

Laparoscopic Radiofrequency Fibroid Ablation: Phase II and Phase III Results

Donald I. Galen, MD, Rodolfo Robles Pemuelier, MD, José Gerardo Garza Leal, MD,
Karen R. Abbott, MD, Janice L. Falls, MD, James Macer, MD

ABSTRACT

Background and Objectives: To review phase II and phase III treatments of symptomatic uterine fibroids (myomas) using laparoscopic radiofrequency volumetric thermal ablation (RFVTA).

Methods: We performed a retrospective, multicenter clinical analysis of 206 consecutive cases of ultrasound-guided laparoscopic RFVTA of symptomatic myomas conducted on an outpatient basis under two phase II studies at 2 sites (n = 69) and one phase III study at 11 sites (n = 137). Descriptive and exploratory, general trend, and matched-pair analyses were applied.

Results: From baseline to 12 months in the phase II study, the mean transformed symptom severity scores improved from 53.9 to 8.8 ($P < .001$) (n = 57), health-related quality-of-life scores improved from 48.5 to 92.0 ($P < .001$) (n = 57), and mean uterine volume decreased from 204.4 cm³ to 151.4 cm³ ($P = .008$) (n = 58). Patients missed a median of 4 days of work (range, 2–10 days). The rate of possible device-related adverse events was 1.4% (1 of 69). In the phase III study, approximately 98% of patients were assessed at 12 months, and their transformed symptom severity scores, health-related quality-of-life scores, mean decrease in uterine volume, and mean menstrual bleeding reduction were also significant. Patients in phase III missed a median of 5 days of work (range, 1–29 days). The rate of periprocedural device-related adverse events was 3.5% (5 of 137). Despite the

enrollment requirement for patients in both phases to have completed childbearing, 4 pregnancies occurred within the first year after treatment.

Conclusions: RFVTA does not require any uterine incisions and provides a uterine-sparing procedure with rapid recovery, significant reduction in uterine size, significant reduction or elimination of myoma symptoms, and significant improvement in quality of life.

Key Words: Radiofrequency ablation, Laparoscopy, Laparoscopic ultrasound, Fibroid, Myoma.

INTRODUCTION

Uterine myomas (leiomyomas) are practically ubiquitous among women. They have a lifetime incidence of 70% to 80%, and approximately 25% of women report being symptomatic.^{1,2} Widespread use of hormonal contraception may minimize symptomatology and may skew the reported incidence downward. Although hormone use results in a temporary reduction in symptoms, it is not a permanent treatment for fibroids. Ultrasound studies have shown that myomas begin to develop in female patients at a young age and increase in both size and number until women reach menopause. Studies have shown ethnic differences in the incidence of leiomyomas, with African-American women having a disproportionately higher occurrence than other races. Growth rates of leiomyomas also are reported to be associated with race. The Fibroid Growth Study included data showing decreasing myoma growth rates among white women as they approached menopause; however, among African-American women, growth rates remained unchanged.^{1,3,4}

Symptoms, including heavy menstrual bleeding, dysmenorrhea, pelvic-abdominal pain or pressure, urinary frequency and incontinence, dyspareunia, infertility, and an increased risk of spontaneous abortion, occur in 20% to 50% of patients with fibroids.^{5,6} Symptomatic uterine fibroids represent the most common indication for hysterectomy, accounting for 150 000 to 200 000 of all of the hysterectomy procedures, or 30% to 40% of cases, that are performed annually in the United States.^{7,8}

San Ramon Ob/Gyn, San Ramon, CA, USA (Dr. Galen).

Department of Obstetrics and Gynecology, Hospital Universitario Esperanza, Guatemala City, Guatemala (Dr. Pemuelier).

Department of Gynecology and Obstetrics, Hospital Universitario de Nuevo Leon, Monterrey, Mexico (Dr. Garza Leal).

Athena Gynecology Medical Group, Reno, NV, USA (Dr. Abbott).

Montefiore Medical Center—Einstein Division, Bronx, NY, USA (Dr. Falls).

Pasadena Premier Women's Health, Pasadena, CA, USA (Dr. Macer).

