Intra-Arterial Dexamethasone for the Alleviation of Pain and Postembolization Syndrome Following Uterine Artery Embolization

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3. INVESTIGATOR AGREEMENT

I confirm that I have read this protocol, I understand it, and I will work according to this protocol and to the ethical principles stated in the latest version of the Declaration of Helsinki, the applicable ICH guidelines for good clinical practices, and the applicable federal, state, and local laws, rules, and regulations relating to the conduct of the protocol.

I have read and understand the information in the Investigators' Brochure (and/or other such pertinent safety information) regarding the risks and potential benefits.

I agree to inform all those who assist/collaborate with me in the conduct of this study of their responsibilities and obligations.

Once the protocol has been reviewed and approved by the Institutional Review Board (IRB) I understand that any change(s) made during the course of the study must also (first) be approved by the IRB prior to implementation, except when such modification is made to remove any immediate hazard(s) to the subject(s).

I certify that I and the study staff responsible have received the requisite training to conduct this research protocol.

I agree to maintain adequate and accurate records in accordance with the University of Miami policies, federal, state and local laws and regulations.

I agree to maintain the confidentiality of all information received and/or developed in connection with this protocol.

eProst Number:	
Protocol Version Number: **09122023**	Protocol Version Date: **09/12/2023**

Signature of Investigator:	Date: **09/12/2023**
Name of Investigator (printed): Prasoon Mohan, MD	Institution: University of Miami

4. PROTOCOL REVISION HISTORY

Version #	Summary of Changes	Version Date
05282020	**Initial Submission**	07/09/2020
09122023	**Revision**	**09/12/2023**

5. PROTOCOL SYNOPSIS

Protocol Title	Intra-Arterial Dexamethasone for the Alleviation of Pain and Postembolization Syndrome Following Uterine Artery Embolization (UFE).
Targeted Patient Population	Women aged 20-50 years with symptomatic uterine fibroids.
Study Design	Randomized double blind placebo control trial.
Treatment Schema	Direct intra-arterial dexamethasone delivery to the uterine arteries at the time of embolization for minimizing the post embolization pain, narcotic use, nausea and vomiting and hospital stay.
Duration of Treatment	Intra-arterial dexamethasone will be administered during standard UFE procedure protocol
Follow-up Required Post-Treatment	**To evaluate specific aim 1**: Pain will be assessed using 11 point visual analog scale as below: The visual analog pain score will be documented as follows: o Time 0 Immediately prior to the procedure o 1 hour intervals for the first 3 hours o 3 hour intervals for the next 9 hours o 6 hour intervals for the next 12 hours o Daily, for the next 3 days o Once at day 7 First 3 of those surveys will be done in the recovery area The amount of narcotic use from PCA pump will also be recorded. **To evaluate specific aim 2:** Post embolization syndrome will be assessed as reporting of nausea, vomiting and pain scores, that will be assessed at least twice during the day of the procedure and then daily for the next 3 days and then at 7 days. We will utilize our previously mentioned *UFE Pain and PED Survey*. **To evaluate specific aim 3:** Symptom relief and patient satisfaction will be measured through the completion of a UFE health-related quality of life (QOL) survey, *UFE QOL Survey*, prior to the procedure and then at 1 month and 3 month after procedure.

	Uterine fibroid volume change will be measured by comparing the pre procedure and 3 month post procedure MRI using volumetric software.
Objectives	SA1: Assess the efficacy of intra-arterially delivered dexamethasone for the alleviation of post-procedural pain following UFE. SA2: Assess the efficacy of intra-arterially delivered dexamethasone for the alleviation of post embolization syndrome in UFE. SA3: Compare the fibroid volume change, symptom relief and patient satisfaction from UFE between patients who received steroids versus those who did not.
Expected Number of Patients	Approximately 42 patients
Expected Number of Centers	University of Miami Health Towers University of Miami Hospital and Clinics Lennar Foundation Medical center
Expected Duration of the Study	2 years
Inclusion Criteria	Women aged 20-50 years undergoing UFE for symptomatic fibroids
Exclusion Criteria	Women aged <20 or >50 years, those pregnant or actively attempting to conceive, those deemed mentally impaired to make their own medical decisions, previous documented allergy to dexamethasone, those currently taking daily steroids for any reason, those with diabetes or deemed to be pre-diabetic, those with contraindications for angiography, and prisoners.

