaints. Based on the reported number of products sold, approximately 750,000 women worldwide have undergone ESSURE hysteroscopic sterilization [17], with France being the largest market among European countries (approximately 180,000 women). Conceptus Inc., which worked on the preclinical development of ESSURE, was a US start-up later bought by Bayer [1]. At least two associations and a web-driven collective have been created recently in France around the safety problems encountered by more than 2000 women, and there is a tendency towards salpingectomy or hysterectomy treatment of many affected women.

The FDA report in September 2019 about biological responses to metal implants includes a discussion about ESSURE implants [19], principally centred on nickel hypersensitivity as a proposed explanation for ESSURE intolerance [3–5].

This study reports 10 cases with mineralogical analysis by scanning electron microscopy (SEM) coupled with energy-dispersive x-ray (EDX) spectroscopy of implants and/or fallopian tubes and uterine horns, and discusses the evidence of tin weld degradation suggested by the analyses.

Patients and methods

Patient population

Ten patients, aged 42–53 years (average 48 years), who requested removal of their ESSURE implant and underwent salpingectomy or hysterectomy were included in this study. Eight patients underwent total hysterectomy and two patients underwent salpingectomy after a mean exposure time of 85.5 months (standard deviation 26.8 months, range 34–105 months). A mineralogical analysis was performed on 13 biopsies (eight fallopian tubes, five uterine horns) and four implants. Table 1 describes the patient population and samples analysed. For Patients 1, 5, 6 and 7, both their biopsy and implant were analysed. Each patient gave their informed consent for study of their fallopian tube or uterine horn tissue by SEM-EDX and, if possible, the implant, and publication of the results.

Preparation of biopsies

Two 5-µm-thick histological sections were made from a paraffin block. HES colouring was applied to the first section, which was placed on an optical slide. The second section was placed on a double-sided adhesive carbon disc (diameter 25 mm) after addition of a mixture of water and albumin glycerin. The disc was subsequently placed on a hot plate at 38 °C until the liquid evaporated.

Preparation of implants

After receiving the ESSURE implant in a dry container from the pathology laboratory, the implant was dipped in a fixator (Roti-Histofix 4%) for 24 h. The implant was subsequently dried under a chemical hood for 12 h and separated using scissors. The part containing the weld was placed on a double-sided adhesive carbon disc (diameter 25 mm).

Scanning electron microscopy analysis

Two unused implants were compared with implants removed surgically from patients. The unused implants were placed on carbon tape and analysed by SEM (Zeiss Supra 55 V P with EDS Oxford Aztec-DDI detector X-Max), operating at 5 kV for secondary electron observations and at 20 kV for backscattered electron observations and EDX analyses. The observation parameters for this work were: working distance 9 mm, high pressure and magnification x228. The histological sections and used implants were also analysed by SEM (JEOL JSM-6010LV Plus) coupled with EDX spectrometry (EDS Oxford Aztec-DDI detector X MAX^N 50). In order to compare the EDX spectra of the different particles, they were analysed under the same experimental conditions: backscattered electrons, intensity 20 kV, working distance 12 mm, spot size SS55, pressure 20 Pa and magnification x500. For the biopsies, each particle was classified into a family according to its chemical composition. The different families of particles identified during these analyses were as follows: endogenous particles (NaPSCa, NaSCa, SCa, NaP, NaClK, NaPSCaFe, PCaFe, PCaS, NaS, NaCl and Cl compounds); tin-based particles (SnAg, SnTi, SnNi, SnPt, SnPtTi, SnAuTi, SnTiCr and SnAgTi); silicon-based particles (aluminosilicates, SiMg, SiCa, SiO and SiAlMg); calcium-based particles (PCa,

Table 1
Description of the patient population and the different samples analysed.

Patient number	Age (years)	Biopsy	Implant	Time before removal (months)
1	49	Two fallopian tubes; two uterine horns	1	96
2	52	One fallopian tube		105
3	46	One uterine horn		35
4	52	One fallopian tube		79
5	45	One fallopian tube	1	59
6	45	One fallopian tube	1	60
7	42	One uterine horn	1	42
8	44	One uterine horn		34
9	53	One fallopian tube		101
10	53	One fallopian tube		75

CaO, CaMg and calcium compounds); steel (FeCrNi, FeCr and FeNi); iron compounds; titanium compounds; tungsten compounds; gold metal; aluminium metal; platinum metal; FeO; ZrPt; fluorine and SBa. The families labelled as compounds corresponded to particles containing multiple elements and in which the given element was present at more than 5 wt%. When several elements were above 5 wt%, either the heaviest element was taken into account, or a new family was added to the list if there were many particles of the same type.

