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U.O.C. Clinica Ginecologica ed Ostetrica
Scuola di Specializzazione in Ginecologia e Ostetricia
Direttore Prof. Giovanni Battista Nardelli

**2015: the year of
cesarean scar pregnancy.
HIFU and new
perspectives**

Dott. Emanuele Ancona

- 1: Zhai JF, Xu M, Zhang B, Gao JW, Chen N. Treatments of caesarean scar pregnancy and the corresponding results in ten years. *Eur Rev Med Pharmacol Sci*. **2015** Jul;19(14):2523-7.
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- 4: Cheung VY. Reply to Letter to the Editor: Methotrexate Treatment for Cesarean Scar Ectopic Pregnancy: Learning Lessons. *J Minim Invasive Gynecol*. **2015** May 16.
- 5: Shokeir T. Methotrexate Treatment for Cesarean Scar Ectopic Pregnancy: Learning Lessons. *J Minim Invasive Gynecol*. **2015** May 16.
- 6: Ng BK, Lim PS, Ahmad S, Kampan NC, Abdul Karim AK, Omar MH. Cesarean scar pregnancy: What can we offer? *Taiwan J Obstet Gynecol*. **2015** Apr;54(2):208-10.
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- 11: Cheung VY. Local Methotrexate Injection as the First-line Treatment for Cesarean Scar Pregnancy: Review of the Literature. *J Minim Invasive Gynecol.* **2015** Jul-Aug;22(5):753-8.
- 12: Timor-Tritsch IE, Khatib N, Monteagudo A, Ramos J, Berg R, Kovács S. Cesarean scar pregnancies: experience of 60 cases. *J Ultrasound Med.* **2015** Apr;34(4):601-10.
- 13: Michaels AY, Washburn EE, Pocius KD, Benson CB, Doubilet PM, Carusi DA. Outcome of cesarean scar pregnancies diagnosed sonographically in the first trimester. *J Ultrasound Med.* **2015** Apr;34(4):595-9.
- 14: Huanxiao Z, Shuqin C, Hongye J, Hongzhe X, Gang N, Chengkang X, Xiaoming G, Shuzhong Y. Transvaginal hysterotomy for cesarean scar pregnancy in 40 consecutive cases. *Gynecol Surg.* **2015**;12(1):45-51. Epub 2014 Oct 22.
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- 16: Peng P, Gui T, Liu X, Chen W, Liu Z. Comparative efficacy and safety of local and systemic methotrexate injection in cesarean scar pregnancy. *Ther Clin Risk Manag.* **2015** Jan 27;11:137-42.
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- 21: He Y, Wu X, Zhu Q, Wu X, Feng L, Wu X, Zhao A, Di W. Combined laparoscopy and hysteroscopy vs. uterine curettage in the uterine artery embolization-based management of cesarean scar pregnancy: a retrospective cohort study. *BMC Womens Health*. **2014** Sep 24;14:116.
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Cesarean section ectopic pregnancy (CSEP) occurs when an early pregnancy (blastocyst) implants on myometrial tissue from an existing cesarean section scar.

If unrecognized and allowed to develop and grow devastating complications:

- Placental abnormalities (accreta)
- Catastrophic life-threatening maternal hemorrhage
- Uterine rupture



Type I

Implantation of a gestational sac in the existing scar with growth toward the uterine cavity.

Case Report

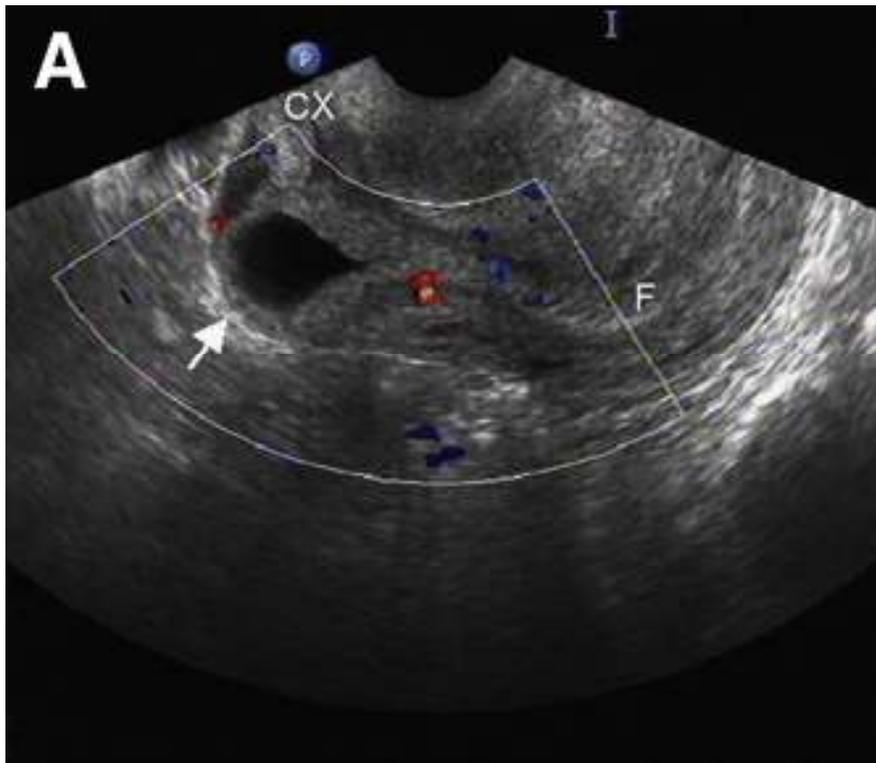
Ectopic Pregnancy within a Cesarean Scar Resulting In Live Birth: A Case Report

Firoozeh Ahmadi MD¹, Deena Moinian MSc¹, Parichehr Pooransari MD¹, Zohreh Rashidi BSc¹, Hadiieh Haghghi BSc¹

At 38 weeks, the baby was safely delivered during a three-hour long cesarean section operation. A placenta previa and 30 % placenta accrete was observed. After delivery, the placenta was stuck to the lower segment which caused bleeding. Despite the efforts made to control the bleeding, a hysterectomy was performed. The fully extracted placenta was transferred to the pathology laboratory for further study. The patient had an uneventful postoperative recovery and was discharged from the hospital on postoperative day 3.

Herman A 1995 Oct;102(10):839-41.

Ahmadi F, 2013 Nov;16(11):679-82



Type II

Deep implantation into the scar defect with growth towards the myometrium, the uterine serosal layer and the bladder

High risk of uterine rupture and uncontrolled hemorrhage

Incidence

1:2,216

6.1% of ectopic pregnancies



- Increased rate of cesarean delivery (50% in China)
- Transvaginal color Doppler sonography diagnosis

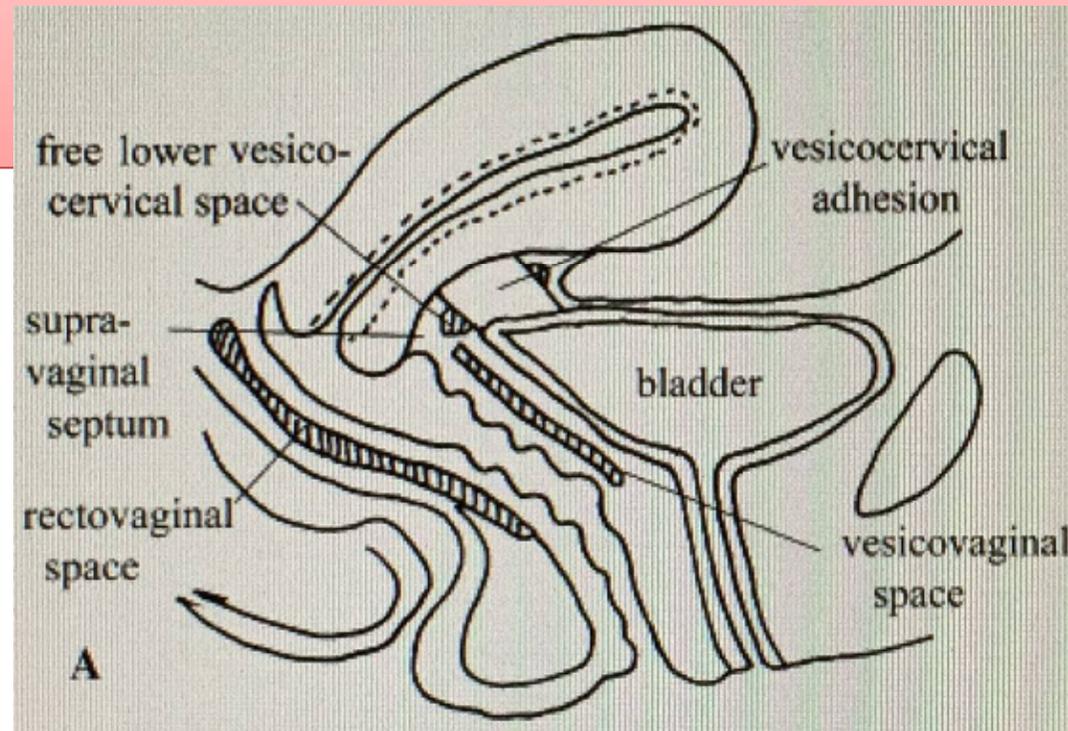


Risk factors

- Cesarean delivery history in rural community hospitals (China)
- Earlier cesarean scar pregnancy
- Repeated cesarean scar pregnancies
- Earlier surgeries (cesarean delivery or Myomectomy)
- Brief interval between the surgery and subsequent conception.

Timing of previous cesarean section

- Elective cesarean section: Isthmic scar and reduced risk of vesical adhesences
- Cesarean section during labour/dilatative phase: cervical/low scar with high risk of adhesences



Maymon R Hum Reprod Update. 2004 Nov-Dec;10(6):515-23

Qian ZD. Fertil Steril. 2014 Jul;102(1):129-134

Rotas MA. Obstet Gynecol. 2006 Jun;107(6):1373-81

Etiology

Invasion of the myometrium through a microscopic tract that develops from the trauma of earlier uterine surgery, such as curettage, CS, or myomectomy.



