

OBSTETRICS & GYNECOLOGY



NOTICE: This document contains comments from the reviewers and editors generated during peer review of the initial manuscript submission and sent to the author via email.

Questions about these materials may be directed to the *Obstetrics & Gynecology* editorial office:
obgyn@greenjournal.org.

Date: Sep 17, 2018
To: "Scott Chudnoff" [REDACTED]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-18-1510

RE: Manuscript Number ONG-18-1510

12-Month Clinical Efficacy of Transcervical Radiofrequency Ablation of Uterine Fibroids: the SONATA Pivotal IDE Clinical Trial

Dear Dr. Chudnoff:

Your manuscript has been reviewed by the Editorial Board and by special expert referees. Although it is judged not acceptable for publication in Obstetrics & Gynecology in its present form, we would be willing to give further consideration to a revised version.

If you wish to consider revising your manuscript, you will first need to study carefully the enclosed reports submitted by the referees and editors. Each point raised requires a response, by either revising your manuscript or making a clear and convincing argument as to why no revision is needed. To facilitate our review, we prefer that the cover letter include the comments made by the reviewers and the editor followed by your response. The revised manuscript should indicate the position of all changes made. We suggest that you use the "track changes" feature in your word processing software to do so (rather than strikethrough or underline formatting).

Your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Oct 08, 2018, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

REVIEWER #1:

This is a prospective cohort study evaluating the safety and effectiveness of transcervical radiofrequency ablation for the treatment of symptomatic uterine fibroids.

1. Title: Please remove the term: the SONATA Pivotal IDE Clinical Trial from the title and change the Short Title accordingly so a brand name does not appear in the title. Do not use the term IDE in the text without defining it.
2. Abstract: Please state in the methods that this is a prospective cohort study.
3. Methods: Please define PBAC in the text as well and define for the reader what values are significant.
4. Methods: Please include a Figure of the FIGO fibroid classification for easy reader reference.
5. Methods: Why choose surgical reintervention at 12 months as a primary endpoint...that seems rather soon for a patient to decide that the treatment failed and to have another surgery although 1 patient did have a hysterectomy. It would make more sense at 24 and 36 months. What about medical interventions?
6. Methods: Why were Type 0 >1 cm fibroids excluded?
7. Methods: Why was the fibroid size limit 5 cm?
8. Methods: If I am reading this correctly, only 1 fibroid was used to calculate the mean maximal total and perfused fibroid volume reductions? Why only 1 fibroid if more than 1 was treated?
9. Methods: How does the physician know if the fibroid needs repeat ablation? Is there a feedback mechanism on the device?
10. Methods: By conscious sedation, are you referring to moderate sedation with midazolam and fentanyl only, or was propofol allowed which would be Deep Sedation?
11. Results: The first two sentences in the 2nd paragraph are confusing as to where the procedures took place. The first sentence implies only offices and procedure rooms, the second sentence adds in hospital ORs. Please clarify.

12. Results: How was mean length of stay calculated?

13. Results: When were mean procedure pain scores and recovery pain scores assessed?

14. Discussion: I would add caveats that the sample size was not large enough to determine the risks of device related adverse events e.g. when this technology enters the real world and more women are exposed, will there be more events e.g. thermal heating outside the uterus?

15. Discussion: This could be shortened, some of the discussion is just repeating the results.

16 Discussion: What is the training required to use this method, how many cases are required for competency?

17. Overall: There is no mention of whether medical therapies were allowed prior to entering the trial or during the trial. Were subjects allowed to take hormonal treatments if their bleeding was unsatisfactory?

REVIEWER #2:

This study summarizes a novel technology for addressing a variety of uterine fibroids. Regarding the disclosures, I have significant concerns that all authors are on advisory board of the company sponsoring the research study. What measures were put in place to avoid undue bias due to the financial associations? Why were sites/investigators without financial conflict included in this trial?

Abstract- objective should be stated in present tense; methods should be more standardize in description (and fibroid diameter belongs in results unless you rephrase as an inclusion criteria); line 67-69 in conclusion should be stricken, it is an over-reach in conclusion and not supported by results that wide variety of fibroid type and sizes could be treated when you include only <5cm fibroid lesions.

