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Research Article

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FemBloc Non-Surgical Permanent Contraception for Occlusion of the Fallopian Tubes

James H. Liu[1,2*], Paul D. Blumenthal[3], Paula M. Castano[4], Scott C. Chudnoff[5], Lori M. Gawron[6], Erica B. Johnstone[6] and Kathy Lee-Sepsick[2]

[1]*Department of Reproductive Biology, Case Western Reserve University, USA.*

[2]*Femasys Incorporated, Suwanee, GA, USA.*

[3]*Department of Obstetrics and Gynecology, Stanford University Medical Center, Stanford, CA, USA.*

[4]*Department of Obstetrics and Gynecology, Columbia University Irving Medical Center, New York, NY, USA.*

[5]*Department of Obstetrics and Gynecology, Maimonides Medical Center, Brooklyn, NY, USA.*

[6]*Department of Obstetrics and Gynecology, University of Utah, Salt Lake City, UT, USA.*

[*]Corresponding Author

James H. Liu, Department of Reproductive Biology, Case Western Reserve University, USA.

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Abstract

Objective: *To assess pregnancy outcomes following non-surgical tubal occlusion using the FemBloc® system in a population of women seeking permanent contraception.*

Methods: *Three prospective, multi-center clinical trials (Clinicaltrials.gov NCT03067272, NCT03433911, and NCT04273594) of females aged 21-45 years desiring permanent contraception, who underwent non-surgical, in-office procedure with the FemBloc system, conducted collectively at twenty-five academic and private medical centers in the United States. An ultrasound-based confirmation test for tubal occlusion with the FemChec® device was performed prior to subject reliance and contraceptive effectiveness assessment of FemBloc through one year. Follow-up continued annually through five years for safety.*

Results: *The pregnancy rate for FemBloc non-surgical permanent contraception subjects, who met trial eligibility and, three months post-FemBloc, were determined bilaterally occluded by investigator after a properly performed ultrasound-based confirmation test with FemChec was 0% (95%UCB: 0.057; n=0/51), which was significantly lower than the performance goal of 6% based on the historical control (one-sided P=0.0426). The safety reports were consistent with those typically observed for intrauterine transcervical procedures, with no on-going safety concerns through five years. There were no reports of serious adverse events, no ectopic pregnancies and no uterine perforations (n=0/228) for subjects that underwent a FemBloc procedure.*

Conclusion: *No pregnancies occurred among eligible subjects who relied on the FemBloc permanent contraceptive system after receiving a properly conducted confirmation test. The FemBloc system involves minimally invasive delivery*

of a proprietary synthetic tissue adhesive to occlude the fallopian tubes, fully degrading and producing nonfunctional scar tissue. It has the potential to offer safe, effective, accessible, non-surgical permanent contraception as an option to surgical sterilization with fewer risks, contraindications, and a substantially lower cost.

Keywords: Permanent Contraception, Permanent Birth Control, Sterilization, Bilateral Fallopian Tube Occlusion, Non-Surgical Permanent Contraception, FemBloc.

1. Introduction

The demand for contraception, including accessible non-surgical permanent options, continues to increase worldwide, with the number of women seeking contraception growing from 900 million in 2000 to nearly 1.1 billion in 2021 [1]. Access to high quality contraceptive services will continue to be an important factor in promoting healthy pregnancies and preventing unintended pregnancy. Despite the progress made in the last century, unintended pregnancies continue to be a significant personal burden for individuals, as well as a major public health issue in the United States and globally. By age 45, it is estimated that about half of US women will have experienced an unintended pregnancy and about one-quarter will have had an abortion [2]. The decision to have an abortion is often challenging, and the procedure can be costly and less accessible due to state restrictions [3]. In the context of acknowledging the risk of unintended pregnancy, the risks of specific contraceptive methods must be carefully weighed. Women typically initiate and discontinue multiple contraception methods over their reproductive lifespan of approximately thirty years, spending only three years trying to become pregnant, being pregnant or postpartum [4]. The high rate of unintended pregnancy points to an unmet need for contraceptive technologies that are safe and effective, accessible, and affordable.

Female surgical sterilization or permanent contraception (PC) is the most commonly used contraceptive worldwide, including 18.1% of contracepting women in the US [5,6]. Effective family planning involves careful consideration of many aspects of available contraceptive methods, including relative effectiveness; misconceptions of contraceptive effectiveness, however, are common [7]. Female PC has traditionally been performed via mini-laparotomy or laparoscopy for tubal resection, clipping, electrocautery, etc. to prevent sperm from accessing an ovulated oocyte [8]. Bilateral salpingectomy is an increasingly employed surgical PC option, with the additional benefit of reducing ovarian cancer risk [9]. These approaches are effective and perceived as generally safe but are also invasive surgical procedures that commonly require general anesthesia or deep sedation [10]. Reported risks include infection, minor or major bleeding, injury to nearby organs, anesthesia-related events, and even death [11,12]. Along with the various surgical risks, some patients may not qualify as surgical candidates for abdominal or laparoscopic surgery due to obesity, adhesive disease, or medical comorbidities [5]. Previously available PC methods, Essure® (Bayer, Germany) and Adiana® (Hologic, Marlborough, MA), offered less invasive alternatives that involved hysteroscopic transcervical placement of permanent, lumen occluding devices into both fallopian tubes [10,13]. These non-degradable permanent implants stimulated localized foreign-body reactions to completely occlude the tubal lumen. Both hysteroscopic PC options required a radiology-based confirmation test three months post procedure. Essure and Adiana have both been discontinued or withdrawn from the global market, thereby eliminating access to less invasive hysteroscopic PC for women. The Essure device had numerous patient safety concerns, including patient-device incompatibility/ biocompatibility, migration, dislodgement or malpositioning of the device or device component, device breakage/ material fragmentation/ fracture, and tubal perforation [14,15]. Market experience with Essure reported unintended pregnancies due to misinterpretation or inadequately performed confirmation tests and high non-compliance in returning for the radiology-based hysterosalpingography confirmation test particularly by patients in certain populations [16,17]. When considering effectiveness, real-world data for laparoscopic PC (n=23,965) and hysteroscopic PC (n=5,906), recently reported pregnancy rates of 5.57% and 4.74% respectively and cumulative pregnancy rates five (5) years after PC of 7.22 and 6.26 per 100 woman-years respectively [18]. Of the reported failures, 7.34% were ectopic pregnancies for laparoscopic PC and pregnancy failures varied by age at time of PC.

