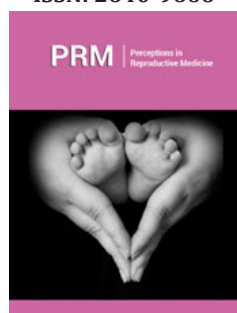


# Sonata® System from a Reproductive Perspective

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ISSN: 2640-9666



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**Submission:** 📅 July 26, 2023

**Published:** 📅 September 14, 2023

Volume 5 - Issue 5

**How to cite this article:** Tomic V\*, Oppelt P, Trautner P and Arnreiter C. Sonata® System from a Reproductive Perspective. *Perceptions Reprod Med.* 5(5). PRM. 000624. 2023.  
DOI: [10.31031/PRM.2023.05.000624](https://doi.org/10.31031/PRM.2023.05.000624)

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## Abstract

**Objective:** A mini-systematic review of pregnancy outcomes after Radiofrequency Ablation (RFA) of uterine fibroids with Sonata® System.

**Data sources:** A literature search was conducted using PubMed, ScienceDirect, Cochrane Library and Medline, from database inception to 20th July 2023.

**Method:** Three reviewers (VT, CA, PT) conducted independent literature searches. Studies that met the criteria based on title, abstract or keyword underwent full-text review. Publications were included if they reported pregnancies and/or obstetric outcomes after transcervical RFA of myomas.

**Result:** A total of 441 publications were initially identified and screened, 41 underwent full-text review, and 6 publications were ultimately included. Among the RFA patients who conceived, the average age at ablation was 37 years old (range, 22-45 years). Most patients had between 1 and 6 myomas ablated and myomas size ranged from 1cm to cm, FIGO type 2-5. There were 8 spontaneous abortions and 36 pregnancies, of which 60% were caesarean deliveries. There were no cases of uterine rupture, invasive placentation, stillbirth, fetal growth restriction nor neonatal complications. Obstetric complications were comparable with the general population.

**Conclusion:** Treatment of uterine fibroids with the Sonata® system did not show any adverse pregnancy outcome, including women with recurrent abortion and women undergoing in vitro fertilization.

**Keywords:** Sonata® system; Transcervical radiofrequency ablation; Uterine fibroid; Systematic review; Pregnancy

**Abbreviations:** FDA: Food and Drug Administration; TFA: Transcervical Fibroid Ablation; RF: Radio Frequency; NOS: Newcastle Ottawa Scale; ART: Assisted Reproductive Technology

## Introduction

Uterine fibroids are benign solid tumors affecting about 70%-80% by the age of 50 years [1]. Myomas can cause various symptoms like heavy menstrual bleeding, dyspareunia, pelvic as well as subfertility [2]. Since many affected women have not yet completed their reproductive desire, there has been increasing interest in organ preserving, minimally invasive treatment options [3]. Hyperthermic ablation of uterine fibroids using Magnetic Resonance-Guided Focused Ultrasound (MRgFUS) and Radio Frequency therapy (RF) has been shown to be an effective and safe alternative for women with a wish for organ preservation [4-8]. MRgFUS has been approved by the Food and Drug Administration (FDA) for use in women who desire fertility and it has been shown that pregnancy outcomes after Focused Ultra Sound (FUS) have been favourably compared with those after laparoscopic myomectomy [9,10]. Transcervical radiofrequency ablation is performed with the Sonata® System (Gynesonics, Inc. Redwood City, CA, USA) and is a minimally invasive, transcervical, incisionless approach to treat uterine myomas. Transcervical Fibroid Ablation (TFA) is associated with clinically meaningful improvement of myoma related symptoms including significant and durable improvements in menstrual bleeding and overall quality of live [7]. Radio Frequency Ablation (RFA) showed significantly greater reduction in mean fibroid volume than Uterine Artery Embolization (UAE) and MRgFUS without major surgical morbidity [11,12]. The clinical trials for laparoscopic and transcervical RFA did not report intraoperative or postoperative complications [13-15] nor serious procedural complications [16].

The preliminary results from the first 160 treated women in SAGE suggest broad applicability of TFA to a wide range of fibroid types and sizes and an excellent safety profile [17]. Until today, there are several reports about successful pregnancy outcomes after transcervical fibroid ablation [18]. The purpose of this systematic-review is to analyse the currently available data regarding pregnancy outcomes after TFA with the Sonata® System.

## Method

### Search strategy and outcome measures

This systematic review was conducted in accordance with the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA). The first step was an electronic literature search in the PubMed, ScienceDirect, MEDLINE and Cochrane Library databases. The following keywords and combinations of them were used: "Sonata-System", "Pregnancy", "In Vitro Fertilization", "transcervical radiofrequency ablation", "uterine fibroid," and "Leiomyoma". Subsequently, all search results in English that were identified in the literature search from its inception through 20th July 2023 were screened for title and abstract. The aim of the review was to provide an overview of the available data regarding impact of sonata-treatment on reproduction and pregnancy outcome, and safety of radiofrequency ablation with the Sonata® System. The full-text analysis therefore included all articles in English addressing at least one of the following outcomes after treatment with the Sonata® system: Apgar scores, birthweight, stillbirth, adverse obstetric outcome, postpartum haemorrhage, mode of delivery, preterm birth, placenta praevia and uterine rupture.

