euro® gine

Technology for women's healthcare

Collaborating entities

UPC
UNIVERSITAT POLITÈCNICA DE CATALUNYA

Politecnic University of Catalonia
Department of materials science and metallurgical engineering

SOCIEDAD ESPAÑOLA DE GINECOLOGIA Y OBSTETRICIA S.E.G.O. MADRID

Spanish Association of Gynecolgy and Obstetrics

Ministerio de Industria y Energía
Miner

Ministry of Industry and Energy
ATYCA
Initiative for the support of technology, quality and industrial safety

CDTI

Technological Industrial Development Department

Intrauterine Device

"Gold T®"

Characterization of the active metals and the intrauterine corrosion thereof

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1998

Objective:

Proposal for a new IUD that encompasses the advantages of the current ones and eliminates the majority of their drawbacks.

Material and the method:

Concrete study on the mechanical performance of the current IUDs, which includes improvements to the insertion process, the geometry of the base frame and the application of new metals.

In the insertion system, a new type of inserter design is chosen, which facilitates insertion mechanics, thus providing a much lesser degree of trauma and avoiding the risk of uterine perforation.

A new base frame design is being studied to improve the performance of the end ring in order to increase its resistance to shear effect of the thread, and additionally, obtaining more space for the placement of the active copper coil without increasing the length of IUD.

Study of intrauterine corrosion in IUDs implanted for 3, 12, 24 and 48 months.

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Results and conclusions:

It has been noted that the corrosion products (copper salts) are produced by the contraceptive function, and from their characterization, the elemental composition of uterine secretions has been deducted.

The interference of calcium carbonate crust deposited on the coil of the IUDs is shown and its influence on the release of corrosion products, inferring that the maximum effectiveness of the IUD is achieved when the body ceases this carbonate deposition.

The observed intergranular corrosion induces, ultimately, the fragmentation of the coil with the risk of loss of efficacy.

Traditionally, to overcome this problem, a silver core has been included in the wire that forms the coil. However, this study shows that intergranular corrosion proceeds in the silver core as a result of the detected existence of sulphur in uterine environment. All this leads to the proposal to replace the silver core with a gold one; gold is a metal immune to any corrosion and completely hypoallergenic, thus the possibility of prolonging the life of the IUD without any risk of fragmentation of the coil that may undermine its contraceptive efficacy.

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INTRODUCTION

Eurogine, S.L. is a company dedicated exclusively to the manufacture and marketing of products designed to enhance the quality of life of women in the gynaecologic medical aspect.

Recently, this company has undertaken a major project in the field of Research & Development (R&D) of new gynaecological products, obtaining support and funding from the Centre for Industrial Technological Development (CDTI) and the ATYCA Initiative of the Ministry of Industry and Energy.

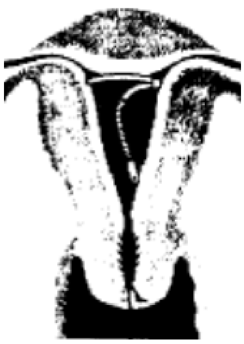
As a result, an R&D agreement has been established with the *Department of Materials Sciences,* of the *Universidad Politécnica de Catalunya,* with the purpose of, amongst other, developing a new generation of IUDs that exceeds the current reliability and whose insertion and removal is as painless as possible for women.

The main established objectives are as follows:

Objectives	IUD
SCIENTIFIC	1) Characterization of the copper metal corrosion by uterine fluid. Increased reliability. Biocompatibility. 2) Characterization of the plastic material. Biocompatibility, viscoelastic memory, tensile strength.
TECHNO-LOGICAL	Design of the base frame in terms of reliability and trauma. Amount of contraceptive copper.

WHAT IS AN IUD?

The **I**ntra**U**terine **D**evices (IUDs) also called *coils* are small objects placed in the woman's uterus as a means of contraception. These devices, which have their origin in antiquity, are nowadays an important element in national family planning programs.



The chemical effect IUD is the most used IUD today. (See IUD.01) It consists of a moulded plastic material base frame in the form of and "anchor" or "T". Along the vertical stem, a copper wire is wound with or without a silver core, of different diameters, 0.25 mm, 0.30 mm and 0.40 mm and different lengths to ensure a minimum area of exposure to the uterine environment.

PROROPOSAL OF THE NEXT GENERATION "GOLD T®" IUD

The clinical practice and its literature clearly indicate that the design of the structure determines the effectiveness of an IUD, in relation to:

1) *Non-traumatic insertion*;

2) *Insertion-extraction method*;

3) *Quantity of contraceptive copper*.

After analyzing the characteristics of the current IUDs, conclusions can be drawn to define the new parameters of a new IUD that optimizes simultaneously all the partial advantages of the current ones.

1) *Non-traumatic insertion;*

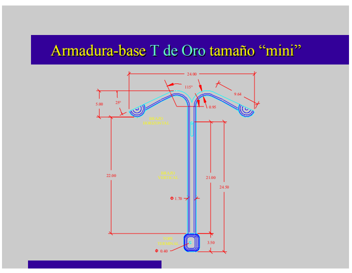
This factor is resolved by adopting the frame-based IUDs with a specific "T" or "Y" shape as are NOVA T and Novaplus, which, when introduced in their cannula before insertion, provide two advantages:

The first one is that the complete IUD is hidden within the insertion cannula and that when the ends of the arms of the IUD base frame are joined during its introduction by pulling the thread through the cannula, they form, by the hemispherical configuration of these ends, a ball that completely avoids them from entering it, preventing the edge of the inserter cannula is hurtful, and at the same time facilitating their passage through the cervical canal.

The other advantage is that the external diameter of the insertion cannula is 3'6 mm, the lowest in the market. Therefore there is no need to dilate the cervical canal, given that the pre-hysterometry performed prior to the insertion would have produced enough dilation. Do not forget that the gentle movements during insertion of an IUD and the rounded shapes make it a lot easier to avoid unnecessary inconvenience to women and severe uterine perforation.