Contraceptive choices are influenced by various factors, with effectiveness, safety and side effects being most commonly prioritized [19]. Therefore, women who desire PC may be using a temporary or reversible method as a compromise because they do not wish to undergo surgical PC. Non-surgical PC offers a more convenient, accessible and lower cost solution than surgical sterilization options. Safe, minimally-invasive, effective approaches for achieving PC non-surgically remains an important goal to provide patients with options that align with their lives and goals [20]. We developed FemBloc to meet this goal and are presenting the results from our initial safety and efficacy assessments.

2. Materials and Methods

2.1 Study Design and Subjects

We conducted three prospective, open-label, clinical trials (clinicaltrials.gov NCT03067272, NCT03433911, and NCT04273594) under US Food and Drug Administration (FDA) approved investigational device exemption (G160106) to evaluate the safety and effectiveness of the FemBloc® permanent birth control. The trials were performed at 25 US tertiary medical centers by 35 investigators beginning April 2017, February 2018, and June 2020 respectively. Enrollment for the three prospective trials included 49, 135, and 45 subjects, respectively and concluded in November 2017, February 2019, and September 2022. Institutional review board (IRB) approvals were obtained for all sites. All subjects provided written informed consent.

2.2 Devices and Procedures

The FemBloc system consists of a sterile single-use delivery device (Delivery System) that is introduced by transcervical placement to deliver a proprietary synthetic tissue adhesive (Blended Polymer) directly into each uterine cavity cornu and both fallopian tubes simultaneously (Fig. 1A). The insertion tube transits the cervix into the uterine cavity to the fundus (Fig. 1B). Two flexible balloon catheters are deployed and exit laterally out of the insertion tube and are advanced a pre-set distance to each uterine cavity cornu, whereupon the balloons are simultaneously inflated with air from syringes contained within the Delivery System handle (Fig. 1C) to prevent retrograde egress and promote forward flow of the subsequently delivered liquid Blended Polymer (Fig. 1D). The Delivery System is then removed, and the Blended Polymer polymerizes to form a pliable, porous structure in each cornual region extending into the proximal end of the fallopian tubes (Fig. 1E). With tissue contact, the Blended Polymer elicits a natural inflammatory response followed by a healing phase. Over the following three-months, the Blended Polymer degrades, leaving nonfunctional scar tissue in a small section of each fallopian tube, resulting in bilateral tubal occlusion. After three months, an ultrasound-based hysterosalpingogram confirmation test with saline-air contrast generated from the FemChec device confirms bilateral occlusion. (Not shown) The subject is then cleared to rely on FemBloc for permanent contraception.

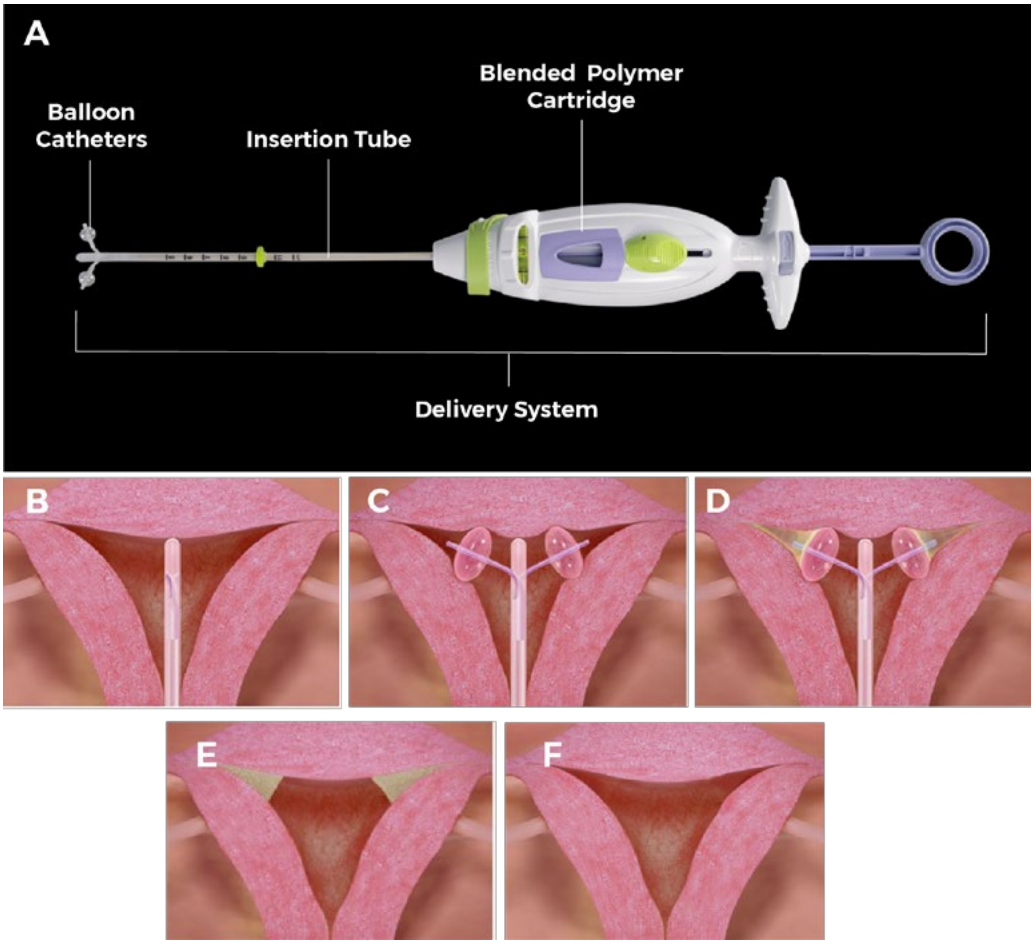

Figure 1: The FemBloc Permanent Birth Control system.

