University of Wisconsin-Madison

Research Subject Information and Consent Form

Title of Study: Advanced MRI for Uteroplacental Flow, Perfusion, Oxygenation & Inflammation

Study Investigators: Dinesh Shah, MD and Oliver Wieben, PhD

INVITATION/SUMMARY

You are invited to participate in a research study about using magnetic resonance imaging (MRI) and ultrasound (U/S) imaging during pregnancy to determine whether these new scanning techniques can provide doctors with more information about the uterus and placenta at different time points throughout pregnancy. You are invited because you are pregnant and expecting to deliver your baby at UnityPoint Health Meriter Hospital. Approximately 200 subjects will participate in this study being conducted at the University of Wisconsin-Madison.

The main study procedures are blood and urine collection, U/S, and MRI, which will occur at weeks 14-16, 20-22, and 28-30 (no MRI) of your pregnancy. These visits will require approximately 30-60 minutes for the ultrasound (Meriter Hospital) and 30-60 minutes for the MRI (University of Wisconsin Hospitals and Clinics, or UWHC). You will need to allow additional time for travel to each of these locations.

Your participation in this research study is voluntary. If you decide not to participate, any relationship you have with the University of Wisconsin-Madison (UW-Madison) or the UWHC will not be affected in any way.

WHAT IS THE PURPOSE OF THE STUDY?

The goal of this study is to be able to measure the blood and oxygen flow to the placenta using advanced U/S and MRI testing at three different time points during your pregnancy. It is believed that the quality of blood flow/oxygen to the placenta determines pregnancy outcomes. In the past this has only been detected in late stage pregnancy when the undesirable event has already occurred. The thought is that if the blood flow and oxygenation can be evaluated earlier in the pregnancy then this could provide a tool to detect and possibly correct the occurrence.

Both the U/S and the MRI scanner and equipment have been approved by the U.S. Food and Drug Administration (FDA). The computer software that is being used to collect the MRI scan is experimental which means it is not FDA approved at this time.

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WHAT WILL MY PARTICIPATION INVOLVE?

If you decide to participate in this research study, you will be asked to read and sign this consent form document. You will be given time to do this and you may ask your study doctor or research staff to answer any questions you might have or to help with information you may not understand. Your participation will last from the time you consent to participate through 6 weeks after you deliver your baby. A blood and urine sample will be collected on the day you deliver in addition to the scheduled study visits at weeks 14-16, 20-22, and 28-30 of your pregnancy. Your medical records will be reviewed throughout your pregnancy. The information that will be collected will include all clinical data from your prenatal visits to include the newborn outcomes such as birth weight and hearing tests that would normally be performed after your delivery.

We may contact your clinical provider to let them know that you are participating in this research study. One of the reasons is so that your provider can report any conditions or illnesses in the course of your prenatal care. We may also use an alert mechanism in your electronic medical record indicating that you are in a research study so that the research staff can be notified of any new conditions and /or illness.

Fetal growth ultrasounds at 28-30 weeks of pregnancy are a regular procedure for pregnant women that have a body mass index (BMI) above 30. If you choose to participate in this study and your BMI is less than 30, you will also have the opportunity to have a fetal growth ultrasound at 28-30 weeks of pregnancy. The results of this U/S will be available to you and your OB provider through your medical record.

The research study plans to bank the leftover blood and urine samples collected from you for this research. If you agree, the leftover samples will be banked for future research. It is not known what your banked samples might be used for.

Samples may be stored indefinitely or until they are used up. The samples will not be labeled with any information that identifies you. Once the samples have been provided to the bank you will be unable to recall them.

Please initial below to indicate your choice:

_____I agree to allow my leftover samples to be banked for future research done at the University of Wisconsin-Madison.

_____I DO NOT agree to allow my leftover samples to be banked for future research done at the University of Wisconsin-Madison.

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Screening Visit

At the screening visit, the physician or the research staff will discuss the research study with you and see if you are eligible to participate, which includes filling out an MRI screening form. This is a routine screening procedure used at UW prior to any MRI imaging. This is required to make sure it is safe for you to have an MRI.
If you are interested you will have time to read the consent form document and ask any questions you might have. You will also be allowed to take this document home for further review and to share it with family members. If you decide to participate you will be asked to sign this document and a copy will be made and given to you for your files. This form must be signed prior to week 16 of your pregnancy in order for you to be eligible to participate.

Study Visits

Blood and urine samples will be collected at each study visit. The collection of blood will total 10 mls (approximately 2 teaspoons) for research purposes. If you would normally have a blood collection at this visit during your regularly scheduled OB visit the 10 ml will be collected in addition to what would normally be collected, thus avoiding an additional needle stick by the research staff. The blood and urine samples will be collected to gain a better understanding of why some proteins increase while others decrease during pregnancy and if this information can be used to monitor how well a pregnancy is progressing.