Address correspondence to: Donald I. Galen, MD, San Ramon Ob/Gyn, 11030 Bollinger Canyon Rd, Ste 250, San Ramon, CA 94582, USA. Telephone: (925) 570-1331; E-mail: drgalen@drgalen.com

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We present the following report of phase II and phase III studies of laparoscopic ultrasound-guided radiofrequency volumetric thermal ablation (RFVTA) of leiomyomas in an effort to address the dearth of new clinical research in the United States on minimally invasive approaches to symptomatic fibroid therapy and to provide descriptions of what we believe to be an emerging, preferred uterine-sparing fibroid treatment modality. Both percutaneous and laparoscopic radiofrequency (RF) ablation studies have been described internationally over the years, as well as recently.^{9–15} No long-term medical therapy exists for symptomatic fibroids; consequently, treatment has been and remains largely surgical. In suitable candidates, myomectomy may be performed. Myomectomy, though allowing for uterine preservation, does require one or more myometrial incisions; can require a postprocedural inpatient hospitalization similar to that of hysterectomy; and may be associated with increased blood loss, longer procedure times, and increased risk for postoperative hemorrhage and/or pelvic adhesions.^{16,17} Interventional radiologists have achieved symptom improvement and fibroid tumor shrinkage through embolization of the uterine arteries.^{16,18} Laparoscopic bipolar coagulation of uterine vessels and uterine nerves has been reported.¹⁸ Laparoscopic myolysis with either bipolar needles or a neodymium:yttrium-aluminum-garnet laser was performed in Europe in the late 1980s and was subsequently reported in the United States by Goldfarb.^{19,20} The procedure initially targeted the entire myoma by using multiple punctures through the uterine serosa with resultant and significant formation of postoperative adhesions.

Lee²¹ performed RFVTA of fibroids in the 1990s and early 2000s under an institutional review board–approved off-label study using an RFVTA system designed for soft-tissue ablation. This procedure involved the insertion of an RF needle with 7 deployable curved electrodes that created a volumetric ablation within the myoma. Lee subsequently developed a system designed specifically to treat uterine fibroids using RFVTA (Acessa™ System; Halt Medical, Brentwood, California). This system was tested in multiple studies enrolling a total of 206 women with symptomatic uterine fibroids.

The primary objectives of the phase II studies, which were conducted under similar but separate protocols, were to assess the safety and efficacy of the Acessa System in women with symptomatic fibroids ≤ 6 cm and to evaluate the treatment's effect on uterine volume.^{13,14} Study endpoints were the incidence of procedure- and device-related adverse events, change in Uterine Fibroid Symptom and Quality-of-Life (UFS-QOL) questionnaire²² responses

over time, and change in uterine volume. The primary objectives of the phase III study, which was conducted under 1 protocol and included 9 sites in the United States and the 2 Latin American sites, from the phase II study were to confirm the safety and efficacy of the Acessa System for the treatment of symptomatic uterine fibroids ≤ 7 cm in diameter in patients with confirmed clinical menorrhagia (indicated by menstrual blood loss of ≥ 160 mL to ≤ 500 mL) based on alkaline hematin testing.¹⁵ Study primary endpoints at 12 months were safety, surgical reintervention rates, and change in menstrual blood loss. Secondary endpoints included changes in uterine and fibroid volumes, evaluation of patients' UFS-QOL and general health status questionnaire responses over time, and patients' satisfaction after treatment. The Acessa System has been approved for commercial use in the United States, Mexico, Canada, and the European Union for the treatment of symptomatic uterine fibroids. Insufficient data exist to evaluate the safety and effectiveness of the Acessa procedure in women who plan future pregnancy. Therefore, the procedure is not recommended for women who are planning future pregnancy.

METHODS

The phase II trial was a prospective, dual-center, longitudinal, open-label, single-arm feasibility study assessing the safety and efficacy of RFVTA of symptomatic myomas in women seeking alternative treatment to hysterectomy. The setting was two urban university hospitals: one in Monterrey, Mexico, and the other in Guatemala City, Guatemala. Participation in the trial was voluntary, the local ethics committee and Ministry of Health of each country approved the recruitment of the study participants, and the principal investigators or designee obtained written informed consent from each enrolled patient according to good clinical practice guidelines, local and federal regulations of Mexico and Guatemala, and international standard EN ISO 14155–1:2003 (Clinical Investigation of Medical Devices for Human Subjects).

