Her Option® Clinical Study Summary

2,159 Patients in 20 Separate Studies

Her Option Efficacy Studies

<table>
<thead>
<tr>
<th>Study &amp; Publication</th>
<th>Authors</th>
<th>Number of Patients</th>
<th>Key Findings</th>
</tr>
</thead>
</table>
| Endometrial Cryoablation: 2-Year Follow-Up, AAGL, 2004       | R. Bruno R. Samuelson J. Hard V. Soto-Wright N. Peterson | 91-at 1 year 86-at 2 years | • 91% effectively treated for menometrorrhagia with 50% amenorrhea or spotting, at 12 mos.  
  • 89% effectively treated for abnormal uterine bleeding with 47% amenorrhea or spotting, at 24 mos.  
  • 6 patients underwent hysterectomy due to treatment failure  
  • Modified freeze technique with 7 minutes in each cornu and a 4-minute pull-back freeze in the lower uterine segment of patients with uteri greater than 9-cm |
| Office-Based Cryosurgical Endometrial Ablation Using The Her Option Cryotherapy System: A Retrospective Review Of 25 Patients, AAGL, 2004 | S. Bush                          | 25                 | • 90% patients reported satisfaction with procedure  
  • 2 patients required additional surgical intervention due to treatment failures  
  • All 25 patients in an office setting under oral analgesia and cervical block |
| Comparison Between Pretreatment Versus No Pretreatment In Treating Menorrhagia By Cryoablation Therapy, ACOG, 2004 | B. Levy D. Whiteside K. Isaacson D. Townsend | 268                | • 80.3% of group 1 were considered successes  
  • 28.0% amenorrhea and spotting rate in group 1  
  • 86.7% of group 2 were considered successfully treated  
  • 35.0% amenorrhea and spotting rate in group 2  
  • It appears that we can achieve comparable results by extending freezing time slightly longer without having to use GnRH before the procedure |
| Endometrial Cryoablation With Adjustment Intracavitory Length: One-Year Follow-Up, AAGL, 2004 | L. Weather                        | 25                 | • 94.7% reported reduction in bleeding to normal levels  
  • 60% amenorrhea rates  
  • No complications  
  • Modified freeze technique using 7-minute freezes in each cornu and an added 3-minute midline freeze in uteri greater than 10 cm  
  • 28% received midline freeze |
| Factors Affecting Outcomes In Cryoablation, AAGL, 2003      | R. Bruno R. McClellan             | 100                | • Over 90% success rate  
  • 40% absolute amenorrhea rate  
  • Modified freeze technique using 7-minute freezes in each cornu, and an added 4-minute pull-back freeze in the lower uterine segment for uteri greater than 9 cm |
| In Office Versus Operating Room Cryoablation: Evaluation Of Patient Tolerance To The Procedure, AAGL, 2003 | B. Levy                          | 310                | • 83.1% of patients treated in-office had normal or better bleeding outcomes  
  • 79.3% of patients treated in hospital had normal or better bleeding outcomes  
  • 78.6% were comfortable with the procedure, and 17.5% were slightly uncomfortable  
  • Cryoablation can be performed in the office under low levels of anesthesia and with good clinical outcomes  
  • No measurable difference in outcomes based on location of service |
### Her Option® Clinical Study Summary

#### Her Option Efficacy Studies (continued)

<table>
<thead>
<tr>
<th>Study &amp; Publication</th>
<th>Authors</th>
<th>Number of Patients</th>
<th>Key Findings</th>
</tr>
</thead>
</table>
| A Safe And Effective Method Of Controlling Abnormal Uterine Bleeding, 2nd World Congress On Controversies In Obstetrics Gynecology And Infertility, 2001 | D. Townsend for the endometrial ablation study group | 222                | • Depth of ablation noted between 8 and 12 mm  
• Depth of ablation should be more effective in women with adenomyosis  
• Chance of freezing through uterine wall is remote  
• Ultrasound monitoring provides precise monitoring of the advancing cryo-edge  
• No significant complications |
| Endometrial Cryoablation With Ultrasound Visualization In Women Undergoing Hysterectomy, J. Am Assoc. Gynecol Laparosc., 2000 | J. Dobak  
J. Williams  
R. Howard  
C. Shea  
D. Townsend | 10                 | • 10 patients scheduled for hysterectomy  
• In all cases the margin was safe and no reduction in serosal surface temperatures occurred  
• There was no full-thickness myometrial destruction  
• Total endometrial destruction was achieved |

#### Scarring Studies

<table>
<thead>
<tr>
<th>Study &amp; Publication</th>
<th>Authors</th>
<th>Number of Patients</th>
<th>Key Findings</th>
</tr>
</thead>
</table>
| Magnetic Resonance Imaging Of The Uterus After Endometrial Resection, British Journal of Obstetrics and Gynecology, 1997 | L. Turnbull  
A. Jumaa  
S. Bowsley  
S. Dhawan  
A. Horsman  
S. Killick | 59 Total Treated  
22 Amenorrhoeic | • Of 22 amenorrhoeic patients, residual endometrium was present in all but 3 of these patients  
• Adenomyosis was present in 3 of the 22 amenorrhoeic patients  
• Haematometra was found in 3 of the 22 amenorrhoeic patients  
• Intraperitoneal fluid was present in 11 of the amenorrhoeic patients  
• Mean volume of endometrium was same in amenorrhoeic as well as menstruating patients |
| Hysteroscopic Evaluation Following Endometrial Ablation, ACOG, 2004                  | D. Townsend  
R. Bruno | 98                | • 98 patients evaluated via hysteroscopy; findings indicated that cryoablation does not induce endometrial scarring, and there is preservation of the uterine cavity  
• 98 patients had a completely visible ostia |
| Prospective Evaluation Of Cryoablation Of The Endometrium, ACOG, 2003                | R. Bruno  
R. McLellan  
N. Peterson  
M. Birdsall  
A. Dick  
J. Hurd | Over 90            | • 90% patients had clinically significant reduction in uterine bleeding at 3 months  
• Nearly 50% amenorrhea rate  
• 40 patients had hysteroscopy; in these cases the contour and depth of the endometrial cavity were maintained, as there was no scarring or intrauterine synechiae |
| Hysteroscopic Findings Following Cryoablation, AAGL, 2003                           | R. Bruno  
R. McLellan | 75                | • Cryoablation maintains the contour and depth of the endometrial cavity with minimal scarring or intrauterine synechiae, when compared to women treated by heat ablation techniques |
### Scarring Studies (continued)

<table>
<thead>
<tr>
<th>Study &amp; Publication</th>
<th>Authors</th>
<th>Number of Patients</th>
<th>Key Findings</th>
</tr>
</thead>
</table>
| Frequency Of Symptomatic Cornual Hematometra And Postablation Tubal Sterilization Syndrome After Total Rollerball Endometrial Ablation: A 10-Year Follow-Up, Am J Obstet Gynecol, 2002 | A. McCausland V. McCausland                 | 50                 | - Rollerball electrode (Valley Laboratory)
- 10 years follow-up
- In all cases, pathologic examination found the endometrial cavity to be a contracted narrow tubular structure with the periphery obliterated because of scarring
- Hematometra or PATL in 10% of patients |
- 2nd look hysteroscopy performed 30 months or more after initial surgery
- During follow-up, bleeding patterns were: 21% eumenorrhea 21% hypomenorrhea 48% dysmenorrhea
- Whereas all random biopsies were normal before ablation, biopsies after ablation revealed diminished endometrial glands with necrosis and scarring |
- Women who had endometrial carcinoma develop after ablation had predictive high-risk factors for subsequent neoplasia, and all eventually underwent a hysterectomy |
- 6 women who had previously undergone tubal ligation followed by rollerball endometrial ablation
- 1.5 year observation period
- In all cases, marked endometrial scarring was noted
- It appears that women who have had a tubal sterilization followed by endometrial ablation are at risk of developing an ectopic-like symptom complex |
| Feasibility of Endometrial Assessment After Thermal Ablation, European Journal of OBGYN and Reproductive Biology, 2009 | S. Ahonkalio A. Liakka H. Martikainen M. Santala | 80                 | - Endometrial assessment is compromised after previous endometrial thermal ablation
- Both endometrial sampling and sonohysterography fail quite often
- Intrauterine adhesions may also decrease the reliability of the endometrial sampling |
- Hematometra was a significant finding in women who underwent hysterectomy because of persistent pain of GEA
- A possible pathological predictor of GEA failure may be intramural leiomyomas |
# Her Option® Clinical Study Summary