The base frame is improved by replacing the end ring thereof by a sphere with a through hole to hold the insertion-extraction wire. This substitution has two purposes, it allows for the lower end of the vertical arm to be atraumatic, and it gains space for the copper coil without changing the total length of the IUD. At the same time, the area has a greater tensile strength at the time of the IUD removal.

The specific "T" or "Y" shape of the designed frame-base, allows for less traumatic insertion, a significant recovery capacity increase (viscoelastic memory) and the folding strength of their arms, all of this resulting in a better response to the attempts of the uterus to expel the IUD, and therefore, better safety in guarantying contraception.



Gold T® Mini Shape

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2) *Optimal insertion-extraction method;*

The IUD insertion system from "Novaplus" and "Nova T," with their six phases, is undoubtedly the most elaborate and allows a more secure attachment in regard to the proper placement of the IUD in the uterine fundus. But at the same time, the inadequate belief that this technique is "complicated," results in their disposal in some cases or the possibility that each professional uses their own interpretation of the method, with the risk posed by the fact that their interpretations are not always successful.

Assuming that the insertion technique is essential to achieve the best results from an IUD with as little inconvenience as possible to the user, the possible improvements must be assessed in this procedure and the elements necessary for its implementation. Clearly, by being inseparable, the two aspects must be treated together, which leads inevitable to the conclusion that an inserter capable of complying with these premises is needed.

Once more, those that should be kept or improved were drawn from the comprehensive analysis of the characteristics of the integration systems of the different models of known IUDs.

KEEP:

- The system to cover-up the IUDs inside the canula.

- The smallest possible diameter of the insertion canula.

IMPROVEMENTS in terms of:

- Process simplification.

- Eliminate possible personal interpretation as much as possible.

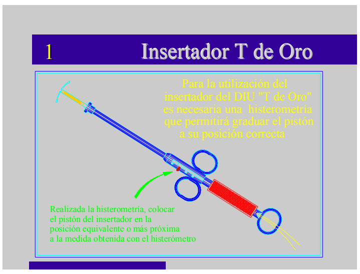
- Eliminate any possibility of perforation during insertion.

- Increase the safety of the implantation of the IUD in the fundus.

- Eliminate the possibility of moving the IUD while removing the cannula.

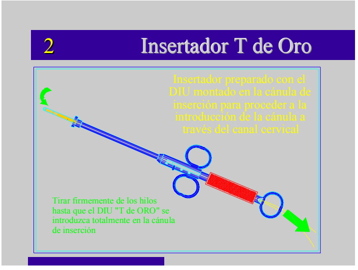
All these features are achieved with the incorporation of a new design inserter to the IUDs, whose description, characteristics and method of operation are simplified and explained below.

<u>Gold T® Insertion System</u>

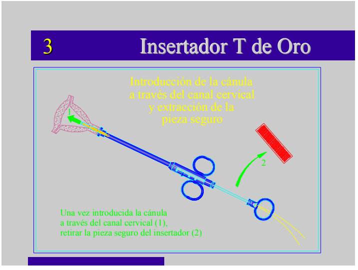


To use the Gold T® Insertion System, it is necessary to perform an histerometry to allow the regulation of the piston to the right position.

Once the histerometry is performed, put the piston in an equivalent position or as closer as possible to the measurement obtained with the uterine sound.

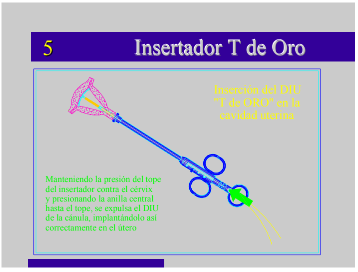


Insertion System ready with the IUD settled into the canula to insert the device through the cervical canal.
Tug firmly the thread until Gold T®is totally inserted into the insertion canula.



Introduction of the canula through the cervical canal and locking-piece extraction.
Once the canula has been introduced through the cervical canal, remove the Insertion System locking-piece.

Placement of Gold T® into the uterine cavity.
Once the locking-piece has been removed and keeping distal end Insertion System with firm and constant pressure against the cervix, place the fingers in the corresponding rings and press the central one.



Placement of Gold T® into the uterine cavity.
Keeping the pressure of the Insertion System against the cervix and pressing the central ring until the end, the Gold T® IUD will be expelled from the canula, being implanted correctly into the uterus.

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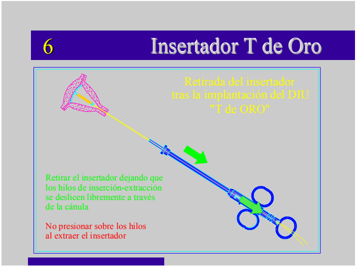
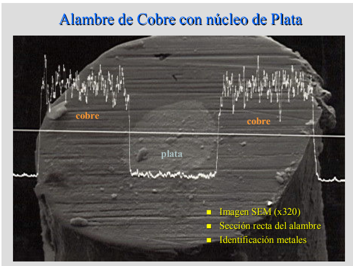


Insertion System removal after Gold T® is placed.
Remove the Insertion System leaving the insertion-extraction threads slide down freely through the canula.
Do not press the threads during the Insertion System removal.

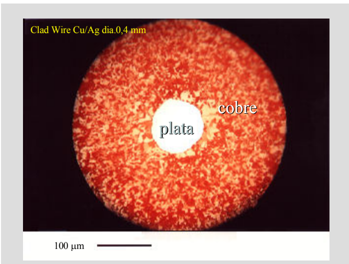
3) *Ideal Copper Quantity*

Clearly, the active copper surface that provides more contraceptive safety is located between 350 and 380 mm², and the one that is best known for its wide use in various IUDs models in recent years is the 375 mm² quantity and contraceptive copper surface, that at the same time has the mandatory registration from the Ministry of Health.

On the other hand, the addition of a silver core to the contraceptive copper wires indicates a very positive addition to functionality, durability and safety of these contraceptive copper wires.