The phase III trial, which is ongoing, is a Food and Drug Administration– and institutional review board–approved, prospective, multicenter, longitudinal, pivotal study in which the patients serve as their own controls. All enrolled study participants were diagnosed with symptomatic fibroids, specifically menorrhagia confirmed by alkaline hematin testing. Eleven urban study centers in the United States ($n = 9$) and in Latin America ($n = 2$) provided the clinical setting. As with the phase II trial, participation by the enrollees was voluntary and written

informed consent was obtained from each patient according to good clinical practice guidelines; federal regulations established by the US Food and Drug Administration, Mexico, and Guatemala; and international standard EN ISO 14155–1:2003 (Clinical Investigation of Medical Devices for Human Subjects).

Patients in both phases have been followed up for a minimum of 1 year after RF ablation of their symptomatic fibroids. At each of the 3-, 6-, and 12-month follow-up visits, the patients were evaluated clinically to assess symptoms and to identify any adverse events; at baseline and at each follow-up visit, they were also asked to complete a UFS-QOL questionnaire. (The questionnaire's mean transformed scores range from 0 to 100. A decrease in symptom score over time from baseline indicates improvement, whereas a higher score for health-related quality of life after the procedure indicates improvement).

Before the intervention, baseline medical data were collected and recorded, including a complete health history, a pregnancy test within 24 hours of surgery, a complete blood panel, and completion of the UFS-QOL questionnaire. For the phase II trial, transvaginal ultrasound was performed for an initial determination of the location, number, and size of fibroid(s) and to measure the uterine volume. For the phase III trial, magnetic resonance imaging was incorporated in the preoperative assessment along with transvaginal ultrasound.

Device Description and Procedure

The device (Acessa System) is composed of an RF generator and a disposable RF handpiece with deployable needle electrodes, two dispersive electrode pads, extension cables, and a foot pedal (**Figure 1**). Each dispersive electrode pad has 3 built-in thermocouples that measure skin



Figure 1. Schema of Acessa System: RF generator with foot pedal, extension cables, RF handpiece, and dispersive pads.



Figure 2. RF handpiece tip showing full deployment of 7-needle array and effective ablation zone.

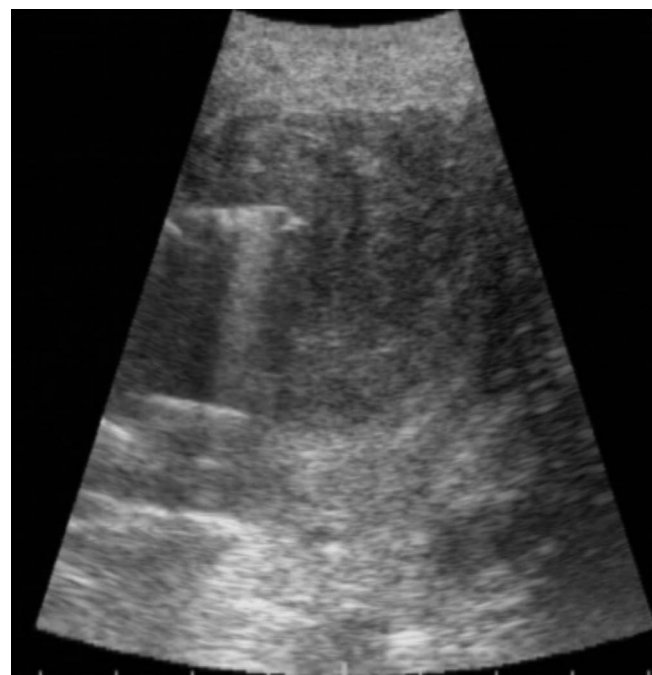


Figure 3. Ultrasound image of RF handpiece tip advancing from left side and located inside fibroid capsule, before deployment of array.

temperature. The two dispersive return pads are designed specifically to minimize the risk of surface skin burns at these points of current return from the patient to the generator. During surgery, laparoscopic ultrasound and video observation locate each target fibroid. The RF handpiece is inserted percutaneously and is introduced into the fibroid through the uterine serosal surface. Simultaneous laparoscopic ultrasound confirms device tip placement within each fibroid. The surgeon then may choose to deploy the 7-needle electrode array to the desired ablation size within the fibroid capsule (**Figures 2 and 3**). RF ablation is carried out with a continuous, low-voltage, high-frequency (45–500 kHz) alternating current with a maximum output of 200 W. Once the tissue temperature reaches 100°C, the watt-

age automatically adjusts to maintain treatment temperature and deliver RF energy to tissue through the handheld disposable RF handpiece. Energy propagation is concentrated in the pelvic region only; thus there is no safety risk to the patient in terms of high levels of current being conducted across the heart, which would otherwise be a concern. The maximum level of current conduction is approximately 2.5 amps, which only occurs under conditions of highest power (200 W) and lowest resistance/impedance (30–40 Ω in the case of RFVTA procedures). The typical current level at 60 W and 60 Ω is 1 amp and is representative of most Acesa RFVTA cases.