Introduction- reads a bit like a brochure written by the company... for example the sentence about integration of real-time imaging being an improvement over hysteroscopy -- this system may well be able to treat a wider variety of lesions than hysteroscopy if they can address lesions not in the cavity, however real-time ultrasound imaging can easily be used along with hysteroscopy as well so please edit sentence to be more clear about what improvements this technique offers. Line 88-90 should be rephrased in terms of study objective and primary outcomes.

Methods- Line 112-114, please explain what you mean that subserous fibroids were treated but not counted? why was antibiotic use not standardized? would antibiotic be routine recommended with this procedure? please report in results what percentage received antibiotic prophylaxis as this could impact periop complications (also please comment on the patient with postop infection in results about antibiotic use); please give more detail on FDA IDE and approval numbers.

Results- sufficiently summarized and reflected in tables however you do not need to report both mean and median- depending on normality of variable you should report one or the other, please see other similar clinical studies for examples of this; please ensure that throughout the paper all abbreviations are defined (LOCF method)

Conclusion- the introductory paragraphs again read like a sales pitch, suggest editing to soften language as per comments to follow; line 348 about morcellation - you need to be careful to address this issue, just because you are not morcellating tissue does not excuse you from issues regarding occult leiomyosarcoma. if you mention morcellation you need to also address the fact that it is unknown what would happen if occult sarcoma is ablated with this system, could lead to delayed diagnosis or altered disease course. line 388, the lack of surgical intervention does not minimize a complication, would strike this portion. line 390, BMI of 28 is not high, please be careful what you are claiming is consistent with your data; please also avoid re-iterating your results here; please comment on need for long-term follow-up, and compare outcomes to other non-extirpative techniques such as UAE and laparoscopic radiofrequency ablation

REVIEWER #3:

1. There is a clear need for new effective minimally invasive surgical options for women with symptomatic leiomyoma.,

2. This need has grown as several minimally invasive techniques have fallen under serious scrutiny.,

3. My comments are based on the fact that any new device for the treatment of symptomatic leiomyomas is going to very closely scrutinized before approval.,

4. As the disclosure statement reveals: each author has received support for the study, serves on Advisory Board and one received stock options. I think it is fair to question if any bias played a role in study.,

5. As acknowledged the Medical Director for the device manufacturer contributed to the manuscript. The manuscript reads like a submission to the FDA for device approval.,

6. I applaud the authors for having such a high follow up at 12 months which is very rare.
- 7., I would like to see more clarification regarding using the 7 patients who did not complete 12 month PBAC questionnaire in the analysis of menstrual bleeding reduction primary endpoint.,
8. I would like to understand the rationale behind protocol change resulting in only 117 patients completing 3 month visit.,
9. Authors state limitation of single arm trial. Why was trial designed in this manner?.,
10. To date no other minimally invasive treatment has results that are as successful as the reported outcomes in this trial. It would be helpful for the authors to offer an explanation.

STATISTICAL EDITOR'S COMMENTS:

1. Table 1: Since there were apparently no missing values, should cite the N at the top of the column, rather than within each variable. Need units for BMI.
2. Table 2: Suggest that if a variable has normal distribution, then may cite as mean±SD, if skewed, then median (Range or IQR).
3. Table 3: If the 3 month data were only collected from 117 women, then the baseline comparison group should only be the same cohort of 117 women, not all 142. Also, for the 6 and 12 month data, if pairwise comparisons are being shown, then only those cases with complete data (not imputed from last visit) should be used. That is, using only the patients with actual data at baseline and at the pre-specified 12 months post-ablation, what proportion experienced ≥ 50% reduction in bleeding and what did the LCL exceed 45%, as defined by lined 176-178?
4. Fig 3, lines 240-244: Should provide a table of these data, indicating either mean(SD) or median(IQR or range) and results of stats testing for baseline vs follow up at 12 months, but only for those cases with no missing data and identifying what stats tests were used to arrive at inferences.