## Her Option Extended Treatment Regimen

<table>
<thead>
<tr>
<th>Study &amp; Publication</th>
<th>Authors</th>
<th>Number of Patients</th>
<th>Key Findings</th>
</tr>
</thead>
</table>
| Impact Of Extended Freeze Patterns on Menorrhagia, Poster, 2004 | D. Townsend R. Bruno | 163 | • In patients treated with a standard freeze pattern (4x6 minutes), amenorrhea and spotting results were 41.2% with 84.5% achieving normal or better results  
• In patients treated with the extended freeze pattern (7x7 minute), amenorrhea and spotting results were 72.7% with 95.4% achieving normal or better results |
| Bleeding and Symptom Reduction With Her Option Office Cryoablation Therapy Using Extended Treatment Regimens, ACOG Poster, 2007 | A. Lukes D. Whiteside S. Herbst J. Manjon K. Roy D. Heilbronn R. Bruno | 82 | • Pain assessment during procedure demonstrated a mean overall score of 1.1  
• Baseline menses impacting normal activities 90%, 12 months following procedure 2%  
• Baseline impact on mood 93%, 12 months following procedure 9%  
• Baseline moderate to severe PMS 85%, 12 months following procedure 14%  
• Baseline pain & cramping 87%, 12 months following procedure 20% |
| Patient Satisfaction In Subjects Treated With Increased Freeze Regimens Using the Her Option Office Cryoablation Therapy For AUB, AAGL | R. Bruno A. Lukes D. Whiteside S. Herbst K. Roy J. Manjon D. Heilbronn R. Bruno | 81 | • Patient expectations (desired outcome) regarding cryoablation therapy for AUB – baseline: Eumenorrhia (29%), Hypomenorrhea (39%) and Amenorrhea (30%)  
• Patient outcomes following cryoablation therapy for AUB: Perception of eumenorrhia or less (98.5%), Moderate to extreme satisfaction (92.2%), Likelihood of recommending procedure (95.3%) |
| An Extended Treatment Regimen Using the Her Option Office Cryoablation Therapy for AUB is Well-Tolerated, AAGL Poster, 2007 | S. Herbst D. Whiteside K. Roy J. Manjon A. Lukes D. Heilbronn R. Bruno | 82 | • Minimal amount of anesthesia used  
• Mean overall Wong-Baker Faces pain score for subjects undergoing 2 freeze cycles was 1.1 and for 3 and 4 freeze cycles was 1.2 and 1.6, respectively |

## Her Option and Essure

<table>
<thead>
<tr>
<th>Study &amp; Publication</th>
<th>Authors</th>
<th>Number of Patients</th>
<th>Key Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>In Vitro Evidence Supporting the Safety of Cryoablation Therapy in Women with Implanted Contraceptive Micro-Inserts, AAGL Poster, 2008</td>
<td>J. Presthus J. Frigstad L. Garlie</td>
<td>Bench Test</td>
<td>• Results provide evidence that harmful cold conduction resulting in unwanted tissue injury is unlikely to occur during cryoablation in women with micro-insert devices</td>
</tr>
</tbody>
</table>
# Her Option® Clinical Study Summary

## Her Option Comparison Studies

<table>
<thead>
<tr>
<th>Study &amp; Publication</th>
<th>Authors</th>
<th>Number of Patients</th>
<th>Key Findings</th>
</tr>
</thead>
</table>
| A Randomized Study Comparing Endometrial Cryoablation And Rollerball Electroablation For Treatment Of Dysfunctional Uterine Bleeding, AAGL, 2003 | A. Duleba, M. Heppard, R. Soderstrom, D. Townsend | 279 patients with cryoablation, 193 patients with electroablation, 86 patients with rollerball | - 84.6% success rate at 1 year in cryoablation patients vs. 88.9% for electroablation patients  
- 92% decline in bleeding in cryoablation patients vs. 94% for electroablation  
- 3 procedure-related or probably procedure-related, serious adverse events were recorded more than 15 days after cryoablation, severe vaginal bleeding and severe cramping. 1 patient underwent a hysterectomy  
- 2 procedure-related or probably procedure-related, serious adverse events were recorded more than 15 days after electroablation; urinary tract infection and infected hematoma |
| Durability Of Treatment Effects After Endometrial Cryoablation Versus Rollerball Electroablation For Abnormal Uterine Bleeding: Two-Year Results Of A Multicenter Randomized Trial, Am J Ob Gyn, 2003 | D. Townsend, A. Duleba, M. Wilkes | 272 patients in cryo group, 156 patients in electroablation group at 1 year, 72 patients in electroablation group at 12 months, 94 pts in cryoablation group at 2 yrs, 43 pts in electroablation group at 2 yrs | - 94% of cryoablation patients did not have AUB at 24 months vs. 93% of electroablation patients  
- 91% of cryoablation patients were very or extremely satisfied with treatment at 24 months vs. 88% of electroablation patients  
- 7.0% of cryoablation patients proceeded to hysterectomy vs. 8.1% of electroablation patients  
- 2.7% of cryoablation patients had repeat ablation vs. 1.2% of electroablation patients |
| Comparison Of Balloon Ablation And Cryoablation For Menorrhagia, ACOG, 2002         | D. Townsend, S. Herbst, S. Bush | 100-balloon endometrial ablation, 100-extended cryoendometrial ablation | - Control of bleeding during first 9 months was better with cryoablation  
- Patients treated with cryoablation had less pain and a more rapid recovery  
- Neither group had any significant complications |
- Patients with minimal superficial adenomyosis had good results |
## Her Option® Clinical Study Summary

### Her Option Comparison Studies (continued)

<table>
<thead>
<tr>
<th>Study &amp; Publication</th>
<th>Authors</th>
<th>Number of Patients</th>
<th>Key Findings</th>
</tr>
</thead>
</table>
| Comparison Of In-office Cryoablation for Menorrhagia When Uterine Fibroids Are     | D. Whiteside             | 51                 | • Compares the results between patients with fibroids up to 4 cm to patients without fibroids  
  • At six months,  
  - 91% of patients without fibroids reduced menstrual flow to normal or less, compared to 82% of patients with fibroids  
  - 45% of patients without fibroids developed amenorrhea or spotting, compared to 36% of patients with fibroids |
| Present Vs. Absent, ACOG Poster, 2004                                               |                          |                    |                                                                                                                                             |
| Bipolar Radiofrequency Compared With Thermal Balloon Endometrial Ablation In The   | T. Clark                 | 81                 | • Procedures were performed in the office  
  • Pain during the procedure on the VAS scale for Thermal Balloon ablation was 6.5 and for Radiofrequency ablation was 7.7  
  • Pain post-procedure on the VAS scale was 6.7 for Thermal Balloon and 5.1 for Radiofrequency ablation  
  • Patients were given a regimen of narcotics and a paracervical block before the treatment started |
| Office, ACOG, 2010                                                                  | N. Samuel, S. Malick,    |                    |                                                                                                                                             |
|                                                                                     | L. Middleton, J. Daniels,|                    |                                                                                                                                             |
|                                                                                     | J. Gupta                 |                    |                                                                                                                                             |
| Endometrial Ablation Devices: Review Of A Manufacturer And User Facility Device     | C. Della Badia           |                    | • 254 adverse events reported in the US from January 1, 2003 to December 31, 2006  
  - Her Option – 10 adverse events  
  - Thermachoice – 43 adverse events  
  - Hydro ThermAblator (HTA) – 67 adverse events  
  - NovaSure – 119 adverse events |
| Experience Database, Journal of Min. Inv. Gyn., 2007                               | P. Nyirjesy, A. Atogho   |                    |                                                                                                                                             |
| Review Of Major Complications Related To Devices Used To Treat Abnormal Uterine    | A. Duleba                |                    | • Rate of complications reported with the use of endometrial ablation devices is low when compared to the rate of complications of hysterectomy  
  • Her Option showed the lowest total number of adverse events at 1/3,000 |
| Bleeding, AAGL Poster, 2004                                                         |                          |                    |                                                                                                                                             |
Endometrial Cryoablation: 2-Year Follow-Up

*R Bruno, R Samuelson, J Hurd, V Soto-Wright, N Petersen
Lahey Clinic, Burlington, Massachusetts

*Obstetrics and Gynecology, April 2003, v. 101(4), suppl., p. 45
Journal of the American Association of Gynecologic Laparoscopists, August 2004, v. 11(3) abstract 40

**Study Objective:** To assess the 2-year durability of a modified extended freeze technique to treat menometrorrhagia in 82 women.