6. Objectives*

Uterine fibroid embolization (UFE) is a proven minimally invasive and uterine sparing technique for the treatment of symptomatic fibroids. The procedure is associated with significant post procedure cramping along with nausea and vomiting which require a high dose of non-steroidal anti-inflammatory medications (NSAID) and IV patient controlled analgesia with opioids. This can sometimes translate to increased length of hospital stay, and the possibility of readmission [1, 2]. Recently, a study by Kim, et. al., has shown that the use of preprocedural oral dexamethasone decreases these clinically apparent side effects seen following UFE [3].

In this proposed randomized double blind placebo control trial, we propose the use of intra-arterial dexamethasone, delivered directly to the uterine arteries at the time of embolization for the treatment of post-UFE pain and post-embolization syndrome. We hypothesize that the anti-inflammatory effects from the high dose of steroids delivered directly to the uterus, bypassing the first pass metabolism and systemic dilution, will lead to lower pain scores, decline in narcotic use, lower incidence of nausea and vomiting and shorter hospital stay.

The specific aims of the study are:

1. To assess the efficacy of intra-arterially delivered dexamethasone for the alleviation of post-procedural pain following UFE.

2. To assess the efficacy of intra-arterially delivered dexamethasone for the alleviation of post embolization syndrome in UFE.

3. To compare the fibroid volume change, symptom relief and patient satisfaction from UFE between patients who received steroids versus those who did not.

7. Background*

Occurring in over half of all women, uterine fibroids are the most common tumor of the female reproductive tract [4]. While most women remain asymptomatic, those with symptomatic uterine fibroids suffer from pain, pelvic pressure, menorrhagia, urinary frequency and infertility [5]. Not surprisingly, such women have

significantly lower health-care quality of life scores [6, 7]. Current management options include medical, surgical, and minimally invasive procedures.

The initial medical management of symptomatic fibroids is pharmacologic, with the first-line treatment being oral contraceptives (OCPs). However, these are generally used to regulate menstrual cycles and have not been shown to reduce the overall volume of the fibroid [8]. In fact, 25% of women with symptomatic fibroids who are medically managed will go on to have a hysterectomy [9]. Gonadotropin-releasing hormone agonists (GnRHa) inhibits the production of estrogen and can shrink fibroids, but they are associated with serious side effects such as menopause like symptoms, osteoporosis and hirsutism. When GnRHa are stopped, the fibroids normally grow back [10].

Hysterectomy is considered the definitive treatment for symptomatic uterine fibroids. In 2005, of all the hysterectomies performed in the United States (~200,000) in women less than 45 years, 25% were for fibroids. Surgery is of course not without risk and two thirds of hysterectomies performed are still performed via open surgery [11]. Hysterectomy is also associated with significant morbidity and longer recovery period. Infection, abdominal herniation, injuries to the bowel or urinary system, hormonal changes that effect mood/weight, the possibility of hirsutism if an oophorectomy is included, and the inability to conceive are all associated complications.

Since it was first introduced into the United States in the late 90's, UFE has presented women with a non-surgical, minimally invasive, and uterine-sparing option for the treatment of their symptomatic fibroids [12]. Since then, multiple randomized controlled trials (RCTs) have shown similar efficacy of UFE compared to hysterectomy. One of the initial studies, the EMbolization versus hysterectoMY (EMMY) trial, found that patients recovered and returned to work significantly sooner in the UFE cohort, and that there was no difference in symptom relief at 2 years between the two groups [13-15]. Other studies, such as the Randomized Trial of Embolization versus Surgical Treatment for Fibroids (REST) found that UFE patients recovered more quickly and had less pain than surgery patients. At 1 year, both groups had similar degrees of improvement in health-related qualify of life and had similar levels of satisfaction. A third study, found that patients who underwent UFE rather than hysterectomy additionally had a shorter hospital stay, thus highlighting some of the financial benefits of UFE [16]. Further, several clinical trials have shown an increased complication rate and lower patient satisfaction scores for those women who underwent hysterectomy for the treatment of their fibroids, as opposed to Uterine Artery Embolization (UFE) [17, 18].