- Scar has a deleterious effect on decidualization
- The scar surface is increased after repeated cesarean sections and the anterior uterine wall may be deficient because of poor vascularity, fibrosis, and impaired healing

Symptoms

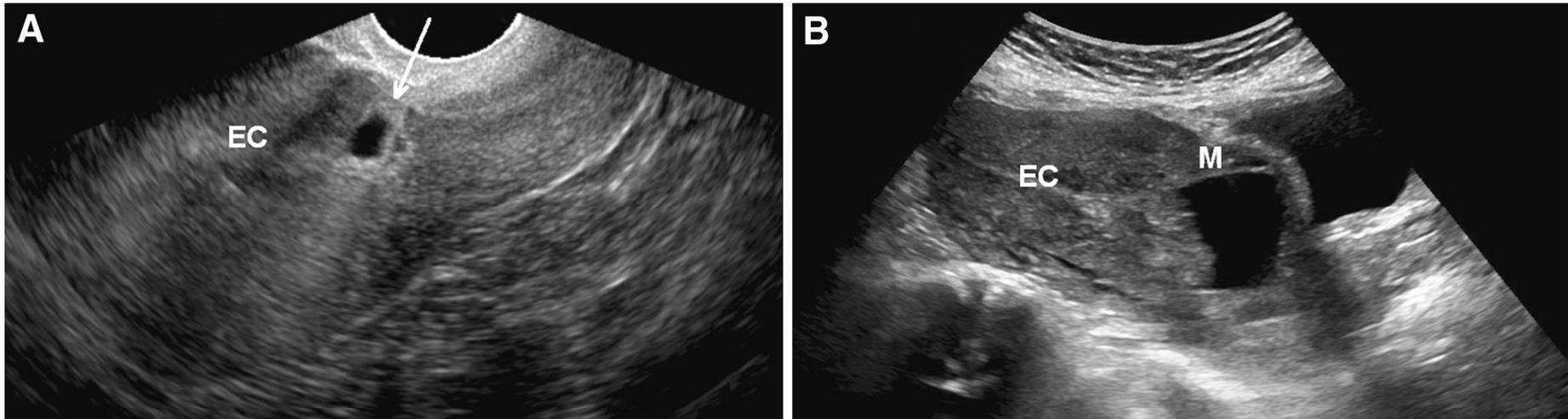
- Vaginal bleeding
 - Spotting
 - Pain or cramping
 - Asymptomatic
-
- Occasional finding during gestational age scanning

Riaz Abdom Imaging. **2015** Jun 13.

Timor-Tritsch J Ultrasound Med. **2015** Apr;34(4):601-10.

1. Endometrial and endocervical canal devoid of a pregnancy
2. Placenta/gestational sac embedded in the hysterotomy scar
3. Triangular gestational sac that fills the niche of the scar
4. A thin (1–3 mm) or absent myometrial layer between the gestational sac and bladder
5. Embryonic/fetal pole with or without heart activity;
6. Prominent and at times rich vascular pattern at or in the area of a cesarean delivery scar
7. All of the above in the presence of positive human chorionic gonadotropin (hCG) levels.

Diagnosis- Ultrasound

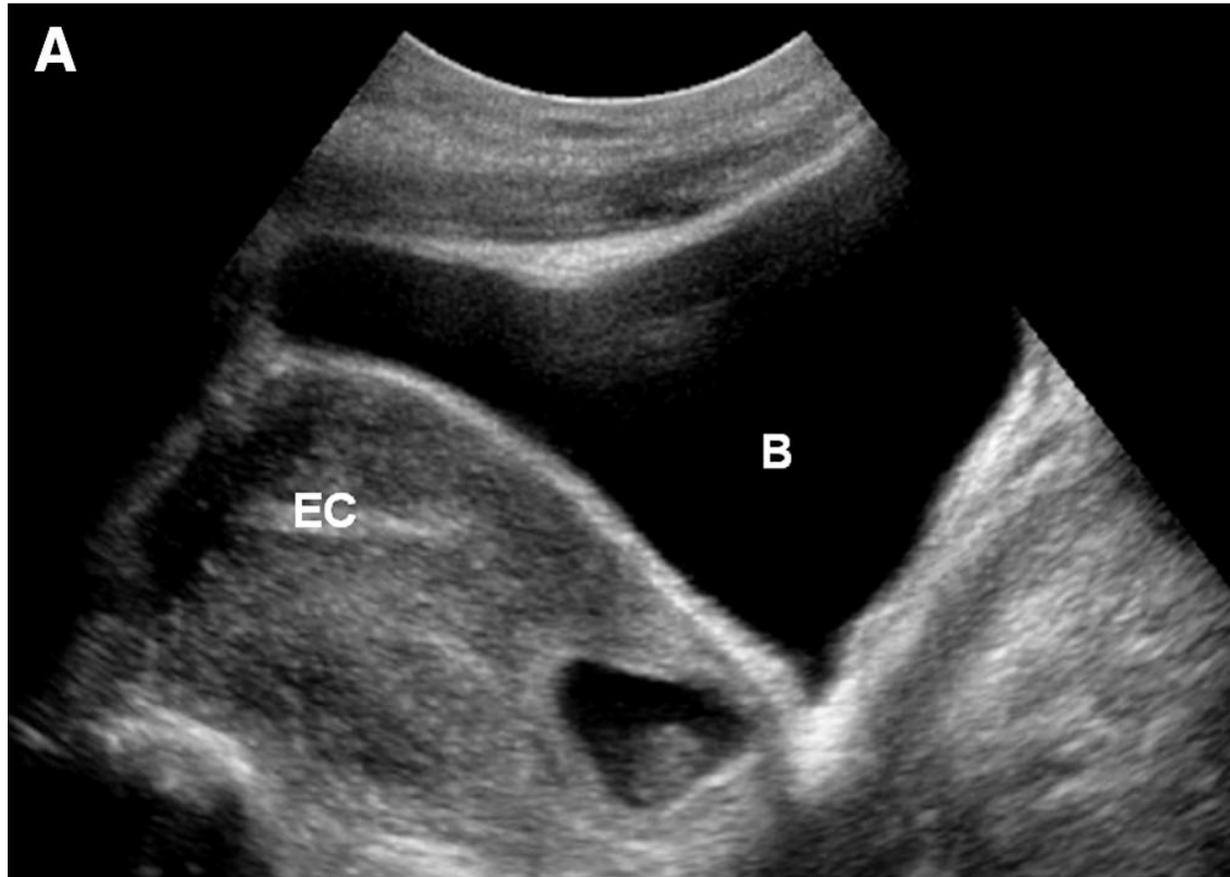


The gestational sac is implanted on the cesarean section scar (arrow) in the anterior LUS, with thinned myometrium (M) anteriorly and an empty endometrial cavity (EC).

Riaz Abdom Imaging. **2015** Jun 13.

Timor-Tritsch J Ultrasound Med. **2015** Apr;34(4):601-10.

Diagnosis- Ultrasound

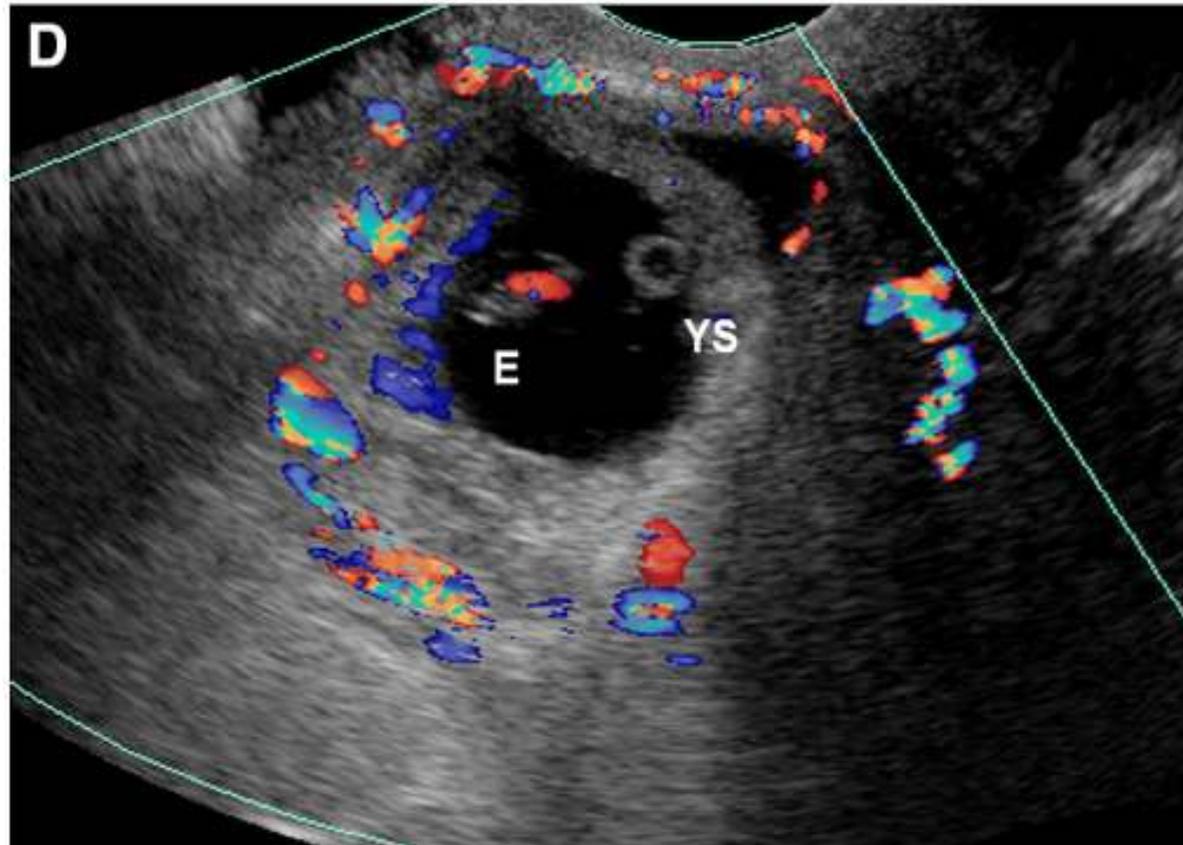


Eccentrically located gestational sac in the LUS in close proximity to the bladder, causing a bulge in the uterine contour at the scar

Riaz Abdom Imaging. **2015** Jun 13.