Copper wire with silver core



Copper wire with silver core

Eurogine, S.L. in collaboration with the UPC (Polytechnic University of Catalonia) has completed a study showing that the substitution of silver for gold in the contraception copper wires represents a marked improvement on them, and both conclusions result in the proposal to incorporate a coil of contraceptive copper to the new "Gold T" IUD with the following characteristics:

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- * Outside diameter of the wire: 0.40 mm
- * Internal bore diameter: 0.10 mm
- * Total area: 375 mm²
- * Metal inner core: Pure Gold

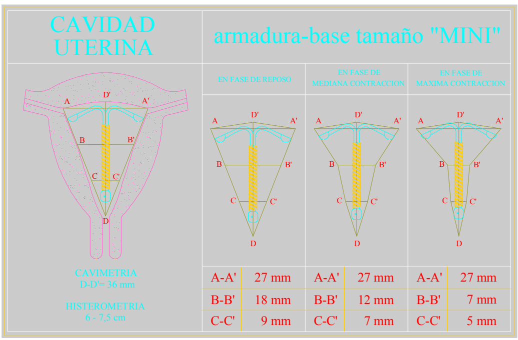
TECHNICAL INNOVATIONS INTRODUCED BY THE "GOLD T®" IUD

The usual end ring of this frame-base type is replaced with a sphere that improves the no trauma condition of the ring, and its improved resistance to be sheared by the traction of the extraction threads in extreme cases in which a force greater than normal is applied.

The new "Gold T" IUD is provided with a high-load copper coil containing an active area of 375 mm². This copper surface is the most effective from the contraception point of view, according to all the publications and clinical experience in recent years.

The increased safety in the copper coil in terms of duration and non-fragmentation during their working life is achieved with a copper wire with a noble metal core or nucleus that will provide the coil with unalterable support ensuring its integrity. For the first time the core is made of noble metal in gold, rather than the traditional silver, ensuring total incorruptibility and biocompatibility.

Another innovation of the "Gold T" is that it comes in three sizes: "Maxi" "Normal" and "Mini", which is presented for the first time active IUDs in the world, reflecting the advantage of choosing the appropriate IUD size depending on the anatomy of each uterus.



Mini size shape in different uterine positions: normal, medium contraction and maximum contraction

ACTION MECHANISM

Multiple theories have attempted to explain the mechanism of the copper contraceptive action inside the uterus, but none has been fully tested and accepted. Among these theories, the most accepted ones

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are those that indicate that copper exerts an anti-anidation action by preventing the implantation of the fertilized egg, and those who maintain that copper causes a certain changes to the uterine wall to prevent passage of sperm and or cause their destruction.

In the first one of them, it has been observed that changes in the endometrium caused by a possible inflammatory reaction, slows the normal hormonal cycle, thus creating an endometrium inhospitable to implantation (1, 2). However, no evidence has emerged that the IUD acts through any fundamental change in hormonal function or in the menstrual cycle (3).

According to the second theory, the numerous cellular and biochemical alterations in the human uterus induced by the IUD in the endometrium would be responsible for the contraceptive effect (4). Non-medicated devices, as well as copper stimulate an inflammatory reaction or foreign body reaction in the uterus wall. After the IUD insertion, numerous polymorphonuclear leukocytes occur in the endometrium and the uterine fluids, followed by giant foreign-body cells, mononuclear cells, plasma cells and macrophages (5, 6, 7, 8).

Medicated IUDs in addition to producing local inflammatory reactions, have local effects, which could exert a contraceptive action. The IUDs containing copper interfere with the enzyme system (9), with the cellular DNA content in the endometrium (10), with the glycogen metabolism (11.12), and with the oestrogen captured by the uterine lining. Copper enhances the inflammatory action (13). In the in vitro reactions, the copper ions are toxic to sperm, but this effect is less important than the interference with the enzyme systems (14, 15). The presence of copper in the cervical mucus inhibits and stops sperm penetration (16).

In summary, we can identify several action mechanisms of the copper IUDs, according to (17):

a) mechanical or physical action, independent of the material of the IUDs.

b) Chemical reaction of at least two components: the reduction of proteins and enzymes through the reduction of disulfide links in their molecular structure, and the release of copper ions, secondary to the first reactions, which can be locally toxic on sperm, eggs or both.

CHARACTERIZATION OF THE CORROSION TO BE PRODUCED IN AN IUD

Copper has become the active ingredient of modern IUDs, noting that this metal dissolves in the uterus due to uterine fluid as a result of intense surface corrosion of the wire. If this corrosion is not uniform across the surface, but contrarily, if it accelerates in certain points or areas, the wire may break and disintegrate before the total dissolution of the metal. This non-homogeneous corrosion reduces the life and the safety of the IUD, without the carrier or the gynaecologist realizing it.

The accompanying sketch "corrosion vs. biocompatibility" shows the factors that influence different types of corrosion that can lead to various processes that cause a significant modification of the metal surface.

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CORROSION FACTORS			
Factors defining the kind of the attack	**Metallurgical Factors**	**Usage Conditions**	**Time dependent factors**
Reagent concentration	Composition	Superficial State	Aging
Oxygen content	Preparation procedure	Shape of the part	Mechanical stress
pH of the medium	Impurities	Mechanical stresses	Temperature
Addition of inhibitors	Heat treatment	Use of inhibitors	Modification of protective coatings
Temperature	Mechanical Treatments	Characteristics of joints	
Pressure	Protective additions		

Whatever the type of corrosion occurring, compounds or copper salts are formed, called "corrosion products," which must be biocompatible with the human body because they are absorbed slowly by the endometrium.

Usually, biocompatibility is associated with the absence of corrosion, but in the case of the copper used in an IUD, biocompatibility should not be total. The corrosion products formed should be local and partially toxic, so that the device may fulfil its function, in other words, to exercise the contraceptive action.

Therefore, it should minimize the risk of localized corrosion of the copper within the uterine environment so as to ensure the minimum effective life of the IUD. For this, the characterization of corrosion is essential.

