

EXEM FOAM KIT BIBLIOGRAPHY  
AS SEEN AT THE PRESENTATION

*SUPPLEKEY HEALTH  
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THE EXCELSIOR HOTEL  
SKG*

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BY ERIC REEP  
IQ Medical Ventures BV

## 1. Bibliography of HyFoSy publications as used in the presentation:

- 2011 | Ultrasound Obstet Gynecol. | Emanuel Exalto | Hysterosalpingo-foam sonography (HyFoSy): a new technique to visualize tubal patency.
- 2011 | Human Reproduction | Chou Phay Lim | hysterosalpingogram first-line investigation diagnose in modern subfertility workup
- 2012 | Hum Reproduction | Emanuel | first experiences with HyFoSy
- 2013 | Gynecol Obstet | Van Schoubroeck | The use of a new gel foam for the evaluation of tubal patency
- 2014 | Am. Soc. Reproductive Medicine | Dreyer Hompes Mijatovic | Hysterosalpingo-foam sonography, (HyFoSy) a less painful procedure for tubal patency testing during fertility compared with (serial) hysterosalpingography: RCT | VU mc Amsterdam
- 2014 | Reproduction Medicine | Exalto Stassen Emanuel | Safety aspects and side-effects of ExEm-gel and foam for uterine cavity distension and tubal patency testing
- 2014 | Reproduction Medicine | Dreyer Hompes Mijatovic | Diagnostic accuracy of hysterosalpingo-foam-sonography
- 2015 | Reproduction Medicine | Van Schoubroeck | Spontaneous conception after hysterosalpingo-foam sonography (HyFoSy)
- 2015 | JMIG | Exacoustos | Can Tubal Flushing With HysteroSalpingo Foam Sonography (HyFoSy) Media increase Woman's chances on Pregnancy
- 2015 | EJOG | Lim, Jung, Ling Yu | Comparison of hysterosalpingo-foam sonography (HyFoSy) and hysterosalpingo-contrast sonography with saline medium (HyCoSy) in the assessment of tubal patency
- 2015 | Gyn & Obs | Van Schoubroeck | The Use of a New Gel Foam for the Evaluation of Tubal Patency (ExEm foam)
- 2016 | Journal of Ultrasound - Piccioni et al | HyFoSy vs HyCoSy with Saline
- 2017 | UltraSound Obst. Gyn | Exacoustos | Foam used for Essure confirmation test
- 2017 | JMIG | Ludwin | Pain intensity during ultrasound assessment of uterine cavity and tubal patency with and without painkiller
- 2018 | UltraSound Obst. Gyn | Zizolvi | [One-step transvaginal three-dimensional hysterosalpingo-foam sonography \(3D-HyFoSy\)](#)
- 2018 | JUM | Rosic | Use of Hysterosalpingo-Foam Sonography for Assessment of the Efficacy of Essure Hysteroscopic Sterilization
- 2018 | ANZJOG | Tanaka | Hysterosalpingo-foam sonography: tolerability, safety and occurrence of pregnancy post-procedure.
- 2018 | Minerva Ginecol | Riganelli I, casorelli a, caccetta J, Merlino I, Mariani M, Savone D, et al. Ultrasonography reappraisal of tubal patency in assisted reproduction technology patients: comparison between 2D and 3D-sonohysterosalpingography. a pilot study.

## 2. ExEm-Foam in Summary:

ExEm-gel and special designed applicators originally were developed for a more stable filling of the uterine cavity, being a patient and doctors friendly alternative for Saline Infusion Sonography (SIS). [1\*\*] Gel Instillation Sonography (GIS) became the first choice diagnostic procedure for uterine anomalies and pathology of the uterine cavity. Hysterosalpingo-Foam Sonography (HyFoSy), using ExEm-gel for

creating stable foam, was developed as an office procedure for tubal patency testing. [2,3\*\*] The technique was tested in a prospective laparoscopy-controlled study. [4\*\*] Hysterosalpingo Contrast Sonography (HyCoSy) is, compared to the Hysterosalpingography (HSG), a first-line investigation to diagnose female tubal subfertility. [5,6\*\*] For tubal patency testing HyFoSy with ExEm-gelfoam is performing better than HyCoSy with saline in terms of accuracy. [7,8\*\*] ExEm-gel is considered to be safe, as the components are well known and have been used intravenously and in the abdominal cavity for other medical purposes. There are no known serious side effects. [9\*\*] In a randomized controlled trial HyFoSy turned out to be less painful than HSG. [10\*\*] Furthermore, there are signs that HyFoSy may improve women's chances of pregnancy, although this has to be investigated in future studies further before firm conclusions can be drawn. [11-12]\*\*.