**Patients:** Ninety-one of the first consecutively treated patients were evaluated at 1 year. Eighty-six of the 91 patients were evaluated at 2 years.

**Measurements and Main Results:** The modified extended freeze technique was performed in the following manner: if the uterus sounded less than 9 cm, a 7-minute freeze was applied to both cornual areas. For uteri 9 cm or greater, an additional 4 min lower uterine segment freeze was also performed. Ninety-one consecutively treated patients were evaluated at 12 months. Ninety-one percent were effectively treated for their menometrorrhagia with 50% reporting amenorrhea or spotting. At 2 years, 5 patients were lost to follow-up leaving 86 patients for evaluation. Eighty-nine percent of patients were still effectively treated for their abnormal uterine bleeding with 47% reporting amenorrhea or spotting. Six patients underwent hysterectomy due to treatment failure. At the 1-year mark, the smaller the uterus, the higher the amenorrhea rate.

**Conclusion:** The extended freeze technique continued to give satisfactory results at 2 years.

Office-Based Cryosurgical Endometrial Ablation Using The Her Option Cryotherapy System: A Retrospective Review Of 25 Subjects

*S Bush
Fox Valley Women's Health Partners, Geneva, Illinois


**Study Objective:** To evaluate cryosurgical endometrial ablation (CEA) using the Her Option Cryotherapy System as a viable in-office treatment for menorrhagia due to benign causes.

**Methods:** A retrospective review of 25 premenopausal women treated in an office setting under oral analgesia and cervical block.

**Measurements and Main Results:** No surgical or long-term complications were observed. Patients reported minimal cramping postprocedure, with all subjects able to return to normal activity by the next day. Postoperative discharge was typically limited to a minimal amount of pink watery discharge for up to 2 weeks. Ninety percent of the subjects reported satisfaction with outcome by 2 weeks postprocedure. To date, 2 women have required additional surgical intervention. Follow-up of subjects is ongoing to assess long-term outcomes.

**Conclusion:** Unlike other procedures currently approved, procedures requiring anesthesia or IV sedation, this therapy can be performed in an office setting using only oral analgesia with a cervical block. In addition, patients are able to resume normal activity quickly, usually by the day after, and experience minimal postoperative discharge.
Comparison Between Pretreatment Versus No Pretreatment In Treating Menorrhagia By Cryoablation Therapy

B Levy, et al.

Objective: To compare outcomes in patients undergoing cryoablation of the endometrium for menorrhagia with and without GnRH endometrial preparation.

Design: Retrospective analysis at 6 months on 208 patients pretreated with GnRH agonist and 60 treated without any endometrial preparation. All of the patients who received pretreatment received two 4- and 6-minute freezes. Freezing times were slightly increased in the untreated patients to produce these equivalent results. Ultrasound guidance was used for all treated patients.

Results: Of the 208 patients pretreated with GnRH agonist, 167 (80.3%) were considered successes. Amenorrhea and spotting rates were 38.0%. Of the 60 patients who received no pretreatment, 52 (86.7%) were considered successfully treated. The amenorrhea and spotting rate was 35.0%.

Conclusion: Based on this retrospective analysis, it appears that we can achieve comparable results by extending freezing time slightly longer without having to use GnRH before the procedure.

Endometrial Cryoablation With Adjustment For Intracavitory Length: One-Year Follow-up

L Weather Jr
Omni Fertility & Laser Institute, New Orleans, Louisiana

Study Objective: To assess the response to treatment at one year or more follow-up of menorrhagia via endometrial cryoablation when uterine cavity length is taken into consideration.

Design: Retrospective analysis of 25 patients treated for menorrhagia with endometrial cryoablation. The freezing procedure consisted of 7 minutes in each cornu; however, when the uterine intracavitary length exceeded 10 cm an additional 3-minute freeze was administrated in the midline of the cavity, 2 cm from the fundus. The study was from August 2001 through September 2003.

Measurements and Main Results: Of the 25 patients who completed one year or more follow-up, 7 (28%) received the midline freeze, 15 (60%) reported amenorrhea, and 94.7% reported reduction in bleeding to normal levels or less, and there were no complications.

Conclusion: Endometrial cryoablation via ultrasound guidance performed with adjustment for uterine cavity length appears to be a safe and effective procedure to treat certain benign causes of menorrhagia in patients who do not desire future pregnancy.
Factors Affecting Outcomes In Cryoablation

R Bruno, R McClellan
Lahey Clinic Foundation, Inc.


Objective: modify an extended freeze technique to different sized uteri

Measurement and main results: 100 women with menometrorrhagia underwent cryoablation in the following manner: If the uterus sounded 9 cm or less, a 7-minute freeze was applied to both corneal areas. With larger uteri up to 12.5 cm, the freezing profile was altered to adjust to the size of the uterus. In these larger uteri an additional 4-minute lower uterine segment freeze was also performed. Results indicated an absolute 40% amenorrhea rate with normal sized uteri, and as uteri became larger the amenorrhea rates declined. The overall success rate in these women was in excess of 90% even with uteri that sounded to over 12.5 cm.

Conclusion: With larger uteri it is apparent that the freeze patterns must be modified in order to obtain satisfactory results for the patient.

In Office Versus Operating Room Cryoablation: Evaluation of Patient Tolerance To The Procedure

B Levy
University of Washington, School of Medicine

Journal of the American Association of Gynecologic Laparoscopists, August 2003, v. 10(3) abstract 191

Design: Retrospective analysis on 141 patients treated in the physician’s office and 169 patients treated in the hospital operating room. Six months prospective data on 71 patients treated in the office. All patients were treated for endometrial ablation using a 5 mm cryoprobe. Six months bleeding outcomes were compared between the patients treated in the office and those treated in the hospital operating room.

Results: Of the 141 women treated in the office, 103 (73%) were given only a Paracervical Block with oral medications. Of these patients 78.6% were comfortable with the procedure, and 17.5% were slightly uncomfortable. Seventy-one patients treated in the office completed 6 months follow-up, with 83.1% having normal or better bleeding outcomes. This is higher than the 79.3% outcome found with patients treated in the hospital operating room.

Conclusion: Cryoablation of the endometrium can be performed in a gynecological office under low levels of anesthesia and with good clinical outcomes.
A Safe And Effective Method Of Controlling Abnormal Uterine Bleeding

DE Townsend for the Endometrial Ablation Study Group
Second World Congress on Controversies in Obstetrics Gynecology & Infertility
Paris (France), September 6-9, 2001

Design: A prospective randomized study between cryosurgical endometrial ablation and rollerball ablation performed in over 200 premenopausal women with a PBAC score of at least 150. Pelvic ultrasound, endometrial biopsy and blood studies to confirm premenopausal state. Uterine sound over 10 cm and those that contained uterine myomas over 2 cm were excluded from study. A single dose of a GnRh agonist 3-4 weeks prior to treatment was provided. An initial 4-minute freeze to one cornu followed by a 6-minute freeze to the opposite cornu.

Patients: 222 premenopausal women who presented with PBAC score of at least 150.