One of the major side effects of UFE is the pain and cramping that patients experience after the procedure, which is most pronounced in the first 12-24 hours. Therefore, much interest has been placed on determining what causes pain following UFE and how best to alleviate it. Some studies have addressed the timing and nature of post-UFE pain, with a finding that the initial pain is due to uterine myometrial ischemia [19, 20]. Later at about 72 hours, some patients begin to report loss of appetite, nausea, vomiting, and fatigue - a constellation of symptoms termed post-embolization syndrome (PES). PES can lead to readmission in up to 10% of patients [2]. Hence, there appears to be two distinct phases of pain in the post-UFE patient: 1. The immediate ischemic pain, and later, 2. The PES symptom constellation.

Treatment of post-UFE pain and PES has largely focused on the use of non-steroidal anti-inflammatory medications (NSAIDs), narcotics, antiemetics, intra-arterially delivered lidocaine, and most recently with dexamethasone. It is this last option that has shown a decrease in both pain scores and biomarkers of inflammation [21]. In this study by Kim, et. al., significant reductions in post-procedural pain were achieved with a single intravenous dose of 10mg of dexamethasone in without any reported complications [3]. Our hypothesis is primarily based on this Randomized study. Instead of giving the steroid orally, administration into uterine artery will lead to a high dose of drug reaching the myometrium, bypassing the first pass metabolism and systemic drug dilution. We hypothesize that the anti-inflammatory effects of the high dose dexamethasone will have a significant beneficial effect on the post procedural pain and PES.

As a single administration, even at high doses, dexamethasone has very favorable efficacy and side effect profiles for the treatment of a wide range of conditions, including inflammation, pain, and nausea [22]. In fact, a recent study involving a single IV dose of dexamethasone was shown to significantly decrease PES following embolization of liver tumors [23].

Delivering dexamethasone directly to the uterus during a UFE has several advantages: bypassing of the first-pass metabolism, the lack of systemic dilution, and importantly, the direct delivery to the targeted region of ischemia and source of pain- *i.e.* the same tissue receiving embolic agent will also receive dexamethasone. This will also be administered as a single dose, eliminating the need for a steroid taper. This is a relatively cheap intervention (cost of Dexamethasone $1.22 USD per dose) which could potentially save money by decreasing the length of hospital stay and transitioning of UFE to an ambulatory/outpatient procedure. Additionally, a concurrent decrease in the incidence of PES should translate to a lower readmission

rate. If true, this work may also have a social impact in that fewer narcotics would be required to control pain. Here we propose a clinical trial designed to address these questions, and if proven true, could be adopted as a standard of practice to this uterine-sparing minimally-invasive procedure.

8. Inclusion and Exclusion Criteria*

All eligible women, in whom UFE is not inherently contraindicated, will be screened based on the following Inclusion/Exclusion criteria during their initial clinic appointment to discuss UFE. This will consist of a standardized questionnaire administered with participation from the primary physician and utilize standardized teach-back techniques to ensure patient understanding [24].

Inclusion: Women aged 20-50 years, undergoing UFE for symptomatic fibroids.

Exclusion: Women aged <20 or >50 years, those pregnant or actively attempting to conceive, those deemed mentally impaired to make their own medical decisions, previous documented allergy to dexamethasone, those currently taking daily steroids for any reason, those with diabetes or deemed to be pre-diabetic, those with contraindications for angiography, and prisoners.

9. Number of Subjects*

The power calculation is primarily based on the paper from Kim et al, which evaluated the effect of IV dexamethasone for treatment of post UFE pain and PES [3]. Based on this study, the mean Visual Analogue Scale for the Dexamethasone group was 2.89 (SD 1.09) compared to 3.91 (SD 2) for controls. However, in contrast to the reference study, the proposed study utilizes intraarterial drug delivery directly into uterus instead of IV routedrug , which results in higher concentration in the uterus [25-27]. For a low flow organ such as uterus, intraarterial delivery of a low clearance drug such as dexamethasone will result in a regional advantage of 10-25 times compared to IV or oral delivery as shown by Daemen et al. [25]. Given the significantly enhanced organ drug concentration in the uterus, an increase in effect size of at least 50% is expected with intraarterial drug administration compared to IV route. To detect a difference 50% larger between control group and intervention group, using a two-sample t test with significance level of 0.05, sample size of 21 per group will provide us with 86% statistical power to detect such an effect size.

