TRACE ELEMENT STATUS OF WOMEN WITH CONTRACEPTIVE PROCEDURE ESSURE®

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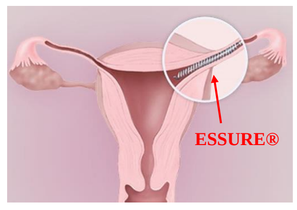
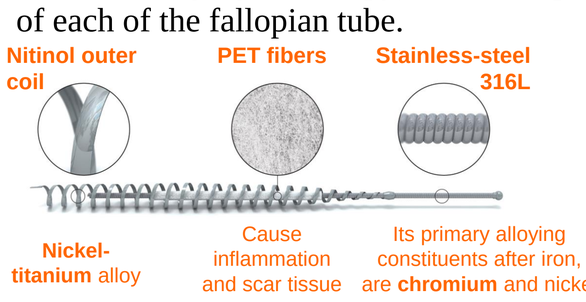
Introduction

Background ESSURE® (Bayer) is a permanent contraceptive procedure that uses a small implant inserted through the vagina and the cervix (by hysteroscopy) into the opening of each of the fallopian tube.





The ESSURE® coils show a complex metal composition, including iron, nickel, chromium, titanium, silver, tin and platinum.

The device has been linked to several serious health complications, including persistent pain, bleeding, allergic reactions possibly leading to removal surgery. Bayer stopped sales of ESSURE® in Sept. 2018.

Objectives: The aims of this study were (i) to measure two main components of ESSURE® devices (chromium and nickel) in urines, peritoneal fluid and fallopian tissues from women who underwent surgical removal of the sterilization devices (1) and (ii) to evaluate the decrease of urinary toxic metals levels during follow-up of the patients.

Material & Methods

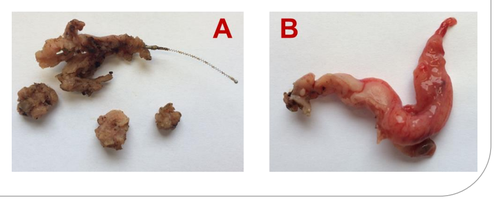
Study design and subjects

- This study was a sub-protocol of the single-center prospective cohort ABLIMCO study: Evaluation of symptom resolution after surgical removal of ESSURE® sterilization devices (2). The results of this study suggest that laparoscopic removal of ESSURE® devices in symptomatic women is associated with short and medium-term improvement in quality of life as well as reduction in pelvic pain.

STUDY SUBJECTS	
PATIENTS Symptomatic women undergoing laparoscopic removal of Essure® devices	**CONTROL PATIENTS** Women undergoing gynecological surgery for other (non-malignant) indications
BIOLOGICAL SAMPLES (on the day of the surgery)	
Urines (U1) Peritoneal fluid (PF) Fallopian tissues (FT)	Urines Peritoneal fluid
FOLLOW-UP	
≈ 1 month: urines (U2) ≈ 6 months: urines (U3)	

Trace metal determination

- Chromium and nickel levels in **urine** and **peritoneal fluid** from patients were compared to levels obtained from control patients.
- Metal levels in **fibrotic fallopian tissues** (close to ESSURE® device) (A) were compared to levels in **non-fibrotic fallopian tissues** (B).



- Chromium and nickel concentrations were determined by **Inductively Coupled Plasma Mass Spectrometry** (ICP-MS) analysis (PerkinElmer NexION 350X) in kinetic energy discrimination (KED) mode. The instrument is operated using helium as the collision cell gas (internal standard: Rh^{103}).