Timor-Tritsch J Ultrasound Med. **2015** Apr;34(4):601-10.

Diagnosis- Ultrasound



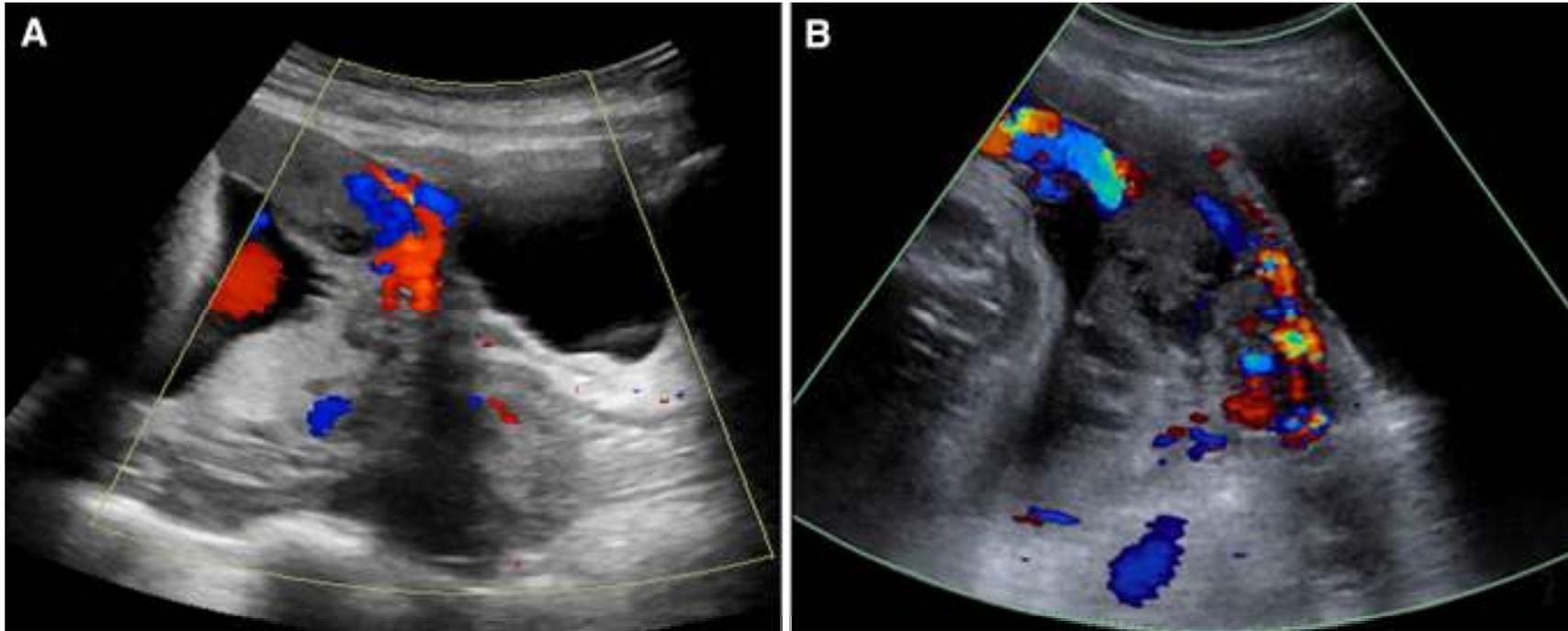
A yolk sac and embryo are seen with significant Doppler flow

Riaz Abdom Imaging. **2015** Jun 13.

Timor-Tritsch J Ultrasound Med. **2015** Apr;34(4):601-10.

Placental invasion

- Partial invasion into the myometrium (placenta accreta)
- Complete invasion of the myometrium (placenta increta)
- Extension through the myometrium (placenta percreta)



- Loss of the normal myometrial **placental interface** with increased or focal loss of Doppler color flow
- **Vascularized lacunae** within the placenta, and outward bulging of the uterine contour.
- Loss of the bladder wall reflector and the presence of placental tissue or vessels within the urinary bladder

Riaz Abdom Imaging. **2015** Jun 13.

Timor-Tritsch J Ultrasound Med. **2015** Apr;34(4):601-10.

Ultrasound criteria for diagnosis were as follows:

Greyscale:

- loss of the retroplacental sonolucent zone
- irregular retroplacental sonolucent zone
- thinning or disruption of the hyperechoic serosa-bladder interface
- presence of focal exophytic masses invading the urinary bladder
- abnormal placental lacunae.

Colour Doppler:

- diffuse or focal lacunar flow
- vascular lakes with turbulent flow (peak systolic velocity over 15 cm/s)
- hypervascularity of serosa-bladder interface
- markedly dilated vessels over peripheral subplacental zone.

Three-dimensional power Doppler:

- numerous coherent vessels involving the whole uterine serosa-bladder junction (basal view)
- hypervascularity (lateral view)
- inseparable cotyledonal and intervillous circulations, chaotic branching, detour vessels (lateral view).

Placenta Praevia, Placenta Praevia
Accreta and Vasa Praevia: Diagnosis
and Management



Placenta Praevia, Placenta Praevia
Accreta and Vasa Praevia: Diagnosis
and Management

The main MRI features of placenta accreta include:⁷⁴

- uterine bulging
- heterogeneous signal intensity within the placenta
- dark intraplacental bands on T2-weighted imaging.



MRI

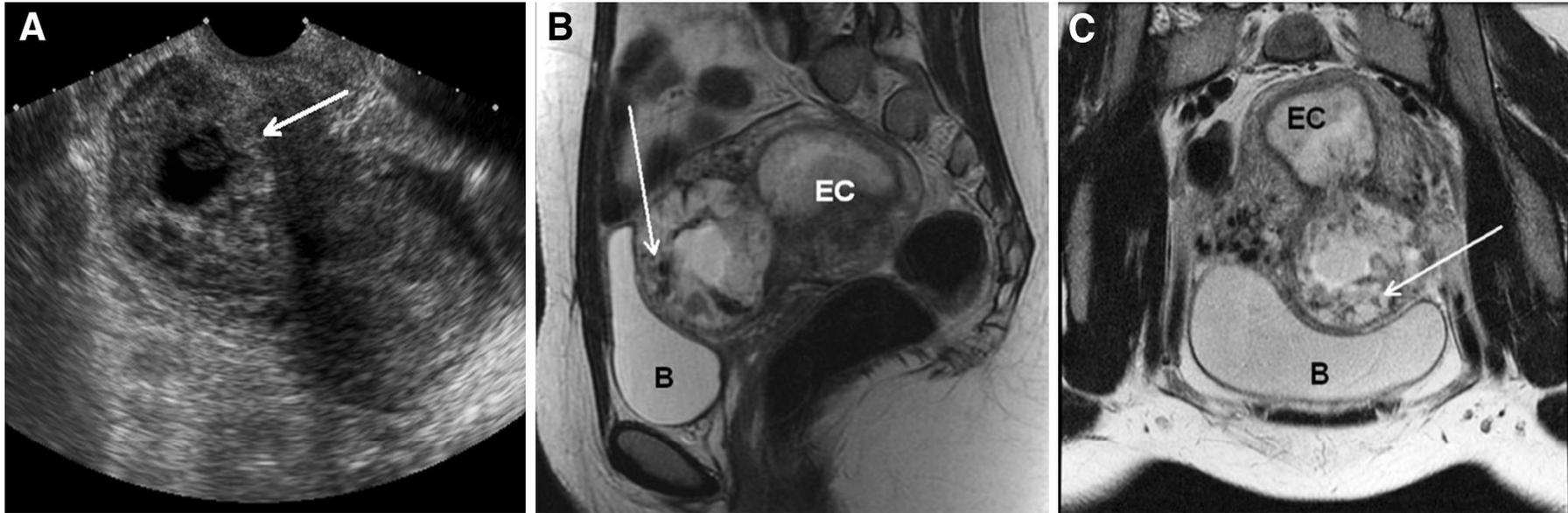
- Confirm the ectopic location of the gestational sac
- Evaluate placentation (determine position relative to adjacent structures).

MR findings of early CSEP are similar to ultrasound

- Implantation of the gestation on the cesarean section scar
- Myometrial defect
- Empty endometrial cavity and endocervical canal