A) The FemBloc consists of a sterile single-use Delivery System that is placed transcervically to deliver Blended Polymer directly into each uterine cavity cornu and both fallopian tubes simultaneously. Following insertion to uterine fundus **(B)**, the flexible balloon catheters exit laterally out of the insertion tube and are advanced a pre-set distance to each uterine cavity cornu, whereupon the balloons are simultaneously inflated with air to seal off each cornu **(C)**. The Blended Polymer is then delivered directly towards the opening and into both fallopian tubes simultaneously **(D)**. The Delivery System is removed, and the Blended Polymer remains where delivered in the cornual region and into each fallopian tube **(E)**. The Blended Polymer elicits a natural healing response and ultimately degrades, leaving nonfunctional scar tissue in a small section of each fallopian tube for bilateral occlusion **(F).**

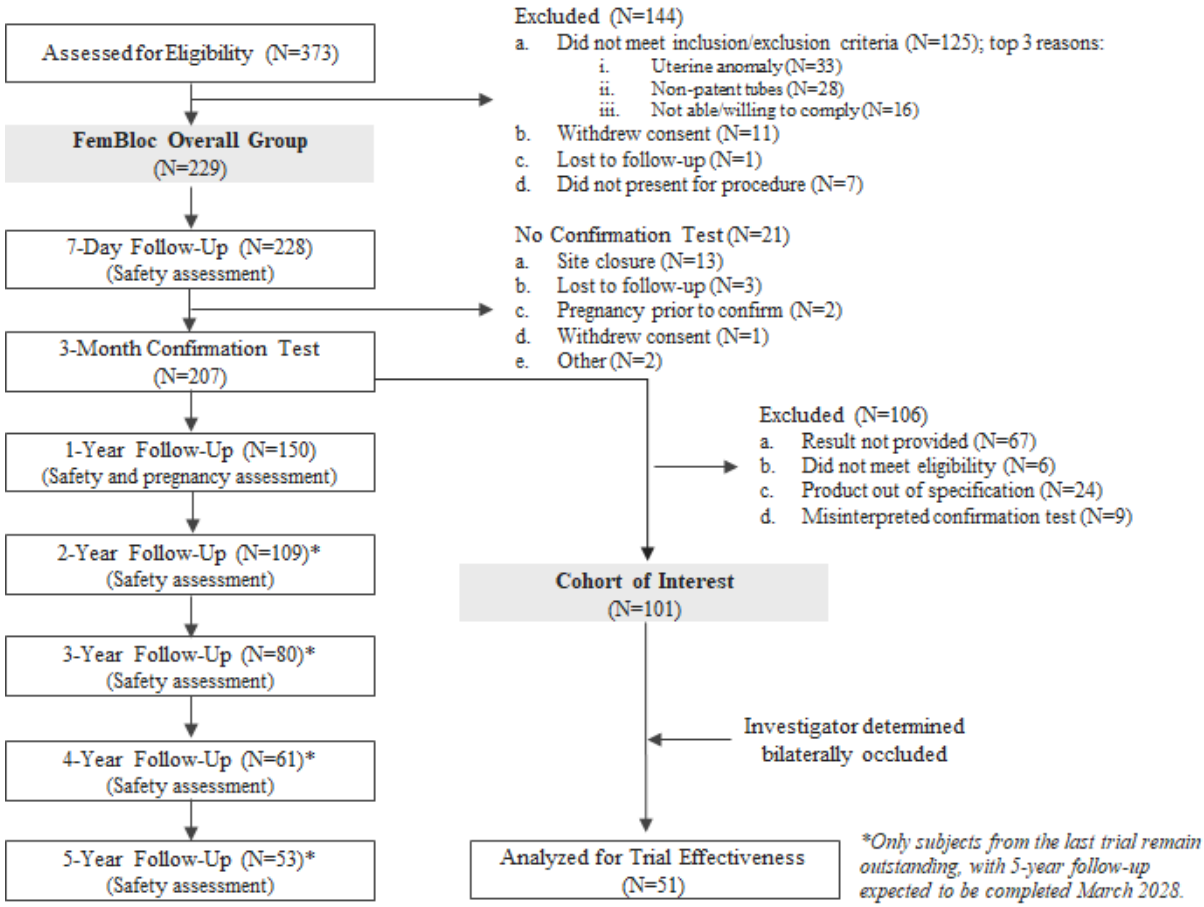

Figure 2: Flowchart of Subject Numbers of the Combined Three Open-Label Trial

2.3 Inclusion/Exclusion Criteria

Primary inclusion criteria were: i) female, 21-45 years of age, desiring permanent contraception; ii) agreement to use temporary contraception until documented bilateral tubal occlusion; iii) sexually active and at low risk of sexually transmitted infection; and iv) willing to accept risk of pregnancy while relying on FemBloc for contraception. For the last two trials, an additional criterion was added requiring normal uterine cavity and patent fallopian tubes demonstrated by sonographic hysterosalpingogram with the FemVue® Saline-Air device (Femasys, Suwanee, GA), a substantially similar product to FemChec.

Primary exclusion criteria were: i) prior tubal surgery or ectopic pregnancy; ii) difficult cervical visualization or instrumentation of the uterus; iii) current or recent infection of cervix, endometrium, or fallopian tubes; iv) presence or suspicion of gynecologic malignancy; v) known uterine anomaly or uterine position that would interfere with insertion tube midline fundal placement, access to uterine cornu, or lateral deployment of the balloon catheters; vi) postpartum or pregnancy termination < 6 weeks from scheduled FemBloc procedure, vii) abnormal uterine bleeding requiring evaluation or treatment, and viii) known hypersensitivity to cyanoacrylate or formaldehyde.