Results

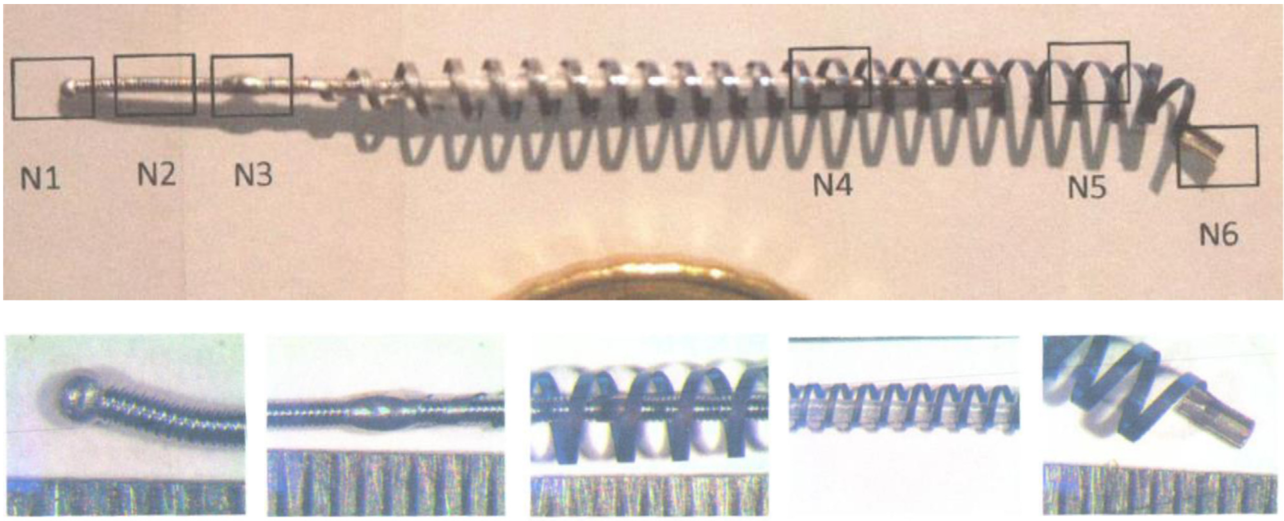
Elemental composition of unused implants

Fig. 1 shows the elemental composition of the different parts of an unused ESSURE implant. The ball and inner coil are made of steel (iron, chromium and nickel), the weld is made of tin and silver, the outer coil is made of nickel and titanium, and the ring of the inner coil and the end of the outer coil are mainly composed of platinum.

Results of mineralogical analysis of biopsies

Each histological section was observed by optical microscopy and then by electron microscopy. Table 2 describes the results of the mineralogical analysis of all biopsies.

Table 2 shows that tin-based particles were detected in Patients 1, 2, 7, 9 and 10. Other metallic particles, such as steel, gold metal, aluminium metal, platinum metal, FeO and ZrPt, were found in smaller proportions. Endogenous and calcium-based particles were found in almost all patients. In Patient 1, mineralogical analysis revealed the presence of a significant accumulation of particles on optical and electron microscopy (Fig. 2). On this fallopian tube biopsy (Sample 1A), a particle cluster >1 mm in diameter was observed.



N1 ball and N2 inner coil	N3 weld	N4 ring of the inner coil	N5 outer coil	N6 end of the outer coil
Fe 58% Cr 17% Ni 14.5% Mo 2.7% Mn 1.6% W 0.5%	Sn 48% Fe 21.6% Ni 7.3% Cr 6.2% Ti 1.3% Ag 0.95% Mo 0.9% Mn 0.6% W 0.2%	Pt 52.4% Fe 25.4% Cr 7.2% Ni 6.2% Ir 6.1% Mn 0.7% W 0.2%	Ni 55% Ti 29.5% Cr 0.23%	Pt 84.7% Ir 9.7%
Traces : Co, Cu, V, Sn, As, Hg, Sb, Mg	Traces : Cu, Co, V, Pb, Sb, Bi, Hg, As, Mg	Traces : Cu, Co, V, Pd, Rh, Mg, Sn, Hg, As, Au, Sb	Traces : Mg, Fe, W, Zn, Au, Mn, Hg, Sn, Co	Traces : Pd, Rh, Fe, Mg, W, Cu, Au, Zn, Bi, Co
Total N1 93.3% Total N2 95.8%	Total 87.1%	Total 99.5%	Total 84.8%	Total 94.4%

Fig. 1. Elemental composition of an unused ESSURE implant analysed by scanning electron microscopy coupled with energy-dispersive x-ray spectroscopy.

Table 2
Results of mineralogical analysis of the biopsies. Endo, endogenous particles; comp, compounds; ZrPt, zirconium + platinum; SBa, barium sulphate.

Patient number	Sample	Endo	Tin-based	Silicon-based	Calcium-based	Steels	Iron comp	Titanium comp	Tungsten comp	Gold metal	Aluminum metal	Platinum metal	Iron oxide	ZrPt	Fluorine	SBa
1A	Fallopian tube		119		12											
1B	Fallopian tube		45	5	102		2			1						1
1C	Uterin horn	2	1		19					1						
1D	Uterin horn		110	3	6	2		2								
2	Fallopian tube		55	1	2											
3	Uterin horn	47		3	3	1	1				5					
4	Fallopian tube	6		10	15	1			22						1	
5	Fallopian tube	5		2	2	9		3								
6	Fallopian tube	34			2						1	1	3			
7	Uterin horn	13	11		1			6	2					1		1
8	Uterin horn	36		17	37	1	7									
9	Fallopian tube	16	2	1	43			8								
10	Fallopian tube	6	45	8	14						2					