Placenta accreta MRI findings

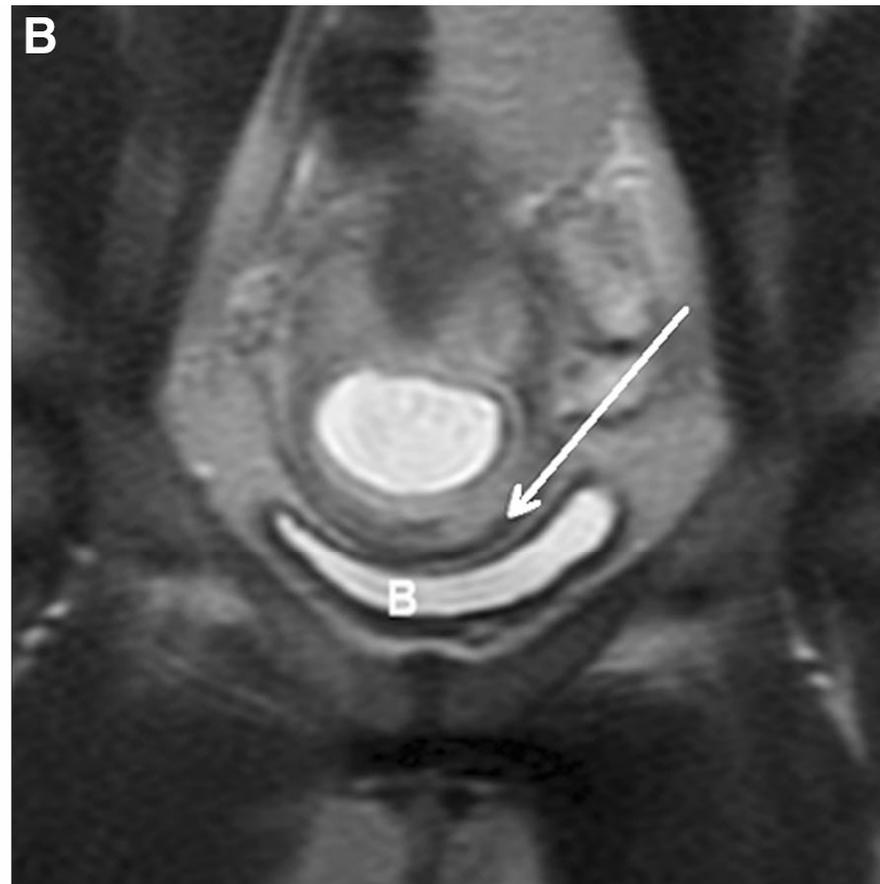
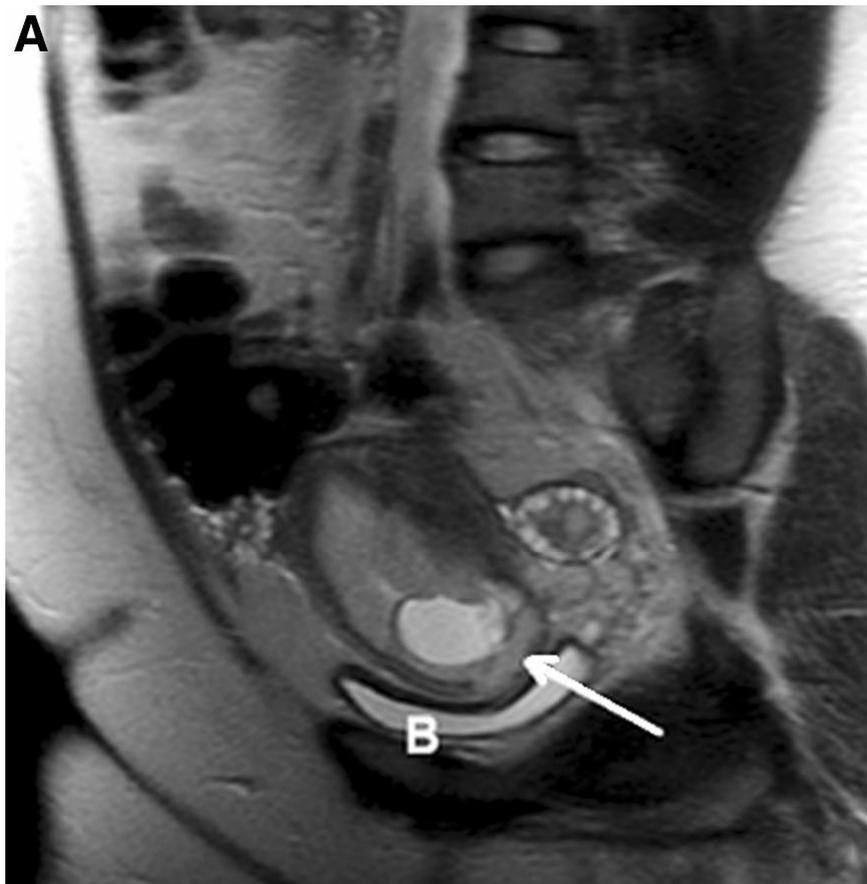
- Dark, irregular intraplacental bands on T2-weighted sequences
- Thinning or loss of the subplacental myometrium
- Abnormal vessels
- Outward bulging of the uterine contour
- Invasion of the anterior abdominal wall or urinary bladder



Empty endometrial cavity (EC), myometrial thinning and proximity of the trophoblastic tissue to the urinary bladder B.

Riaz Abdom Imaging. **2015** Jun 13.

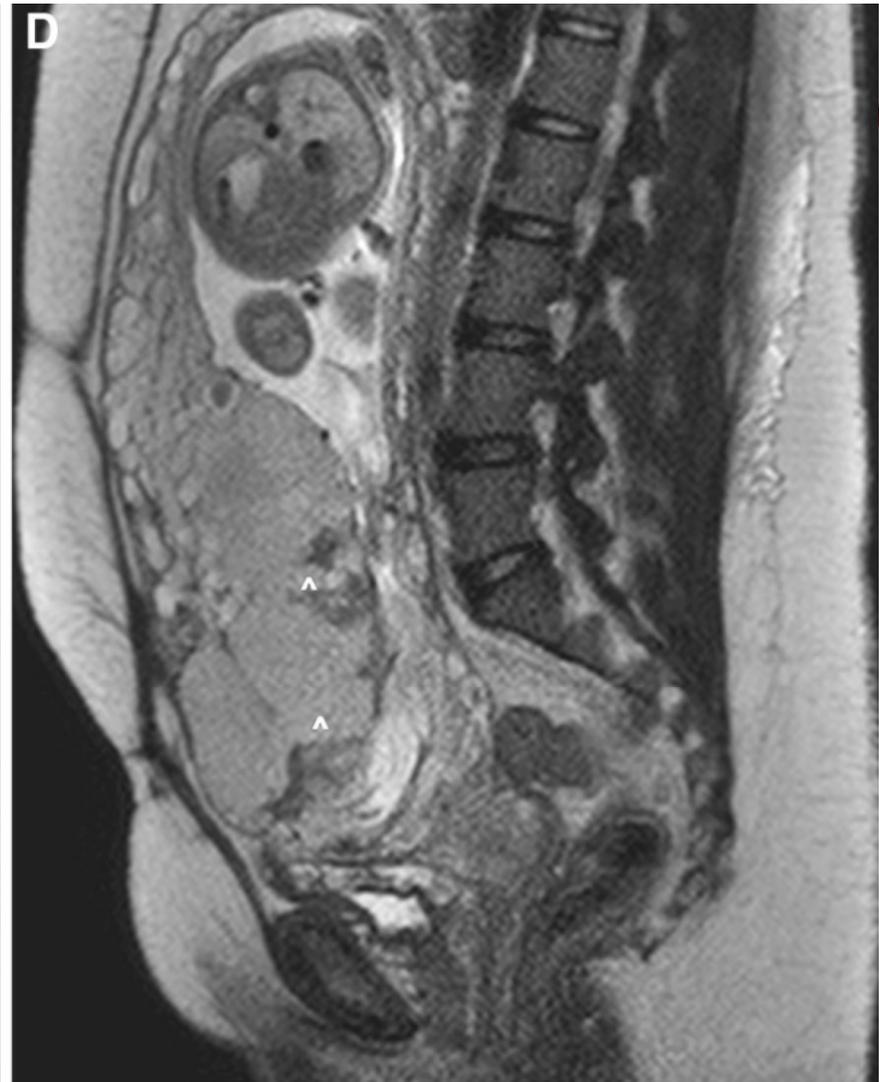
Timor-Tritsch J Ultrasound Med. **2015** Apr;34(4):601-10.



Bulging of the LUS contour and a focal absence of the myometrium anteriorly

Riaz Abdom Imaging. **2015** Jun 13.

Timor-Tritsch J Ultrasound Med. **2015** Apr;34(4):601-10.

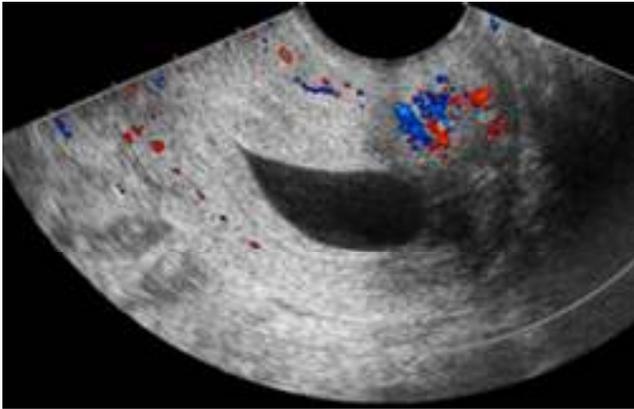


Dark T2 placental bands (^), thought to represent areas of placental hemorrhage and infarction.

Riaz Abdom Imaging. **2015** Jun 13.

Timor-Tritsch J Ultrasound Med. **2015** Apr;34(4):601-10.

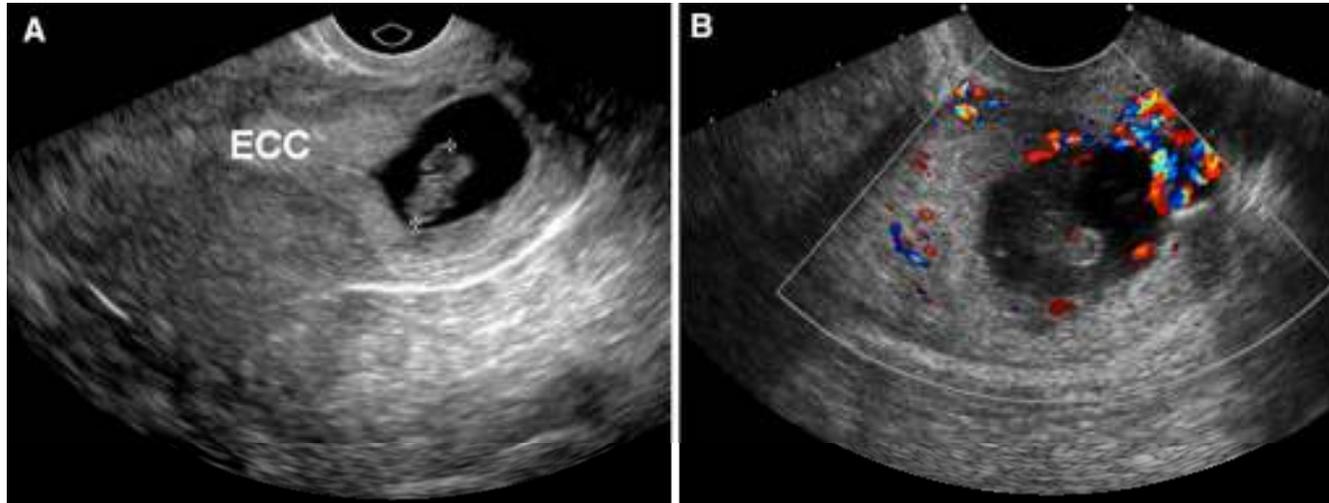
First trimester US differential diagnosis



Spontaneous abortion in progress:

gestational sac will be located in the endometrial canal and does not demonstrate the surrounding flow on color Doppler

First trimester US differential diagnosis



Cervical ectopic pregnancy :

- Sac will be located within the endocervical canal rather than within the anterior LUS.
- Myometrium remains intact
- Surrounding color flow

Riaz Abdom Imaging. **2015** Jun 13.