To carry out this study. the following analytical techniques have been used:

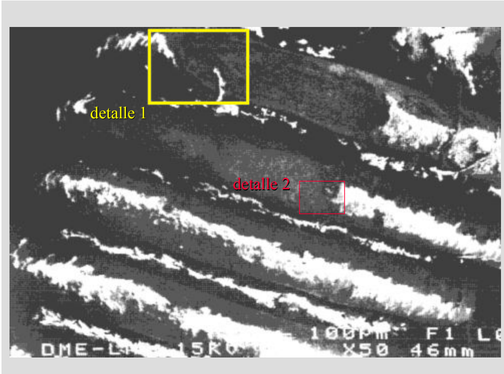
- Scanning electron microscopy (SEM)
- Analyzer by Energy-dispersive X-ray spectroscopy (EDX)
- with IUDs samples with different moments of implantation (3, 6-18, 24 and 48 months). These samples were provided by gynaecologists by specific indication from Eurogine, SL

Politecnic University of Catalonia
Metal materials and metallurgical engineering department

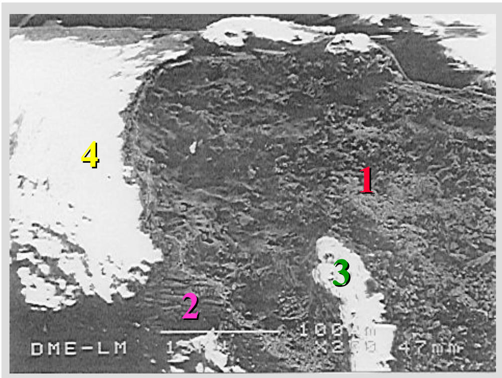
The results are outlined below:

a) <u>Characterization of a silver core IUDs after 3 months of implantation</u>.

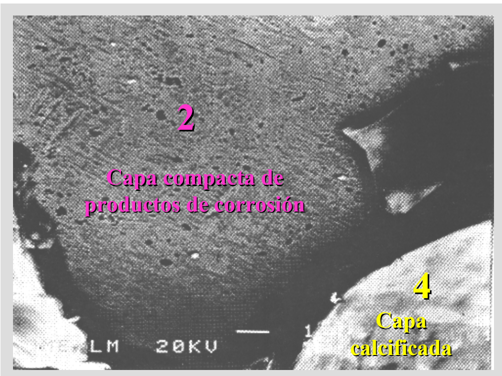
The surface of the copper wire of an IUD within 3 months of implantation has the appearance of shown on images SEM-11 and 12, with four clearly distinct layers.



SEM-11 Image



SEM-12 Image (detail of the yellow square at SEM-11)



SEM-13 Image (detail of the yellow square at SEM-11)

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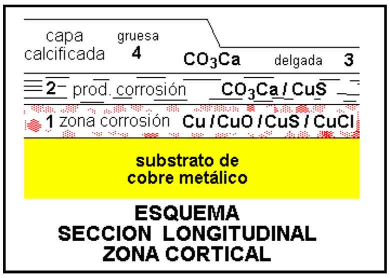
CHARACTERIZATION OF THE CORROSION LAYERS



Longitudinal section. Cortex zone.

Layer 1: Metallic copper substrate. It presents a very rough surface as a result of corrosion.

Layer 2: Corrosion products compact layer

Layer 3: Thin white layer of lime carbonate.

Layer 4:Thick layer of lime carbonate.

The EDX microanalysis provides the following information:

Layer 1 (EDX-01): Corroded copper layer

It is highly rugged with no apparent pitting. It consists of the metallic copper substrate surface with surface presence of corrosion products.

Element	Origin	Presence
Cu	Metallic substrate	Corrosion product (c.p.)
O	Uterine fluid	c.p. (oxides)
S	Uterine fluid	c.p. (sulphides)
Cl	Uterine fluid	c.p. (chlorides)
C	Uterine fluid	Corrosion products

Layer 2 (EDX-02): Corrosion products layer

Compact layer with intergranular degradation by pitting. Presence of metallic elements (Al, Mg) which have not been detected as impurities in the initial copper.

It consists of:

1) copper compounds: oxides, oxalates, sulphides, chlorides;

2) aluminium and magnesium salts;

3) carbonate in significant quantities.

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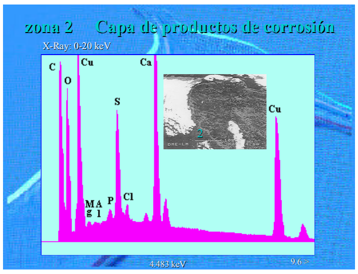
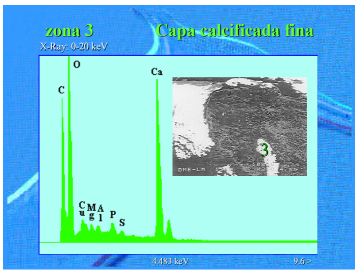


Element	Origin	Presence
Cu	Metallic substrate	Corrosion products (c.p.)
Ca	Uterine fluid	Surface deposition
C	Uterine fluid	Corrosion products
O	Uterine fluid	c.p. (oxides)
S	Uterine fluid	c.p. (sulphides)
Cl	Uterine fluid	p.c. (chlorides)
P	Uterine fluid	p.c. (phosphates)
Al	Uterine fluid	p.c. (aluminates)
Mg	Uterine fluid	Surface deposition

Layer 3 (EDX-03): <u>Thin calcified layer</u>

It consists mainly of calcium carbonate with small amounts of the detected elements in layers 1 and 2.



Element	Origin	Presence
O	Uterine fluid	Corrosion product (c.p.)
Ca	Uterine fluid	Surface deposition
C	Uterine fluid	Corrosion product (c.p.)
Cu	Metallic substrate	Corrosion product (c.p.)
Cl	Uterine fluid	c.p. (chlorides)
P	Uterine fluid	c.p. (phosphates)

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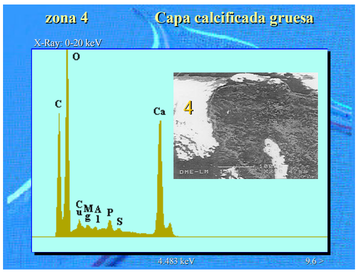
Al	Uterine fluid	Surface deposition
Mg	Uterine fluid	Surface deposition
S	Uterine fluid	Corrosion product (c.p.)