2.4 Visits

FemBloc procedure and confirmation test were conducted according to FemBloc Instructions for Use and training, with the following parameters documented: i) pre-medication use (e.g., NSAIDs, acetaminophen); ii) FemBloc procedure/ confirmation test time; iii) discomfort rating using a visual analog scale; iv) investigator assessment of FemBloc procedure/ confirmation test performance; and v) Adverse Events (AE) during the procedure/ test.

Subjects received a phone call 7 days (±2 days) after FemBloc procedure, for subject and AE assessments. Subjects returned 3 months (+30 days) after the FemBloc procedure for the confirmation test. Three months (±14 days) after the confirmation test, subjects returned for AE assessments. A phone follow-up call was conducted 1 year (+30 days) after the confirmation test for pregnancy and safety assessment, and annually 2-5 years (±30 days) for safety assessment. Subjects were instructed to report any suspected pregnancy to the investigational site immediately. If pregnancy was diagnosed, clinical management was at the subjects' and investigators' discretion.

3. Statistical Analysis

Exact 95% upper confidence bound (UCB) was calculated for the effectiveness analysis. *P*-values <.05 were considered indicative of a statistically significant difference and were one-tailed. Software was SAS v.9.4 (SAS Institute, Cary, NC). A performance goal of 6% was chosen based on the reported pregnancy rate for surgical sterilization PC of 5.57% [18].

3.1 Outcome Measures

The effectiveness endpoint was confirmed pregnancy rate post FemBloc procedure and positive confirmation test result (i.e., investigator determined bilateral tubal occlusion) in subjects who met trial eligibility; received FemBloc Blended Polymer that met pre-determined product specifications; and received a confirmation test result without misinterpretation adjudicated by an independent clinical events committee. Safety outcomes included incidence of uterine perforation, ectopic pregnancies, and any AEs that were investigator assessed to be possibly or definitely related to the device and/ or procedure.

4. Results

The subject flow of the three clinical trials combined is shown in Figure 2. Of the Intention-to-Treat (ITT) subjects, 228/229 (99.6%) underwent a successful FemBloc procedure, defined as Delivery System placement and Blended Polymer delivery, performed by 31 investigators. Of the 228 subjects who completed the FemBloc procedure, 90.8% (n=207) had a completed confirmation test, defined as intrauterine catheter placement and ultrasound hysterosalpingography with saline-air contrast generated from FemChec. The confirmation test was performed by 28 of the 31 investigators who performed the FemBloc procedure (a different gynecologist performed the confirmation test at three academic centers). Due to US-FDA concerns with unintended pregnancies (n=9) among the first 117 cases, attributed to misinterpretation of the confirmation test, as adjudicated by an independent clinical events committee, 67 subjects (50% of second trial) underwent the confirmation test but were not permitted to receive a result and were followed for safety only. Adjudication of trial eligibility and product specification analysis resulted in 101 subjects who met the trial requirements and received a confirmation test result, constituting the Cohort of Interest (Figure 2). Pregnancy rate effectiveness was analyzed for the 51 subjects determined bilaterally occluded by the investigator. Safety assessment was analyzed for all subjects through 5 years.

Among all subjects, the average age was 34.7 years-old (range 22-45 years), 79.9% were multiparous with a mean BMI of 30.9. Approximately 63.8% of subjects at time of screening were utilizing a hormonal contraceptive method, of which 18% were using a levonorgestrel-releasing IUD and had to agree to removal prior to the FemBloc procedure. 28.8% of subjects were using a condom for contraception (Supplemental Table S1).

All FemBloc procedures and confirmation tests were performed in an office setting. All subjects received pre-medication prior to the FemBloc procedure and 78.6% received a transvaginal ultrasound prior to the procedure to accurately assess the cavity for fluid/blood prior to Blended Polymer delivery. The vast majority (98%) received pre-medication prior to the confirmation test (Supplemental Table S2).

Almost all (99.6%, n=228) of the ITT procedures were successfully completed with one failed attempt. The majority (91.2%, n=208) had a confirmation test approximately 3 months post the FemBloc procedure, 99.5% of which were successfully completed. The FemBloc procedure time (speculum insertion-to-speculum removal) was 6 minutes 43 seconds (median) and the confirmation test (speculum insertion-to-catheter removal) was 15 minutes (median) (Supplemental Table S3).

Some women received cervical anesthesia (18.3%) for the FemBloc procedure or (2.4%) the confirmation test. In 94.3% of cases, the FemBloc procedure was performed with one insertion attempt. Use of post-procedure medication was limited for the FemBloc procedure (15.6%) or the confirmation test (1.9%).

4.1 Cohort of Interest

The pregnancy rate (PR) in the 51 subjects who the investigator determined bilaterally occluded was 0% (95%UCB: 0.057; n=0/51) and was statistically significantly lower than the 6% PR performance goal (one-sided P-value=0.0426) (Table 1).

Of 229 subjects who had FemBloc procedure attempted (ITT) in the safety analysis (Table 2), there were no serious adverse events (SAE) reported, including no uterine perforations and no ectopic pregnancies (to-date). Data from the majority of subjects (87%) through the 5-year follow-up has been reported. There was one (1) report of uterine perforation during placement of an HSG catheter for the confirmation test. The most commonly reported (≥1%) adverse events (AEs) post the FemBloc procedure related to the device or procedure were vaginal spotting/ bleeding (58.5%), pelvic/ abdominal pain (37.1%), abdominal/ uterine cramps (18.8%), nausea (3.5%), musculoskeletal cramps (2.6%), and abdominal bloating (1.3%). The majority (61.1%) of these events occurred on the day of the FemBloc procedure and most (85.8%) resolved within 3 days. Of all 208 subjects who had a confirmation test attempted, there were only 11 AEs reported related to the device or procedure, including vaginal spotting/ bleeding (1.4%) and nausea (1.0%). There was no evidence of cervical scarring or adhesions, no hematometra, no intrauterine adhesions observed during the confirmation test (Supplemental Table S3).