Timor-Tritsch J Ultrasound Med. **2015** Apr;34(4):601-10.

First trimester US differential diagnosis

Sliding organ sign

- The sac position and shape will change on short-term follow-up imaging as the abortion progresses.
- Ability to move a failed pregnancy within the endometrial canal with transducer pressure

Both CSEP and cervical ectopic pregnancies frequently contain live embryos with cardiac activity while an abortion in progress will not.

Riaz Abdom Imaging. **2015** Jun 13.

Timor-Tritsch J Ultrasound Med. **2015** Apr;34(4):601-10.

TREATMENT



- Eliminate the embryo
- Decrease the risk of bleeding
- Preserve the uterus to maintain further fertility before the gestational sac rupture and hemorrhage

Observational management

Not recommended

Complications increase as pregnancy progresses.
Catastrophic life-threatening maternal hemorrhage

Growth towards the uterine cavity has been documented sonographically (Cesarean section with hysterectomy)

The natural course of CSEP may be a spontaneous abortion even when carriage to term is desired.

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Timor-Tritsch J Ultrasound Med. **2015** Apr;34(4):601-10.

Methotrexate (MTX)

Methotrexate is an antimetabolite that binds to the catalytic site of dihydrofolate reductase, interrupting the synthesis of purine nucleotides and the amino acids serine and methionine, thus inhibiting DNA synthesis and repair and cell replication.

Affects actively proliferating tissues

- Bone marrow
- Buccal and intestinal mucosa
- Respiratory epithelium
- Malignant cells
- Trophoblastic tissue.



Hemodynamically stable patients

Methotrexate Treatment Protocols

*Single-dose regimen:**

Single dose MTX 50 mg/m² IM day 1

Measure hCG level on posttreatment days 4 and 7

Check for 15% hCG decrease between days 4 and 7.

Then measure hCG level weekly until reaching the nonpregnant level.

If results are less than the expected 15% decrease, re-administer MTX 50 mg/m² and repeat hCG measurement on days 4 and 7 after second dose. This can be repeated as necessary.

If, during follow-up, hCG levels plateau or increase, consider repeating MTX.

Two-dose regimen:†

Administer 50 mg/m² IM on day 0.

Repeat 50 mg/m² IM on day 4.

Measure hCG levels on days 4 and 7, and expect a 15% decrease between days 4 and 7.

If the decrease is greater than 15%, measure hCG levels weekly until reaching nonpregnant level.

If less than a 15% decrease in hCG levels, readminister MTX 50 mg/m² on days 7 and 11, measuring hCG levels.

(continued)

Methotrexate Treatment Protocols (continued)

Two-dose regimen:† (continued)

If hCG levels decrease 15% between days 7 and 11, continue to monitor weekly until nonpregnant hCG levels are reached.

If the decrease is less than 15% between days 7 and 11, consider surgical treatment.

Fixed multidose regimen:‡

Administer MTX 1 mg/kg IM (on days 1, 3, 5, 7), alternate daily with folinic acid 0.1 mg/kg IM (on days 2, 4, 6, 8).

Measure hCG levels on MTX dose days and continue until hCG has decreased by 15% from its previous measurement.

The hCG level may increase initially above pretreatment value, but after 15% decrease, monitor hCG levels weekly until reaching the nonpregnant level.

If the hCG level plateaus or increases, consider repeating MTX using the regimen described.

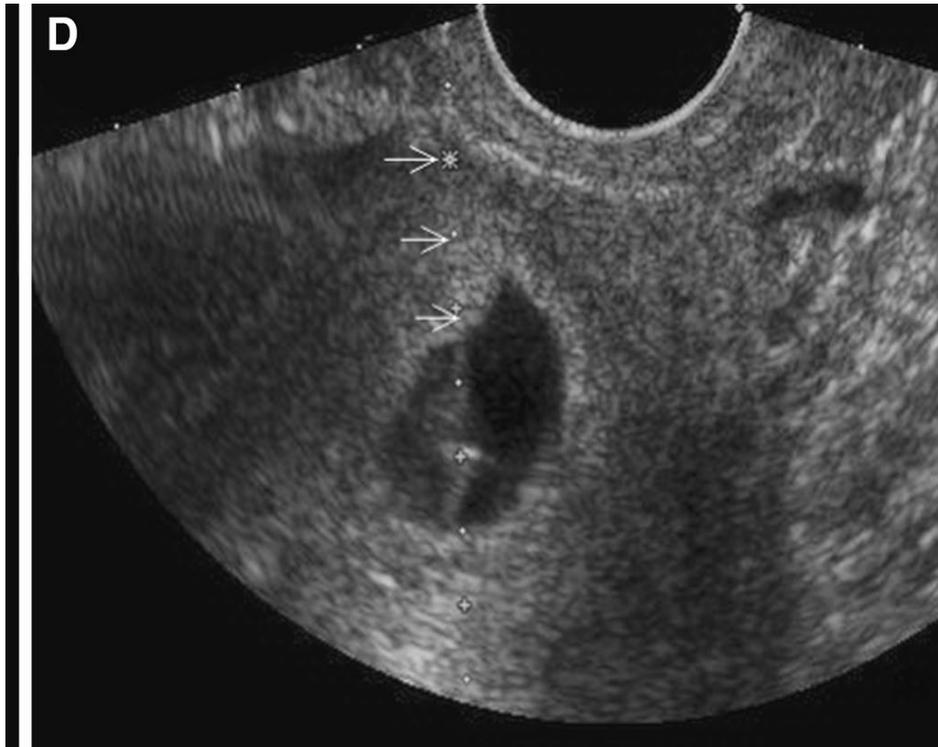
ACOG
PRACTICE
BULLETIN



Mifepristone (RU-486)

Misoprostol (Cytotec)

Can be used in conjunction to stimulate uterine contraction and help expel retained products of conception



Local methotrexate

- Transabdominally or transvaginally
- Amniotic sac is aspirated
- (Potassium chloride)

Table 1

Summary of case characteristics and outcomes

Study, year	Number of cases	Patient age (yr)	Gestational age at treatment (yr)	HCG (IU/L)	Local methotrexate dosage	Success rate (1 dose, with additional doses)	Surgical intervention (n)
Ko et al, 2014 [2]	10	34.9 ± 4.8 (26–41)	6.7 ± 1.6 (4.5–9.0)	50 666 (1962–139 653)	25–58.5 mg	80% (NA)	2
Yamaguchi et al, 2014 [4]	7	31.7 ± 4.3 (25–38)	7.5 ± 1.2 (6.5–9.4)	31 105 (10 957–95 707)	50 mg	71.4% (100%)	0
Cox et al, 2014 [5]	18	33.7 ± 3.4 (27–40)	6.2 ± 1.0 (5.1–8.3)	12 699.5 (2378–149 405)	25–50 mg/m ²	61.1% (83.3%)	3
Yin et al, 2014 [6]	22	28.5 ± 3.9 (NA)	9 ± 5.9 (NA)	40 154.2 ± 2249.2	50–80 mg	95.5% (NA)	1
Seow et al, 2013 [7]	11	33.8 ± 4.1 (29–42)	6.3 ± .7 (5.2–7.4)	20 520 (1290–81 586)	50 mg	45.5% (100%)	0
Pang et al, 2012 [8]	3	36.7 ± 6.1 (30–42)	7.3 ± 1.2 (6–8)	63 352 (22 305–205 321)	50 mg	66.7% (NA)	1
Frishman et al, 2012 [9]	1	27	6.4	32 673	50 mg/mL	100% (NA)	0
Tagore et al, 2010 [10]	1	38	7	11 546	20 mg	100% (NA)	0
Bij de Vaate et al, 2010 [3]	3	35.0 ± 3.6 (31–38)	6.5 ± 1.2 (5.1–7.4)	26 400 (14 000–40 000)	50–75 mg	66.7% (NA)	1
Pascual et al, 2007 [11]	1	38	First trimester	11 838	50 mg	100% (NA)	0
Hasegawa et al, 2005 [12]	2*	32	10.5 ± 2.1 (9–12)	NA	NA	100% (NA)	0
Hwu et al, 2005 [13]	1	31	6	29 377	50 mg	100% (NA)	0
Tan et al, 2005 [14]	2	37.0 ± 2.83 (35–39)	8.3 ± .4 (8.0–8.6)	93 615 (587–186 643)	50 mg	0% (100%)	0
Seow et al, 2004 [15]	6	32.2 ± 5.2 (27–41)	6.5 ± .9 (6.0–8.4)	21 725 (16 628–47 752)	1 mg/kg	100% (NA)	0
Jurkovic et al, 2003 [16]	6	39.4 ± 3.8 (34–43) [†]	6.7 ± 1.5 (5.0–9.0)	20 895 (3823–92 880)	25 mg	66.7% (NA)	2
Godin et al, 1997 [17]	1	33	9	62 000	60 mg	100% (NA)	0
Lai et al, 1995 [18]	1	27	7	5789	50 mg	0% (NA)	1

NA = not available/not applicable.

* In 1 patient with recurrent CSP.

[†] n = 5.