Layer 4 (EDX-04): <u>Thick calcified layer</u>

It consists mainly of considerable thickness calcium carbonate.



Element	Origin	Presence
O	Uterine fluid	Corrosion product (c.p.)
Ca	Uterine fluid	Surface deposition
C	Uterine fluid	Corrosion product (c.p.)
Cu	Metallic substrate	Corrosion product (c.p.)
Cl	Uterine fluid	c.p. (chlorides)
P	Uterine fluid	c.p. (phosphates)
Al	Uterine fluid	Surface deposition
Mg	Uterine fluid	Surface deposition
S	Uterine fluid	Corrosion product (c.p.)

The elemental EDX analysis shows that copper corrosion is caused by uterine secretions that dissolve and degrade the metal, forming various salts thereof. These include oxides, oxalates, sulphides, chlorides and carbonates. The white surface layer is identified as calcium carbonate deposited by the body as a result of a rejection phenomenon that is produced by the presence of a foreign body (IUD) within the uterus. The thickness of this deposition decreases with time the IUD spends inside the uterus, disappearing completely in IUDs with a time of implantation longer than 48 months.

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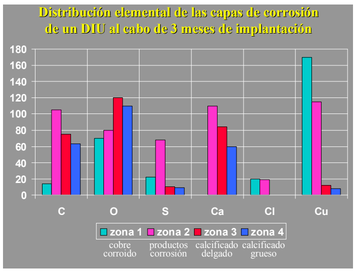
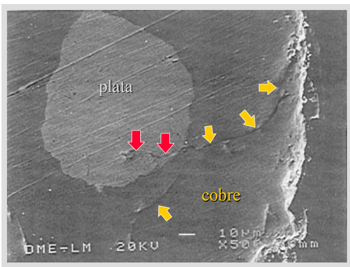


Elemental distribution of corrosión layers within 3 months
of implantation
Zone 1. corroded copper 2. Corrosion products 3. Thin calcified 4. Thick calcified

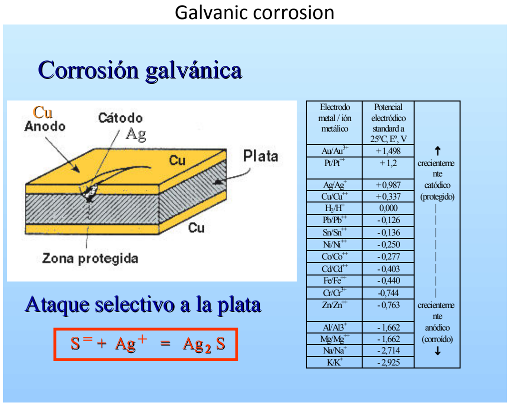
This calcified layer is very compact and impermeable to the passage of fluid and ions, so it has a screening effect on the corrosion of the copper wire, preventing the release of corrosion products (copper salts) that are concentrated in large numbers between it and the metal substrate, and the appearance of pitting corrosion. This results in a lower density of the salts in the uterine fluid and a significant risk of wire breakage. Both factors lead, without doubt, to a decrease in contraceptive effectiveness.

The SEM-14 image shows a section of the copper wire with the silver core. There are two lines of intergranular corrosion that have increased in depth from the outer surface of the wire and that have not stopped when the silver core was found. This means that sulphur has been the corrosive element (found in quantity on the surface), because this is the only thing that can cause corrosion in the metal with the formation of silver sulphide. This indicates the likelihood of the fragmentation of the wire, although the silver core eliminates this risk according to the consulted texts.



SEM-14 Image. Cross section with silver core.
Intergranular cracks of a silver core IUD after 3 months of implantation.

Galvanic corrosion



Selective attack to silver

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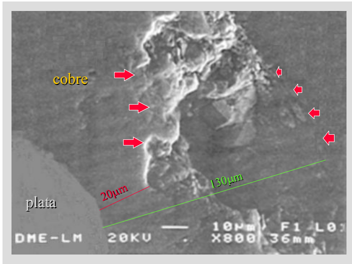
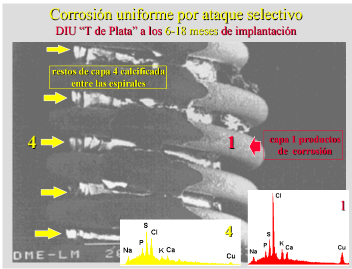
The SEM-15 image shows the localized intergranular corrosion of the copper. The central section shows copper polycrystals.



SEM-15 Image. Cross section with silver core.
Cavernous type Intregranular pitting corrosion

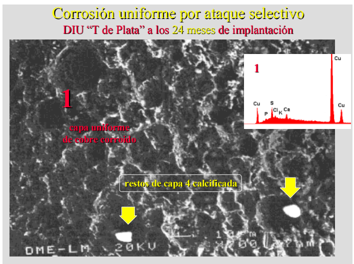
b) <u>Characterization of a silver core IUDs after 12 months of implantation</u>.

The SEM-21 image shows the typical corrosion of the IUDs with intrauterine implantation time of 12 months. The EDX -21/1 and 21/2 spectrums show the absence of calcified layer



SEM-21 Image. (6-18 months)
Uniform corrosion by selective attack
Calcified rests of layer 4 between the spiral
Layer 1 – corrosion products

c) <u>Characterization of a silver core IUDs after 24 months of implantation</u>.



SEM-31 Image. (24 months)

The total absence of calcified layer should be noted.