The surgeon makes selections from a menu on the generator that is controlled through a set of “scroll and select” buttons on the RF handpiece. The surgeon initiates treatment by depressing the foot pedal, and the RF generator increases the tissue temperature to 100°C and maintains that temperature for the duration of the ablation. The total time of treatment for each fibroid is determined by a treatment algorithm, which is based on the volume of tissue to be ablated. The generator is specifically designed for use with this RF device and has real-time temperature or power displays (depending on the mode being used) that facilitate monitoring and control of the ablation throughout the procedure. The generator also monitors the return tem-

perature from each dispersive electrode pad and automatically stops RF treatment if any of the dispersive pad thermocouples register a skin temperature $>40^{\circ}\text{C}$. Multiple uterine fibroids can be treated during the procedure and often by use of only one insertion through the uterine serosa. The technology and the laparoscopic ultrasound mapping allow the surgeon to target only the fibroids and to spare the surrounding myometrium, with the exception of a 3.4-mm puncture followed by coagulation of the tract during probe withdrawal. Because there is no requirement for uterine incisions, there is no need for suturing of the myometrium after RF treatment.

After fibroid ablation, the surgeon withdraws the electrode array into the 3.4-mm primary needle and removes the handpiece while simultaneously performing standard needle-track RF coagulation by applying a lower wattage (8–15 W) of intermittent coagulation mode to the needle tip (**Figure 4**). On occasion, depending on the fibroid's shape and size, multiple ablations may be required for a single fibroid. Fibroids can be treated virtually in any portion of the uterine myometrium (anterior, posterior, or lateral), including those that are subserosal, intramural, transmural, or submucosal. Pedunculated (type 0) intracavitary fibroids usually are not treated by this method because hysteroscopic resection is the preferred therapy for these myomas.

RESULTS

Patient demographic data and myoma symptom characteristics at baseline for both the phase II and phase III trials are presented in **Table 1**. Phase II participants were



Figure 4. Laparoscopic image of probe tip after standard needle-track RF coagulation. One should note the laparoscopic ultrasound transducer behind the probe.

all of Hispanic or Latino origin (100%), whereas 55.1% of phase III participants reported not being Hispanic or Latino. After intervention in the phase II study, 69 patients (100%) were seen at the 3-month follow-up visit, 65 (94.2%) at the 6-month follow-up visit, and 58 (84.1%) at the 12-month visit. The flow of patients through the phase III study has been similar through 12 months: 137 patients (100%) were treated at baseline, 134 (97.8%) have been followed up through 3 months, 134 (97.8%) have been followed up through 6 months, and 132 (96.4%) have been followed up through 12 months. The phase III study is ongoing.

Four pregnancies occurred within the first 12 months in both phases. One patient in the phase II trial conceived after ablation, delivered a healthy, full-term infant by elective repeat cesarean section, and was excluded from further participation in the study. Three patients in the phase III trial conceived after ablation and were excluded from further participation in the study. One patient delivered a

Table 1.
Phase II and Phase III Patient Demographics and Myoma Symptom Characteristics at Baseline^a

| Baseline Characteristics | Phase II (n = 69) | Phase III (n = 135) ^a |
|--|----------------------|-------------------------------------|
| Mean age (SD) (y) | 42.1 (5.5) | 42.4 (4.7) |
| Mean height (SD) (cm) | 156.0 (6.5) | 162.6 (8.1) |
| Mean weight (SD) (kg) | 68.1 (11.3) | 81.0 (19.1) |
| Race [n (%)] | | |
| White | 0 (0) | 62 (45.3) |
| African American | 0 (0) | 46 (33.6) |
| Asian | 0 (0) | 2 (1.5) |
| Other ^b | 69 (100.0) | 27 (19.7) |
| Ethnicity [n (%)] | | |
| Hispanic or Latino | 69 (100.0) | 62 (45.3) |
| Not Hispanic or Latino | 0 (0) | 75 (54.7) |
| Mean transformed UFS-QOL symptom severity score (SD) | 53.9 (22.5) | 61.4 (18.4) |
| Mean transformed UFS-QOL health-related quality-of-life score (SD) | 48.5 (24.4) | 37.1 (19.6) |
| Mean uterine volume (SD) (cm ³) ^c | 204.4 (11.9) | 303.1 (160.6) |

^aThe baseline population for phase III does not include two patients who, after RFVTA, did not meet all inclusion criteria.