Cheung J Minim Invasive Gynecol. **2015** Jul-Aug;22(5):753-8.

Peng PTher Clin Risk Manag. **2015** Jan 27;11:137-42.

Local methotrexate dosage	Success rate (1 dose, with additional doses)
25–58.5 mg	80% (NA)
50 mg	71.4% (100%)
25–50 mg/m ²	61.1% (83.3%)
50–80 mg	95.5% (NA)
50 mg	45.5% (100%)
50 mg	66.7% (NA)
50 mg/mL	100% (NA)
20 mg	100% (NA)
50–75 mg	66.7% (NA)
50 mg	100% (NA)
NA	100% (NA)
50 mg	100% (NA)
50 mg	0% (100%)
1 mg/kg	100% (NA)
25 mg	66.7% (NA)
60 mg	100% (NA)
50 mg	0% (NA)



Cheung J Minim Invasive Gynecol. **2015** Jul-Aug;22(5):753–8.

Peng PTher Clin Risk Manag. **2015** Jan 27;11:137-42.

Peng P, Gui T, Liu X, Chen W, Liu Z. Comparative efficacy and safety of local and systemic methotrexate injection in cesarean scar pregnancy.

Ther Clin Risk Manag. 2015 Jan 27;11:137-42.

Table 2 Clinical outcome of local injection and systemic administration of MTX

Clinical outcome	Local injection	Systemic administration
Overall cure rate (%)	69.2%	67.3%
Time for serum β -hCG remission (days)	56 (24–92)	42 (21–69)
Time for uterine mass disappearance (d)	53 (23–88)	40 (20–67)
Hospitalization time (days)	12.4 \pm 6.1	10.9 \pm 7.0
Hospitalization fee (RMB)	4,976.3 \pm 4,339.4	4,384.4 \pm 4,009.7

Note: Data is presented as median with range and mean \pm SD.

Abbreviations: MTX, methotrexate; hCG, human chorionic gonadotropin.

Peng PTher Clin Risk Manag. 2015 Jan 27;11:137-42.

Contraindications to Medical Therapy

Absolute contraindications

Breastfeeding

Overt or laboratory evidence of immunodeficiency

Alcoholism, alcoholic liver disease, or other chronic liver disease

Preexisting blood dyscrasias, such as bone marrow hypoplasia, leukopenia, thrombocytopenia, or significant anemia

Known sensitivity to methotrexate

Active pulmonary disease

Peptic ulcer disease

Hepatic, renal, or hematologic dysfunction

Side effects

Nausea

Diarrhea

Leukopenia

Hepatic dysfunction

Arthralgias

Leg swelling

-
- Preserving future fertility
 - Slow resolution of the CSP
 - Variable success of systemic MTX (relative de-vascularized fibrous tissue surrounding the gestational sac and short half-life of MTX, which limits drug exposure when given systemically.)
 - Persisting risk of uterine rupture and hemorrhage

Suction Curettage

Suction curettage as first line treatment in cases with cesarean scar pregnancy: feasibility and effectiveness in early pregnancy.

Polat J Matern Fetal Neonatal Med. **2015** Apr 21:1-6.

- Contraindicated in an unruptured CSP because it might result in rupture of the implanted gestation and **massive hemorrhaging**.
- The trophoblastic tissue is outside the uterine cavity and thus **unreachable by a curette**
- Foley balloon catheter** to be inserted for tamponade because of persistent vaginal bleeding (**84% success rate**)

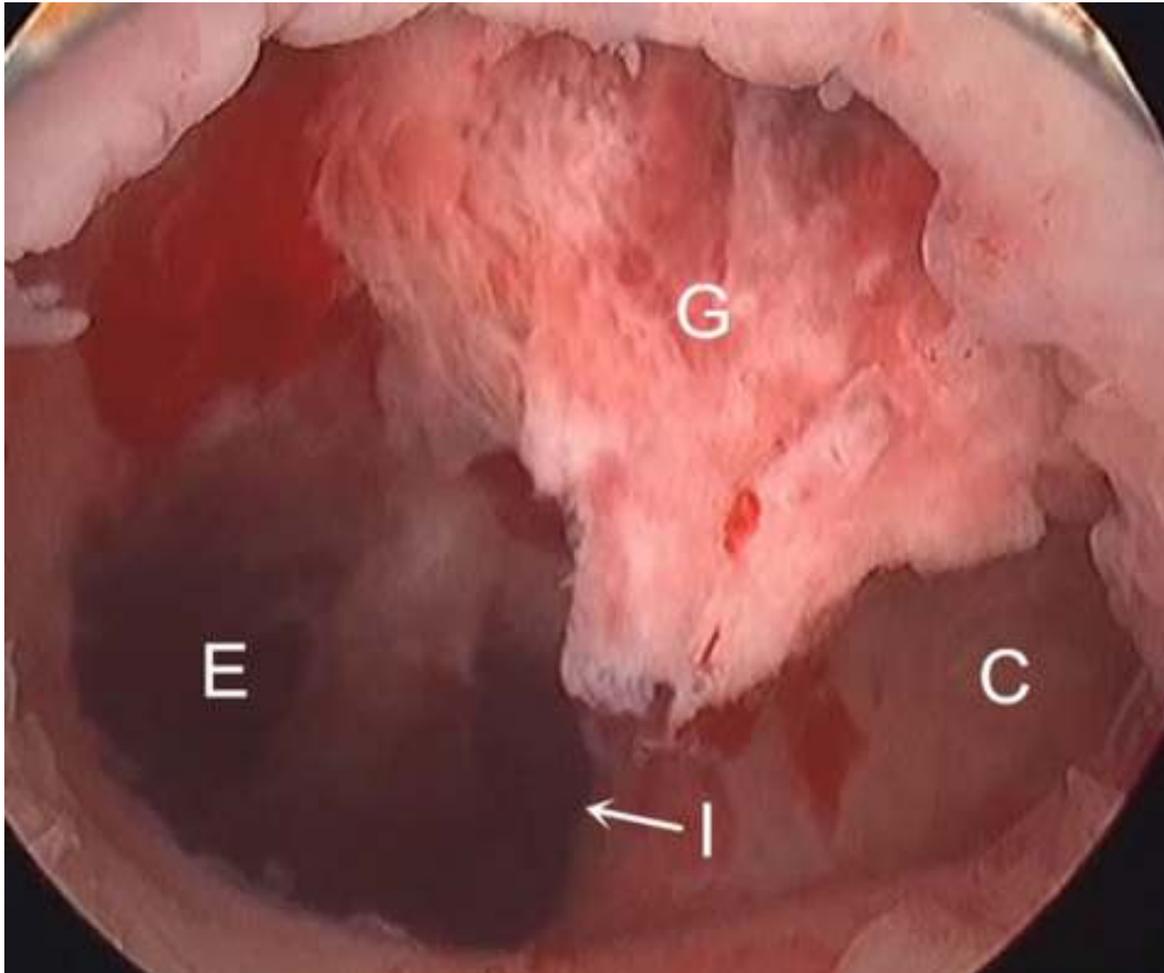
Hysteroscopy

Curettage or operative hysteroscopy in the treatment of cesarean scar pregnancy.

Qjian Arch Gynecol Obstet. **2015** May 3.

- Visualization of implantation site
- Separate gestational sac from myometrium under direct vision
- Loosened embryonic tissue removed by curettage
- Check bleeding and perform electrocoagulation.
- Rapid return to normal b-hCG level (reduction in follow-up time, rapid return to fertility)

Qian ZD Arch Gynecol Obstet. **2015** May 3.



C cesarean scar diverticulum
E endometrial cavity
G gestational Tissue
I internal os

-
- Not suitable for an inexperienced surgeon (skillful at manipulating hysteroscopic instruments and familiar to prevent massive bleeding)
 - Possible damage to bladder
 - Possible uncontrollable bleeding
 - Facilities for immediate laparoscopy or laparotomy must be available

Table 2 Outcomes of two groups

Characteristic	D&C after UAE	HSC after UAE
Total hospitalization time (days)	7.97 ± 2.49	7.61 ± 3.81
Hospitalization time after surgery (days)	4.79 ± 2.09	4.85 ± 3.93
Estimated intraoperative blood loss [mL, median (range)]	20.00 (5.00–100.00)	20.00 (5.00–1500.00)
Hospitalization cost [CNY, median (range)]	11,186.53 (8585.52–15,721.39)	12,576.01 (10,032.90–25,492.93)
Decline of serum β-hCG the day after surgery (%)	74.53 ± 12.60	74.27 ± 11.51
Side effect rate [<i>n</i> (%)]	1 (3.03)	4 (12.12)
Success rate [<i>n</i> (%)]	33 (100.00)	30 (90.91)
Hysterectomy rate [<i>n</i> (%)]	0 (0)	1 (3.03)
Time of bleeding after surgery [days, median (range)]	8.00 (3.00–60.00)	10.00 (2.00–60.00)
Time of serum β-hCG resolution after surgery (days)	30.15 ± 9.55	34.18 ± 14.12
Time of CSP mass disappearance [days, median (range)]	60.00 (14.00–92.00)	60.00 (0–91.00)
Intrauterine pregnancy after CSP [<i>n</i> (%)]	3 (9.09)	3 (9.09)

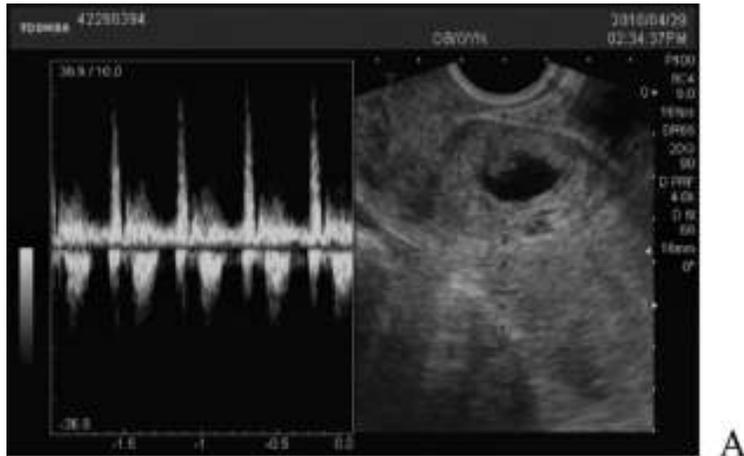
Preventive Uterine Artery embolization for all patients

Laparoscopy

- Remove ectopic gestational tissue
- Repair the defect
- Rapid bhcg decrease
- Preserve uterine integrity
- Future fertility
- Exclude bladder involvement



Wang YL, Weng SS, Huang WC, Su TH. Laparoscopic management of ectopic pregnancies in unusual locations. Taiwan J Obstet Gynecol. **2014** Dec;53(4):466-70.