ClinChek® Controls (Recipe®)	Repeatability		Inter-day precision	
	Value	CV	Value	CV
Ni (analysis of Ni^{60})	2,2 µg/L	6,3%	2,5 µg/L	11,5%
Ni	7,5 µg/L	2,4%	7,9 µg/L	5,9%
Cr (analysis of Cr^{52})	1,7 µg/L	11,8%	1,6 µg/L	14,2%
Cr	6,7 µg/L	2,6%	6,3 µg/L	8,4%

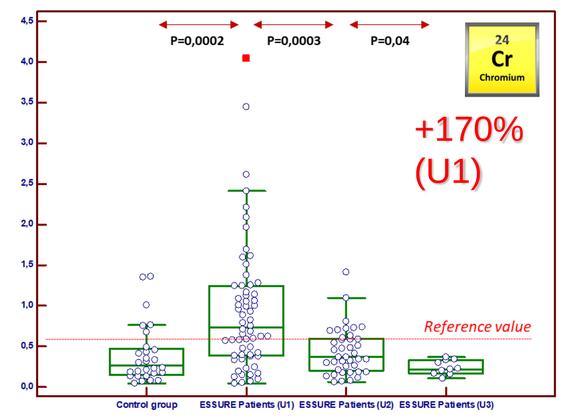
- **Limits of quantification** (LOQ): 0,6 and 0,3 µg/L for Ni and Cr, respectively. Values below the LOQ were replaced with half the LOQ.

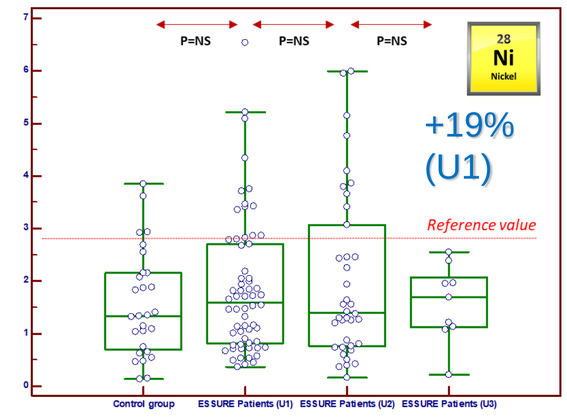
Results

Summary of demographics and other characteristics of the subjects

	Patients	Controls patients	P
n	63	33	
Median age (min-max) (yrs.)	48 (38-56)	43 (22-59)	<0,001
Delay between ESSURE® insertion and surgical removal (min-max) (yrs.)	5.4 (1,2-11,2)	//	
Follow-up (days) • Urines 1 • Urines 2 • Urines 3	 n=63 ; Day 0 (D0) n=42 ; D0+41 (min: 9 - max: 137) n=42 ; D0+197 (min: 111- max: 264)	 n=28 ; D0	

Chromium and nickel levels in **URINES** (µg/g creatinine)





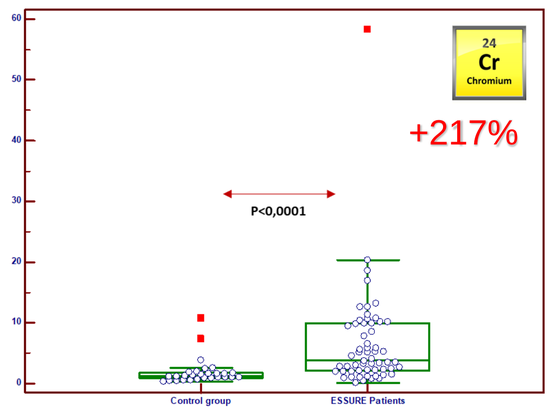
U-Cr (µg.g creat.)	n	Median	IQR	U-Ni levels exceeding the reference value
Control group	28	0,27	[0,15-0,47]	21%
ESSURE Patients (U1)	62	0,73	[0,39-1,25]	66%
ESSURE Patients (U2)	38	0,37	[0,20-0,60]	35%
ESSURE Patients (U3)	10	0,22	[0,17-0,33]	0/10

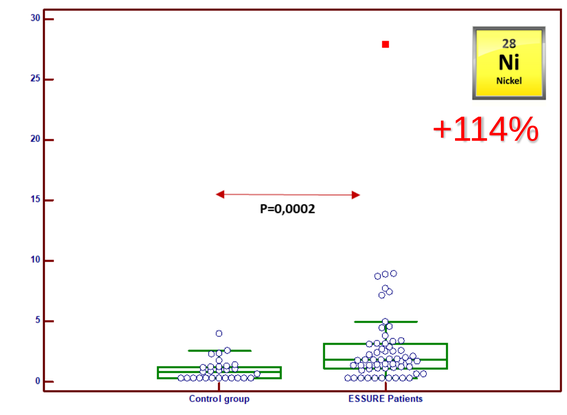
Reference values : Cr < 0,54 µg/g creatinine (95th percentile) (3)