EDITORIAL OFFICE COMMENTS:

1. The Editors of Obstetrics & Gynecology are seeking to increase transparency around its peer-review process, in line with efforts to do so in international biomedical peer review publishing. If your article is accepted, we will be posting this revision letter as supplemental digital content to the published article online. Additionally, unless you choose to opt out, we will also be including your point-by-point response to the revision letter, as well as subsequent author queries. If you opt out of including your response, only the revision letter will be posted. Please reply to this letter with one of two responses:
 1. OPT-IN: Yes, please publish my response letter and subsequent email correspondence related to author queries.
 2. OPT-OUT: No, please do not publish my response letter and subsequent email correspondence related to author queries.
2. Clinical trials submitted to the journal as of July 1, 2018, must include a data sharing statement. This statement must appear at the end of your Materials and Methods section. The statement should indicate 1) whether individual deidentified participant data (including data dictionaries) will be shared; 2) what data in particular will be shared; 3) whether additional, related documents will be available (eg, study protocol, statistical analysis plan, etc.); 4) when the data will become available and for how long; and 5) by what access criteria data will be shared (including with whom, for what types of analyses, and by what mechanism). Examples of statements can be found online at http://www.icmje.org/news-and-editorials/data_sharing_june_2017.pdf.
3. Responsible reporting of research studies, which includes a complete, transparent, accurate and timely account of what was done and what was found during a research study, is an integral part of good research and publication practice and not an optional extra. Obstetrics & Gynecology supports initiatives aimed at improving the reporting of health research, and we ask authors to follow specific guidelines for reporting randomized controlled trials (ie, CONSORT), observational studies (ie, STROBE), meta-analyses and systematic reviews of randomized controlled trials (ie, PRISMA), harms in systematic reviews (ie, PRISMA for harms), studies of diagnostic accuracy (ie, STARD), meta-analyses and systematic reviews of observational studies (ie, MOOSE), economic evaluations of health interventions (ie, CHEERS), and quality improvement in health care (ie, SQUIRE 2.0). Include the appropriate checklist for your manuscript type upon submission. Please write or insert the page numbers where each item appears in the margin of the checklist. Further information and links to the checklists are available at <http://ong.editorialmanager.com>. In your cover letter, be sure to indicate that you have followed the CONSORT, MOOSE, PRISMA, PRISMA for harms, STARD, STROBE, CHEERS, or SQUIRE 2.0 guidelines, as appropriate.
4. Standard obstetric and gynecology data definitions have been developed through the reVITALize initiative, which was convened by the American College of Obstetricians and Gynecologists and the members of the Women's Health Registry Alliance. Obstetrics & Gynecology will be transitioning as much as possible to use of the reVITALize definitions, and we encourage authors to familiarize themselves with them. The obstetric data definitions are available at <http://links.lww.com>

/AOG/A515, and the gynecology data definitions are available at <http://links.lww.com/AOG/A935>.

5. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Original Research reports should not exceed 22 typed, double-spaced pages (5,500 words). Stated page limits include all numbered pages in a manuscript (i.e., title page, précis, abstract, text, references, tables, boxes, figure legends, and appendixes).

Please limit your Introduction to 250 words and your Discussion to 750 words.

6. Titles in Obstetrics & Gynecology are limited to 100 characters (including spaces). Do not structure the title as a declarative statement or a question. Introductory phrases such as "A study of..." or "Comprehensive investigations into..." or "A discussion of..." should be avoided in titles. Abbreviations, jargon, trade names, formulas, and obsolete terminology also should not be used in the title. Titles should include "A Randomized Controlled Trial," "A Meta-Analysis," or "A Systematic Review," as appropriate, in a subtitle. Otherwise, do not specify the type of manuscript in the title.

7. Specific rules govern the use of acknowledgments in the journal. Please edit your acknowledgments or provide more information in accordance with the following guidelines:

* All financial support of the study must be acknowledged.

* Any and all manuscript preparation assistance, including but not limited to topic development, data collection, analysis, writing, or editorial assistance, must be disclosed in the acknowledgments. Such acknowledgments must identify the entities that provided and paid for this assistance, whether directly or indirectly.