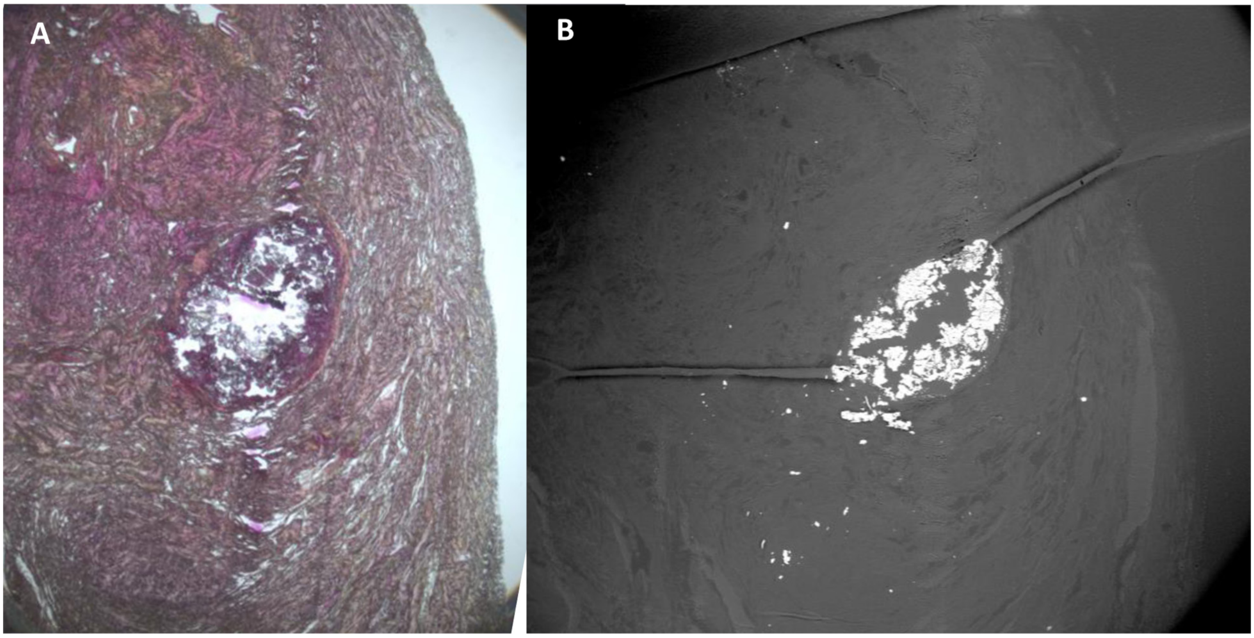


Fig. 2. Correlative observation in optical (A) and scanning electron microscopy (B) of a field of the histological section of the uterine tube of Patient 1 (Sample 1A) at original magnification x25 and x27.

Analysis of the particles present in this cluster showed that they were mainly composed of tin, with an elemental composition similar to the two spectra shown in Fig. 3.

In another field of this sample, tissue-integrated particles were observed in the wall of the fallopian tube (Fig. 4). In this region, all of the particles analysed were mainly composed of tin. Phosphorus comes from the phosphate buffer used to fix the tissue, and sulphur comes from paraffin.

For this patient, the pathology report mentions macrophagic granuloma and multinucleated giant cells associated with particles.

Results of mineralogical analysis of used implants

Table 3 describes the results of the mineralogical analysis performed on the implants.

