Magnetic Resonance Imaging in Pregnancy

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Magnetic resonance imaging is commonly used in pregnant women to evaluate, most frequently, acute abdominal and pelvic pain or placental abnormalities, as well as neurological or fetal abnormalities, infections, or neoplasms.

pregnancy magnetic resonance imaging (MRI)

1. Background

In recent years, due to a greater availability of imaging resources, technological advances in diagnostic imaging, and an increase in forensic litigation, there has been an exponential increase for medical imaging.

However, this type of examination requires a series of profound reflections as they involve the health of both the pregnant woman and the fetus, raising a series of medical, ethical, and legal assessments [1][2]. Ultrasound (US) and magnetic resonance imaging (MRI) are the most commonly used imaging modalities in pregnancy as they lack ionizing radiation. Compared to US, MRI also has the advantages of not being operator-dependent, and of providing greater anatomical details, due to the continuous progress made since its advent in the mid-1980s [3][4]. Particularly, the use of MRI, as also suggested by the guidelines proposed by the American Congress of Obstetricians and Gynaecologists (ACOG), is recommended when the ultrasound examination shows unclear results as it can improve diagnostic accuracy, especially in cases of posterior localization of the placenta or abnormally invasive placenta (AIP), by visualizing the utero-placental interface [5][6]. Moreover, during pregnancy there are various physiological changes that may have an influence on MRI. Indeed, during pregnancy, the abdomen is the site of profound anatomical changes. The uterus increases its size with the passing of the weeks of gestation, becoming an abdominal organ as early as the second trimester [7]. As a result, all abdominal organs undergo compression from the uterus [8]. In particular, the hollow organs are the ones that are most affected by compression from the uterus: the stomach is pushed more cranially, the intestine laterally, and the bladder more caudally [7][8]. The diaphragm also suffers from the reduction of space at the abdominal level, being pushed cranially by at least 4 cm. The veins, whose wall is more compressible than that of the arteries, are also affected by the increase in size of the uterus [7]. In particular, a flattening of the lower third of the vena cava is often observed in the last weeks of gestation. All these aspects should be considered during MRI evaluation in pregnancy.

2. Non Contrast MRI during Pregnancy

To date, few data have been reported about eventual effects of MRI during pregnancy. There are theoretical risks regarding the process of deposition of energy in the body in the form of heat, which is quantified by the specific

absorption ratio (SAR), measured in units of watts per kilogram (W/kg). In animal models, it has been observed that tissue heating caused by elevated SAR during pregnancy resulting in an increase in maternal body temperature of more than 2–2.5 °C for at least 30–60 min causes fetal harm [9]. In light of this, the Food and Drug Administration (FDA) advises, in clinical practice, not to exceed the maximum SAR for the whole body of 4 W/kg, which is capable of increasing the body temperature by 0.6 °C for 30 min of MRI. It was also observed that the heating of the tissues is lower in the deep tissues, where the fetus is located, compared to the maternal body surface. Therefore, observing the SAR limits imposed, the heating of the tissues is not considered a serious risk factor for the fetus. Therefore, the International Electrotechnical Commission (IEC), as a precaution, to reduce the effects of tissue heating, imposes a limit for pregnant patients of whole-body SAR of 2 W/kg [10].

During the first trimester of pregnancy, fetal cells proliferate, differentiate, migrate and implant, going through one of the most crucial phases of pregnancy, namely, organogenesis.

Precisely during this delicate phase, the main risks are related to an altered organogenesis or to a possible miscarriage [11].

Although several in vitro studies on mammals stem cells have shown that exposure to MRI influences cell proliferation, differentiation, and migration, via altered cell signalling [12][13], and that in animal models during pregnancy was associated with reduced birth weight and increased stillbirth [14], to date, no observational studies in humans have shown adverse effects, such as teratogenic effects, or differences in birth weight or perinatal mortality rate, of MRI on the fetus during pregnancy (as well as on children born to pregnant women exposed to MRI). However, major limitations of available human studies are their retrospective nature and the lack of long-term data [15][16][17][18][19][20].