Measurement and Main Results: Depth of destruction by rollerball ablation was around 2-4mm. The same depth of destruction was found to be true of Hydrotherm ablation as well as balloon ablation. In women with "deep" adenomyosis (6mm of glands extending into the uterine wall) would likely be treatment failures by preceding techniques. Cryoablation depth of destruction was noted to be between 8-12mm, depths that should be more effective in women with adenomyosis.

Conclusion: When compared to other commonly used techniques for endometrial ablation i.e. rollerball, endometrial resection and thermal balloon, cryoablation has major advantages. Cryoablation is easier to learn and is much safer with the chance of hyponatremia eliminated. Ultrasound monitoring accurately depicts the precise location of the cryoprobe and monitors the advancing edge of the cryozone.

Endometrial Cryoablation With Ultrasound Visualization In Women Undergoing Hysterectomy

J Dobak, J Willems, R Howard, C Shea, D Townsend
Scripps Clinic, La Jolla, California

Study Objectives: To evaluate tissue effects of cryosurgical endometrial ablation in women just before hysterectomy, characterize ultrasound monitoring of freezing, determine the feasibility of a new probe-angling procedure, and assess the safety profile by monitoring serosal surface temperatures.

Design: Single-arm safety study enrolling 10 women at two centers.

Patients: Ten women scheduled for hysterectomy.

Intervention: Hysterectomy with a new cryosurgical device (First Option, CryoGen, Inc., San Diego, CA) that achieves surface temperatures below -90° C to freeze endometrium.

Measurements and Main Results: The freeze protocol involved angling the probe toward each cornu. Maximum ice front diameter at the end of the first angled freeze ranged from 24 to 34 mm, and maximum ice ball diameter at the end of the second freeze ranged from 28 to 37 mm. The margin between the advancing ice front and serosal surface was monitored by ultrasound. In all cases the margin was safe and no reduction in serosal surface temperatures occurred. Depth of necrosis ranged from 9 to 12 mm as determined by tetrazolium staining and electron microscopy, and there was no full-thickness myometrial destruction. Total endometrial destruction was achieved.

Conclusion: Cryosurgical ablation of the endometrium with the First Option system with angled freezes and ultrasound monitoring appears to be feasible and safe given our preliminary data.
Magnetic Resonance Imaging Of The Uterus After Endometrial Resection

L Turnbull, A Jumaa, S Bowsley, S Dhawan, A Horsman, S Killick
Hull Royal Infirmary, United Kingdom

Objective: Diagnostic hysteroscopy following endometrial resection is frequently unsatisfactory and transvaginal ultrasound is unable to detect subtle changes in endometrial morphology. Magnetic resonance imaging was employed to evaluate the uterus.

Design: Retrospective study: 59 women – 22 amenorrhoeic– were studied for 34 months after endometrial resection, using a 1.5 Tesla magnetic resonance imaging system with a pelvic-phased array coil for signal reception. T2-weighted FSE images were acquired through the long and short uterine axis and volumetric assessment of each uterine layer performed.

Results: Residual endometrium was demonstrated in all but 3 amenorrhoeic women, with a similar mean volume present in menstruating and amenorrhoeic groups. Adenomyosis, haematometra, fallopian tube dilation and free intraperitoneal fluid were also identified.

Conclusions: The majority of amenorrhoeic and all menstruating women have residual endometrium after endometrial resection.

Hysteroscopic Evaluation Following Endometrial Ablation

D Townsend, R Bruno
Park City, Utah
Obstetrics and Gynecology, April 2004, v. 103(4), p. 56S

Objective: To evaluate the effects of cryoablation upon the preservation of the uterine cavity and the extent of uterine scarring, a retrospective analysis of 98 patients.

Design: All patients underwent pretreatment hysteroscopy and endometrial sampling with no preoperative treatment. Hysteroscopic evaluation was performed between 3 and 15 months posttreatment.

Results: Hysteroscopy findings indicated that cryoablation does not induce endometrial scarring, and there is preservation of the uterine cavity. All 98 cryo patients had completely visible ostia.

Conclusion: Cryoablation is a safe and effective treatment for abnormal bleeding and does not result in significant uterine scarring. Results of treatment are due to destruction of the endometrium through cell dehydration and not dependent upon uterine scarring. In contrast to heat ablation techniques where scarring is quite common, the possibility of hiding an occult carcinoma after ablation is extremely unlikely.
Prospective Evaluation Of Cryoablation Of The Endometrium

Objective: To prospectively observe the effects of endometrial cryoablation to reduce menometrorrhagia as well as the effect of cryoablation upon the preservation of the uterine cavity and extent of intrauterine scarring.

Methods: Over 90 women who suffered from significantly heavy uterine bleeding underwent endometrial cryoablation. Patients underwent pretreatment hysteroscopy and endometrial sampling. No preoperative treatment of the endometrium was employed. The contour of the uterine cavity was recorded. Following cryoablation, patients were evaluated at 1 month, 3 months, 6 months, and 12 months. Hysteroscopy was performed between 3 and 12 months after the procedure.

Results: Greater than 90% of patients more than 3 months from the procedure had a clinically significant reduction in uterine bleeding. Nearly 50% had amenorrhea. No immediate or long-term complications have been noted to date. In over 40 women, hysteroscopy was performed after ablation. In these cases the contour and depth of the endometrial cavity were maintained as there was no scarring or intrauterine synechiae.

Conclusion: Cryoablation is safe and effective with virtually no significant side effects. It requires minimal analgesia. Early results indicate that none to minimal uterine scarring develops, thus avoiding hematometra. The lack of scarring and its long-term implications are discussed.

Hysteroscopic Findings Following Cryoablation – 75 Cases

Objective: To hysteroscopically evaluate the effect of cryoablation upon the uterine cavity.

Design: 75 women that had undergone cryoablation of the endometrium subsequently underwent hysteroscopy.

Measurement and Main results: Hysteroscopy was performed from 3 to 15 months flowing cryoablation; minimal scarring of the endometrial cavity was noted. In the majority of cases the ostia of the fallopian tube remained visible.

Conclusion: Cryoablation of the endometrium maintains the contour and depth of the endometrial cavity with minimal scarring or intrauterine synechiae, when compared to women treated by heat ablation techniques.
Frequency Of Symptomatic Cornual Hematometra And Postablation Tubal Sterilization Syndrome After Total Rollerball Endometrial Ablation: A 10-Year Follow-Up

A McCausland, V McCausland
Sutler Medical Group and University of California at Davis Medical School, USA
Sacramento, California

Objective: This study was undertaken to determine the frequency of symptomatic cornual hematometra and postablation tubal sterilization syndrome after total rollerball endometrial ablation

Study design: Retrospective cases of 50 consecutive patients who received total rollerball endometrial ablation for dysfunctional uterine bleeding and were followed up for 10 years.

Results: Symptomatic cornual hematometra or postablation tubal sterilization syndrome was diagnosed by ultrasound scanning and/or magnetic resonance imaging in 5 of 50 patients (10%) who had a total endometrial ablation. Two patients had cornual hematometra, and 3 patients had postablation tubal sterilization syndrome 4 months to 90 months after rollerball ablation.

Conclusion: Uterine contracture, which obstructs bleeding from persistent cornual endometrium and leads to symptomatic cornual hematometra or postablation tubal sterilization syndrome, is not uncommon after total rollerball endometrial ablation, with an incidence of 10% in our series. Satisfactory treatment requires hysterectomy with salpingectomy, but modifications such as partial endometrial ablation can prevent these complications.

Long-Term Histopathologic And Morphologic Changes After Thermal Endometrial Ablation

O Taskin, A Onoglu, M Inal, E Turan, S Sadik, E Vardar, H Postaci, J Wheeler
Department of Obstetrics and Gynecology, Inonu University Medical School, Turkey

Study Objective: Prospective longitudinal study outlining long-term histologic features of endometrial ablation.

Patients: Twenty-six patients.

Intervention: Thermal ablation followed by second-look office hysteroscopy with endometrial biopsy.