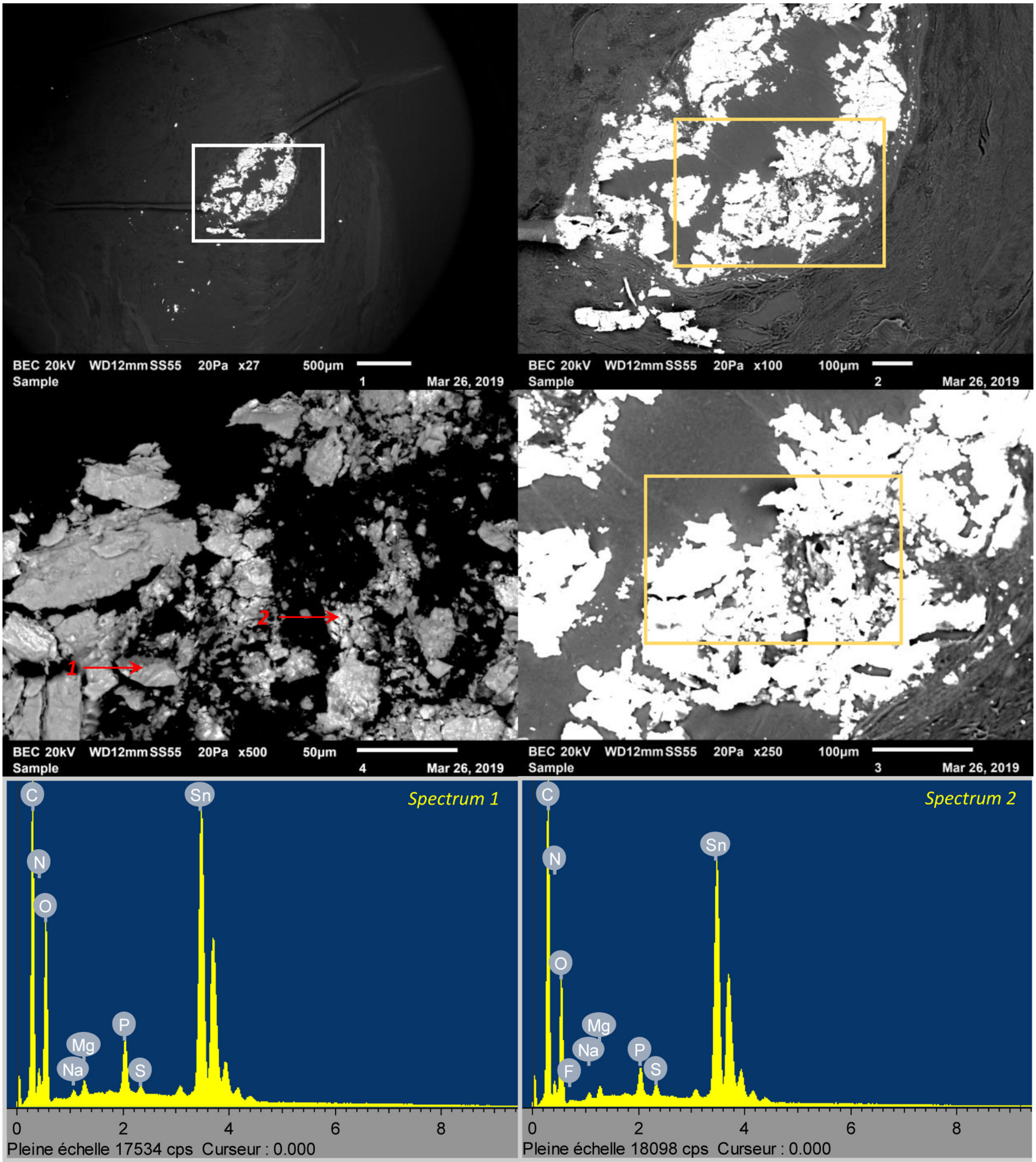


Fig. 3. Scanning electron microscope observation of a field of the histological section of the uterine tube of Patient 1 (Sample 1A) at original magnifications x27, x100, x250 and x500, and the spectrum of two tin particles.

If one excludes the nitrogen and oxygen elements resulting from the analysis conditions (degraded vacuum), tin represented a major proportion (19–46 %) of a large number of particles analysed from the four implants. With the exception of Patient 5, an important proportion of silver was found in many particles. Titanium, chromium, iron and nickel were found in variable proportions depending on the sample analysed, while sodium, magnesium, aluminium, silicon, phosphorus, sulphur, chlorine, potassium and calcium were found in smaller proportions (<5 wt%).

Fig. 5 shows an unused implant and the implants of Patients 1 and 7 observed by SEM at the weld zone. On the unused implant, the weld, the outer coil and the inner coil are clearly visible. The implant from Patient 1 shows dark and light areas. The dark areas appear to be mainly composed of organic compounds, and the light areas are mainly composed of tin, sometimes associated with