According to the American College of Radiology (ACR) and ACOG guidelines, MRI, performed with 3.0 T scanners or less, is not associated with any adverse effects on the fetus, but it should be used prudently in any gestational ages [21][22]. Hence, MRI is recommended if the information provided may affect the medical treatment of the pregnant woman or fetus, if it is not possible to wait for the term of pregnancy, and if it is not possible to perform an alternative method that does not use ionizing radiation, such as US. Furthermore, the exposure, compatibly with the pursuit of the pre-established diagnostic goals, must be as short as possible [23].

3. Gadolinium-Based Contrast Agents (GBCAs) MRI during Pregnancy

Gadolinium-based contrast agents (GBCAs) are intravenously administered contrasts for MRI approved for clinical use in patients over 20 years. These agents enhance the clarity and detection of images, improving diagnoses [24]. Chemically, there are currently two different types of GBCAs: linear contrast agents and macrocylic contrast agents (**Table 1**). Macrocylic contrast agents appear to have lower dissociation constants and lower retention within the body than linear agents [24][25]. Gadolinium, used in about one third of MRI exams, is toxic in its free ionic form

(gadolinium 3+) but biologically inert in its complexed form, which is why chelates to a ligand (GBCA) are used [26][27][28].

Table 1. Commercially available gadolinium-based contrast agents (GBCAs) in Europe approved during pregnancy.

Trade Name	Marketing Authorisation Holder	Compound	Chemical Structure	Use
Dotarem®	Guerbet Diagnostic Imaging	Gadoterate meglumine	Macrocyclic	Intraarticular/Intravenous
Gadovist®	Bayer Pharmaceuticals	Gadobutrolo	Macrocyclic	Intravenous
Magnevist®	Bayer Pharmaceuticals	Gadopentetate dimeglumine	Linear	Intraarticular
Multihance®	Bracco Imaging	Gadobenate dimeglumine	Linear	Intravenous
Primovist®	Bayer Pharmaceuticals	Gadoxetate disodium	Linear	Intravenous
Prohance®	Bracco Imaging	Gadoteridol	Macrocyclic	Intravenous

4. Risks Related to GBCA Administration

The literature suggests that both short and long-term risks after GBCA administration were observed in pregnant patients as in the general population; however, reactions to contrast agents that are unique to pregnancy have also been reported [29]. Short-term risks include allergic reactions and non-allergic reactions, such as nausea and vomiting. However, there are severe reactions to the contrast agent that are characteristic of pregnancy, such as recurrent late decelerations, prolonged fetal bradycardia on fetal heart tracing, and preterm labor [30][31][32].

Long-term risks include nephrogenic systemic fibrosis (NSF) and retained intracranial gadolinium.

NSF is a rare and debilitating disease characterized by fibrosing skin lesions and organ failure, observed in patients with impaired renal function. It was first described in 2000, but only in 2006 was it related to the intravenous administration of GBCA. To date, however, no cases of NSF have been reported in a pregnant patient or newborn after intrauterine exposure [33][34]. The retained intracranial gadolinium, first described as observed T1 shortening predominantly in the globus pallidus and dentate nucleus, and also observed in patients with normal renal function, has been related to multiple administrations of GBCA during the life, leading to greater caution in the use of the contrast agent [35][36]. Moreover, subsequent biopsy and autopsy-based studies revealed retained gadolinium in other parts of the body, including the bones, the skin, the liver, and the bone marrow, following the use of mainly linear but also macrocyclic agents, in a dose-dependent manner. To date, however, no symptoms have been observed following retained gadolinium, whose clinical significance remains uncertain [37][38][39]. Although human studies performed during pregnancy are still lacking, the deposition of gadolinium in the fetus is of particular interest due to the rapid development of the brain and other organs during this period, as well as a

greater probability of undergoing further administration during the course of life [40][41]. Notably, recent studies examining the degree of gadolinium deposition associated with in-utero exposure in mammalian animal models have shown detectable concentrations of gadolinium in the brain, bone, and liver [42][43]. Hence, intravenous administration of clinically approved GBCAs, although not contraindicated during pregnancy, should be avoided unless necessary, such as when the potential benefits outweigh the risks. Its use should therefore be assessed on a case-by-case basis.

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