A



B



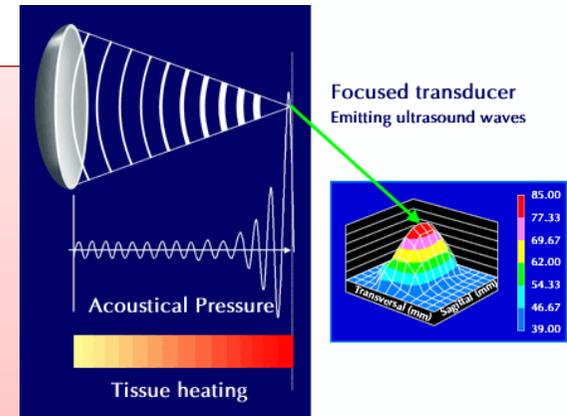
C

- Hemorrhaging remains a major concern
- Few literature reports
- Risks associated with laparoscopy and further adhesions
- Possible conversion to laparotomy

Wang YL, Weng SS, Huang WC, Su TH. Laparoscopic management of ectopic pregnancies in unusual locations. *Taiwan J Obstet Gynecol.* **2014** Dec;53(4):466-70.

HIFU (High Intensity Focused Ultrasound)

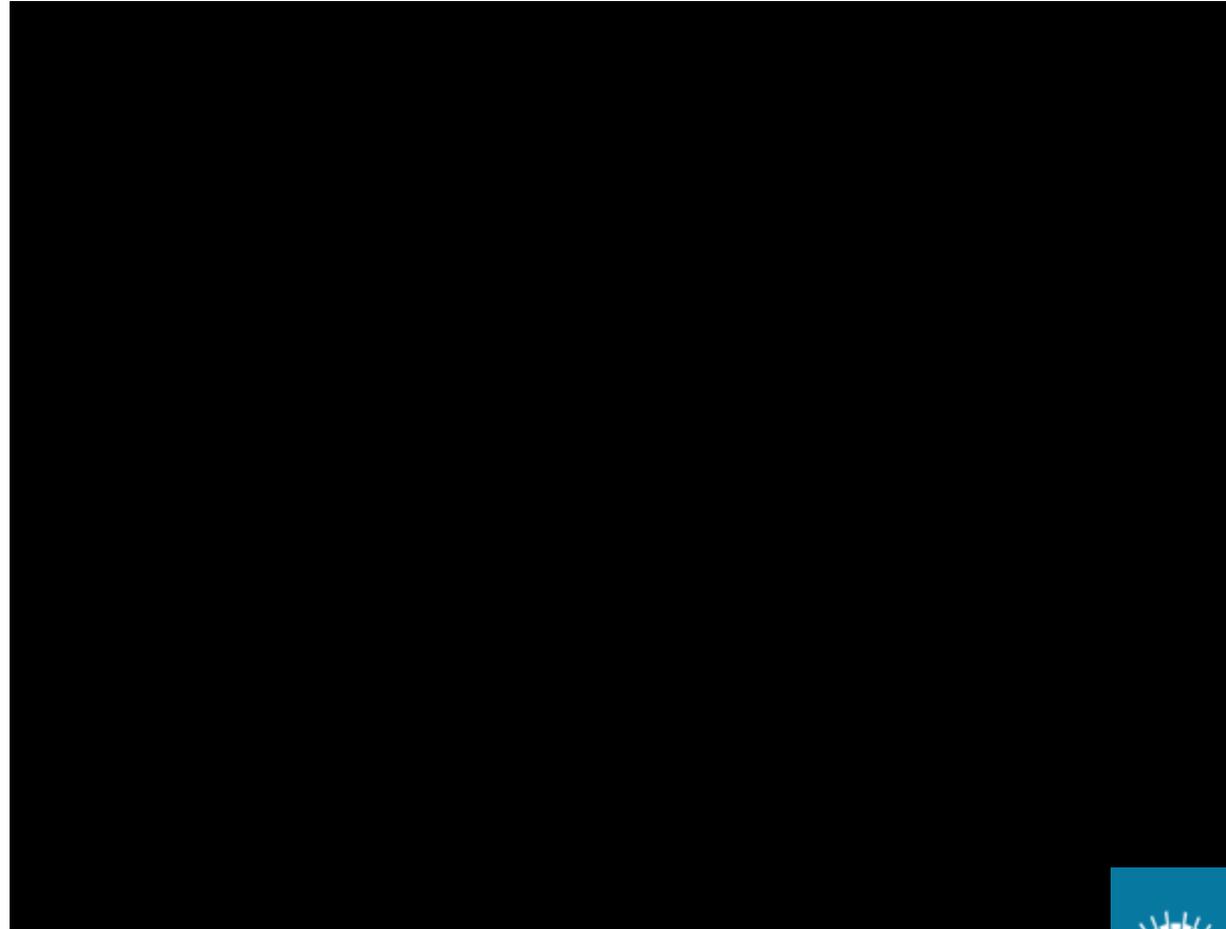
- Focused ultrasound
- Ultrasound imaging



Acoustic lens concentrate multiple intersecting beams of ultrasound on a target in the body

Target can be 1x1.5mm or as large as 10x16mm in diameter.

HIFU (High Intensity Focused Ultrasound)



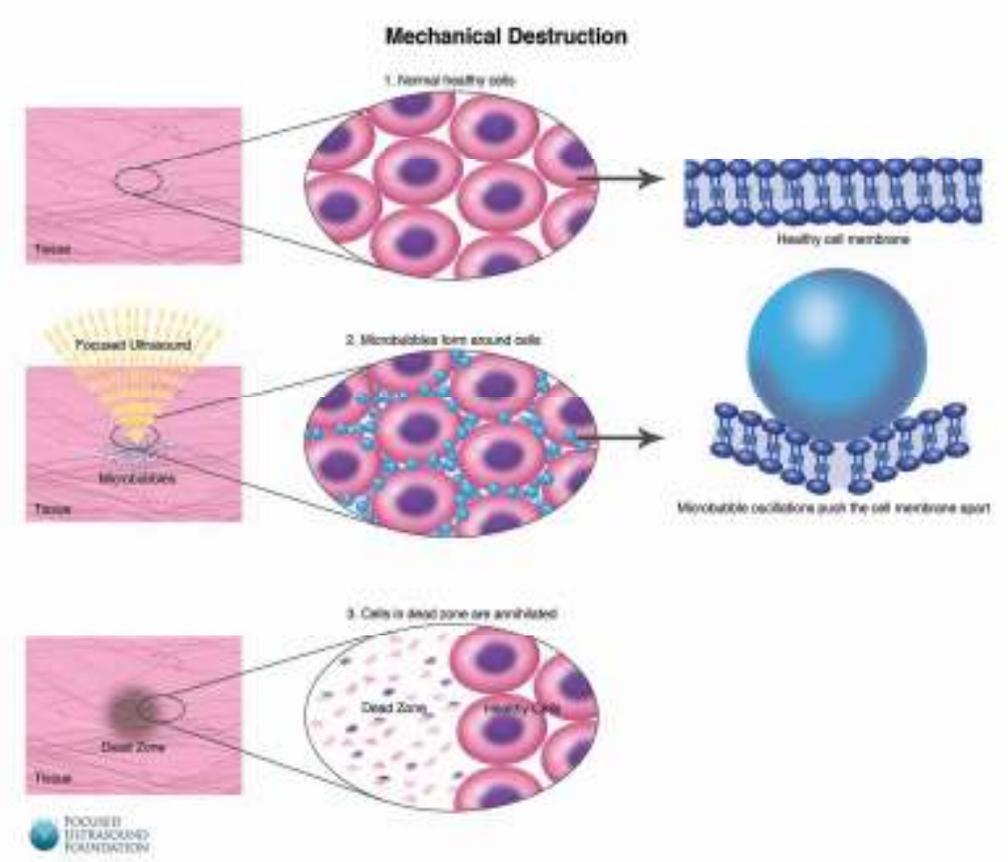
Biological Mechanisms and Disease Targets of Focused Ultrasound



Mechanisms	Diseases																		
	CARCINOMAS				NEUROLOGICAL								ONCOLOGICAL		WOMEN'S HEALTH				
	Alzheimer's	Cancer Metastasis	Depression	Yeast Metastasis	Alzheimer's Disease	Epilepsy	Essential Tremor	Hypothalamic Neurostimulation	Stroke Repair	Motor Neuron Disease	Migraine Pain	Parkinson's Disease	Psychotic Disorders	Tinnitus & Deafness	Uterine Fibroids	Surgical Injury (uterus, ovaries)	Endometriosis	Tamoxifen Injury (mammary glands)	
TISSUE DESTRUCTION																			
Thermal Ablation		•	•			•	•			•	•	•	•	•	•				
Mechanical Destruction		•												•					
DRUG DELIVERY																			
Sonoporation												•	•	•					
Increased Vascular Permeability					•							•		•					
Local Hyperthermia														•					
Drug Delivery Vehicles	•				•							•		•					
Vasodilation														•					
OTHER MECHANISMS																			
Vasoconstriction				•										•		•			•
Chemotherapy Sensitization														•					
Radiation Sensitization														•					
Neuromodulation						•	•			•	•	•	•						
Immunomodulation					•									•					
Cell Lysis	•							•	•										
Sonodynamic Therapy														•					
Blood Vessel Occlusion/Coagulation				•										•		•			•
Amplification of Cancer Biomarkers														•					
Stem Cell Homing					•							•					•		

Non-thermal cavitation

Mechanical process of vaporization of tissue water which leads to rapidly expanding microbubble production that subsequently collapse and release shock waves and high-speed liquid jets which are associated with extremely high pressures and temperatures.