Measurements and Main Results: Mean follow-up time to second-look hysteroscopy after ablation was 33.4 ± 2.1 months. Complete atrophy, partial adhesions or obliteration of the cavity, and fibrosis were observed at second-look hysteroscopy. Whereas all random biopsies were normal before ablation, biopsies after ablation revealed diminished endometrial glands with necrosis and scarring. The number of endometrial glands was not correlated with amount of bleeding or menstrual pattern. No premalignant or malignant lesions were found after ablation.

Conclusion: Although efficacy of endometrial ablation is related to initial thermal destruction and correlated with postablation hysteroscopic and histologic findings, endometrial regrowth is an expected development, not a failure of ablation.
Endometrial Carcinoma After Endometrial Ablation: High-Risk Factors Predicting Its Occurrence

R Valle, M Baggish
Department of Obstetrics and Gynecology, Northwestern University Medical School, Illinois

Purpose: Our purpose was to review reported cases of endometrial carcinoma after endometrial ablation and to evaluate high-risk factors predicting its occurrence. We present guidelines for the treatment of abnormal uterine bleeding unresponsive to medical therapy in this high-risk group of patients. Eight detailed reports on endometrial carcinoma after endometrial ablation were reviewed. The indications, methods of treatment, follow-up, and associated high-risk factors for endometrial carcinoma were analyzed. A focused list of high-risk factors for endometrial carcinoma was developed on the basis of the data collected. Women who had endometrial carcinoma develop after ablation had predictive high-risk factors for subsequent neoplasia, and all eventually underwent a hysterectomy. Women with abnormal uterine bleeding and high-risk factors for endometrial carcinoma who did not respond to medical treatment may safely undergo endometrial ablation but must have a pre-ablation biopsy indicating normal endometrium. Persistent hyperplasia unresponsive to hormonal therapy should influence the selection of a hysterectomy. Careful screening of patients before undergoing endometrial destructive procedures is prescient because minimally invasive, nonhysteroscopic ablative techniques are now emerging.

Post-Ablation-Tubal Sterilization Syndrome

D Townsend, V McCausland, A McCausland, G Fields, K Kauffman
Salt Lake City, Utah

Objective: To determine the cause of unilateral or bilateral pelvic pain associated with vaginal spotting in women who had previously undergone tubal ligation followed by rollerball endometrial ablation.

Results: During a 1.5 year observation period, 6 women with the symptom complex had laparoscopy and hysteroscopy. In all cases, marked endometrial scarring was noted. In every case, the proximal portions of either one or both fallopian tubes were swollen, and 2 cases had the appearance of an early ectopic pregnancy. In the remaining cases, the fallopian tubes were rubbery and swollen to as much as twice normal size. Symptoms in 5 of 6 patients subsided after laparoscopic removal of the oviduct.

Conclusion: It appears that women who have had a tubal sterilization followed by endometrial ablation are at risk of developing an ectopic-like symptom complex. Salpingectomy appears to be effective in relieving symptoms.
Feasibility Of Endometrial Assessment After Thermal Ablation

S Ahonkallio, A Liakka, H Martikainen, M Santala
University of Oulu, Oulu, Finland

European Journal of Obstetrics & Gynecology and Reproductive Biology, June 2009

Study Objective: To evaluate the feasibility of endometrial assessment after endometrial thermal ablation.

Study Design: Prospective observational study. A total of 57 women (age 47-52 years), who had undergone endometrial thermal ablation as a treatment for heavy menstrual bleeding (HMB) 3-10 years (mean 6 years) earlier, were examined with transvaginal ultrasound and saline sonohysterography. Endometrial samples were collected with a Pipelle device. Visualization of endometrium, access to uterine cavity, change in cavity length, success in outpatient endometrial sampling and success in sonohysterography were evaluated.

Results: Endometrial thickness was 4.5 mm in amenorrheic women (n=17), 5.6 mm in eumennorrheic women (n=37) and 6.6 mm in hypermenorrheic women (n=3). An endometrial sample was successfully taken in 44 (77%) women, and in 13 (23%) women endometrial sample failed. The length of the uterine cavity compared to the length measured before endometrial thermal ablation was 0.5-5 cm (mean 2 cm) shorter in 34 women, unchanged in 4 women, and longer in 5 women. The uterine cavity distended regularly in only 9 (16%) women. In 14 (25%) women the cavity distended irregularly or only partially, and in 24 (42%) women the uterine cavity did not distend at all, but appeared as a narrow tube. In 10 (18%) women the sonohysterography catheter did not enter the uterine cavity at all.

Conclusion: Endometrial assessment is compromised after previous endometrial thermal ablation. Both endometrial sampling and sonohysterography fail quite often, causing problems in diagnosis of abnormal bleeding. Intrauterine adhesions may also decrease the reliability of the endometrial sampling.

Pathologic Characteristics Of Hysterectomy Specimens In Women Undergoing Hysterectomy After Global Endometrial Ablation

E Carey, S El-Nashar, M Hopkins, D Creedon, W Cliby, A Famuyide
From the Department of Obstetrics and Gynecology, University of North Carolina (Dr. Carey), and the Department of Obstetrics and Gynecology, May Clinic, Rochester Minnesota (Drs. El-Nashar, Hopkins, Creed, Cliby and Famuyide).


Study Objective: To describe uterine pathologic features in women who underwent hysterectomy because of failed global ablation (GEA).

Design: Retrospective cohort study from 1998 through 2005 (Canadian Task Force classification III).

Setting: Tertiary referral center.

Patients: Sixty-nine women who underwent hysterectomy because of GEA failure.

Interventions: Pathology reports were available for 67 patients. Descriptions of hysterectomy specimens after GEA were reviewed.

Measurements and Main Results: Rates of pathologic findings in hysterectomy specimens after failed GEA were determined. Reasons for hysterectomy in the 67 patients with available pathology reports were bleeding in 34 (51%), pain in 19 (28%), and bleeding and pain in 14 (21%). The pathology reports of these specimens showed leiomyomas in 33 specimens (49%); intramural myomas were present in 15 women (44%) who underwent hysterectomy because of bleeding and 8 women (42%) who underwent hysterectomy because of pain. Hematometra was identified in 7 pathologic specimens (10%). Specifically, hematometra was identified in specimens from 5 of 19 women who underwent hysterectomy because of pain (26%).

Conclusion: Hematometra was a significant finding in women who underwent hysterectomy because of persistent pain after GEA. A possible pathologic predictor of GEA failure may be intramural leiomyomas.
Impact Of Extended Freeze Patterns On Menorrhagia

D Townsend, R Bruno

Objective: To compare outcomes between recommended and extended freeze patterns in patients undergoing endometrial cryoablation for treatment of menorrhagia.

Materials and Methods: Retrospective analysis at 12 months on total of 163 patients with uterine cavities up to 9 cm treated for menorrhagia using Her Option Cryoablation Therapy System. From the 163 patients treated, 119 patients were treated by 4x6 (left and right cornu) minute freeze pattern with Lupron pretreatment. The remaining patients were treated by a 7x7 minute freeze pattern without any pretreatment. Treatment was performed in 12 ambulatory surgical centers in the US and included patients who presented with menorrhagia, benign endometrial pathology, and no desire for future pregnancy.

Results: Of the 119 patients treated by the 4x6 freeze pattern, amenorrhea and spotting results were 41.2%, with 84.5% achieving normal or better results. Of the 44 patients treated by the extended freeze pattern, amenorrhea and spotting results were 72.7%, with 95.4% of the patients achieving normal or better results.

Conclusion: When extended freeze patterns are used during cryoablation with ultrasound guidance, significantly higher amenorrhea rates and clinical outcomes are noted when compared to currently recommended freeze patterns.

Bleeding And Symptom Reduction With Her Option® Office Cryoablation Therapy Using Extended Treatment Regimens

A Lukes, Duke University Medical Center, Durham, North Carolina
D Whiteside, S Herbst, J Manjon, K Roy, D Heilbronn, R Bruno

Background: The Her Option Office Cryoablation Therapy System is a closed-loop cryosurgical device that is used to ablate the endometrial lining in reproductive-aged females with abnormal uterine bleeding due to benign causes.