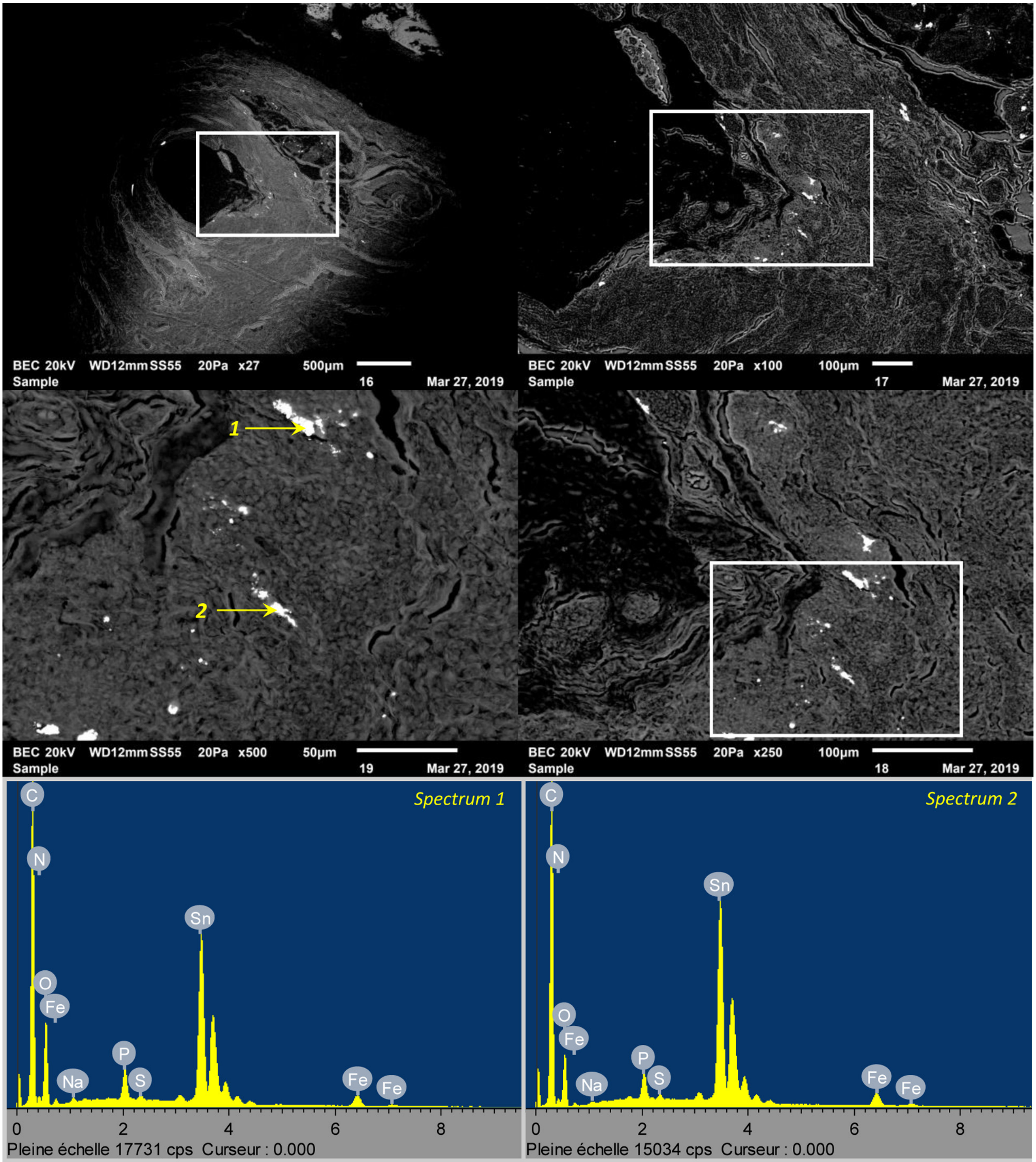


Fig. 4. Scanning electron microscope observation of a field of the histological section of the uterine tube of Patient 1 at original magnifications x27, x100, x250 and x500, and the spectrum of two tin particles.

silver. The weld zone from the implant of Patient 7 is surrounded by an organic sleeve (dark grey) on which inorganic particles can be seen. As shown in Table 3, the majority of the particles analysed in this area had a spectrum comparable to Spectrum S1. For the two used implants, it was also possible to analyse the inner and the outer coils (Spectra S2 and S3, respectively). These spectra show traces of elements that appear to come from the weld and from the inner and outer coils.

Discussion

This analysis of implants and uterine biopsies shows that tin particles were found most frequently in the samples. However, other element constituents of the implant were also identified (silver, nickel, gold, chromium, platinum and titanium). It is therefore possible that supplementary toxicity could be added to tin toxicity. In Patient 4, tungsten compound particles probably

Table 3
Results of the mineralogical analysis of the weld area of the ESSURE implants (expressed in mass percent for each element).

Patient number		N	O	Na	Mg	Al	Si	P	S	Cl	K	Ca	Ti	Cr	Mn	Fe	Ni	Cu	Mo	Ag	In	Sn	Sb	W	I	Ta
1	Mean	22.9	45.4	1.6	0.4	0.8	0.4	2.7	1.8	0.3	3.3	1.8	7.1	5.2	1.1	13.3	5.0	0.7	2.6	6.7	6.5	19.6	10.3	0.7		
	Min	0.7	0.3	0.1	0.1	0.1	0.1	0.2	0.2	0.2	0.4	0.2	0.1	0.2	0.5	0.2	0.1	0.3	2.6	0.3	6.5	0.5	10.3	0.7		
	Max	42.6	94.6	7.8	1	5.4	1.1	13.1	14.3	0.4	19	8.2	39	20.3	3.3	62.8	60.3	1.3	2.6	55.8	6.5	83.6	10.3	0.7		
	n	67	87	36	51	14	9	80	74	5	44	68	14	22	10	26	40	4	1	36	1	75	1	1		
5	Mean	14.6	44.6	1.4	0.5	0.3	2.9	1.4	0.3	0.3		3.7	1.8	4.1		6.6	2.3			1.3		30.2				
	Min	1.5	15.6	0.3	0.2	0.3	0.5	0.3	0.3	0.3		0.4	0.3	0.2		0.2	0.3			1.3		2.4				
	Max	49.2	83.9	3.6	1	0.3	14.5	6.2	0.3	0.3		24.4	3.7	9.8		31.2	9.7			1.3		75.4				
	n	40	60	57	27	1	57	60	1	1		34	15	24		57	37			1		56				
6	Mean	14.0	35.7	2.0	0.3	0.4	2.2	1.3	0.5	0.4	1.3	1.4	7.3	0.5	18.0	3.2	0.5	1.3	2.5	8.3		29.2			1.7	0.6
	Min	0.9	4.8	0.1	0.2	0.1	0.3	0.2	0.2	0.1	0.4	0.3	0.3	0.4	0.3	0.2	0.5	0.4	1.5	0.5		1.3			1.7	0.6
	Max	46.5	77.3	8.3	0.5	1.1	9.1	5.4	1.5	1.1	2.1	3.5	20.4	0.7	57.3	11.6	0.5	2.1	3.6	69.5		75.3			1.7	0.6
	n	49	66	66	23	9	66	56	15	9	8	16	23	4	28	38	1	8	8	51		66			1	1
7	Mean	10.9	38.7	1.5	0.4			1.5	0.6	0.4		1.7	0.6	0.5		2.4	0.6	9.2	4.6	6.8		40.7			2.2	0.5
	Min	1.1	11.3	0.5	0.1			0.3	0.2	0.1		0.7	0.6	0.2		0.2	0.2	0.3	4.6	0.6		4.3			1.6	0.4
	Max	65.6	65.1	5	1.2			7.9	2.7	1.8		3.1	0.6	0.8		6.8	2.2	50	4.6	35.9		83.1			2.7	0.5
	n	51	80	54	23			73	64	19		10	1	2		6	28	57	4	39		80			2	2