10. Study-Wide Recruitment Methods*

As with the discussion of Inclusion/Exclusion criteria, participants will be introduced to the study at the time of their initial clinical visit (referred for UFE through typical channels), and once they have already met criteria for undergoing a UFE for symptomatic fibroids. The patients will not be actively recruited for this study, per say, but will be offered admission to it providing they meet criteria.

11. Study Timelines*

We intend to start the study by 10/2020 and to complete recruitment in 2 years, completing in 10/2022

Unless a patient chooses to opt-out of the study, a participant's duration will be limited to a total of 15 days beyond the procedural date. This will include periodic assessments of a subjective and objective measure, as outlined later in this proposal.

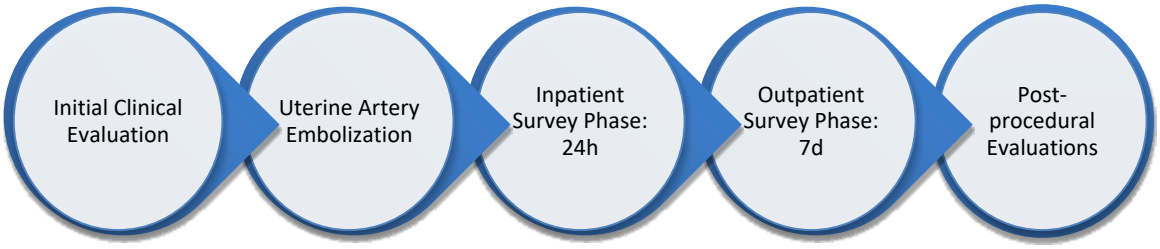
Enrollment and data analysis will be conducted on a rolling basis and deemed complete upon either meeting the primary endpoints (detailed below) or in the face of severe adverse events related to the procedural modification (detailed below).

12. Study Endpoints*

Primary end point of this study is post procedure pain. As such, pain is measured using a modified Visual Analogue Score (VAS), a numerical rating system that each patient assigns to their level of pain, at a particular time [28]. The study endpoints will include qualitative and quantitative collection of data. Pain following UFE is subjective and unique to each patient and can be based on the location, number of the fibroid(s) and the volume of fibroid(s). A modified VAS, termed *UFE Pain and PES Survey*, will be utilized to assess pain prior to and following the procedure (Pre, immediately after the procedure, and periodically for the next 13 days, as described below). Our primary endpoint will be a 3-point decrease in the UFE Pain & PES score between test and controls.

Secondary endpoints will include assessment of PES based on the measurement of nausea, vomiting, subjective fevers or chills, subjective data obtained from return to work times and readmission rates. This will be assessed in part using our *UFE Pain and PES Survey*, which includes a previously validated numerical scoring system

(0-3) to categorize nausea and vomiting, as well as a "Yes" or "No" scoring system to evaluate subjective fevers or chills.



13. Procedures Involved*

The Uterine Artery Embolization procedure with the proposed intervention is detailed below, italicized section denotes the interventions which are additions to the standard of care. The procedure is separated into Pre-Procedure Assessment and Imaging, Uterine Artery Embolization Procedure, and Post-Procedure Assessment and Imaging.

Pre-Procedure Assessment and Imaging:

- All accepted UFE study participants will be initially assessed using the attached UFE Pain & PES Survey to ascertain their current baseline pain.
- Current medication requirements (e.g. OCPs, NSAIDs, narcotics, anti-emetics) will also be assessed at this time.
- Basic laboratory studies will be conducted at this time. This will include a Complete Metabolic Panel (CMP), Complete Blood Counts (CBC), Hemoglobin A1c, and qualitative urine pregnancy test (UPT).
- Each patient will further undergo (or have recent) pre-procedural imaging to determine fibroid burden, approximate volume, and arterial anatomy. This should be an MRI of the pelvis.