You will have an ultrasound (a noninvasive diagnostic test that uses sound waves to create a visual image of your placenta) performed at all study visits (weeks 14-16, 20-22 and 28-30 of your pregnancy). Research related ultrasounds should take approximately 30-60 minutes. This is an abdominal U/S done by applying gel to your abdomen and then using a probe to show images on a screen. If you are uncomfortable, you can take a break halfway through the U/S to adjust your position. This U/S will be performed in the Perinatal Clinic located on the main floor at Meriter Hospital.

You will have an MRI at the study visits during weeks 14-16 and weeks 20-22 of your pregnancy. The MRI will be performed at the UWHC. Before your MRI you will be screened again for MRI safety and compatibility. You will be placed in the center of a large metal doughnut-shaped magnet. The MRI technologist will make every effort to ensure you are comfortable. The MRI machine produces a magnetic field that passes through your body without disturbing any of its parts. Radio signals will be sent into your body. A small proportion of the water in your body will send back radio signals that the machine receives. The MRI machine uses a computer to determine where these radio signals came from to make a picture showing us what the inside of your body looks like. During a scan, the scanner will make a tapping or “chirping” noise. Ear plugs or headphones will be provided to minimize any discomfort. The MRI exam is expected to take approximately 30-60 minutes with some additional time to get you comfortably placed in the scanner. Once

you are situated in the scanner you will receive a call button that will allow you to signal the MRI technologist conducting the scan in case you need to stop the scan.

You will have to travel to Meriter Hospital for your U/S and UWHC for your MRI. Parking will be provided free of charge at both Meriter Hospital and UWHC for all of your research related study visits.

At Time of Delivery

Prior to delivery, blood and urine will be collected from you for research purposes. After you deliver your baby, we will record information from your medical record about your labor, delivery and laboratory results. We will also collect information from your newborn's medical record.

Post Delivery Follow-Up

A member of the research staff will contact you within 6 weeks after you deliver your baby to ask about any adverse events you may have experienced within the past month.

Summary of Study Procedures

	Screening Visit	Visit 1 (14-16 Weeks)	Visit 2 (20-22 Weeks)	Visit 3 (28-30 Weeks)	Delivery	6 weeks After Delivery
Review Eligibility	X					
Obtain Informed Consent	X					
Collect Blood and Urine		X	X	X	X	
Ultrasound		X	X	X		
MRI		X	X			
Review Adverse Events		X	X	X		X

ARE THERE ANY RISKS?

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Associated Risks with Blood Collection

- Minor bruising at the needle stick site
- Slight pain
- In rare instances, fainting
- In rare instances, infection could occur at the needle stick site

Associated Risks with U/S (Ultrasound)

The study will be using standardized ultrasound for imaging the uteroplacental blood flow (which will evaluate the flow of blood from the mother to the placenta). Diagnostic ultrasounds have been used during pregnancy for many years and is considered safe. These standard techniques do not pose any significant risk to you or your fetus. The ultrasound equipment used at Meriter hospital does not require you to have a full bladder which will help with any discomfort you might have felt from having a full bladder. U/S for pregnant women are considered minimum risk.

Associated Risks with MRI

Although no known ill effects have been directly attributed to exposure to the radio waves or the strong magnetic field used in MRI, it is not safe to scan people with certain types of metallic implants in their bodies. In order to determine if it is safe for you to have an MRI exam you will be asked a series of questions. It is very important that you answer these questions accurately and thoroughly.

MR imaging can potentially heat up body tissue. This process is monitored by the "specific absorption rate", also called SAR, which is a measure of the amount of energy that the human body is taking up from scanning. Most people don't feel any sensation from SAR but some have experienced a warming sensation in parts of their body as a result of SAR levels. The SAR is continuously measured during imaging to ensure that the increase in maternal and fetal body temperature is less than 0.5 degree Celsius.

The MRI scanner makes loud tapping and beeping noises while images are being collected. You will be provided with ear protection (ear plugs or headphones) to wear during the scan but what about your baby? Tests have been done to see how much a mother's body and the fluid around the fetus help to protect the noise level created by an MRI scanner, it turns out, the loudest level the fetus is exposed to from any MRI scan is about the same level that a lawnmower creates. In addition, there have been no reports of MRI causing any hearing damage in babies whose mother had an MRI scan during pregnancy.

There are no reported risk for you or your baby when undergoing a MRI during the second and third trimester of your pregnancy. Occasionally some individuals experience feeling claustrophobic during an MRI exam. Support will be provided to keep you from becoming uncomfortable, and you will be able to stop at any time. Using a microphone built into the

scanner which you can use to talk with the technician if you need assistance. Please inform the technician of any discomfort you may experience during the MRI exam.