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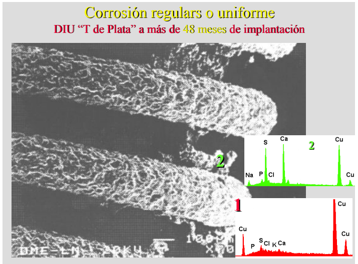
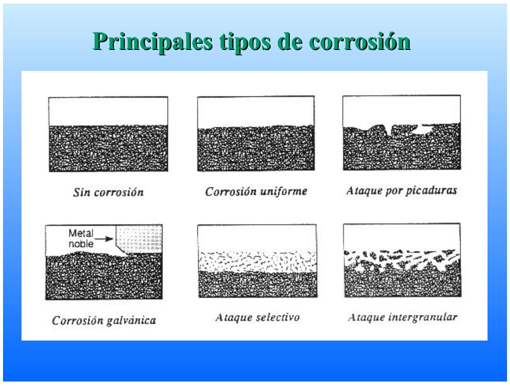
d) <u>Characterization of a silver core IUDs after 48 months of implantation</u>.



SEM-41 Image. (> 48 months)

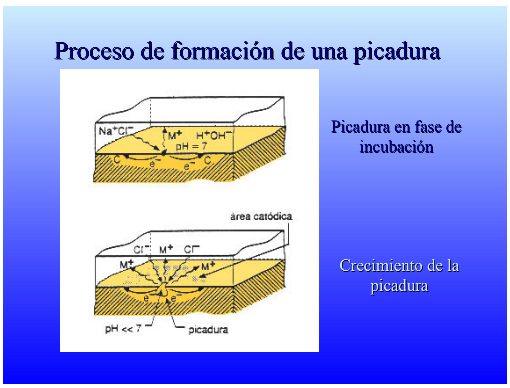
<u>TYPES OF CORROSION</u>

The intrauterine corrosion from the copper wire is a combination of several types of corrosion, which are listed below:



Main types of corrosion
Without corrosion · Uniform corrosion · Pitting corrosion
Galvanic corrosion · Selective corrosion · Intergranular corrosion

Chemical corrosion: It is produced by an heterogeneous reaction between the solid phase (copper) and the agressive liquid phase (uterine secretion) that attacks copper with consequent formation of corrosion products (organic and inorganic salts of copper).



Formation process of a pitting
Incubation phase · Pitting growth

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Electrochemical corrosion: When there is some heterogeneity (impurity) in the metal, a battery effect is produced; electrical current flows between micro-anodes and micro- cathodes. The copper is cathodic to hydrogen in the electrochemical dissolution series, and it is a cathode in the galvanic pairs formed with other metals such as iron, aluminium, lead, magnesium, tin and zinc. The elements that are formed as anodes are attacked, that is, the impurities in the copper. For this reason, corrosion occurs primarily in an intergranular manner that advances in depth and that can break the copper wire.

This is why copper has low resistance to corrosion by oxidizing acids, halogens (Cl) in a wet environment, sulphides (S) and solutions containing the ammonium radical. It has been noted repeatedly that the main products of corrosion are chlorides and sulphides.

Biochemical corrosion: Sometimes adherent deposits can be observed on the metal surface resulting from the attack, not from the metal itself, but from certain aggressive environmental constituents, mainly bacteria. The result is the formation of pitting on the metal in the place where the deposit occurred, according to a corrosion process by the difference in oxygen concentration. This type of corrosion that occurs in depth, can be intergranular or transgranular.

Corrosion with erosion: The corrosion products form an adherent and continuous deposit on the surface of the metal, decreasing the rate of corrosion. In the case of IUDs, it has been noted that the accumulation of this layer is caused by the surface deposition of calcium carbonate when the IUD has spent little time inside the uterus.

UTERINE SECRETIONS

COMPOSITION:

Uterine secretions are responsible for the corrosion and dissolution of the IUD’s copper wire, representing the aggressive environment. As seen in the image, SEM-21 is a more or less viscous liquid.

Its composition and concentration is variable and depends on many factors such as hormonal status, infections, medical treatment, secretory phase, proliferative phase, rejection phase.

This variability also affects the various areas that makeup the inside of the uterus from the fundus to the cervix.

To conclude, the characterization of the metal corrosion's overall elemental qualitative analysis, regardless of its particular or local variability, is as follows:

Oxygen, calcium, carbon, phosphorus, chlorine, sulphur, aluminium and magnesium.

The composition is also altered by an effect of the rejection phenomenon of the IUD from the uterus. However, sulphur is the element that stays constant in the rest of the corrosion products remaining on the copper surface, perhaps because the formed copper sulphide is not very soluble in the uterine fluid. The corrosion products are more soluble as the rejection phenomenon lowers, so we may assume that the solubility of these in the uterine fluid is also variable.

The degree of dissolution of the copper depends on the acidic or basic nature of the uterine fluid (when the uterus detects a foreign body inside the fluid, it shifts from basic to acidic, concurrent with uterine contractions, and all of that with the aim of furthering their expulsion through the cervix), on its oxygen saturation level and temperature.

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Furthermore, the pH of the medium also influences the degree of dissolution of the corrosion products, and its possible absorption by the endometrium, although the mechanism that allows it is unknown.

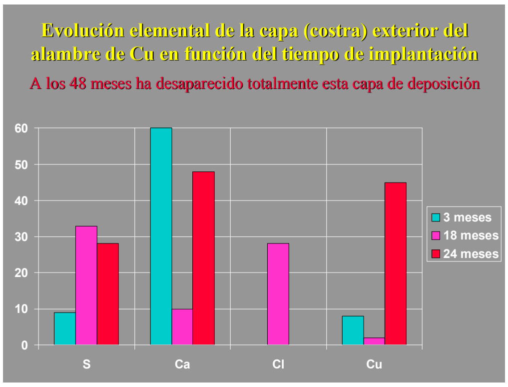
All these factors, concentration, composition, acidity-basicity balance, temperature, define the type of the uterine fluid attack on the copper and in turn determine the types or the corrosion that occurs on the metal surface.

QUANTITY:

The amount of discharge directly affects the rate of corrosion and dissolution of copper, and hence the weight loss experienced by the wire. Ultimately, it affects the life of IUDs and their contraceptive activity. A high rate of dissolution in IUDs was observed when removed after the menstrual period.