Initial FDA clinical studies were conducted with a 2-freeze treatment regimen consisting of a 4-minute freeze in one cornu followed by a second freeze of 6 minutes with the contralateral cornu. Since completion of the early studies, many Her Option uses have used varying freeze patterns using longer freeze durations and/or additional freeze cycles at the fundus and the lower uterine segment.

Objective: To evaluate safety and effectiveness of extended treatment regimens with Her Option Office Cryoablation Therapy for females with menorrhagia.

Methods: A prospective, multicenter study conducted under an investigational device exemption was performed using extended treatment regimens with Her Option Office Cryoablation Therapy.

Seven study sites included 2 academic and 5 private practices. Eligible subjects were premenopausal adult females who had completed childbearing. A normal endometrial biopsy and a baseline pictorial bleeding assessment chart (PBAC) score ≥150 was required. Subjects received pretreatment with luprolide.

Freeze patterns were determined by uterine measurements and included up to 4 freeze cycles. Symptoms relating to mood and quality of life were evaluated. Effectiveness was measured with change in PBAC scores and quality of life measurements. Evaluations were done at baselines, then at 3, 6 and 12 months.
Results: A total of 82 subjects were assessed and qualified for treatment. At baseline, the mean age of subjects was 40.3 years and mean parity was 2.2. Myomas (< 3 cm) were found in 43% of subjects, and the mean baseline PBAC score was 423.9 (range: 160-2755).

Uterine dimensions were assessed at baseline to determine placement and duration of freeze cycles. Overall, larger uterine dimensions required more or extended freezes. The number of freezes performed in subjects were as follows: two freeze in 9 subjects, three in 50 subjects, and four in 23 subjects.

Subjects were treated in the office or day-surgery center at the discretion of the investigator. Pain assessment (0-10 scale) during procedure demonstrated a mean overall pain score of 1.1 (SD 1.68) corresponding to mild, annoying pain. Setting did not significantly impact subject tolerability.

The majority of subjects reported moderate to extreme symptoms of PMS (70/82) and impact on social activities (74/82) due to heavy menses at baseline. Most subjects reported some level of improvement of symptoms.

A significant reduction in PBAC scores was seen throughout follow-up. Improvement in PBAC score below 75 is considered a ‘success’ within the study protocol.

Four subjects elected to undergo further treatment for their condition prior to the 1-year evaluation; 1 repeat cryoablation, 1 rollerball EA, 1 hysterectomy and 1 transcervical resection of the endometrium. Two additional subjects elected to undergo hysterectomy following their 1-year visit.

Importantly, this extended freeze study highlights the underlying safety of Her Option In-Office Cryoablation. There were no serious intra-operative complications. The majority of adverse events were mild in nature and required pharmacological or no intervention. One subject experienced a device-related adverse event deemed serious in nature at the 6-month visit, cervical stenosis leading to hysterectomy. Another subject had a serious adverse event related to a pre-existing condition, polycystic ovarian syndrome, which led to hysterectomy.

Conclusion: Preliminary analyses indicate that Her Option® Office Cryoablation Therapy using extended treatment regimens is a safe and effective treatment for menorrhagia. Additionally, subjects reported improvement in social activities and reduced symptoms of cramping and PMS.

Patient Satisfaction In Subjects Treated With Increased Freeze Regimens Using The Her Option® Office Cryoablation Therapy For Abnormal Uterine Bleeding

R Bruno, Lahey Clinic, Burlington, MA; AS Lukes, Duke University Medical Center, Durham, NC; DC Whiteside, Center for Endometrial Ablation, Charlotte, NC; SJ Herbst, Institute for Women’s Health, West Palm Beach, FL; K Roy, Banner, Good Samaritan Medical Center, Phoenix, AZ; JM Manjon, Camp Hill, PA; D Heilbronn, Valley Ob-Gyn Clinic, Saginaw, Mi.

Presented at the AAGL 36th Global Congress of Minimally Invasive Gynecology, Washington, DC, Nov. 13 – 17, 2007

Introduction: Initial studies with Her Option® Office Cryoablation Therapy were performed with 2 freeze cycles of 4 and 6 minutes duration, respectively, in each cornu of the uterus1,2, which has become the standard freeze regimen. Since then, several Her Option users have provided evidence suggesting a regimen using additional or longer freeze cycles (extended freeze regimen) may be more beneficial.3,4

Study Objective: The primary objective of this study was to evaluate the benefits of an extended freeze regimen with Her Option for the treatment of AUB. Secondary objectives included assessment of patient satisfaction after 12 months following cryoablation.

Design: This was a 12-month, prospective, nonrandomized, multi-center study. Additional 24- and 36-month evaluations are ongoing.

Setting: The setting for each procedure was determined by physician preference with (78%) performed in an office setting and the remainder performed in surgery centers.

Participants: Subjects were premenopausal women ≥ 30 years of age with AUB, confirmed by baseline PBAC scores ≥ 150, and who were unresponsive to prior treatment.

Interventions: Subjects received a GnRH agonist 21-28 days prior to treatment. Subjects were excluded from participation if uterine fibroids > 3 cm were detected during
baseline assessments. The number and location of freeze cycles was determined a priori based on uterine dimensions and performed as described elsewhere. The protocol permitted up to 4 freeze cycles: midline fundal freeze durations of ≤ 4 minutes; corneal and lower uterine segment freezes ≤ 10 minutes.

Measurements and Main Results: The primary measurement in this trial was a 12-month PBAC score ≤ 75. Prior to undergoing cryoablation and following patient counseling about global endometrial ablation treatment outcomes, patient expectations included amenorrhea (30.5%), hypomenorrhea (39.0%) and eumenorrhea (29.3%). However, QOL data collected 12 months postprocedure indicate perceived eumenorrhea rate of 98.5%. Additionally, 92% of patients would recommend procedure.

Conclusions: Preliminary data suggest that subjects undergoing Her Option Cryoablation Therapy were satisfied and perceived their outcomes to be better than actual PBAC measurement indicates. These results support the suggestion that patient satisfaction and perception of results should define success rather than PBAC scores.

Acknowledgements: The study was sponsored by American Medical Systems, Inc., Minnetonka, MN 55343 and conducted under an investigational device exemption. These results are currently undergoing FDA review.

References:

An Extended Treatment Regimen Using The Her Option® Office Cryoablation Therapy For Abnormal Uterine Bleeding (AYB) Is Well-Tolerated

SJ Herbst, Institute for Women’s Health, West Palm Beach, FL; DC Whiteside, Center for Endometrial Ablation, Charlotte, NC; K Roy, Banner Good Samaritan Medical Center, Phoenix, AZ; JM Manjon, Camp Hill, PA; AS Lukes, Duke University Medical Center, Durham, NC; D Heilbronn, Valley Ob-Gyn Clinic, Saginaw, MI; R Bruno, Lahey Clinic, Burlington, MA.


Introduction: The original studies with Her Option® Office Cryoablation Therapy were performed with 2 freeze cycles of 4 and 6 minutes duration, respectively, in each cornu of the uterus1 2 which has become the standard freeze regimen. Since then, several Her Option users have provided evidence suggesting a regimen using additional or longer freeze cycles (extended freeze regimen) may be more beneficial.3 4

Study Objective: The primary objective of this study was to evaluate the benefits of an extended freeze regimen with Her Option for the treatment of AUB. Secondary objectives included assessment of safety and tolerability of cryoablation procedure.

Design: This was a 12-month, prospective, nonrandomized, multicenter study. Additional 24- and 36-month evaluation are ongoing.

Setting: The setting for each procedure was determined by physician preference with (78%) performed in an office setting and the remainder performed in surgery centers.

Participants: Subjects were premenopausal women ≥ 30 years of age with AUB, confirmed by baseline PBAC scores ≥ 150, who were unresponsive to prior treatment.