Subject comfort was reflected in self-reported scores at the time of the procedure/test utilizing a visual analog scale from 0–10, averaging 4.6 discomfort for the FemBloc procedure and 3.4 for the confirmation test (Table 3). For the FemBloc procedure and the confirmation test, mean discomfort scores were notably lower for multiparous (4.1, 3.0) versus nulliparous (6.3, 5.3) subjects, respectively. 96.1% of subjects stated they would probably or definitely recommend the FemBloc permanent birth control to friends and family. All investigators (100%) stated they would recommend FemBloc to a colleague. Investigator mean ratings for overall satisfaction of the FemBloc procedure was “extremely satisfied” and when compared to surgical tubal ligation and hysteroscopic sterilization was “much easier” (Table 3).

Statistic	Result (N=51) [a]
Overall, % (n/N)	0% (0/51)
Exact 95% upper confidence bound for p_1	0.057
One-sided p-value	0.0426

Table 1: Pregnancy Effectiveness Assessment, Cohort of Interest

[a] N=51 subjects who were determined bilaterally occluded by the investigator.

Adverse Event Category	Subjects Reporting AE FemBloc Procedure N=229 [a]	Subjects Reporting AE Confirmation Test N=208 [a]
Serious AE, SAE, any, n	0	0
SAE, device-related	0	0
Uterine perforation	0	1 (0.48)
SAE, ectopic pregnancy	0	0
Non-serious AE, device-or procedure-related, n [b]	352	11
Severity Rating, n (%) [c]		
Mild	269 (76.4)	5 (45.5)
Moderate	75 (21.3)	6 (54.5)
Severe [d]	8 (2.3)	0
Time of AE reporting from procedure/test, n (%)		
1 day	215 (61.1)	9 (81.8)
2 days	30 (8.5)	0 (0)
3 days	57 (16.2)	0 (0)
4 days	12 (3.4)	0 (0)
5 days	2 (0.6)	0 (0)
6 days	2 (0.6)	0 (0)
7 days	3 (0.9)	0 (0)
>7 days	29 (8.2)	2 (18.2)
Not reported	2 (0.6)	0 (0)
AE lower level term, ≥1%, n (%)	N=229	N=208
Spotting vaginal or uterine/vaginal bleeding [e]	134 (58.5)	3 (1.4)
Pelvic or abdominal pain [e,f]	85 (37.1)	1 (0.5)
Abdominal or uterine cramps [g]	43 (18.8)	1 (0.5)
Nausea	8 (3.5)	2 (1.0)
Musculoskeletal cramps	6 (2.6)	0 (0)
Abdominal bloating [h]	3 (1.3)	0 (0)
Any AE, regardless of seriousness or relatedness, n	610	

Table 2: Safety Assessment, All Subjects

[a] N=229 total subjects who had an attempted or completed FemBloc procedure and N=208 total subjects who had an attempted or completed confirmation test.
[b] AEs listed were adjudicated to be possibly or definitely related to the device or procedure.
[c] Severity rating of "Mild" indicates an AE that does not interfere with usual activities, "Moderate" indicates an AE that interferes with usual activities, and "Severe" indicates an AE that prevents usual activities.
[d] The following AEs were noted as "Severe" by the investigator: 2- pelvic pain, 2- muscle spasms, 1- uterine spasm, 1- abdominal distension, 1- pain, and 1- abdominal pain.
[e] Includes eight AEs coded as 'post procedure bleeding' and one AE coded as 'uncoded-spotting'.
[f] Includes one AE coded as 'post procedure pain'.
[g] Includes four AEs coded as 'Abdominal crampy pains'.
[h] Three AEs were reported in first trial only.

Parameter	N=228 [a] FemBloc Procedure	N=207 [a] Confirmation Test
Subject-reported discomfort, all [b]	N=228	N=205
Mean ± SD	4.6 (2.9)	3.4 (2.8)
Median (range)	4 (0-10)	3 (0-10)
Subject-reported discomfort, nulliparous [b]	N= 46	N=39
Mean ± SD	6.3 (2.3)	5.3 (3.0)
Median (range)	6 (0-10)	5 (0-10)
Subject-reported discomfort, multiparous [b]	N=182	N=166
Mean ± SD	4.1 (2.8)	3.0 (2.6)
Median (range)	4 (0-10)	2 (0-10)
Subject recommendation to friend/ relative [c], n (%)	N=179	
Yes	136 (76.0)	NA
Probably	36 (20.1)	NA
No	7 (3.9)	NA
Investigator overall satisfaction rating [d]	N=228	N=205
Mean ± SD	1.3 (0.6)	1.6 (0.8)
Median (range)	1 (1-4)	1 (1-4)
Investigator "ease of procedure" rating, Mean ± SD [e]	N=179	N=156
Compared to surgical tubal ligation	1.2 (0.5)	NA
Compared to hysteroscopic sterilization	1.3 (0.6)	NA
Compared to IUD procedure	2.9 (0.8)	NA
Compared to saline infusion sonogram	NA	2.8 (0.7)
Investigator recommendation to colleague, n (%) [f]	N=228	N=205
Yes	191(83.8)	123 (60.0)
Probably	37 (16.2)	76 (37.0)
No	0 (0)	6 (2.9)

Abbreviations: SD=standard deviation; IUD=intrauterine device.

Table 3: Discomfort and Satisfaction Ratings, All Subjects

[a] A total of 228 FemBloc procedures and 207 confirmation tests were completed.
[b] Pain assessed using the Wong Baker FACES® Pain Rating Visual Analog Scale (VAS) score on a scale from 0 to 10, with 10 being the highest pain rating.
[c] Subject satisfaction results were queried at 7-day follow-up, before confirmation test status was known. Probably rating includes possibly.
[d] The ratings for Investigator rating of satisfaction and subject tolerability were converted as follows: 1 - Extremely Satisfied, 2 - Very Satisfied, 3 - Neither Satisfied nor Dissatisfied, 4 - Very Dissatisfied, 5 - Extremely Dissatisfied.
[e] The ratings for Investigator impression of ease of procedure compared to other procedures/tests were converted as follows: 1 – Much Easier, 2 - Easier, 3 - Same, 4 - Difficult, 5 – More Difficult. f Probably rating includes possibly.
[f] Probably rating includes possibly.