SURFACE DEPOSITIONS

It has been proven that a layer of calcium carbonate is deposited on the metal surface of the wire together with organic compounds, the latter to a lesser degree. The amount of the deposition and the thickness of the deposition are greater the shorter the time that the IUD has remained inside the uterus. On devices with a long period of time spent in the uterus (from age 2), deposition is practically zero. As discussed above, this may be due to the phenomenon of rejection that a foreign body causes on the body.



Elemental evolution of the outer layer of copper wire in terms of implantation time
Deposition layer has disappeared completely at 48 months of implantation
3 months · 18 months · 24 months

This deposition causes pitting in the copper, either as a result of electrochemical corrosion or biochemical corrosion effect. On the other hand, it is a layer little impermeable to the passage of the corrosion products formed between it and the metallic copper substrate. That's why in the inner layer of calcium carbonate, an accumulation of various salts is produced that as a consequence, dissolve in smaller numbers in the uterine fluid at the same time reducing the corrosion rate. It seems reasonable that these effects produce a decrease in the contraceptive effectiveness.

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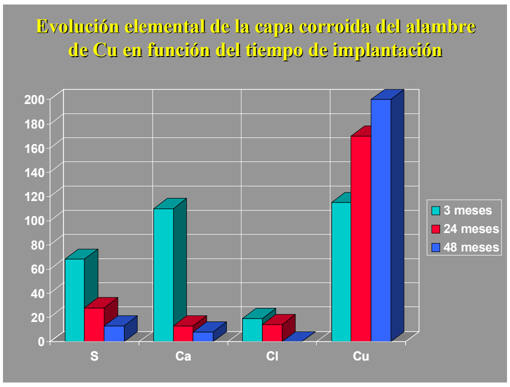
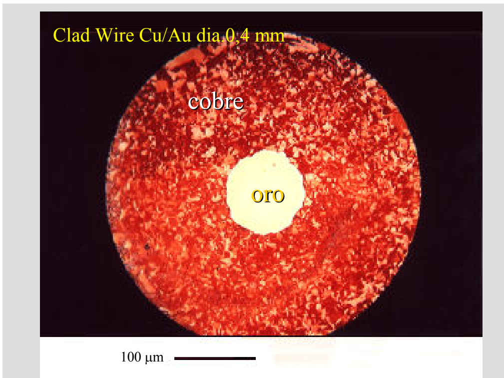


Elemental evolution of the corroded copper wire in terms of implantation time
3 months · 24 months · 48 months

The abovementioned biochemical corrosion occurs because of the effect of the deposition of an adherent layer of certain constituents of the uterine fluid, especially bacteria. The result is the formation of pitting corrosion as a process by the difference in oxygen concentration.



Copper wire with gold core

FINAL CONCLUSIONS

In the long term IUDs (> 2 years) to remain inside the uterus and as a result of the total absence of calcification (the phenomenon of rejection has been overcome), a transgranular corrosion is present and virtually all corrosion products are dissolved by the uterine fluid and incorporated therein from the moment of its formation. Under these conditions, the contraceptive effect is greater when the dissolution power and a higher corrosion rate exist, and therefore, a higher concentration of corrosion products in both the fluid and the uterine endometrium. However, corrosion may vary depending on the particular composition of the uterine secretions of each organism, as well as different degrees of calcification that may occur.

As a final conclusion and in general, we can say that the contraceptive effectiveness of IUDs is higher from the second year of implantation, and that when the implantation time is less than 24 months, the

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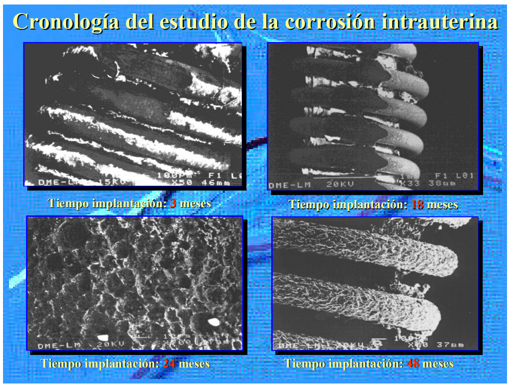
greater the risk of ineffectiveness, provided the risk of rupture and fragmentation of the wire is not eliminated.

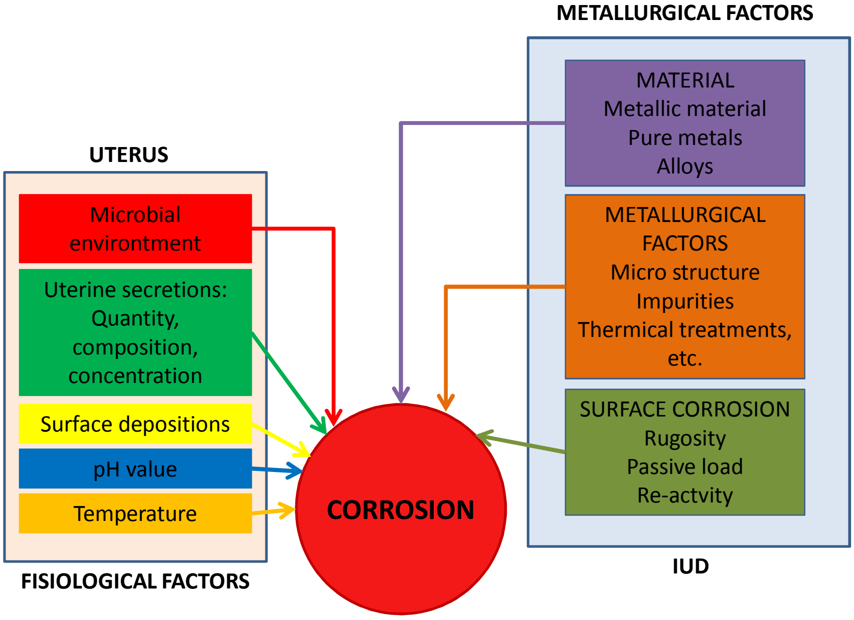
The precious metals group includes gold, silver and metals of the platinum family (Pt, Pd, Ir, Rh, Ru and Os). Except for silver, all have excellent resistance to corrosion. The use of silver is not appropriate when the corrosive environment contains any sulphur compound (S), since this is the only element that combines with silver to form silver sulphide. This sulphidation can lead to accelerated corrosion of the copper itself from the electrochemically effect and can break its core. This affects negatively the lifespan of the IUD and its contraceptive effectiveness.