Uterine Embolization Procedure:

No changes are proposed to the standard UFE procedure except for the intraarterial delivery of dexamethasone.

Pre-UFE patients will receive the following medications for conscious sedation, pain control and nausea/vomiting during the procedure as per the standard departmental protocol, unless contraindicated:

- 50-300 mg IV Fentanyl
- 0.5- 3.0 mg IV Versed
- 30 mg IV Toradol
- 1 g IV acetaminophen

Procedure technique:

No changes are proposed to the standard UFE procedure except for the intraarterial delivery of dexamethasone.

Common femoral or radial artery access is used for the procedure. Using a combination of base catheters, microcatheters and different wires, each uterine artery is catheterized and angiograms are performed. *Following this, prior to embolization, 5 mg of IV dexamethasone or placebo are injected via the microcatheter placed in the uterine artery.* This is followed by particle embolization using particles of size ranging from 500-1000μM, until near stasis as per standard technique. The same procedure is then repeated on the contralateral uterine artery. Finally, catheters and sheaths will be removed and hemostasis achieved at the access sites using closure device or manual compression. Patients will be admitted to the general medicine ward for overnight observation.

Post-UFE patients will receive the following pain/anti-emetic regimen post procedure:

Inpatient Medications

- 30 mg IV Ketorolac q6h
- 650 mg PO Acetaminophen q6h (continued for 4 days post procedure)
- 0.2 mg demand dose, 10 minute lockout, 1.2 mg/hour, Hydromorphone PCA
- 4 mg IV Ondansetron q6h PRN

Discharge Medications

- 650 mg PO Acetaminophen q6h (4 days post procedure, then q12h)
- 800 mg PO Ibuprofen q6h (4 days post procedure, then q12h)
- 5/325 mg PO Percocet q6h PRN
- 100 mg PO Docusate Sodium (Colace) q12h (4 days post procedure, then PRN)
- 4 mg SL Ondansetron q6h PRN

Post-Procedure Assessment and Imaging:

- *Pain, nausea, vomiting and fever will be documented using the visual analog score and nausea and vomiting score at:*
  - *Time 0 Immediately prior to the procedure*
  - *1 hour intervals for the first 3 hours*
  - *3 hour intervals for the next 9 hours*
  - *6 hour intervals for the next 12 hours*
  - *Daily, for the next 3 days*
  - *Once at day 7*
- *Each patient will complete* uterine fibroid symptom & health-related quality of life questionnaire prior to the procedure and then 1 month and 3 month after.
- Each patient will undergo post-procedural MRI imaging to determine residual fibroid burden and approximate volume at 3 months in order to gauge treatment response.
- PCA usage statistics.

Study Design:

This study is designed as a double blinded, placebo controlled randomized control trial. As previously mentioned, the study will divide the patients into two groups. The test group will receive intra-procedural intra-arterial dexamethasone and the control group, a saline placebo. Block randomization (Size: 8) will be done using a random number generator.

The drug or placebo will be prepared by research pharmacy and be delivered to the Interventional Radiology Department in identical containers with specific serial numbers. The physician performing the UFE, the patient and the research team will be unaware of the nature of the administered drug/placebo or the patient grouping. The drug preparation will be coordinated by the University of Miami Pharmacy Department's Research Coordinator, Daniel W. Nobel. Once the uterine artery is catheterized, the drug or placebo will be injected intra-arterially. Embolization is then performed as usual.

Following UFE, all patients will be admitted to the general inpatient unit for observation, as is standard of care for all UFE patients. Following this observation period, patients will be discharged with appropriate instructions of when and how to follow-up with the treatment team. This will include explicit instructions to self-monitoring for unusual bleeding, swelling, bruising at the femoral artery access site, abnormal uterine bleeding, cramping, extended bouts of nausea, vomiting, fever, chills, and malaise. All patients will be given the number of an on-call physician for questions and concerns they may have. As mentioned above, all patients will be telephoned daily by a member of the research team on day 2, 3, 4, and 7 post-UFE.

