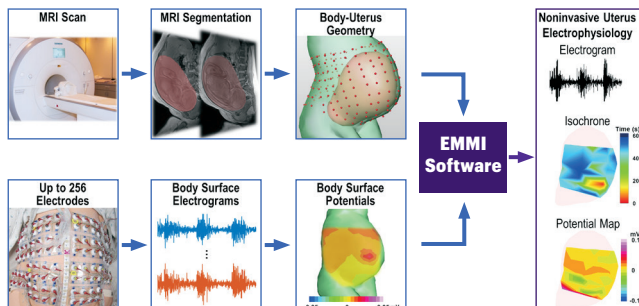


What causes contractions to start in a pregnant woman’s uterus at only 22 or 26 weeks of pregnancy? And why do they stop for some women, allowing them to deliver at term (40 weeks), while for others they continue, resulting in preterm birth? This question has stymied researchers for years.

“In our work to understand preterm birth, the uterus has always been a key piece of the puzzle, as it develops the ability to contract and change the cervix,” says Alison Cahill, M.D., M.S.C.I., in the Department of Obstetrics and Gynecology at Washington University in St. Louis, who is also a practicing high-risk obstetrician and a leader of Theme Two. “But nobody knows why contractions start for some women weeks or months before term and result in a preterm birth.

“In Theme Two, we are thinking about the uterus in a new way. With the help of the March of Dimes, we are bringing together a group of leading thinkers that have never before thought about this to try and discover something totally new.”



Noninvasive electromyometrial imaging (EMMI) combines the shape of the uterus obtained from an MRI image with the electrical information from the abdominal skin to study “four-dimensional” electrical properties of uterine contractions.

The premise is exciting and out of the box: they are looking to another muscular organ—the heart—to determine whether it will be possible to create images of uterine contractions with the richness and detail that is now possible in cardiac imaging.

“In cardiology we have a rich set of tools developed over 50 years to image and study how the heart beats,” says Phillip Cuculich, M.D., a cardiologist in the Department of Medicine, and also a theme leader whose involvement is reflective of the team’s innovative transdisciplinary approach. “Without touching the heart we can determine where each beat comes from, the direction in which it goes, how fast it moves, and whether it is starting at the top chamber or bottom, or on the left side or right. Noninvasive cardiac imaging has become an invaluable tool for understanding the pathophysiology of various forms of heart disease.

“The current standard for uterine monitoring essentially determines whether the uterine is contracting or not, and some fundamental idea of contraction strength — but that’s it.”

Studies have shown that the uterus undergoes electro physiological changes over the course of pregnancy, eventually resulting in contractions that change the cervix and result in delivery. But why does this happen earlier for some women, resulting in preterm birth?

### BIOMEDICAL ENGINEERING TEAM ALSO ENGAGED

The team will build on a technology recently developed at Washington University in St. Louis in the Department of Biomedical Engineering by world-renowned researcher, Dr. Yoram Rudy, Ph.D., called electrocardiographic imaging (ECGI). ECGI is a novel, noninvasive electrical imaging modality that combines a detailed body surface electrical map (obtained by using a vest containing 256 electrodes) with a patient-specific heart-torso model to image the electrical activation of the heart with remarkable accuracy. Now, the team will be engaged to modify ECGI to image uterine contractions, a method called electromyometrial imaging (EMMI).

Using EMMI, the team will test its central hypothesis that untimely electrical maturation of the uterine smooth muscle at a preterm gestational age contributes to the mechanism of labor resulting in preterm birth.

### WATCHING A CONTRACTION’S MOVEMENTS

Once software has been developed specifically for the uterus and tested for safety, Drs. Cahill and Cuculich will develop a reference group by imaging normal uterine maturation of women who deliver at term. These 3D color-coded images and movies will enable researchers to identify the pacemaker sites where contractions begin, and the velocity, direction, and coordination of uterine contractions in women in labor at term.

They then will compare the images of the term births with those of women who deliver preterm. “We will have 3D color images showing us how a contraction wave moves over and through the uterine muscle,” says Dr. Cuculich. “Our hope is that we will find one type of contraction pattern consistently in preterm that we don’t see at term.”

*“We will have 3D color images showing us how a contraction wave moves over and through the uterine muscle.”*

*Alison Cahill, Md.D. M.S.C.I.*

Moms and babies in the U.S. are facing an urgent health crisis:

- In this country 1 in 10 babies is born prematurely each year
- Worldwide 15 million babies are born prematurely each year.
- Premature birth and its complications are the largest contributors to infant death in the United States and globally.
- More than 380,000 babies are born prematurely in the U.S. each year.
- In addition to the human toll, the societal cost of premature birth is more than \$26 billion in the U.S. per year.
- Women of color are up to 50 percent more likely to give birth prematurely and their children can face a 130 percent higher infant death rate.
- In this country black women have maternal death rates over three times higher than women of other ethnicities.
- More than 20 percent of premature babies are born to black women—that's 1 in 5 babies.
- Employers pay 12 times as much in health care costs for premature/ low birthweight babies compared to babies born without these complications.

Because premature birth has many possible causes, each PRC is charged with exploring a different transdisciplinary research target that is likely to be crucial to the prevention of premature birth. Washington University in St. Louis have unique strengths in studying the following areas: sleep patterns, the role of the cervix, and building an imaging device to analyze uterine contractions—all to understand how to predict and prevent preterm birth.

The researchers will try to identify how and where the contractions start, and understand how pacemaker cells develop over the course of pregnancy.

“With the heart, we have many medications and treatments dealing with heart beats that are too slow or too fast,” Dr. Cuculich adds. “We also have many other treatments for arrhythmias; ways to stimulate the heart to beat stronger or ways to make the heart stop beating in harmful ways.

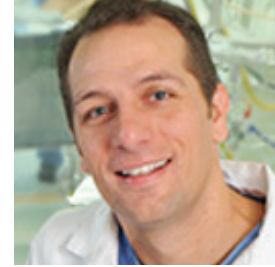
“I see this as a golden opportunity to study the uterus in the same way and hopefully one day develop similar drugs and treatments that can help reduce preterm birth.”

## THEME 2 LEADERS



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