Mean, average over all particles on which the element was detected; min, minimum value over all particles on which the element was detected; max, maximum value over all particles on which the element was detected; *n*, number of particles on which the element was detected.
Number of particles analysed for each patient: Patient 1, 87; Patient 5, 60; Patient 6, 66.

came from the electrode of the electric scalpel used during salpingectomy. The many calcium-based particles found in the biopsies were probably caused by calcification and do not have a toxic effect.

In seven of the 10 cases in this study, possible degradation of the weld was identified, with local dissemination of tin in the fallopian tube or uterine horn, sometimes accompanied by an inflammatory reaction and/or encystment of particles. All analyses of used implants showed an important level of degradation, with a destructive appearance of the tin weld and the presence of organic tissue around the damaged weld, as well as tin particle dissemination inside the organic tissue. In two cases, implant analysis showed abnormal deterioration of the weld without evidence of tin particles in the tissue. It is possible that these specimens came from tissue distant from the tin solder. Future prospective studies should focus on tissue closer to the tin solder.

Local inflammatory lesions associated with the presence of tin particles may explain the pelvic pain and dyspareunia reported by patients. Organotin bioproduction after leaching and tin corrosion, similar to the processes observed for mercury [20–22], could explain some systemic symptoms. Although most mineral tin salts are considered to have low toxicity for mammals, the issue is less clear for organic compounds that could potentially interfere with many biochemical intracellular mechanisms. Indeed, organotin compounds are considered very toxic, with headaches, depression, asthenias and visual disturbances among the symptoms frequently observed among ESSURE cases [23–26]. In 1953 in France, oral treatment with diiodoethyltin was proposed for furunculosis. Iodide contamination led to a high number of cases of severe organotin intoxication, with some deaths. Since then, tin compounds have been omitted from all medications [27].

Further studies should be undertaken to investigate the role of premature degradation of the tin weld, with microstructural and chemical analyses on implant and anatomopathological specimens, and a systematic study of tissue surrounding the tin weld.

In the preclinical study performed by Conceptus and cited by the French Safety Agency [28], a report on corrosion susceptibility of the Conceptus ESSURE micro-insert is included in the 6-month report. After SEM was used to look for signs of corrosion, it was concluded that, 'As expected the tin solder showed signs of corrosion resulting in pitting and increasing porosity with the worst corrosion damage on the ball tip. At the 3-month time point, approximatively 25–50 % of the solder had corroded. At the 6-month time point, the ball tips of some of the samples were almost completely corroded, but all the solder bonds continued to hold together. In all cases the outer coil remain attached to the fibered inner coil'. The authors of the report considered that it was an acceptable level of solder corrosion because it did not result in the loss of mechanical integrity. However, the perspective that this insert would remain in the women's bodies for their entire lives should have led to consideration that the release of tin, by leaching, could have increased over time, and given rise to complications related to tin toxicity.

A second preclinical study in the manufacturer's report was an animal study on pigs implanted with ESSURE. The presence of inorganic particles was observed in the fallopian tubes, but the study was limited to optical microscopy observation, without identification of the chemical nature of the mineral particles. In the present study, the largest number of observed particles were identified as tin particles, thus proving the value of using SEM-EDX for this type of investigation.

An important finding of this study was the presence of tin particles in the uterine horn distant from the fallopian tube in some patients, suggesting that one should systematically consider hysterectomy with salpingectomy for symptomatic patients, whose clinical recovery has been confirmed in many cases [29].