Baseline Characteristics	N=229 [a]
Age, years	
Mean ± SD	34.7 ± 5.6
Median (range)	35 (22–45)
Ethnicity, n (%)	
Hispanic or Latino	47 (20.5)
Not Hispanic or Latino [b]	182 (79.5)
Race, n (%)	
American Indian or Alaska Native	4 (1.7)
Asian	1 (0.4)
Black or African-American	23 (10.0)
Native Hawaiian or Other Pacific Islander	1 (0.4)
Other [c]	5 (2.2)
White or Caucasian	200 (87.3)
Weight, kg, mean ± SD	81.9 ± 20.5
Height, cm, mean ± SD	176.7 ± 56.6
BMI, kg/m^2, mean ± SD	30.9 ± 7.0
Pregnancy history	
Nulliparous, n (%)	46 (20.1)
Multiparous, n (%)	183 (79.9)
Gravidity, mean ± SD	2.6 ± 1.9
Parity, mean ± SD	1.9 ± 1.3
Contraception at Screening, n (%) [d]	
Hormonal short-term method (pill, patch, ring)	81 (35.4)
Hormonal injection (Depo Provera)	15 (6.6)
Hormonal IUD	41 (17.9)
Implant (Nexplanon)	9 (3.9)
Sponge	1 (0.4)
Condom	66 (28.8)
Spermicide	2 (0.9)
Diaphragm	1 (0.4)
None	15 (6.6)

Abbreviations: BMI=body mass index; SD=standard deviation; IUD=intrauterine device.

Supplemental Table S1: Demographic and Baseline Characteristics, All Subjects

[a] N=229 total subjects who had an attempted FemBloc procedure.
[b] Includes two subjects that were not permitted to respond due to local regulations
[c] Subjects reporting multiple races are counted in each race category.
[d] Subjects reporting multiple contraceptive methods are counted in each contraception category.

Pre-Procedure/Test Parameter	N=229 FemBloc Procedure [a]	N=208 Confirmation Test [a]
Location procedure/ test performed		
Office	229 (100)	208 (100)
Operating room (hospital)	0 (0)	0 (0)
Outpatient surgical center	0 (0)	0 (0)
Positive pregnancy test, n (%)	0 (0)	0 (0)
Pre-medication prior to procedure, ≥1%, n (%) [b]	229 (100)	204 (98)
Acetaminophen, paracetamol	11 (4.8)	7 (3.4)
Acetaminophen, other (i.e., codeine, aspirin, caffeine, oxycodone)	5 (2.2)	3 (1.5)
Alprazolam	1 (0.4)	2 (1.0)
Diazepam	5 (2.2)	2 (1.0)
Hydrocodone	5 (2.2)	1 (0.5)
Ibuprofen	69 (30.1)	63 (30.9)
Ketorolac	119 (52.0)	103 (50.5)
Meperidine HCL	0 (0)	2 (1.0)
Misoprostol	11 (4.8)	3 (1.5)
Naproxen	30 (13.1)	21 (10.3)
Tramadol	1 (0.4)	0 (0)
Transvaginal ultrasound evaluation, n (%) [c]		
Pre-scan	180 (78.6)	208 (100)
No pre-scan	49 (21.4)	0 (0)
Uterus positioning, n (%)	N=180	N=158
Mid-plane	96 (53.3)	83 (52.5)
Anteverted	56 (31.1)	50 (31.6)
Retroverted	19 (10.6)	16 (10.1)
Anteflexed	2 (1.1)	6 (3.8)
Retroflexed	7 (3.9)	3 (1.9)

Supplemental Table S2: Pre-FemBloc Procedure/ Confirmation Test Assessments, All Subjects

[a] A total of 229 FemBloc procedures were attempted and total of 208 confirmation tests were attempted.
[b] Subjects reporting multiple pre-medications are counted in each pre-medication category.
[c] Transvaginal ultrasound pre-scan was added to the FemBloc procedure instructions for use to evaluate uterine cavity for presence of fluid/ blood, which if present required rescheduling.

Procedure/ Test Parameter - Attempted	N=229 FemBloc Procedure [a]	N=208 Confirmation Test [a]
Completed procedure/test	228 (99.6)	207 (99.5)
Cervical anesthetic use during procedure/test, n (%)		
Paracervical	32 (14.0)	5 (2.4)
Intracervical	10 (4.4)	0 (0)
Instrument use, n (%)		
Tenaculum	229 (100)	101 (48.6)
Dilator	95 (41.5)	15 (7.2)
Uterine sound	229 (100)	17 (8.2)
Procedure/ Test Parameter – Completed	**N=228 [b]**	**N=207 [b]**
Duration of procedure/test, min:sec [c]	N=228	N=203
Mean (SD)	07:36 (04:38)	16:37 (08:42)
Median (range)	06:43 (02:16-36:52)	15:00 (01:49-45:00)
Insertion attempts, n (%)	N=228	
One	215 (94.3)	NA
Two	11 (4.8)	NA
More than two	2 (0.9)	NA
Uterine sound measurement, n (%)	N=228	N=17
5-6 cm	21 (9.2)	0
7 cm	93 (40.8)	7 (41.2)
8 cm	70 (30.7)	9 (52.9)
9 cm	38 (16.7)	0
10-11 cm	6 (2.6)	0
Not reported	0 (0)	1 (5.9)
Blended Polymer ultrasound assessment, n (%)	NA	N=207
Evidence of cervical scarring or adhesions	NA	0 (0)
Evidence of hematometra	NA	0 (0)
Evidence of intrauterine adhesions	NA	0 (0)
Medication post-procedure, n (%) [d]	N=179	N=154
No	151 (84.4)	151 (98.1)
Yes	28 (15.6)	3 (1.9)
Overall visit time, min:sec [e]	N=179	N=154
Mean (SD)	1:30:52 (40:06)	1:39:04 (32:45)
Median (range)	1:23:00 (10:00-3:57:00)	1:40:00 (40:00-3:35:00)

Abbreviations: SD=standard deviation.