To avoid the totally and absolutely the absence of corrosion in the copper wire core along with a high degree of biocompatibility, it is proposed to replace the silver core with a gold one.



Intrauterine corrosion study chronology
3 months · 18 months
24 months · 48 months

FACTORS AFFECTING METAL CORROSION



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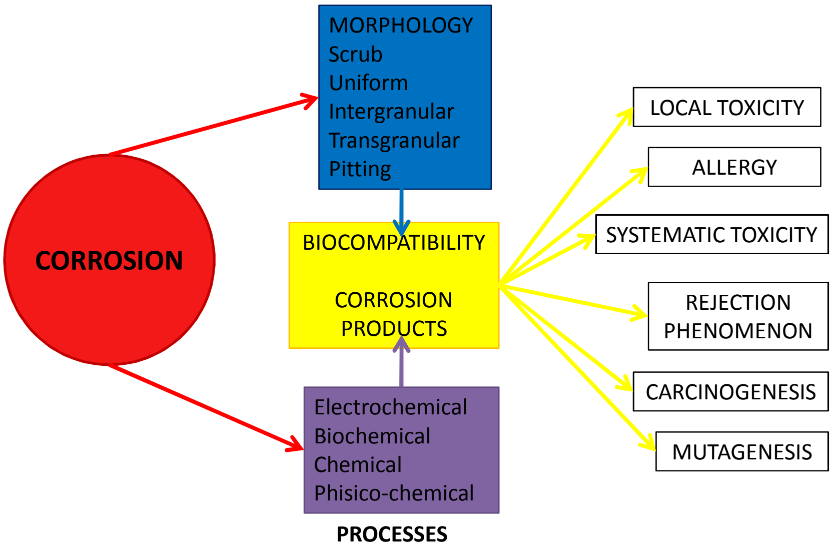
CORROSION AGAINTS CORROSION PRODUCTS



NEW DESIGN PHILOSOPHY

*A) **TAKE ADVANTAGE** and maintain the progress achieved to date in accordance with the experience from the majority of international experts in the field of contraception by IUD, which can be summarized as follows:*

*A.1. Maintain **HIGH COPPER CONTENT**, (375 mm^2 of the surface in our model) as an active principle.*

*A.2. Preserve the **geometry** of the base frame shape in the specific "T" or "Y".*

*B) **IMPROVE:***

*B.1. The **lifespan** of the IUD*

*B.2.The **rupture risk** by secondary fragmentation in the corrosion process.*

*B.3.The **comfort** in the process, for its insertion and for its removal.*

*B.4.The **individual adaptability** to different uterine sizes.*

*B.5. The **accuracy** of its endouterin placement.*
*B.6.The **risk of uterine perforation** during manoeuvres required for its placement.*

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COMMENTS AND CONCLUSIONS ON THE IMPROVEMENTS MADE

- *The **B.1** and **B.2** improvements have been achieved by incorporating a gold core as the central support to the outer copper coating.*
  The gold gives the coil unchanging support that also ensures full biocompatibility.

  So far, the most "advanced" progress was the use of silver. Our study shows that the use of silver is not appropriate when the environment contains a sulphur compound (such as in the intrauterine ecosystem) as this is the only element that combines with silver to form the metal sulphide. This sulphidation accelerates the very copper corrosion by electrochemical effect can break the silver core. This will obviously adversely affect the life of the IUD and ultimately its contraceptive effectiveness. To achieve the total absence of corrosion of the copper wire core along with a high degree of biocompatibility, we have proposed replacing the silver core with a gold core.

- *The comfort in the insertion process **B.3** involves several points or benefits:*

  1. *The first one is that the complete IUD is hidden within the insertion cannula, and that when the ends of the arms of the IUD base frame are joined during its introduction by pulling the thread through the cannula, they form, by the hemispherical configuration of these ends, a ball that completely avoids them from entering it, preventing the edge of the inserter cannula is hurtful, and at the same time facilitating their passage through the cervical canal.*

  2. *The second advantage is that the external diameter of the insertion cannula is 3'6 mm, the lowest in the market. Therefore there is no need to dilate the cervical canal, given that the pre-hysterometry performed prior to the insertion would have produced enough dilation. Clearly, the absence of cervical dilation avoids the woman many hassles.*

- *The third one is improving the base-frame by replacing the end ring with a perforated sphere to let the fastening thread through (which provides guidance and traction control by the user at the time of its removal). The purpose of this substitution is twofold: it allows the lower end of the vertical arm not to be traumatic and make room for the metal coil without changing the total length of the IUD. At the same time, the area has greater tensile strength at the time of IUD removal, as the old rings could be sheared by the guide wire in extreme cases of tensile strength. Also, the geometry of the sphere avoids the possibility of wedging and of endocervical trauma on its descent towards the outside, during the pullout or extraction manoeuvre.*

- *Improving **individual adaptability B.4** is achieved by creating different "sizes" of the same model (with the same load of 375 mm^2), resulting in a more accurate choice for different receptors wombs. Also, the plastic device end section allows a certain degree of malleability, which allows adjusting its angle in different types of positions of the uterus.*

- *The **accuracy** in its final endouterin placement **B.5** is facilitated by a special "piston" in the inserter that can be secured in various positions, always selecting the closest to the previously performed histerometry ("adjustable piston"). Another important fact is that there has been a marked increase in the recovery capacity (which is called "viscoelastic memory") and the resistance of the folding arms, tall of this resulting in a better response to the attempts of the uterus to expel the IUD, and therefore, better safety in guarantying contraception.*

- *Finally, in addition to those described in paragraphs **B.3, B.4.** and **B.5** during the **decline in the risk of perforation B.6** also contributes to the inclusion of a "safety-part" in the insertion system, a safety plate that is removed from the assembly prior to the insertion of the IUD.*

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