All patients will have a routine 2 week post-procedural phone call to review their symptoms, 1 month clinic visit and then 3 month clinic visit after MRI imaging.

All data collected from the Surveys will be stored and analyzed as described elsewhere in this proposal. Again, we expect that this study will reach its recruitment goal and Primary Endpoint in approximately 2 years.

To evaluate specific aim 1:
Pain will be assessed using 11 point visual analog scale as below:

The visual analog pain score will be documented as follows:

- Time 0 Immediately prior to the procedure
- 1 hour intervals for the first 3 hours
- 3 hour intervals for the next 9 hours
- 6 hour intervals for the next 12 hours
- Daily, for the next 3 days
- Once at day 7

First 3 of those surveys will be done in the recovery area. The amount of narcotic use from PCA pump will also be recorded.

To evaluate specific aim 2:
Post embolization syndrome will be assessed as reporting of nausea, vomiting and pain scores, that will be assessed at least twice during the day of the procedure and then daily for the next 3 days and then at 7 days. We will utilize our previously mentioned UFE Pain and PED Survey.

To evaluate specific aim 3:
Symptom relief, patient satisfaction and fibroid volume change will be measured through the completion of a UFE health-related quality of life (QOL) survey, UFE QOL Survey, prior to the procedure and then at 1 month and 3 month after procedure.

Uterine volume will be compared from the pre-procedure and 3 month post procedure MRI using volumetric software.

14. Data and Specimen Banking*

No specimen will be collected or stored. Data will be kept in password protected, HIPAA compliant University approved Box folder, accessible only to investigators.

15. Data Management*

All data will be stored, accessed, and analyzed utilizing server and computer workstations previously approved as HIPAA compliant. Data will be kept in password protected, HIPAA compliant University approved Box folder, accessible only to investigators. Anonymized data will include age, pre and post MRI imaging, UFE Pain & PES Survey, narcotic use, vital signs, subjective reports of nausea, vomiting, daily dietary intake, bowel movements, length of hospital stay, readmission rate, and days to return to baseline.

A single computer system managed by the Pharmacology Research Coordinator, Daniel W. Nobel, will be maintained to ensure blinding of the cohorts. Collected data will be analyzed by Prasoon Mohan, MD, and done so prior to unblinding.

16. Provisions to Monitor the Data to Ensure the Safety of Subjects*

All data will be analyzed as it arrives and on a rolling basis by the primary physicians and researchers directly involved in this study, to ensure that the clinical findings and participant reported responses to the Pain & UFE Survey are not deviating in a way that could lead to undue harm.

As stated previously, all participants will be admitted to the hospital for observation for the first 24 hours and discharged with 2-week clinical follow-up in place and the contact information of a research team member. All participants will be contacted daily for the first 3 days, then at 7 and 14 days following the procedure. Any adverse effects of safety issues would be discovered in this follow up.

At 6 months we will analyze the interim data for any difference in the efficacy of treatment between the groups. All data will be analyzed using IBM SPSS software. We will use Student's T test for analysis of continuous variables, Chi square test for categorical variables with significance level set at two tailed p value of <0.05.

Although we expect that this trial exposes the participants to minimal risk, we consider the following statistically-significant differences between the two arms to be grounds for immediate trial termination: excessive abnormal uterine bleeding, infection, and sepsis.

17. Withdrawal of Subjects*

Subjects will be immediately withdrawn if it is deemed at any time prior to the procedure date that they fall into any of the previously outlined Exclusion criteria, suffer an intra-procedural adverse reaction to the use of dexamethasone, or willingly choose to leave the trial at any time.

Once terminated from the trial, a subject can continue to undergo a UFE if they both meet the previously prescribed criteria and choose to do so. If a subject chooses to withdrawal post-UFE, a termination letter will be issued to their current address and all attained medical documents will be delivered through standard channels to their Primary Care Provider / referring physician. They can continue to receive standard post-UFE follow-up care through the University of Miami Interventional Radiology Department, if they so choose and without any punitive consequences. This is outlined in the Study Consent Form.