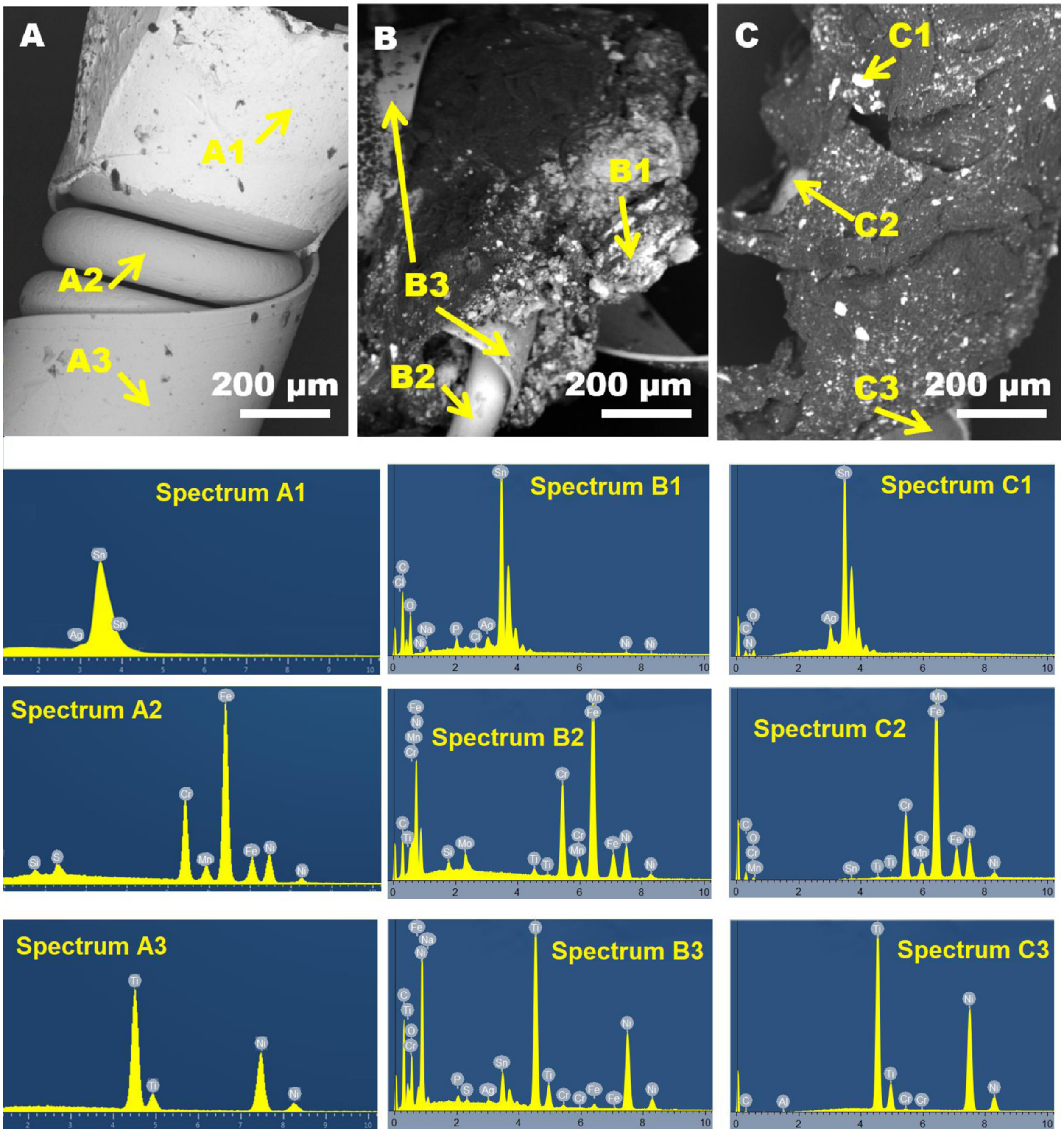


Fig. 5. Scanning electron microscopy coupled with energy-dispersive x-ray analysis of an unused ESSURE implant (A) and the implants of Patient 1 (B) and Patient 7 (C). For each implant, spectra were made on the weld zone (Spectra A1, B1 and C1), the inner coil (Spectra A2, B2 and C2) and the outer coil (Spectra A3, B3 and C3).

Conclusions

The microstructural analysis and EDX chemical analysis of ESSURE implants and proximal tissues supported the hypothesis of a causal relationship between abnormal degradation of the implant and locoregional symptoms. In terms of systemic symptoms, analysis of possible granulomas outside uterine tissue and plasmatic studies of chromium, nickel and tin levels are needed. The fact that inorganic particles were found in the uterine horn of some patients suggests that hysterectomy and salpingectomy should be considered during ESSURE explantation.

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None.

Declaration of Competing Interest

Michel Vincent is Chief Executive Officer of Minapath Développement, and Mickaël Catinon and Elisabeth Roux are employees of Minapath Développement. The other authors declare no conflict of interests.

References

[1] Dhruva SS, Ross J, Gariepy AM. Revisiting Essure – toward safe and effective sterilization. N Engl J Med 2015;373: e17.1–3.

[2] Valle RF, Carigan CS, Wright TC. The STOP Prehysterectomy Investigation Group. Tissue response to the STOP microcoil transcervical permanent contraceptive device: results from a prehysterectomy study. Fertil Steril 2001;76:974–80.

[3] Al-Safi Z, Shavell VI, Katz LE, Berman JM. Nickel hypersensitivity associated with an intratubal microinsert system. Obstet Gynecol 2011;117:461–2.