There may be risks to pregnant women and fetuses that are not known at this time.

Associated Risks with Banking Specimens

The banked specimens may be used by other researchers with the University of Wisconsin-Madison. The information they receive will be de-identified; however, the research staff associated with this study will have a key that could identify you. This key is not to be shared with others outside of this research project. Once the study is completed this identifying key will be destroyed and your banked samples will not be able to be traced back to you. The risk of being identified is very low and there are elements in place to protect your private health care information.

ARE THERE ANY BENEFITS?

You are not expected to benefit directly from participating in this study. Your participation in this research may benefit other people in the future by helping us learn more about blood and oxygen flow to the placenta in early pregnancy. The ultrasound and MRI done for this research study will not be used for your health care.

Possible Financial Benefit

The research proposal does not have the intent of commercialization. There is a possibility that some software applications that may have commercial application which may result in possible financial benefits to the three departments in which the investigators belong. Those departments are Obstetrics and Gynecology, Radiology, and Medical Physics at the University of Wisconsin-Madison.

ARE THERE ANY COSTS?

There will be no costs associated to you or your insurance company for participating in this study. The ultrasounds that will be done as part of your normal routine pregnancy care will be billed to you or your insurance as usual.

The costs for extra ultrasounds done for research purposes only will be paid for by the research study.

WILL I BE PAID FOR MY PARTICIPATING IN THE STUDY?

You will be paid $100 for completing the MRI at Study Visit 1 (14-16 weeks) and another $100 for completing the MRI at Study Visit 2 (20-22 weeks). The maximum amount of money you may receive is $200.

WILL THERE BE COMPENSATION FOR INJURY?

In the event that you are physically injured as a result of participating in this research, emergency care will be available. You will, however, be responsible for the charges for the emergency care. There is no commitment to provide any compensation for research-related injury. You should realize, however, that you have not released this institution from liability for negligence. Please contact the investigator, Dr. Shah at 608-417-6099 if you are injured or for further information.

Possible Discovery of Findings Related to Medical Imaging

Whenever an MRI scan is done, there is the chance of finding something unexpected. There may be benefits to learning such results (such as early detection and treatment of a medical condition), but there are risks as well (such as problems with getting insurance or a job, or feeling worried about a finding for which no treatment is required or appropriate).

The MRI we are using in this research study is not the same as a clinical MRI scan that you may have as part of your health care. The images from this research MRI will not be reviewed by a physician who normally reads such images (such as a radiologist). As a result, you will not be informed of any MRI findings. The results of your MRI scan will not be placed in your medical record. If you believe you are having symptoms that may require clinical imaging, you should contact your primary care physician.

IF I DECIDE TO START THE STUDY, CAN I CHANGE MY MIND?

Your decision to participate in this research is entirely voluntary. You may choose not to participate. If you do decide to participate, you may change your mind at any time without penalty or loss of benefits that you had prior to the study. You will be told of any new and significant findings which may affect your willingness to continue. Your decision of whether or not to participate in this study will not affect the quality of your medical care at this institution.

This study can be stopped at any time without your permission. The study can be terminated by the investigators, the FDA, or the study doctor.

WILL MY CONFIDENTIALITY BE PROTECTED?

The researchers might use information learned from this study in scientific journal articles or in presentations. None of this information will identify you personally. Your information will be protected by using a code instead of your name. All information will be stripped of identifiers prior to the information going into the database where the collected study information will be stored. The database is password protected and will only be utilized by research staff entering the data and the investigators associated with the study. These computers are located in a locked office with limited access.

Research ultrasound data collected at Meriter Hospital will be stored securely to a dedicated, password protected computer terminal. Only the research team will have access to these images and data. U/S images and associated data will have the same coded subject number as all the other data collected.

MRI data will be stored securely on the UW Department of Radiology system.

Meriter IRB, UW IRB, the US Food and Drug Administration (FDA), Health and Human Services, and/or other government officials may need to review your study records to make sure that the study is done properly.

The University of Colorado, Denver has been asked to consult with the process of reviewing ultrasounds.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

WHAT IF I HAVE QUESTIONS?

If you have questions about this research, please contact the study investigator, Dr. Shah, at 608-417-6099 or the research office by calling 608-417-6941. If you have any questions about your rights as a research subject or complaints about the research study that you could not resolve with the study team contact UWHC Patient Relations Representative at 608-263-8009 or the University of Wisconsin Medical Foundation Patient Relations Representative at 800-552-4255 or 608-821-4819.

Authorization to participate in the research study:

I have read this consent form describing the research study procedures, risks, and benefits. I have had a chance to ask questions about the research study and I have received answers to my questions. I agree to participate in this research study. I have received a copy of this consent form.

_____	_____
Signature of Subject	**Date**
_____	_____
Signature of Person Obtaining Consent	**Date**

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