Interventions: Subjects received a GnRH agonist 21-28 days prior to treatment. Subjects were excluded from participation if uterine fibroids > 3 cm were detected during baseline assessments. The number and location of freeze cycles were determined a priori based on uterine dimensions and performed as described elsewhere.5 The protocol permitted up to 4 freeze cycles: midline fundal freeze durations of ≤ 4 minutes; corneal and lower uterine segment freezes ≤ 10 minutes.
Measurements and Main Results: Of the 82 subjects who enrolled, 65 (79%) had the procedure performed in an office setting. One-half received cervical dilation but 35 of these (85%) only required dilation to ≤ 6 mm. Minimal or moderate anesthesia was used in 65 (79%) and 17 (21%) procedures, respectively.

Subjects rated their comfort levels following each freeze cycle of the procedure using the Wong-Baker Faces pain scale, an 11-point visual analog scale ranging from 0 (no pain) to 10 (worst possible pain). The mean (SD) overall pain score for all subjects was 1.1 (1.68), corresponding with mild, annoying pain. Scores were also comparable between the treatment cycles.

The mean pain scores for the subjects undergoing 3 and 4 freeze cycles were 1.2 (1.9) and 1.6 (1.8), respectively, and were not appreciably different from a mean score of 1.1 (1.6) in subjects undergoing 2 cycles. Additionally, office setting scores of 1.1 (1.53) were not statistically different from surgery center setting score of 1.0 (2.20). No procedures were prematurely terminated due to patient discomfort.

No serious intra-operotive complications occurred and the severity of most reported adverse events was mild.

Conclusion: Receiving only minimal to moderate amounts of pretreatment analgesia, subjects undergoing 3-4 freeze cycles tolerated the procedure as well as those receiving 2 cycles. Some degree of cryoanalgesia caused by the low temperatures used during the procedure may contribute to Her Option tolerability. Tolerability was unaffected whether the procedures were performed in office or surgical center. Based on pain scale data collected, Her Option is appropriate for in-office use even when longer, additional freeze cycles are used.

Acknowledgements: The study was sponsored by American Medical Systems, Inc. Minnetonka, MN 55343 and conducted under an investigational device exemption. These results are currently undergoing FDA review.

References:

In Vitro Evidence Supporting The Safety of Cryoablation Therapy In Women With Implanted Contraceptive Micro-Inserts

J Presthus, MD, Minnesota Gynecology and Surgery, Edina, MN 55435; J Frigstad, MS, and L Garlie, American Medical Systems, Minnetonka, Minnesota 55343

Introduction: Endometrial cryoablation was developed as an alternative to hysterectomy for the treatment of abnormal uterine bleeding (AUB) (Duleba et al., 2003; Townsend et al., 2003) and is currently indicated for the treatment of AUB in premenopausal women with normal endometrial cavities who have completed childbearing; however, the application of extreme cold may pose a safety concern in women with implanted contraceptive micro-inserts. The primary objective of the following in vitro study was to test the hypothesis that uterine cryoablation does not pose a safety hazard in women with implanted permanent contraceptive micro-inserts.

Methods: Cryoablation was simulated using the Her Option® Office Cryoablation Therapy System (American Medical Systems, Inc., Minnetonka, MN). During normal cryoablation therapy, an ice front advances through the uterine tissue, creating a cryozone with temperatures below -20°C resulting in tissue necrosis (Hoffmann and Bischof, 2002). Ten thermocouples embedded in gel were used to measure the conduction of cold through a contraceptive micro-insert device (Essure® micro-inserts, Conceptus Inc., Mountain View, CA). The cryoprobe, micro-insert and thermocouples were configured as shown in Figures 1-3.

The cryoprobe was aligned with the main axis of the implant and placed in contact with the proximal end. Thermocouples 1-4 were in contact with the implant/probe tip and the nitinol ribbon; thermocouples 5-8 were either in contact with the stainless steel inner coil or within the diameter of the nitinol ribbon.

Thermocouples 9 and 10 were in contact with the distal end of the implant with respect to the cryoprobe. Temperatures were recorded at 15-second intervals during the 10-minute freeze cycle. Temperatures above -20°C were regarded as being nondestructive to tissue (Hoffmann and
Results: Eight micro-implants were each used 2-3 times to achieve a sample size of 22 cold conduction assessments. After each experiment, the coil was retrieved from the gel, cleaned, and inspected for any evidence of damage prior to reuse. The mean (SD) temperature of the thermocouples in contact with the cryoprobe was -71.5 (7.8) °C. The edge of the cryozone terminated between thermocouples 5 and 6 located 9.0 and 11.7 mm from the cryoprobe, which reached average temperatures of -5.1 (1.8) and 2.9 (2.0) °C, respectively. The mean temperature of each thermocouple is shown in Table 1. The recorder temperatures were virtually identical during the control tests.

Discussion: Nonresectoscopic techniques for performing endometrial ablation and the use of implanted micro-inserts as a technique for achieving permanent contraception are both relatively new treatments in the field of women's health. As the use of these treatments increases, there is greater likelihood that some women may undergo both procedures. To date, one study has reported that an ablation procedure using thermal energy appears to be safe in women with implanted micro-inserts (Valle et al., 2006); however, data from a post-approval study suggests a 3-month hysterosalpingogram prior to ablation to insure tubal occlusion should be encouraged. The results of the current study provide preliminary evidence that the use of cryotherapy may also be used to perform endometrial ablation in women with implanted micro-inserts.

Conclusion: The results of this in vitro experiment provide evidence that harmful cold conduction resulting in unwanted tissue injury is unlikely to occur during cryoablation in women with micro-insert devices. Future in vitro testing will be necessary to further evaluate the findings of this work.

References:

Acknowledgements: This study was sponsored by American Medical Systems Inc., Minnetonka, MN.

A Randomized Study Comparing Endometrial Cryoablation And Rollerball Electroablation For Treatment Of Dysfunctional Uterine Bleeding

A Duleba, M Heppard, R Soderstrom, D Townsend
Department of Obstetrics, Yale University, School of Medicine, New Haven, Connecticut

Study Objective: A prospective, randomized study to determine the effectiveness of endometrial cryoablation in comparison with rollerball electroablation.

Intervention: Endometrial ablation using a Her Option cryoablation device in 193 women and rollerball electroablation in 86.

Measurements and Main Results: Women treated by cryoablation received significantly less general anesthesia (46%) than those treated by electroablation (92%). Subjects maintained menstrual diaries for at least 1 cycle before and for 12 months after the procedure. Success was defined as reduction of menstrual bleeding to a score of 75 or less in the absence of retreatment. Success rates in the cryoablation and electroablation groups were 77.3% and 83.8%, respectively. Bleeding declined by 92% and 94%, respectively. Both procedures led to significant improvements in a broad range of symptoms including menses-related pain and mood, an overall improvement in quality of life.

Conclusion: Endometrial cryoablation is a safe and effective procedure in treatment of dysfunctional uterine bleeding. Its advantages include technical ease of performance, direct ultrasonographic view of depth of ablation, little anesthetic, and avoidance of potential complications related to distention media.
Durability Of Treatment Effects After Endometrial Cryoablation Versus Rollerball Electroablation For Abnormal Uterine Bleeding: Two-Year Results Of A Multicenter Randomized Trial

D Townsend, A Duleba, M Wilkes
LDS Hospital, Department of Obstetrics and Gynecology, Park City, Utah

In a randomized trial, 93% of cryoablation patients who were evaluated at both 12 and 24 months and not retreated were free of abnormal uterine bleeding at 12 months and 94% at 24 months versus 92% of electroablation patients at both times. The retreatment rate was similar after cryoablation (12.9%) and electroablation.

Endometrial cryoablation using the Her Option system effectively and safely relieves AUB, and treatment effects are stable through at least 2 years. Procedural simplicity and flexibility and reduced anesthesia requirements make this form of therapy highly appropriate for the office setting.

Comparison Of Balloon Ablation And Cryoablation For Menorrhagia

D Townsend, S Herbst, S Bush
Park City, Utah
Obstetrics and Gynecology, April 2002, v. 99(4), suppl., p. 39S

Material and Methods: A retrospective review was carried out of two private practices in which balloon endometrial ablation, with 100 patients, and extended cryoendometrial ablation, with 100 patients, were used in an attempt to control refractory menorrhagia.