[4] Zurawin RK, Zurawin L. Adverse events due to suspected nickel hypersensitivity in patients with Essure microinserts. J Minim Invasive Gynecol 2011;18:475–82.

[5] Bibas N, Lassere J, Paul C, Aguilar C, Giordano Labadie F. Nickel-induced systemic contact dermatitis and intratubal implants: the baboon syndrome revisited. Dermatitis 2013;324:35–6.

[6] Beckwith AW. Persistent pain after hysteroscopic sterilisation with microinserts. Obstet Gynecol 2008;111:511–2.

[7] Brito LGO Cohen SL, Goggins ER, Wang KC, Einarsson JI. ESSURE surgical removal and subsequent symptom resolution: case series and follow-up survey. J Minim Invasive Gynecol 2015;22:910–3.

[8] Kamenic H, Thiel L, Karreman E, Thiel J. Does Essure cause significant de novo pain? A retrospective review of indications for second surgeries after Essure placement. J Minim Invasive Gynecol 2016;23:1158–62.

[9] Maassen LW, Van Gastel DM, Lentjes MY, Bongers MY, Veersema MY. Intracavitary deposits on Essure hysteroscopic sterilization devices: a case report. Case Reports Women Health 2017;15:3–5.

[10] Rezai S, Labine M, Roberts HAG, et al. Essure microinsert abdominal migration after hysteroscopic tubal sterilization of an appropiately placed Essure device: dual case reports and review of the literature. Case Rep Obstet Gynecol 2015;2015:402197.

[11] Ricci G, Restaino S, Di Lorenzo G, Fanfani F, Scrimin F, Mangino FP. Risk of Essure microinsert abdominal migration: case report and review of literature. Ther Clin Risk Manag 2014;10:963–8.

[12] Sills ES, Li X, Jones CA, Wood SH. Contraceptive failure after hysteroscopic sterilization: analysis of clinical and demographic data from 103 unplanned pregnancies. Obstet Gynecol Sci 2015;58:487–93.

[13] Bouillon K, Bertrand M, Bader G, Lucot JP, Dray-Spira R, Zurelk M. Association of hysteroscopic versus laparoscopic sterilization with procedural, gynecological and medical outcomes. JAMA 2018;319:375–87.

[14] Fernandez H, Legendre G, Blein C, Lamarsalle L, Panel P. Tubal sterilization: pregnancy rates after hysteroscopic versus laparoscopic sterilization in France, 2006–2010. Eur J Obstet Gynecol Reprod Biol 2014;180:133–7.

[15] Franchini M, Zizolfi B, Coppola C, et al. Essure permanent birth control, effectiveness and safety: an Italian 11-year survey. J Minim Invasive Gynecol 2017;24:640–5.

[16] Ouzounelli M, Reaven NL. Essure hysteroscopic sterilization versus interval laparoscopic bilateral tubal ligation: a comparative effectiveness review. J Minim Invasive Gynecol 2015;22:342–52.

[17] Walter JR, Ghobadi CW, Hayman E, Xu S. Hysteroscopic sterilization with Essure. Summary of the US Food and Drug Administration actions and policy implications for postmarketing surveillance. Obstet Gynecol 2017;129:10–9.

[18] Bahk CY, Gosgharian M, Donahue K, et al. Increasing patient engagement in pharmacovigilance through online community outreach and mobile reporting applications: an analysis of adverse event reporting for the Essure Device in the US. Pharmaceut Med 2015;20:331–40.

[19] US Food and Drug Administration. Biological responses to metal implants. Silver Spring, MD: FDA; 2019. Available at: https://wayback.archive-it.org/7993/20191212150415/ https://www.fda.gov/media/131150/download (last accessed 4 April 2020).

[20] Hirner AV, Rettenmeier AW. Methylated metalloid species in humans. Met Ions Life Sci 2010;7:465–521.

[21] Manceau A, Enescu M, Simionovici A, et al. Cheical forms of mercury in human hair reveal source of exposure. Environ Sci Technol 2016;50:10721–9.

[22] Schafer SG, Femefert U. Tin – a toxic heavy metal? A review of the literature. Regul Toxicol Pharmacol 1984;4:57–69.

[23] Winship KA. Toxicity of tin and its compounds. Adv Drug React Ac Pois Rev 1988;1:19–38.

[24] Graf GG. Tin, tin alloys and tin compounds. Ullmann's encyclopedia of industrial chemistry 2012;37:. p. 1–34.

[25] Rudel H. Case study: bioavailability of tin and tin compounds. Ecotoxicol Environ Saf 2003;56:180–9.

[26] Anger JP. Tin and organotins in the environment. Ann Toxicol Anal 2001;13:196–202.

[27] Bonah C. L'affaire du stalinon. Rev Prat 2007;57:1501–5.

[28] https://www.anasm.sante.fr/var/ansm_ite/storage/original/application/&114c59313992db5144689be838ed5a36pdf.

[29] Merviel P, Kurtz D, Lelievre C, Le Gourrierec A, Postec-Ollitrault E, Dupré PF. Assessment of non-gynecological symptoms before and after removal of the Essure sterilization device. A 6-month follow up study. Minerv Gynecol 2019;71:404–11.