\*\*References:

### GIS and HyFoSy

1. Exalto N, Stappers C, van Raamsdonk LAM, Emanuel MH. Gel instillation sonohysterography: first experience with a new technique. *Fertil Steril* 2007; 87: 152-155.
2. Emanuel MH, Exalto N. Hysterosalpingo-foam sonography (HyFoSy): a new technique to visualize tubal patency. *Ultrasound Obstet Gynecol.* 2011; 37: 497-499.
3. Emanuel MH, van Vliet M, Weber M, Exalto N. First experiences with hysterosalpingo-foam sonography (HyFoSy) for office tubal patency testing. *Human Reprod* 2012; 27: 114-117.
4. Van Schoubroeck D, Van den Bosch T, Meuleman Ch, Tomassetti C, D'Hooghe Th, Timmerman D. The use of a new gel foam for the evaluation of tubal patency. *Gynecol Obstet Invest* 2013; 75: 152-156  
Tubal Patency testing.
5. Lim CP, Hasafa Z, Bhattacharya S, Mahesahwari A. Should a hysterosalpingogram be a first-line investigation to diagnose female tubal subfertility in the modern subfertility workup? *Human Reprod* 2011; 26: 967-971.
6. Luciano DE, Exacoustos C, Luciano AA. Contrast Ultrasonography for tubal patency. *J Min Inv Gynecol* 2014; 21:994-998.
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### Safety and side effects

9. Exalto N, Stassen M, Emanuel MH. Safety aspects and side-effects of ExEm-gel and foam for uterine cavity distension and tubal patency testing. *Reprod Biomed Online* 2014; 29: 534-540.

10. Dreyer K, Out R, Hompes PGA, Mijatovic V. Hysterosalpingo-Foam Sonography (HyFoSy): a less painful procedure for tubal patency testing during fertility work-up compared to (serial) hysterosalpingography. A Randomised Controlled Trial. Fertil Steril 2014; 102: 821-825

Enhanced pregnancy rate

11. Exacoustos C, Tiberio F, Szabolcs B, Romeo V, Romanini E, Zupi E. Can tubal flushing with Hysterosalpingo-Foam Sonography (HyFoSy) media increase women's chances of pregnancy? Virtual Poster in: J Min Inv Gynecol. 2015; 22: S238 (Pregnancy chance 6M after HyFoSy: prim. infert. 30% / sec. infert. 38%).

12. Van Schoubroeck D, Van den Bosch T, Van Tornout K, D'Hooge T, Timmerman D. Spontaneous conception after hysterosalpingo-foam sonography (HyFoSy). Ultrasound Obstet Gynecol 2015; 46; 51 (suppl. 1; OC24.01) (Nr of pregnancies – after 359 procedures – highest in HyFoSy cyclus and two cycli afterwards).

### 3. Benefits of ExEm® Foam

Tubal patency test using Ultrasound

Office based procedure

Highly echogenic foam – resulting in superior fill images

Gel foam is simple to use, easy to inject, enabling short and convenient procedure

Specificity and Selectivity are comparable with HSG – [minimizing the need for Radiation\\*](#)

Reduced discomfort for patient – [VAS pain score 50% less compared to HSG \\*\\*](#)

Perfect control over administration of gel foam, excellent tubal transit

Scientifically proven with multiple publications in renowned magazines

World wide 300.000 procedures performed – distributed in over 50 countries

#### Procedure

##### A. procedure steps

1. Place side opening speculum
2. Insert catheter ( without air and incl. foam )

3. Remove speculum > place TVUS transducer
4. Inject 1ml foam > access to Uterine Cavity (?)
5. Confirmed > Inject 2-3ml and fill the tubes
6. Start longitudinally > turn to transverse plane
7. Spot intra mural of right tube, continue to distal
8. Look for flow > spillage
9. Repeat at left side.

#### B. Procedural tips and tricks

a) Inject some gel foam through catheter after introduction of catheter into cervix. Gel foam will be visible immediately, confirming proper placement of catheter.

b) When checked, continue to add 2-3 ml of gel foam. Gel foam will be visible in uterine cavity and continues to flow through the tubes.

c) Rotation of the ultrasound transducer (from longitudinal plane to transversal plane) can visualize the movement of gel foam through fallopian tubes.

d) Tubal patency is proved by filling of the tubes and/or by spreading of gel foam intra-abdominally. Gel Foam is absorbed in 48hrs.

e) ExEm Foam can be visualized with any 2D or 3D UltraSound equipment.