^bIncludes Hispanic, Hispanic indigenous, or Caribbean.

^cBaseline uterine volume for phase II and III patients measured by transvaginal ultrasound.

Table 2.

Distribution of Myomas by Type and by Study for Phase II and Phase III as Found on Laparoscopic Ultrasound^a

| Fibroid Type | Phase II (n = 69) | Phase III (n = 135) |
|----------------|-------------------|---------------------|
| Intramural | 139 (50.2%) | 462 (58.0%) |
| Subserosal | 106 (38.3%) | 212 (26.6%) |
| Submucosal | 17 (6.1%) | 173 (21.7%) |
| Transmural | 7 (2.5%) | 39 (4.9%) |
| Uncategorized | 8 | 22 |
| Median (range) | 3 (1–20) | 4 (1–29) |
| Total | 285 | 818 |

^aA myoma could be of more than one type. Percentages were based on the number of myomas with categorized types.

full-term, healthy infant by cesarean section; one woman delivered a full-term, healthy infant vaginally²³; and one patient miscarried at 10 weeks.

A total of 128 myomas were visualized in the 69 patients by transvaginal ultrasound at baseline, and 285 myomas were mapped and treated by RF ablation in phase II (median, 3; range, 1–20). During intraoperative laparoscopic ultrasound mapping during phase III, 818 myomas were visualized and 640 were treated (median, 4; range, 1–29). The distribution of imaged leiomyomas by type and study phase is presented in **Table 2**. In phase II surgeons treated a median of 3 fibroids per patient (range, 1–20) in 2.33 hours (range, 0.70–4.83 hours) (timed from first incision to close of last incision). Phase III surgeons treated a median of 4 fibroids per patient (range, 1–29) in 1.88 hours (range, 0.35–5.55 hours) (timed from initiation of pneumoperitoneum to close of last incision).

A comparison of phase II and phase III uterine volume measurements (by transvaginal ultrasound) from baseline to 12 months after the procedure is provided in **Figure 5**. The mean uterine volume decreased over time from baseline through 12 months for the phase II patients: the mean volume reduction at 3 months (n = 68), 6 months (n = 64), and 12 months (n = 58) was 20.3%, 25.2%, and 28.7%, respectively. Similarly, the mean uterine volume for the phase III patients decreased from baseline (n = 134) by 14.6% at the 3-month follow-up visit (n = 129), by 20.6% at the 6-month follow-up visit (n = 128), and by 25.7% at the 12-month follow-up visit (n = 127).

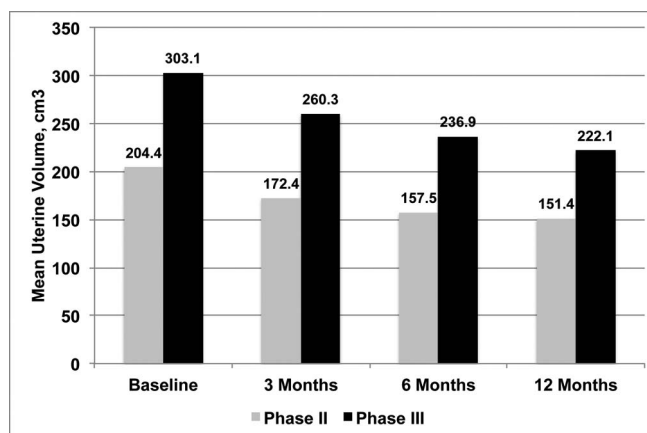


Figure 5. Uterine volume measurements by transvaginal ultrasound over time from baseline to 12 months after procedure for phases II and III.

Improvements in phase II and phase III UFS-QOL mean transformed symptom severity and health-related quality-of-life scores and subscale scores over time are presented in **Table 3**.

Symptom severity decreased from baseline to 12 months in phase II by 83.7% (53.9 to 8.8, n = 58); health-related quality of life improved from baseline to 12 months by 89.8% (48.5 to 92.0, n = 58). In the phase III study, symptom severity decreased by 56.5% from the mean transformed score of 61.1 at baseline (n = 127) to 26.6 at 12 months (n = 124) and health-related quality of life improved by 110.4% over the mean baseline value of 37.3 to 79.5 at 12 months after the procedure (n = 124).