Supplemental Table S3: FemBloc Procedure/ Confirmation Test Details, All Subjects

[a] A total of 229 FemBloc procedures and 208 confirmation tests were attempted.

[b] A total of 228 FemBloc procedures and 207 confirmation tests were completed.

[c] Duration of FemBloc procedure was determined by procedure stop time (time speculum removed from subject) minus procedure start time (time speculum placed in subject) and duration of confirmation test was determined by test stop time (time intrauterine catheter removed from subject) minus test start time (time speculum placed in subject).

[d] Excludes existing medication use. Response provided for 179 subjects who completed FemBloc procedure and 154 subjects who completed confirmation test.

[e] Duration of FemBloc procedure and confirmation test visits were determined by subject departure time minus subject arrival time. Response provided for 179 subjects who completed FemBloc procedure and 154 subjects who completed confirmation test.

5. Discussion

Non-surgical permanent contraception performed exclusively in an office setting with the FemBloc system, resulted in a pregnancy rate of 0% in the Cohort of Interest. Although each individual data set from the three trials was feasibility-sized, the collective results provide compelling evidence of FemBloc effectiveness once bilateral occlusion is confirmed. The FemBloc system was easy to use, associated with high practitioner satisfaction, and with mild discomfort reported by subjects. No uterine perforations were noted, and no serious AEs occurred. Non-serious AEs reported were primarily spotting or bleeding, low-grade peri-procedural pelvic pain, and abdominal cramping events that resolved quickly without sequelae. Early in the second trial, procedure instructions were updated to include a mandatory transvaginal ultrasound pre-scan for evaluating the uterine cavity for fluid/blood, the presence of which accelerates Blended Polymer polymerization inhibiting forward flow into the fallopian tubes. In addition, during the second trial, a minor design feature was incorporated in the Delivery System, specifically addition of a bubble level indicator, to improve device placement accuracy in the horizontal plane. Early in the third trial, frequency of post-production monitoring for Blended Polymer viscosity was increased, as maintaining viscosity within the acceptable pre-established range is a critical factor for the material's ability to flow properly in its liquid state to the desired location in the fallopian tubes before complete polymerization. The formulation of the Blended Polymer remained unchanged throughout all trials.

Overall, non-surgical PC with FemBloc demonstrated effectiveness and an excellent safety profile, offering a viable alternative to surgical PC. This method presents a significantly lower risk compared to traditional surgical PC and is particularly applicable for women who have contraindications to surgery [5,11,12]. This minimally-invasive non-surgical PC method using a Blended Polymer delivered transcervically through a Delivery System offers a distinct advantage over earlier, more-invasive, and technically challenging hysteroscopic sterilization approaches, which are no longer available [10,13-15]. FemBloc provides a safer, simpler alternative with reduced procedural complexity and cost.

The confirmation test using FemChec, performed in an office setting with standard ultrasound, was easy to perform, yielded high practitioner satisfaction, and caused mild subject discomfort with minimal safety events. The diagnostic accuracy of fallopian tube patency using ultrasound has been well-established with high concordance to fluoroscopy [21]. When considering fallopian tube assessment for bilateral occlusion confirmation, sonography was shown to be equivalent or highly concordant to fluoroscopy with a high degree of diagnostic accuracy following the Essure procedure [22-24]. Procedure times and pain scores were established as similar, and it was believed that an ultrasound-based confirmation test would improve patient compliance [22,24]. According to Essure's instructions for use, a proper modified fluoroscopy hysterosalpingogram (HSG) required adequate uterine cornua distension, deemed essential for accurate imaging to confirm procedure success. During the conduct of the FemBloc confirmation test, it was observed that the pressure limiter feature in the FemChec device activated prior to achieving adequate uterine cornua distension in some subjects and the amount of saline-air contrast entering the uterine cavity was limited. During the second trial, procedure instructions and training were updated to deactivate the pressure limiter feature, ensuring adequate contrast and uterine cornua distension, both necessary for conducting an effective test. The ultrasound-based confirmation test using FemChec offers distinct advantages over the historic radiology approach, which involves radiation exposure and requires referral to a radiology center. The FemBloc confirmation test provides a safer, more convenient, accessible and cost-effective solution.

Study limitation was the modest individual sample study size, in particular for the trial effectiveness analysis, and varying training programs, including improved procedure instructions, as the trials progressed. A larger multicenter pivotal trial will clarify more precisely the effectiveness outcome of non-surgical FemBloc permanent birth control versus the traditional surgical PC.

6. Conclusion

The FemBloc permanent birth control system involves minimally invasive transcervical delivery of a proprietary cyanoacrylate-based blended polymer to occlude the fallopian tubes, fully degrading and leaving nonfunctional scar tissue, offering a safe and effective option to reduce the risk of unintended pregnancy. To encourage patient compliance, returning to the same office for the ultrasound-based confirmation test provides a safe and reliable approach to verify procedure success before relying on FemBloc for contraception. No pregnancies occurred among eligible subjects who relied on FemBloc after receiving a properly conducted confirmation test and safety through five years was established. In contrast to historic surgical sterilization, the FemBloc approach offers a non-surgical, more accessible alternative with fewer risks, contraindications, and likely at a substantially lower cost.

Declarations

Data Sharing Statement: The anonymized datasets used in the clinical trials are available from the corresponding author upon reasonable request.

Prior Presentation: These data have not been previously presented or published.

Funding: These trials were supported by Femasys Inc., (Suwanee, GA), the study device manufacturer.

Attestation Statement:

- The subjects in these trials were not concomitantly involved in other trials.
- Data regarding any of the subjects in the trials have not been previously published unless specified.
- Data will be made available to the editors of the journal for review or query upon request.
- The appropriate checklist for this study design (STROBE) was followed.