The authors (VT, CA, PT) reviewed the articles independently. The fourth author (PO) provided expert opinion and in the case of disagreement final decision. The exclusion criteria included reviews, as well as studies in which radiofrequency ablation was not performed with the Sonata® System (or formerly VizAblate®) or studies where outcomes listed in the inclusion criteria were not reported.

### Quality assessment and analysis

Quality assessment of the single arm trials was performed using the Newcastle Ottawa Scale (NOS). This scale provides a maximum of 9 points for quality of selection (up to 4 points), comparability (up to 2 points) and outcome (up to 3 points) of study participants. Study quality was defined as poor (for a score of 0-3), fair (for a score of 4-6), or good (for a score of 7-9). Case report studies were also included in review. All statistical analyses were performed with IBM SPSS® Statistics 23.0 (Statistical Package for Social Sciences).

## Result

A total of 6 articles were included in final analysis. All of the reviewed studies were non-randomized controlled trials (non-RCTs), and as such prone to a high risk of selection bias. The included studies scored from 4 to 6. There was marked heterogeneity in the outcome parameters, timing of follow-up, and use of different tools to evaluate patient-reported outcomes, which limited direct

comparisons. To date, there have been 36 pregnancies representing 20 deliveries among 28 women who were treated with TFA. A four of them conceived through Assisted Reproductive Technology (ART). Outcomes include 8 vaginal deliveries, 12 Caesarean sections, 3 therapeutic abortions, and 8 first-trimester pregnancy losses of the 8 miscarriages, four occurred in a women with a history of recurrent abortion and an antiphospholipid syndrome, which subsequently had a delivery at term. All 5-minute Apgar scores were >7 and all neonates weighed >2500 grams. Deliveries occurred at ≥37 weeks, except for one delivery at 35 6/7 weeks. There were no uterine ruptures or abnormal placentation and no reports of postpartum hemorrhage. Cesarean sections were performed for standard obstetric indications, including non-reassuring fetal monitoring, HELLP syndrome, fetal macrosomia or elective upon patients' choice.

## Discussion

Treatment of uterine fibroids with the sonata® system did not show any adverse pregnancy outcome, including women with recurrent abortion and women undergoing in vitro fertilization. The quality assessment of the studies included demonstrated fair quality with NOS score ranged from 4 to 6. Results of this systematic review suggest that transcervical fibroid ablation with the sonata® system could be appropriated method for women in reproductive age with a desire for future fertility. The number of 36 pregnancies after treatment with the sonata® system is a result of initial clinical studies that excluded women with desire of pregnancy and the novelty of the method. In 2015, the US FDA has approved the use of MRgFUS (Magnetic-Resonance-Guided Focused Ultrasound) in women with the desire for future pregnancy [19]. Sonata® system on the other hand has received the Conformité Européenne (CE) mark in the European Union and has been cleared by the FDA in the United States, labelling notes that treatment with the Sonata system as a uterus-conserving treatment option does not rule out the possibility of pregnancy [20].

The fertility and pregnancy outcome after TFA-Sonata system have been favourable since there have been no reports on adverse outcome regarding uterine rupture, stillbirths, postpartum haemorrhage or any abnormal placentation [21]. Such complication have been reported with pregnancies following uterine artery embolization [22,23]. The spontaneous abortion rate did not differ from general population of the women of same age and parity [18]. All spontaneous abortions occurred in the first trimester, and there was no late abortion reported [18,21,24]. Impact of TFA on mode of delivery showed higher rate of caesarean section (60%) when compared with general population but comparable rate after LFA (50%) as reported by Berman et al. [25]. However it has to be noted that half of the patient giving birth after TFA were more than 37 years of age and 2 CS where on patient desire. Case-series studies [18,20,26] included individual case reports of 3 pregnancies after treatment with the Sonata® system [27-29]. No complications occurred during the pregnancies or deliveries in the 3 case reports. The surgical report showed no abnormalities, and there was no evidence of a pre-existing uterine defect due to fibroids or the radiofrequency ablation performed. Results from the OPEN clinical

trial and INTEGRITY trial did not show higher risk of intrauterine adhesion nor negative impact of TFA on the integrity of uterine wall [30,31] that could compromise the future fertility.

Our findings presented that radiofrequency myoma ablation may offer a safe and effective treatments for women who desire future fertility. The main limitation of the systematic review is the small number of total pregnancies after TFA available for analysis. Therefore, future studies should be focused on the pregnancy outcome after the TFA treatment with Sonata-system including also patients in non-advanced maternal age [32-35].

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