In terms of safety, there was one serious adverse event in phase II (1.4%, 1 of 69): early postoperative bleeding at the abdominal wall resulting in a hematoma, which was related to the procedure and possibly related to the device. It resolved postoperatively without sequelae. There were no hospital readmissions for any of the phase II patients. There were 6 adverse events (10.0%, 6 of 69): 4 cases of abdominal pain and 2 urinary tract infections, which may have possibly been related to the procedure. Device-related adverse events were reported in 5 patients (3.7%, 5 of 137) in phase III (**Table 4**). One study patient (1 of 137, 0.7%), who withdrew early from the phase III trial, later had a surgical reintervention (uterine artery embolization) for her heavy menstrual bleeding.

The study patients in phase III who were employed (n = 88) missed a median of 5 days of work (range, 0–29 days). Thirty-nine patients in phase II described themselves as

Table 3.
Mean UFS-QOL Transformed Scores and Health-Related Quality-of-Life Subscale Scores for Phase II and Phase III Studies^a

| | Phase II | | | | Phase III ^b | | | |
|--------------------------------|----------------------|------------------|------------------|-------------------|------------------------|-------------------|-------------------|--------------------|
| | Baseline (n = 69) | 3 mo (n = 68) | 6 mo (n = 65) | 12 mo (n = 58) | Baseline (n = 127) | 3 mo (n = 124) | 6 mo (n = 125) | 12 mo (n = 124) |
| Symptom severity | 53.9 ± 22.5 | 18.8 ± 14.5 | 14.0 ± 18.8 | 8.8 ± 14.2 | 61.1 ± 18.6 | 29.1 ± 18.9 | 28.5 ± 19.3 | 26.6 ± 19.0 |
| Health-related quality of life | 48.5 ± 24.4 | 84.1 ± 15.4 | 88.2 ± 19.3 | 92.0 ± 19.1 | 37.3 ± 19.1 | 75.1 ± 22.1 | 77.8 ± 20.2 | 79.5 ± 20.6 |
| Subscale scores | | | | | | | | |
| Concern | 38.9 ± 27.2 | 79.6 ± 20.9 | 85.8 ± 22.4 | 64.5 ± 45.0 | 24.7 ± 20.7 | 67.1 ± 26.0 | 69.4 ± 25.9 | 71.4 ± 25.9 |
| Activities | 53.5 ± 28.3 | 86.6 ± 16.8 | 90.5 ± 20.0 | 93.9 ± 18.5 | 37.1 ± 24.1 | 76.9 ± 23.9 | 79.3 ± 23.9 | 79.9 ± 23.5 |
| Energy/mood | 47.5 ± 26.2 | 83.3 ± 18.0 | 86.2 ± 22.6 | 91.7 ± 20.4 | 38.1 ± 21.8 | 75.1 ± 24.2 | 79.0 ± 20.7 | 80.3 ± 20.7 |
| Control | 50.9 ± 27.0 | 86.0 ± 16.6 | 90.0 ± 20.9 | 93.4 ± 18.1 | 45.5 ± 24.9 | 80.7 ± 23.1 | 84.0 ± 19.9 | 86.3 ± 18.1 |
| Self-consciousness | 56.7 ± 28.9 | 86.9 ± 20.0 | 90.9 ± 17.8 | 91.5 ± 20.7 | 38.2 ± 28.3 | 74.7 ± 26.7 | 77.1 ± 24.6 | 79.8 ± 24.5 |
| Sexual function | 46.0 ± 35.2 | 80.7 ± 27.6 | 84.6 ± 25.4 | 86.4 ± 25.0 | 45.5 ± 29.8 | 75.1 ± 29.3 | 75.4 ± 30.4 | 78.5 ± 28.8 |

^aScores range from 0 to 100. A lower symptom severity score indicates a decrease in symptoms, and a higher health-related quality of life score indicates an improvement in health-related quality of life.

^bTen patients were removed from the UFS-QOL analysis because of pregnancy, amenorrhea/menopause, loss to follow-up, or baseline parameters outside the inclusion criteria.