U-Ni (µg.g creat.)	n	Median	IQR	U-Ni levels exceeding the reference value
Control group	28	1,34	[0,70-2,16]	4%
ESSURE Patients (U1)	62	1,60	[0,82-2,7]	6%
ESSURE Patients (U2)	38	1,40	[0,76-3,07]	11%
ESSURE Patients (U3)	9	1,69	[1,12-2,07]	0/9

Reference values : Ni < 3,8 µg/g creatinine (95th percentile) (3)

Chromium and nickel levels in **PERITONEAL FLUID** (µg/L)

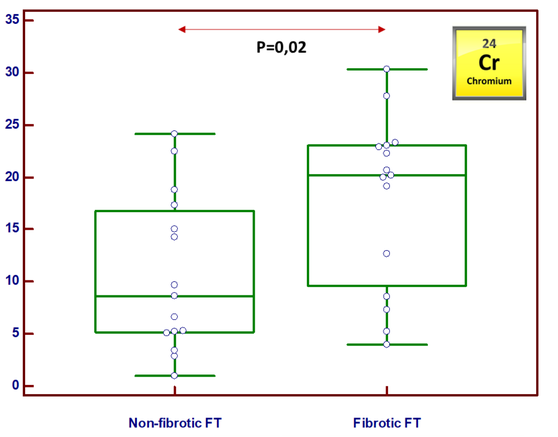


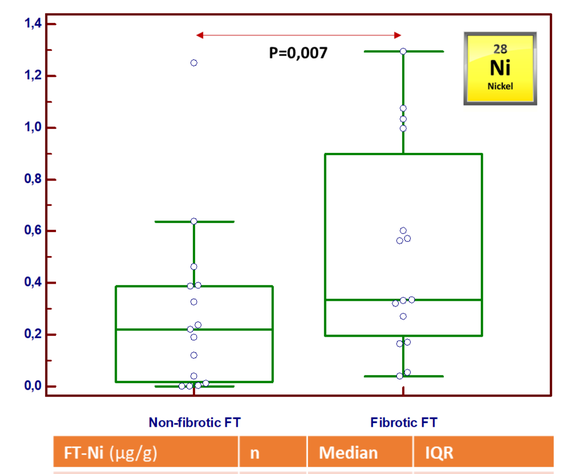


PF-Cr (µg/L)	n	Median	IQR
Control group	28	1,23	[0,87-1,23]
ESSURE Patients	58	3,91	[2,13-9,92]

PF-Ni (µg/L)	n	Median	IQR
Control group	28	0,84	[0,3-1,25]
ESSURE Patients	59	1,80	[1,10 -3,14]

Chromium and nickel levels in **FALLOPIAN TISSUES** (µg/g of dry tissue)





FT-Cr (µg/g)	n	Median	IQR
Non-fibrotic FT	15	8,62	[5,12-16,75]
Fibrotic-FT	15	20,15	[9,59-23,02]

FT-Ni (µg/g)	n	Median	IQR
Non-fibrotic FT	15	0,22	[0,02-0,39]
Fibrotic FT	15	0,33	[0,19-0,90]

Conclusion

Our data suggested significant metal released from ESSURE® devices. Consequently, this raises the question about the physiological or toxic effects of metal release into the peritoneal fluid and systemic circulation. Additional studies are warranted regarding the potential clinical consequences.

Références **1. CHENE G. et al.** How I do. . . laparoscopic removal of Essure® device by mini-cornuectomy without fragmentation? Gynecol Obstet Fertil Senol. 2018 Jul - Aug;46(7-8):608-609

2. CHENE G. et al. Quality of life after laparoscopic removal of Essure® sterilization devices. Journal of Mini-Invasive Gynecology. *Submitted for publication*.

3. FRÉRY N, Saoudi A, Garnier R, Zeghnoun A et al. - Exposition de la population française aux substances chimiques de l'environnement. Saint- Maurice: Institut de veille sanitaire ; 2011 : 151 p.