Disclosures: KLS is the founder of Femasys Inc., the study device manufacturer, is an officer and board member of Femasys, has stock and stock options with Femasys, and holds patents associated with the study device. JHL is the Chief Medical Officer for Femasys and receives a stipend for services performed.

Author Contributions:

Conceptualization: KLS
Protocol Development: KLS, JHL
Data Collection: JHL, PDB, PMC, SCC, LMG, EBJ
Data Analysis: KLS, JHL
Funding Acquisition: KLS
Study Administration: KLS, JHL
Study Supervision: KLS, JHL
Writing – Original Draft: KLS, JHL
Writing – Review and Editing: All authors.
Manuscript approval: All authors.

References

1. World Health Organization. WHO Fact sheet: Family planning/contraception methods. 2023. Updated Sep 5, 2023.
2. Jones, R. K., & Kavanaugh, M. L. (2011). Changes in abortion rates between 2000 and 2008 and lifetime incidence of abortion. *Obstetrics & Gynecology, 117*(6), 1358-1366.
3. United States, Abortion, Guttmacher Institute.
4. Guttmacher Institute. Unintended pregnancy in the United States. Fact Sheet, January 2019.
5. Sung S, Abramovitz A. Tubal Ligation. StatPearls Publishing; January 2021.
6. Daniels, K. (2020). *Current Contraceptive Status Among Women Aged 15-49;: United States, 2017-2019* (No. 388). US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics.
7. Schwarz, E. B., Lewis, C. A., Dove, M. S., Murphy, E., Zuckerman, D., Nunez-Eddy, C., ... & Gariepy, A. M. (2022). Comparative effectiveness and safety of intrauterine contraception and tubal ligation. *Journal of General Internal Medicine, 37*(16), 4168-4175.
8. Gormley, R., Vickers, B., Cheng, B., & Norman, W. V. (2021). Comparing options for females seeking permanent contraception in high resource countries: a systematic review. *Reproductive Health, 18*, 1-18.
9. Committee on Gynecologic Practice. (2019). ACOG committee opinion no. 774 summary: opportunistic salpingectomy as a strategy for epithelial ovarian cancer prevention. *Obstetrics and Gynecology, 133*(4), 842-843.
10. Lawrie, T. A., Kulier, R., & Nardin, J. M. (2016). Techniques for the interruption of tubal patency for female sterilisation. *Cochrane Database of Systematic Reviews*, (8).
11. Bartz, D., & Greenberg, J. A. (2008). Sterilization in the United States. *Reviews in Obstetrics and Gynecology, 1*(1), 23.
12. Marino, S., Canela, C. D., Jenkins, S.M., & Nama, N. (2024). Tubal Sterilization.
13. Bouillon, K., Bertrand, M., Bader, G., Lucot, J. P., Dray- Spira, R., & Zureik, M. (2018). Association of hysteroscopic vs laparoscopic sterilization with procedural, gynecological, and medical outcomes. *JAMA, 319*(4), 375-387.
14. US FDA. Problems reported with Essure. Current as of Apr 9, 2024.
15. Adelman, M. R., Dassel, M. W., & Sharp, H. T. (2014). Management of complications encountered with Essure hysteroscopic sterilization: a systematic review. *Journal of Minimally Invasive Gynecology, 21*(5), 733-743.
16. Shavell, V. I., Abdallah, M. E., Diamond, M. P., Kmak, D. C., & Berman, J. M. (2008). Post-Essure hysterosalpingography compliance in a clinic population. *Journal of Minimally Invasive Gynecology, 15*(4), 431-434.
17. Munro, M. G., Nichols, J. E., Levy, B., Vleugels, M. P. H., & Veersema, S. (2014). Hysteroscopic sterilization: 10-year retrospective analysis of worldwide pregnancy reports. *Journal of Minimally Invasive Gynecology, 21*(2), 245-251.
18. Gariepy, A. M., Lewis, C., Zuckerman, D., Tancredi, D. J., Murphy, E., McDonald-Mosley, R., ... & Schwarz, E. B. (2022). Comparative effectiveness of hysteroscopic and laparoscopic sterilization for women: a retrospective cohort study. *Fertility and Sterility, 117*(6), 1322-1331.
19. Madden, T., Secura, G. M., Nease, R. F., Politi, M. C., & Peipert, J. F. (2015). The role of contraceptive attributes in women's contraceptive decision making. *American Journal of Obstetrics and Gynecology, 213*(1), 46-e1.
20. Whittum, M., Schickler, R., Fanarjian, N., Rapkin, R., & Nguyen, B. T. (2021). The history of female surgical sterilization. *Journal of Gynecologic Surgery, 37*(6), 459-464.
21. Exacoustos, C., Zupi, E., Carusotti, C., Lanzi, G., Marconi, D., & Arduini, D. (2003). Hysterosalpingo-contrast sonography compared with hysterosalpingography and laparoscopic dye pertubation to evaluate tubal patency. *The Journal of the American Association of Gynecologic Laparoscopists, 10*(3), 367-372.
22. Luong, E., Ludwin, A., Winter, T., Yaklic, J., Maxwell, R. A., Bhagavath, B., & Lindheim, S. R. (2020). Saline-Air Hysterosalpingo–Contrast Sonography Is Equivalent to the Modified Hysterosalpingogram Following Hysteroscopic Sterilization. *Ultrasound Quarterly, 36*(2), 138-145.
23. Luciano, D. E., Exacoustos, C., Johns, D. A., & Luciano, A. A. (2011). Can hysterosalpingo-contrast sonography replace hysterosalpingography in confirming tubal blockage after hysteroscopic sterilization and in the evaluation of the uterus and tubes in infertile patients? *American Journal of Obstetrics and Gynecology, 204*(1), 79-e1.
24. Connor, V. (2008). Contrast infusion sonography in the post-Essure setting. *Journal of Minimally Invasive Gynecology, 15*(1), 56-61.