18. Risks to Subjects*

In this study, patients will be asked to assume the standard risks associated with UFE. These include known complications of bleeding, infection, adverse reaction to contrast agent, pain, need for further intervention/embolization. Further, there is a additional risk with the addition of a single dose of dexamethasone, as below which will be explained to patients.

Even at large doses, dexamethasone is known to have an excellent safety profile, with few adverse effects. Of those reported, anaphylaxis is exceedingly rare (incidence of ~ 0.1%) and the risk of transient hyperglycemia should be mitigated by the exclusion of pre-diabetic and diabetic patients (Determined by Hemoglobin A1c percentage) [29, 30]. It is important to note that there is no increased risk for delayed wound healing or infection in surgical patients receiving a single dose of dexamethasone [30]. Further, as a single dose will be administered, there is no need for a dedicated taper as suppression of the hypothalamic-pituitary-adrenal axis does not occur until weeks of steroid therapy.

19. Potential Benefits to Subjects*

If observed, the major benefit to women participating in the dexamethasone arm of this study will be a fall in pain level and PES following UFE. Other benefits may be a faster recovery and faster return to work or baseline activity.

20. Vulnerable Populations*

N/A

21. Multi-Site Research*

N/A

22. Community-Based Participatory Research*

N/A

23. Sharing of Results with Subjects*

All imaging findings, diagnostic studies, complications, and follow-up treatments will be shared with both patient and their appointed primary care/obstetrics physicians. However, the study will remain blinded to both patient and clinician until the study is deemed closed, an adverse event occurs, or the study is prematurely terminated for any of the reasons previously stated. Any shared health information will be done so utilizing HIPAA-compliant channels.

24. Setting

Recruitment will occur in our already-established Interventional Radiology clinics located at University of Miami, at the professional arts center (PAC). Likewise, UFE procedures will be carried out at University of Miami Health Towers or University of Miami Hospital and Clinics or Lennar Foundation Medical center, utilizing similar or identical equipment and the previously stated methods. Data analysis will

be carried out on University of Miami computer systems on a rolling basis to ensure participants are not placed at undue risk.

25. Resources Available

The below members will meet monthly and on an as-needed basis, share all data via a University-approved means, a shared Box folder. This will include this IRB proposal, the Study Consent Form, the Patient Information Packet, and a data spreadsheet to compile the UFE Pain & PES Survey scores. The Principal Investigator shall have the responsibility of coordinating the study effort, and together with the Participating Physicians shall be responsible for the UFE procedures and the monitoring of study participants to ensure safety. This will include coordination between the Advanced Care Practitioners and the Research Coordinator to monitor for any participant adverse events. The Clinical Pharmacist will be responsible for compounding the Dexamethasone and Saline placebo, as well as blinding the study by assigning serial numbers to the medicine vials.

Principal Investigator:
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26. Prior Approvals

All approvals have been granted by the Vascular and Interventional Radiology Department at the University of Miami for this study. This includes funding for a dedicated Research Coordinator and the costs associated with compounding the materials required in the study.

27. Recruitment Methods

Recruitment will occur at the first clinical encounter between Physician and Patient in the IR clinic. Patients considering UFE generally placed in contact with the Vascular and Interventional Radiology team through a standard physician referral system. Referring physicians typically include Obstetric/Gynecologic specialists, Hospitalist, Emergency Physicians, and Primary Care Practitioners. Patients are seen in clinic prior to determining candidacy for the procedure and it is at this time that the research is introduced. If deemed a candidate for a UFE (please see listing of Inclusion/Exclusion Criteria), participants will be introduced to the study utilizing the same simplified language and pelvic models currently utilized to describe the

procedure, and the risks and benefits associated with such. As mentioned, standard teach-back techniques will be employed to gauge participant understanding.

28. Local Number of Subjects

We anticipate that there will be approximately 21 local participants in each arm of this trial. As described above, this number appears to be the minimum required to ensure adequate statistical power. We anticipate to take approximately 2 years to recruit the patients.

29. Confidentiality

X On a University of Miami electronic device (e.g. encrypted, password-protected computer).

X On a cloud-based storage system that is approved by the University of Miami.

X JHS Secured SharePoint.

