In Pursuit of the “Pacemaker of the Uterus”

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.”

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.

Premature birth is one of the most intractable health challenges in modern medicine:

- One in nine babies in the United States is born prematurely each year
- Premature birth is the leading cause of newborn death in children from birth to age five
- Nearly half a million babies are affected annually
- Premature birth costs society at least $26 billion a year, according to the Institute of Medicine
- 15 million children are born prematurely every year worldwide
- Premature birth often leads to a lifetime of significant health challenges

The consequences of preterm birth extend to the entire family in terms of healthcare costs and impaired quality of life for the parents and siblings.

The March of Dimes Prematurity Research Center At Washington University in St. Louis is a robust, integrated cross-institutional effort. Its goal is to develop fundamental new insights into the biology of human pregnancy and the disease mechanisms of preterm birth to decrease the rate of prematurity and its associated complications.

The March of Dimes intends to invest $75 million over five years to support the National Campaign to End Premature Birth. To accomplish its goal, the March of Dimes Prematurity Research Center at Washington University in St. Louis has developed three interrelated theme areas, each bringing together renowned thinkers, researchers, physicians and top academics to focus on key aspects of the underlying causes of preterm birth.
Studies have shown that the uterus undergoes electrophysiological 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.”