Results: Control of bleeding during the first 9 months was better with cryoablation. Anesthesia requirements were similar; however, when light sedation was used, patients treated with cryoablation had less pain and a more rapid recovery. Neither group had any significant complications.

Conclusion: Cryo-endometrial ablation when compared with thermal balloon ablation is associated with less pain and better control of abnormal uterine bleeding. Because it is performed with ultrasound guidance, it permits the deeper destruction of tissue, thereby likely destroying deep as well as superficial adenomyosis.
Depth Of Endometrial Penetration In Adenomyosis Helps Determine Outcome Of Rollerball Ablation

AM McCausland, VM McCausland

Objective: Determine whether depth of endometrial penetration into the myometrium correlates with outcome of rollerball endometrial ablation.

Design: Fifty patients with hysteroscopically normal-appearing cavities had endometrial ablations for menorrhagia and were studied for greater than or equal to 3.5 years. A posterior myometrial biopsy to determine the amount of endometrial penetrations was performed and correlated with an outcome.

Patients: Fifty consecutive patients with normal-appearing cavities.

Measurement and Main Results: Patients with deep endometrial penetration into the myometrium had poor outcomes after ablation. Those with no or minimal endometrial penetration had good results.

Conclusion: Superficial adenomyosis can be treated definitively with ablation. Deep adenomyosis responds poorly to ablation. Hysterectomy should be considered when myometrial biopsy, preoperative ultrasonography or magnetic resonance imaging demonstrates deep adenomyosis.

Comparison of In-Office Cryoablation for Menorrhagia When Uterine Fibroids Are Present Vs. Absent

D Whiteside

Objective: To compare the results of in-office cryoablation for menorrhagia between patients who had uterine fibroids to those who did not have uterine fibroids.

Materials and Methods: Retrospective analysis of 51 patients treated with cryoablation for menorrhagia over a 3-month follow-up and 33 patients over a 6-month follow-up. All patients’ endometrial cavities were treated in a single physician’s office with a 5 mm cryoprobe for 6-8 minutes in either uterine cornua under direct ultrasound guidance. Paracervical block and oral medications were used for anesthesia. Three- and six-month outcome data were compared between patients who had uterine fibroids and those patients who did not have uterine fibroids.

Results: Three months after cryosurgery, 88% of the patients without fibroids reduced their menstrual flow to normal or less as compared to 82% of the patients with fibroids. Thirty-eight percent of the patients without fibroids developed amenorrhea or spotting compared to 24% of the patients with fibroids. Six months after cryosurgery, 91% of patients without fibroids reduced their menstrual flow to normal or less as compared to 82% of the patients with fibroids. Forty-five percent of the patients without uterine fibroids developed amenorrhea or spotting as compared to 36% of the patients with fibroids.

Conclusion: Cryoablation of the endometrium is an effective method of endometrial ablation in patients with and without uterine fibroids. However, the success rate decreased somewhat, from 91% to 82%, when comparing patients without fibroids to those with fibroids.
Bipolar Radiofrequency Compared With Thermal Balloon Endometrial Ablation In The Office

TJ Clark, N Samuel, S Malick, LJ Middleton, J Daniels, JK Gupta
From the Birmingham Women’s Hospital, Birmingham, United Kingdom; and the Birmingham Clinical Trials Unit, University of Birmingham, Birmingham, United Kingdom.

Objective: To estimate the feasibility of local anesthetic endometrial ablation in the office using bipolar frequency endometrial ablation or thermal balloon ablation technologies and to estimate which procedure alleviates heavy menstrual bleeding and improves quality of life more effectively.

Methods: A single-center, single-blind, randomized controlled trial was conducted based in an office hysteroscopy clinic in a university teaching hospital. Eighty-one women with heavy menstrual bleeding without significant intracavity pathology were randomly allocated to bipolar radiofrequency endometrial ablation or thermal balloon ablation in an office setting, avoiding use of general anesthesia or conscious sedation. The primary outcome assessed was the rate of amenorrhea at 6 months after treatment. Secondary outcomes included procedure-related data (feasibility, pain, acceptability, complications) and health-related quality of life.

Results: Amenorrhea rates were higher at 6 months after surgery with bipolar procedures, but not statistically significant (39% compared with 21%, risk ratio 1.9, 95% confidence interval 0.9–4.3, P=.1). All bipolar procedures were successfully completed, whereas the treatment cycle was not completed in 2 of 39 (5%) balloon procedures (P<.1) because of patient discomfort. The office bipolar procedure was significantly shorter, by 6.2 minutes on average (P<.001), and associated with more complete coverage of the endometrial surface (88% compared with 58%, P≤.002). Health-related quality of life was significantly improved after both treatments.

Conclusion: Office endometrial ablation using the bipolar radiofrequency or thermal balloon procedures is feasible and effective. The bipolar procedure was significantly quicker and achieved a greater degree of endometrial destruction than the thermal balloon, although there was no significant difference in amenorrhea rates at 6 months.

Endometrial Ablation Devices: Review Of A Manufacturer And User Facility Device Experience Database

C Della Badia, P Nyirjesy, A Atogho

Objective: To evaluate complications reported to the Manufacturer and User Facility Device Experience (MAUDE) database and to look for trends of complications among various endometrial ablation devices. This database was not intended to be used either to evaluate rates or adverse events or to compare adverse event occurrence rates across other devices.

Methods: We performed a retrospective review of the Food and Drug Administration’s MAUDE database. The database was queried for adverse events associated with the use of endometrial ablation devices. The following data were collected: event number, date reported, date of occurrence, type of ablation device, type of complication, adherence to manufacturer’s protocol, brief description, disposition, who reported incident, report source, and cause of problem.

Results: The total number of adverse events reported in the United States for the time period of January 1, 2003, through December 31, 2006, was 254. The largest number of major complications for cryoablation was bowel injury (n=5), for microwave was bowel injury (n=6), for hot water balloon was complications leading to hysterectomy (n=7), for free circulating hot water was severe burns (n=22), and for bipolar mesh was bowel injury (n=19.)

Conclusion: The MAUDE database is useful to both the physician and manufacturer to look at trends and types of complications.
Review Of Major Complications Related To Devices Used To Treat Abnormal Uterine Bleeding

A Duleba

Department of Obstetrics and Gynecology, Yale University School of Medicine, New Haven, Connecticut

Introduction:
- Menorrhagia affects 14–20% of women in reproductive age, generating 2.7 million office visits in the US each year.1
- Approximately 650,000 hysterectomies are performed in the US every year.2
- Menorrhagia contributes to nearly 50% of hysterectomies.
- Hysterectomy is associated with 3–11% rate of major complications.3,4
- Several endometrial ablation techniques facilitate rapid and effective outpatient treatment of menorrhagia.
- This study summarized major complications associated with endometrial ablation devices.

Methods:
- US Food and Drug Association database: Manufacturer and User Facility Device Experience (MAUDE) lists reports of complications related to the use of medical devices. MAUDE database was used to identify adverse events reported from January 2001 to September 2003 on the following devices: ThermaChoice (Gynecare), Hydrothermal Ablator (HTA; Boston Scientific), NovaSure (NovaCept), and Her Option System (American Medical Systems). Data on Microwave Endometrial Ablation (MEA, Microsulis) were extracted from the report submitted to FDA panel review board in June 2003.
- All adverse events except uncomplicated uterine perforations were analyzed.
- Statistical analysis was carried out using the chi-square test.

Results:
- Table summarizes adverse events and presents estimates of rates of complications.
- The number or reported complications may exceed the number of patients, as in some patients multiple complications were separately reported.
- Frequencies of complications differed between devices (P<0.0001).

Conclusions:
- The rate of complications with the use of endometrial ablation devices is low when compared to the rate of complications of hysterectomy.
- There is marked variability in the rate of major complications related to the devices used for treatment of abnormal uterine bleeding.
- The present findings should be interpreted with caution, as the estimates of the number of cases performed using individual devices and reporting complications may not be accurate.5

References:
* A select number of abstracts and articles were chosen.