X The Investigator (or research staff) will record (e.g. write down, abstract) data collected in a manner that does not include any indirect or direct identifiers and the recorded data will not be linked to the individual's identity.

X The investigator (or research staff) will record (e.g. write down, abstract) the data collected in a manner that does not include any direct identifiers of the subject. The investigator will assign a code to each subject and link the code to the subject's identity. The research team will maintain the link to the subject's identity on a document separate from the research data. Both documents will be stored in separate files on a University of Miami encrypted device or on a University of Miami approved cloud storage system. The research team will destroy the identifiers at the earliest opportunity.

X The research team will maintain the research data incompliance with applicable regulatory requirements and University of Miami data retention requirements as described in the Investigator Handbook.

X Bio-Specimens obtained for this research will be stored without any direct or indirect identifiers.

X Bio-Specimens obtained for this research will be stored in a de-identified coded manner.

X When required to transport data or bio-specimens for this research, the research team will transport the data and bio-specimens in a de-identified (or anonymous) manner with a link to the individual subject's identity maintain separately from the data and/or bio-specimen.

30. Provisions to Protect the Privacy Interests of Subjects

All aforementioned members of this clinical trial hold certain responsibilities to the privacy and comfort of the participants. As such, real-time transparency of incoming clinical data and patient concerns will be compiled in a shared, password protected University Box Folder for monitoring by all. However, some members will be restricted in their access to HIPAA-protected materials. This will include Ancillary Staff members and those not directly involved in the daily care of the participant.

The topics of Privacy, Comfort, and Patient Rights will be explicitly discussed during every patient encounter to ensure that ongoing participant-membership remains voluntary *in the eyes of the patient.* This will include a discussion about the right to withdrawal from the study without penalization.

31. Compensation for Research-Related Injury

N/A

32. Economic Burden to Subjects

N/A

33. Consent Process

Participants will be introduced to the study at the time of their initial clinical visit, and a standardized questionnaire will be administered by the primary physician with standardized teach-back techniques to ensure patient understanding of the risks and benefits of the altered procedure **[24]**. Participants will not be obligated to enter into the study at this time, and can do so, at any time prior to the procedure.

The patient will be given the following documents, which are included in this proposal, during the initial visit:

1. Procedural Consent Form (IMed UFE Consent Form)
2. Study Informed Consent
3. Study Timeline Graphic
4. Adverse Event Reporting Form (FDA Form 3500)
5. UFE Pain & PES Survey
6. QOL Survey

Non-English Speaking Subjects

- Spanish
- Portuguese
- French
- French Creole (French and Haitian)
- Chinese (Mandarin and Cantonese)

All participants will be consented and instructed by a certified native linguist or translation phone line, used by the University of Miami Hospital System.

34. Process to Document Consent in Writing

We will utilize the consent form attached at the end of this document, Study Consent Form, a derivative of HRP-502a.

35. Authorization for Use and Disclosure of Protected Health Information (HIPAA)

Type of Request:

X Waiver of Authorization for access to medical record for subject identification/recruitment.

X Waiver of Authorization for access to medical record to obtain data for the research.

Confirm that you will destroy or de-identify the information you collect at the earliest opportunity.

X I confirm

Confirm that the information you collect will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study or for other research for which the use or disclosure of PHI is permissible.

X I confirm

36. Drugs or Devices

All vials/syringes of dexamethasone or saline will be compounded by the Pharmacology Research Coordinator, Daniel W. Nobel, PharmD, BCOP, BCPS, at University of Miami Hospital. 8 mg dexamethasone intravenous preparation or placebo will be dispensed in identical vials or syringes with unique serial numbers. A log of the serial numbers will be kept in the pharmacy. The medication will be delivered to the IR Angiography suite and will be administered by the interventional radiologist performing the procedure. Storage is not required as the drug is prepared and administered the same day.

	Applicable to:		
FDA Regulation	***IND Studies***	***IDE studies***	***Abbreviated IDE studies***
21 CFR 11	*X*	*X*	
21 CFR 54	*X*	*X*	
21 CFR 210	*X*		
21 CFR 211	*X*		
21 CFR 312	*X*		
21 CFR 812		*X*	*X*
21 CFR 820		*X*	

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