#### c. Visible indicators

*Main indicator:*

Movement in the tubes:

> Patent tubes

In case you spot:

No spil but just flow in a (thin) tube. > Patent tubes

Only Spillage and no tubes? > Patent tubes

In case you spot:

A tube increasing in diameter size  
> indicates a potential blockage

No tube, no flow and no spillage > Stick to Lap & dye ( chromopertubation)

Expectation for Hydro Salphinx? > No foam echo or HSG > Stick to Lap & dye

## 4. F A Q

### 1. What is the ExEm Foam Kit made of?

ExEm Foam consists of:

ExEm gel – hydroxyethyl cellulose & glycerol.

Purified water.

When mixed together, a foam of micro-air bubbles is formed.

### 2. What does the ExEm Foam Kit consist of?

ExEm Foam Kit FK05 contains a 10ml syringe with 5ml of ExEm® gel, a 10ml syringe with 5ml ExEm purified water and includes a coupling device.

### 3. Is the ExEm Foam Kit a drug?

No. According to the European Medical Device Directive, ExEm Foam Kit is a CE marked, Class I Medical Device

This is valid in Europe and some countries in the Middle East, Africa, Asia, South America and Canada.

### 4. Is the ExEm Foam Kit a single use device?

Yes. For single use only. Do not reuse.

### 5. Is the ExEm Foam Kit licensed for my country?

Yes. CE marked for Europe specifically for intra-uterine investigations.

According to the European Medical Device Directive, ExEm Foam Kit is a CE marked, Class I Medical Device.

This is valid in Europe and some countries in the Middle East, Africa, Asia, South America and Canada.

#### 6. How long has the ExEm Foam Kit been on the market?

ExEm Gel has been available as a component of the GIS Kit (intra-uterine scanning) since 2007 and as part of the ExEm Foam Kit (tubal patency testing) since its launch in March 2010.

#### 7. Is the ExEm Foam Kit safe? Evidence?

Yes. Since its launch in 2010, over 250.000 patency tests have been carried out world wide with no reported adverse or allergic reactions. 'The combination of glycerol, hydroxyethyl cellulose and purified water is considered to be safe for intrauterine application and tubal patency testing'

Niek Exalto, Mario Stassen, Mark Hans Emanuel. Safety aspects and side effects of ExEm gel and foam for uterine cavity distension and tubal patency testing. Reproductive Biomedicine Online 2014; <http://dx.doi.org/10.1016/j.rbmo.2014.07.015>. Further evidence and publications are available on our website. Click the link 'literature and studies'.

More safety data is available upon request.

#### 8. Is the HyCoSy procedure uncomfortable for the patient?

No. 'HyCoSy is known as a well-tolerated examination with a very low rate of side effects and no late complications that required no atropine or anti-inflammatory drugs'

Luca Savelli, Paola Pollastri et al. Tolerability, side effects and complications of hysterosalpingo contrast Sonography (hycosy). Fertility and sterility 2009 October; Vol. 92, issue 4, pp. 1481-1486.

#### 9. What is the difference between HyCoSy and HyFoSy?

In principle, there is none. HyFoSy is the HyCoSy procedure using the ExEm Foam, where Contrast is replaced by Foam.

#### 10. What catheter should you use?

Preferably the GIS LN970 Nulli para catheter, which we offer next to the ExEm Foam Kit, but any transcervical catheter designed for intrauterine application can be used as long as the syringe fits to the catheter opening.

NB: a 5 French catheter may be used but care should be taken as the reduced lumen may require a slightly greater force when infusing.

### 11. What is the GIS catheter?

The GIS catheter has a tapered soft tip that is inserted gently into the external OS adapting to each individual patient. By removing the need to insert a balloon catheter fully into the uterus (or inflating a balloon catheter in the cervical canal) some of the discomfort experienced by some patients may be reduced.

### 12. How do you use the ExEm Foam Kit?

Dilute the 5 ml ExEm® gel with the 5 ml ExEm® purified water by mixing the fluids from one syringe through the coupling device into the other syringe (at least 10 times). This creates a gel foam. Leave the gel foam in one syringe and disconnect the other syringe and coupling device.

Connect the syringe containing the gel foam to a suitable catheter and infuse the gel foam within approximately 5 minutes.

### 13. How do you best perform the HyFoSy examination ?

Follow the Instructions for Use. You can find the IFU on our webpage, please click the link corresponding to your language.