Table 4.
Device-Related Adverse Events Reported in Phase III Trial Through 12 Months

| Serious Adverse Event | Occurrence | Relationship to Device | Relationship to Procedure | Anticipated |
|---|----------------------|------------------------|---------------------------|-------------|
| Pelvic abscess in posterior cul-de-sac; patient did not follow recommendation regarding pelvic rest and engaged in sexual activity with a new partner at 2 wk after procedure | 1 mo after procedure | Possibly related | Probably related | Anticipated |
| 2-cm superficial laceration in sigmoid colon serosa caused by ultrasound probe | Intraoperative | Definitely related | Definitely related | Anticipated |
| Mild superficial uterine serosal burn | Intraoperative | Definitely related | Possibly related | Anticipated |
| Severe lower abdominal pain | After procedure | Possibly related | Probably related | Anticipated |
| Postprocedural vaginal bleeding | 5 d after procedure | Possibly related | Probably related | Anticipated |

working outside of the home, and they reported missing a median of 4 days of work (range, 2–10 days).

DISCUSSION

Laparoscopic, ultrasound-guided RFVTA of fibroids was developed by Lee²¹ after using a system designed primarily for liver ablation. The current device used in this study was the result of years of testing the principles of volumetric fibroid tissue ablation by which the treatment effect is limited to the fibroid and spares the myometrial tissue. RFVTA contrasts with current methods for laparoscopic or

abdominal myomectomy procedures, with which only a portion of the existent fibroids can be identified and/or removed. With RFVTA, gynecologic surgeons have been able to treat all fibroid types in all locations, with the exception of type 0 (pedunculated) intracavitary fibroids, which are best removed with operative hysteroscopic resection. Performance of laparoscopic RFVTA requires 3 basic gynecologic skills: laparoscopy, ultrasound, and probe placement under ultrasound guidance. The method described in this report targets only the fibroids, leaving the endometrium intact without incision of the myome-

trium. Because no myometrial incisions are created, there is little blood loss and there is no need for laparoscopic uterine suturing. Patients are normally discharged the same day of treatment and require minimal pain management, similar to diagnostic laparoscopy. In addition, it is normal to have—and we expected to see—small amounts of vaginal discharge after placement of a cervical tenaculum; we saw such discharge, and in all cases the amount was minimal.

Because neither the phase II nor the phase III studies were designed as randomized controlled trials or trials comparing RFVTA with other methods of myoma treatment, we are restricted by the regulatory authorities from making comparative statements. We can report that there are two different comparative/randomized controlled trials under way in Canada (ClinicalTrials.gov identifier NCT01563783) and in Germany (ClinicalTrials.gov identifier NCT01750008). These studies, which will be reported in upcoming articles, describe the following myoma treatments: RFVTA, laparoscopic and abdominal myomectomy, and uterine artery embolization.

The 12-month phase II and interim phase III results of RFVTA of symptomatic fibroids show significant clinical reduction in symptoms and improvement in health-related quality of life within an acceptable safety profile. Despite the fact that the phase III patients displayed greater mean baseline uterine volumes, lower baseline health-related quality-of-life scores, and higher baseline symptom scores, the improvements in all 3 measures were similar across all 3 studies. Phase II and III reductions in uterine volume over time (−20.3% and −28.7%, respectively, at 3 months and −14.6% and −25.7%, respectively, at 12 months) are meaningful and likely contribute significantly to the decline in symptoms and improvement in health-related quality of life as reflected in the follow-up UFS-QOL questionnaire scores.

CONCLUSIONS

Twelve-month phase III results provided a rigorous setting to substantiate the phase II safety and efficacy results of RFVTA of leiomyomas: the decreases in uterine volume and severity of symptoms over time accompanied by a significant improvement in health-related quality of life for up to 12 months after treatment indicate the potential for long-term clinically significant outcomes over the 3-year life of the phase III trial and beyond.