* All persons who contributed to the work reported in the manuscript, but not sufficiently to be authors, must be acknowledged. Written permission must be obtained from all individuals named in the acknowledgments, as readers may infer their endorsement of the data and conclusions. Please note that your signature on the journal's author agreement form verifies that permission has been obtained from all named persons.

* If all or part of the paper was presented at the Annual Clinical and Scientific Meeting of the American College of Obstetricians and Gynecologists or at any other organizational meeting, that presentation should be noted (include the exact dates and location of the meeting).

8. The most common deficiency in revised manuscripts involves the abstract. Be sure there are no inconsistencies between the Abstract and the manuscript, and that the Abstract has a clear conclusion statement based on the results found in the paper. Make sure that the abstract does not contain information that does not appear in the body text. If you submit a revision, please check the abstract carefully.

In addition, the abstract length should follow journal guidelines. The word limits for different article types are as follows: Original Research articles, 300 words. Please provide a word count.

9. Abstracts for all randomized, controlled trials should be structured according to the journal's standard format. The Methods section should include the primary outcome and sample size justification. The Results section should begin with the dates of enrollment to the study, a description of demographics, and the primary outcome analysis. Please review the sample abstract that is located online here: http://edmgr.ovid.com/ong/accounts/sampleabstract_RCT.pdf. Please edit your abstract as needed.

10. Only standard abbreviations and acronyms are allowed. A selected list is available online at <http://edmgr.ovid.com/ong/accounts/abbreviations.pdf>. Abbreviations and acronyms cannot be used in the title or précis. Abbreviations and acronyms must be spelled out the first time they are used in the abstract and again in the body of the manuscript.

11. The journal does not use the virgule symbol (/) in sentences with words. Please rephrase your text to avoid using "and/or," or similar constructions throughout the text. You may retain this symbol if you are using it to express data or a measurement.

12. Our readers are clinicians and a detailed review of the literature is not necessary. Please shorten the Discussion and focus on how your results affect or change actual patient care. Do not repeat the Results in the Discussion section.

13. Please review the journal's Table Checklist to make sure that your tables conform to journal style. The Table Checklist is available online here: http://edmgr.ovid.com/ong/accounts/table_checklist.pdf.

14. The Journal's Production Editor has the following to say about the figures in your manuscript:

"Figure 3: Was this created using an Office product? If so, please upload the original file. If not, please upload a higher resolution version of this figure."

When you submit your revision, art saved in a digital format should accompany it. If your figure was created in Microsoft Word, Microsoft Excel, or Microsoft PowerPoint formats, please submit your original source file. Image files should not be copied and pasted into Microsoft Word or Microsoft PowerPoint.

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If the figures were created using a statistical program (eg, STATA, SPSS, SAS), please submit PDF or EPS files generated directly from the statistical program.

Figures should be saved as high-resolution TIFF files. The minimum requirements for resolution are 300 dpi for color or black and white photographs, and 600 dpi for images containing a photograph with text labeling or thin lines.

Figures should be no smaller than the journal column size of 3 1/4 inches. Art that is low resolution, digitized, adapted from slides, or downloaded from the Internet may not reproduce. Refer to the journal printer's web site (<http://cjs.cadmus.com/da/index.asp>) for more direction on digital art preparation.

If you choose to revise your manuscript, please submit your revision via Editorial Manager for Obstetrics & Gynecology at <http://ong.editorialmanager.com>. It is essential that your cover letter list point-by-point the changes made in response to each criticism. Also, please save and submit your manuscript in a word processing format such as Microsoft Word.

If you submit a revision, we will assume that it has been developed in consultation with your co-authors, that each author has given approval to the final form of the revision, and that the agreement form signed by each author and submitted with the initial version remains valid.

Again, your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Oct 08, 2018, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

The Editors of Obstetrics & Gynecology

2017 IMPACT FACTOR: 4.982

2017 IMPACT FACTOR RANKING: 5th out of 82 ob/gyn journals

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