### 14. User tips and tricks:

- a) Inject some gel foam through catheter after introduction of catheter into cervix. Gel foam will be visible immediately, confirming proper placement of catheter.
- b) When checked, continue to add 2-3 ml of gel foam. Gel foam will be visible in uterine cavity and continues to flow through the tubes.
- c) Rotation of the ultrasound transducer (from longitudinal plane to transversal plane) can visualize the movement of gel foam through fallopian tubes.
- d) Tubal patency is proved by filling of the tubes and/or by spreading of gel foam intra-abdominally. Gel Foam is absorbed in 48hrs.
- e) ExEm Foam can be visualized with any 2D or 3D UltraSound equipment.

### 15. How much Gel foam will I use per examination?

Typically, approximately 2-3 ml. On occasions, more may be required.

### 16. Are there any contraindications?

ExEm Foam Kit: Do not use the gel foam in case of allergy to any of the constituents of ExEm gel (hydroxyethyl cellulose, glycerol and purified water).

Tubal patency test: During pregnancy.

If the patient may be pregnant. Between ovulation and menstruation.

If the patient has co-morbidities. In the presence of active pelvic infection, sexually transmitted diseases and profuse bleeding.

#### 17. Ultrasound scanning of the uterus;

a) Which should I do first, the tubal patency test or the uterine scan?

When conducting a combined diagnostic session, the intrauterine scan should always be conducted prior to the tubal patency test. The Uterine scan may highlight conditions that negate the need for the patency test – Hydrosalpinx.

b) Can I use the ExEm Gel on its own (without mixing with purified water) to scan the Uterus?

Yes. The ExEm Gel on its own is an excellent dilator and will facilitate enhanced images due to its highly echogenic nature. Caution: due to the high viscosity of the ExEm Gel, a wait of at least 2 hours is recommended before then conducting a tubal patency test.

c) How long should I wait between the uterine scan and the patency test?

This will depend upon the contrast solution used for the uterine scan. No contrast: immediately.

Saline – wait for a few minutes for the cavity to empty (remove the catheter).

ExEm Gel – min 2 hours.

#### 18. When should I perform the patency test?

'Tests of tubal patency are usually performed during the follicular phase of the cycle after menstruation has ceased'

The Fallopian Tube in Infertility and IVF Practice, chapter on Fallopian Tube Patency Testing – Stephen R. Killick: Cambridge Medicine

#### 19. What should I do in the event of tubal spasm?

Wait a few minutes for the spasm to stop and then continue scanning. It should not be necessary to infuse more foam unless echogenicity has been low.

#### 20. How long do the microbubbles stay as a foam?

At least 7 minutes (sealed syringe). The remaining solution may be remixed in the syringe to re-introduce the air bubbles.

#### 21. How long do you have visualisation once the foam has been infused?

Once the required amount of the foam has been infused (2 – 3 ml) echogenicity should be maintained for approximately 7 minutes. If the test is prolonged, it may be necessary to infuse more of the Foam.

#### 22. Storage requirements

Store in suitable room and at a temperature between +5°C and +25°C.

#### 23. Temperature thresholds

During transport of the ExEm Foam Kit, a temperature in the tolerance range between +5°C and +25°C must be maintained. However, the products may temporarily (no longer than one week) be exposed to temperatures up to +40°C.

#### 24. Shelf life

Typically, 4 years of shelf life, detailed on the label which is attached to the packaging, unopened.

25. For any remaining questions, please contact [info@iq-medicalventures.com](mailto:info@iq-medicalventures.com)

## 5. Extended Literature list ExEm-gel® & HyFoSy

### HyFoSy historical data

1. Emanuel MH, Exalto N. Hysterosalpingo-foam sonography (HyFoSy): a new technique to visualize tubal patency. *Ultrasound Obstet Gynecol.* 2011; 37: 497-499
2. [With ExEm-gel a stabile foam can be achieved](#)
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4. [HyFoSy is a true "office procedure" for tuba tests.](#)
5. Van Schoubroeck D, Van den Bosch T, Meuleman Ch, Tomassetti C, D'Hooghe Th, Timmerman D. The use of a new gel foam for the evaluation of tubal patency. *Gynecol Obstet Invest* 2013; 75: 152-156.
6. [HyFoSy is a reliable and successful method in tuba tests](#)

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3. Resorption test of hydroxyethyl cellulose by mesothelial cells in vitro, 2013. BioTeSys GMBH, Esslingen. Code No. BTS 703/13
4. **Glycerol**
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2. [HyCoSy is superior and should replace HSG](#)
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4. [HyFoSy is reliable in a laparoscopic controlled study](#)
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#### Less Pain

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