References:

1. Day Baird D, Dunson DB, Hill MC, Cousins D, Schectman JM. High cumulative incidence of uterine leiomyoma in black and white women: ultrasound evidence. *Am J Obstet Gynecol.* 2003;188:100–107.
2. Laughlin SK, Stewart EA. Uterine leiomyomas: individualizing the approach to a heterogeneous condition. *Obstet Gynecol.* 2011;117(2):396–403.
3. Peddada SD, Laughlin SK, Miner K, et al. Growth of uterine leiomyomata among premenopausal black and white women. *Proc Natl Acad Sci U S A.* 2008;105:19887–19892.
4. Eskenazi B, Warner M, Samuels S, et al. Serum dioxin concentrations and risk of uterine leiomyoma in the Seveso Women's Health Study. *Am J Epidemiol.* 2007;166:79–87.
5. Buttram VC Jr, Reiter RC. Uterine leiomyomata: etiology, symptomatology, and management. *Fertil Steril.* 1981;36(4):433–445.
6. Yoo EH, Lee PI, Huh C-Y, et al. Predictors of leiomyoma recurrence after laparoscopic myomectomy. *J Minim Invasive Gynecol.* 2007;14(6):690–697.
7. Fauconnier A, Chapron C, Babaki-Fard K, Dubuisson J-B. Recurrence of leiomyomata after myomectomy. *Hum Reprod Update.* 2000;6(6):595–602.
8. Farquhar CM, Steiner CA. Hysterectomy rates in the United States 1990–1997. *Obstet Gynecol.* 2002;99(2):9–34.
9. Bergamini V, Ghezzi F, Cromi A, et al. Laparoscopic radiofrequency thermal ablation: a new approach to symptomatic uterine myomas. *Am J Obstet Gynecol.* 2005;192(3):768–773.
10. Milic A, Asch MR, Hawrylyshyn PA, Allen LM. Laparoscopic ultrasound-guided radiofrequency ablation of uterine fibroids. *Cardiovasc Intervent Radiol.* 2006;19(4):694–698.
11. Recaldini C, Carrafiello G, Lagana D, Cuffari S, Bergamini V, Ghezzi F. Percutaneous sonographically guided radiofrequency ablation of medium-sized fibroids. *AJR Am J Roentgenol.* 2007;189(6):1303–1306.
12. Carrafiello G, Recaldini C, Fontana F, et al. Ultrasound-guided radiofrequency thermal ablation of uterine fibroids: medium-term follow-up. *Cardiovasc Intervent Radiol.* 2010;33(1):113–119.
13. Garza Leal JG, Hernandez Leon I, Castillo Saenz L, Lee BB. Laparoscopic ultrasound-guided radiofrequency volumetric thermal ablation of symptomatic uterine leiomyomas: feasibility study using the Halt 2000 Ablation System. *J Minim Invasive Gynecol.* 2011;18(3):364–371.
14. Robles R, Aguirre VA, Arguets AI, Guerra MR. Laparoscopic radiofrequency volumetric thermal ablation of uterine myomas

with 12 months of follow-up. *Int J Gynaecol Obstet.* 2013;120(1): 65–69.

15. Chudnoff SG, Berman JM, Levine DJ, Harris M, Guido RS, Banks E. Outpatient procedure for the treatment and relief of symptomatic uterine myomas. *Obstet Gynecol.* 2013;121(5): 1075–1082.

16. Moss JG, Cooper KG, Khaund A, et al. Randomised comparison of uterine artery embolisation (UAE) with surgical treatment in patients with symptomatic uterine fibroids (REST trial): 5-year results. *BJOG.* 2011;118:936–944.

17. Tinelli A, Malvasi A, Guido M, et al. Adhesion formation after intracapsular myomectomy with or without adhesion barrier. *Fertil Steril.* 2011;95(5):1780–1785.

18. Hald K, Noreng HJR, Istre O, Klow NE. Uterine artery embolization versus laparoscopic occlusion of uterine arteries for leiomyomas: long term results of a randomized comparative trial. *J Vasc Intern Radiol.* 2009;20(10):1303–1310.

19. Goldfarb HA. Laparoscopic coagulation of myoma (myolysis). *Obstet Gynecol Clin North Am.* 1995;22:807–819.

20. Goldfarb HA. Bipolar laparoscopic needles for myoma coagulation. *J Am Assoc Gynecol Laparosc.* 1995;2:175–179.

21. Lee BB. Radiofrequency ablation of uterine fibroids: a new minimally invasive hysterectomy alternative. *Obstet Gynecol.* 2002;99(Suppl):S9.

22. Spies JB, Coyne K, Guaou Guaou N, et al. The UFS-QOL, a new disease-specific symptom and health-related quality of life questionnaire for leiomyomata. *Obstet Gynecol.* 2002;99(2):290–300.

23. Berman JM, Puscheck EE, Diamond MP. Full-term live birth after laparoscopic radiofrequency ablation of a large, symptomatic intramural fibroid. *J Reprod Med.* 2012;57:159–163.