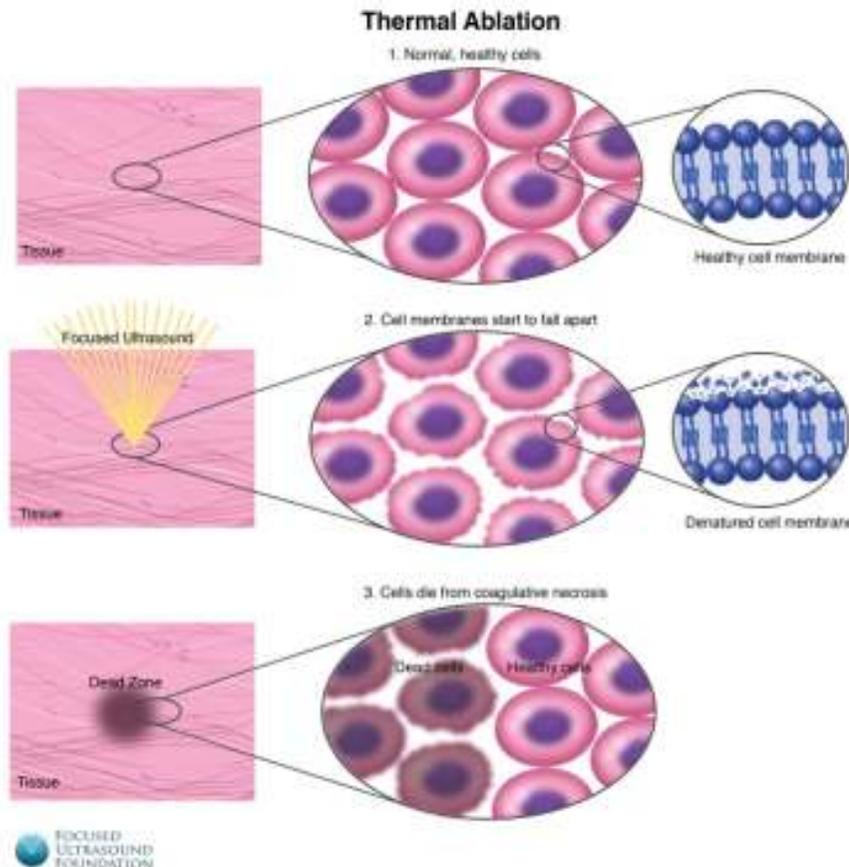




Thermal effects

Absorption of acoustic energy in tissues from viscous shearing and relaxation mechanisms.

Target spot reaches temperature greater than 55°C , denaturation and coagulative necrosis of the cells occurs, leading to cell death.





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Accelerating the Development and
Adoption of Focused Ultrasound



PHILIPS

Verasonics



PROMEDICA
BIOELECTRONICS



APPROVALS

Europe: CE

China: SFDA

Korea: KFDA

Russian Federation approval



Women's Health

Uterine Fibroids	
Breast Fibroadenomas	
Uterine Adenomyosis	
Tubal Pregnancy	
Fetal Surgery	
Ovarian Cancer	
Polycystic Ovarian Syndrome	

TECHNICAL REPORT

Efficacy of extracorporeal ultrasound-guided high intensity focused ultrasound: An evaluation based on controlled trials in China

Jun Luo¹, Xueyi Ren² & Tinghe Yu³

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Could Vessel Ablation by Magnetic Resonance-Guided Focused Ultrasound Represent a Next Future Gynecological Fertility-Sparing Approach to Fibroids?

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Salvatore Gizzo, MD¹, Emanuele Ancona, MD¹, Omar Anis, MD¹, Carlo Saccardi, MD, PhD¹, Tito Silvio Patrelli, MD², Donato D'Antona, MD¹ and Giovanni Battista Nardelli, MD¹

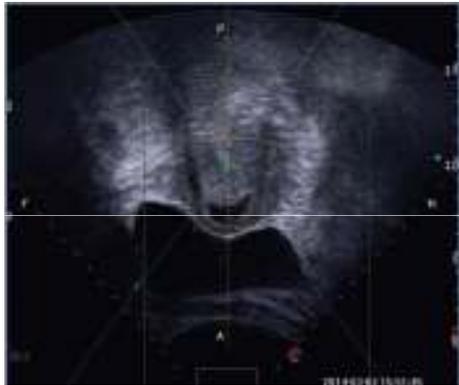
Magnetic Resonance-Guided Focused Ultrasound Myomectomy: Safety, Efficacy, Subsequent Fertility and Quality-of-Life Improvements, A Systematic Review

Salvatore Gizzo, MD¹, Carlo Saccardi, MD, PhD¹, Tito Silvio Patrelli, MD², Emanuele Ancona, MD¹, Marco Noventa, MD¹, Simone Fagherazzi, MD¹, Bruno Mozzanega, MD¹, Donato D'Antona, MD¹, and Giovanni Battista Nardelli, MD¹



High-intensity focused ultrasound combined with suction curettage for the treatment of cesarean scar pregnancy.

Zhu X et al. Medicine (Baltimore). 2015 May;94(18):e854. Impact Factor:5.723



Haifu 

No. of patients	53
Age, y	31.8 ± 4.8 (range, 22–44)
Low-segment cesarean delivery, n	
1	37
2	16
Previous caesarean pregnancies, n	
1	48
2	5
Interval time from the last CS, mo	48 (4–218)
Gestational age, d	47.7 ± 5.0 (37–56)
Subjective symptoms, n	
Painless vaginal bleeding	22
Abdominal pain	1
Vaginal bleeding and abdominal pain	10
No subjective symptoms, n	20
Serum β-hCG, mIU/mL	36645 (207.7–108257)
Largest diameter of the sac/mass, mm	37 (13–60)
Fetal heart activity detected, n	19
Thickness of the intervening myometrium, mm	3.7 ± 2.0 (1–9)

Inclusion

Gestational age <8 weeks

Exclusion

- Pelvic inflammatory
- Diseases
- Previous treatment for CSP

HIFU	
Median total treatment time, min	73 (range, 13–160)
Median sonication time, s	600 (range, 100–1538)
Sessions of HIFU ablation	1
Hysteroscopy	
Depth of the uterus, cm	10.0 ± 1.5 (range, 8–14)
Median blood loss, mL	20 (range, 10–400)
Follow up	
Ultrasound result 1 month later	
No pregnancy tissue retained	49
Pregnancy tissue retained*	4
Median duration of vaginal bleeding after HIFU, days	15 (range, 2–40)
Normal menstrual recovery, days	33.2 ± 8.1 (17–60)
Time for β-hCG reduction to an normal level, days	27.6 ± 6.4 (10–40)
Time of hospital stay, days	7.8 ± 1.5 (5–11)

Suction curettage under hysteroscopic guidance 2.9 days after HIFU ablation.

TABLE 3. Incidence Rate of Adverse Effects or Complications After HIFU Treatment (n = 53)

SIR Class	Description	No. (%)	Complications	No. (%)
A	No therapy, no consequences	7 (13.2)	Lower abdominal pain Vomiting	6 (11.3) 1 (1.9)
B	Nominal therapy, observation, no consequences	0		
C	Required therapy, minor hospitalization (<48 h)	0		
D	Major therapy, unplanned increase in level of care, prolonged hospitalization (\geq 48 h)	0		
E	Permanent adverse sequelae	0		
F	Death	0		

HIFU = high-intensity focused ultrasound, SIR = Society of Interventional Radiology.

These adverse effects can be explained by uterus contraction after HIFU.

Xiao J. Cesarean scar pregnancy: noninvasive and effective treatment with high-intensity focused ultrasound.

Xiao J. Am J Obstet Gynecol. 2014 Oct;211(4):356.e1-7 Impact Factor of **3.973**

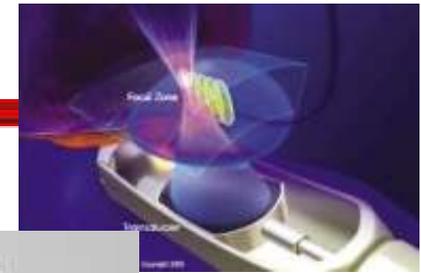
OBJECTIVE: The aim of this preliminary study was to investigate whether ultrasound-guided high-intensity focused ultrasound (HIFU) can play a role in treating cesarean scar pregnancy (CSP).

STUDY DESIGN: Between November 2011 and December 2012, **16 patients** with CSP were treated with ultrasound-guided HIFU ablation. Successful treatment was defined as disappearance of CSP mass, undetectable serum beta human chorionic gonadotropin, and **no serious complications such as severe bleeding, uterine rupture, or hysterectomy.**

RESULTS: All patients were successfully treated in the outpatient department and none required readmission. After 2-5 treatment sessions, the mean time for achieving undetectable serum beta human chorionic gonadotropin was **4.94 ± 2.32 weeks**, and the mean time for CSP mass disappearance was 6.69 ± 3.36 weeks. Three patients experienced moderate abdominal pain that subsided in 1-2 days, and nine patients experienced mild vaginal bleeding (<30 mL) that resolved within 2-3 days. All 16 patients had recovered their normal menstruation function at follow-up.

CONCLUSION: These preliminary results suggest that ultrasound-guided HIFU ablation is a noninvasive, feasible, and effective method for the treatment of CSP.

-
- HIFU ablation could be used to kill CSP tissues and destroy small blood vessels around the CSP.
 - HIFU may help reduce the blood loss during the procedure of suction curettage under hysteroscopic guidance.
 - Removing cardiac activity there is no longer growth of the CSP
 - Thermal effect of HIFU can destroy the pregnancy tissue by damaging the microvascular system within the tissue



WHAT'S
NEXT?

