Quality and Safety in Medical Imaging During Pregnancy and Lactation — Part I

Aurela Clark, MD; Xiaoqin Wang, MD; Riham El Khouli, MD; Margaret Szabunio, MD

Editor's note: Parts 1 and 2 are both published in the September/October 2024 issue of Applied Radiology.

Introduction

Imaging in pregnant patients has increased over the last decades as part of the overall rise in imaging utilization in North America. Lazarus et al reported that radiological utilization rates in pregnant patients more than doubled from 1997 to 2006, with the greatest increase seen in CT scans.[1]

Before imaging a pregnant patient, physicians should assess whether the information gained by imaging will change their clinical decision. If so, is it possible to establish a diagnosis without ionizing radiation?

Not all imaging examinations during pregnancy require informed consent. Examinations with negligible exposure to the fetus such as mammography, CT, or radiographs (excluding the abdomen or pelvis, except for third-trimester chest radiographs) do not typically require informed consent. It is advisable to counsel and seek informed consent from pregnant patients in low-risk exposure settings (< 50 mGy fetus dose) such as abdominal or pelvic radiographs, single-phase abdominal or pelvic CT, and most nuclear diagnostic studies. In higher radiation exposure settings, pregnancy verification and informed consent are typically obtained, as is calculation of dose estimation by a medical physicist.[2]

The American College of Radiology (ACR) practice parameters revised in 2023 do not specifically recommend for or against consenting pregnant patients without direct radiation exposure to the conceptus.[3] Such practices vary by institutional policies and local legal requirements. Documentation that is consistent with institutional policies and state laws must be entered in the patient's medical record.

Per ACR guidelines, imaging examinations of the abdomen and pelvis using ionizing radiation, where the fetus is in the field of view, require informed consent, which may be written or verbal. The ACR guidelines provide examples of consent forms.[3,4]

Nonionizing Radiation Imaging Modalities

US

US is a key diagnostic tool and arguably the most widely used diagnostic imaging modality used in pregnant patients. It is convenient, safe, and yields immediate images. Practice parameters based on consensus among the ACR, American College of Obstetrics and Gynecology (ACOG), American Institute of Ultrasound in Medicine, and Society of Radiologists in Ultrasound deem that US is generally safe for the fetus, regardless of gestational age; however, obstetric US examinations should be performed only when there is a valid medical reason, using the lowest possible ultrasonic exposure settings, and keeping acoustic levels "as low as reasonable achievable" (ALARA principle).[5-7]

Diagnostic US has been used clinically for over half

Affiliation: UK Healthcare, College of Medicine, University of Kentucky, Lexington, KY.
Disclosure: The authors have no conflicts of interest to disclose. None of the authors received outside funding for the production of this original manuscript and no part of this article has been previously published elsewhere.

Published: October 1, 2024. https://doi.org/10.1016/10.37549/AR-D-24-0026

a century without reports of harmful effects in humans, despite reported effects in embryo/fetus animal studies.[7] Nonetheless, US is a form of energy with potential effects in the tissues it transverses (bioeffects). The physical mechanisms responsible for these effects are thermal and nonthermal (mechanical). Thermal effects are an indirect result from the passage of the waveform, with conversion of the acoustic energy into heat. Potential theoretic risks may result from tissue heating owing to acoustic energy deposition associated with prolonged scanning times, particularly in early gestation. In fetal animal studies, this seems to be the case, with temperature increases greater than 1.5°C above physiological levels. Therefore, using high-power techniques prudently (eg, duplex Doppler imaging) and keeping dwell time to a minimum during the first trimester of pregnancy are recommended to minimize such risk.[7]

Nonthermal mechanisms are a direct result of the altering pressure and do not seem to be a major concern in obstetric US owing to the lack of cavitation foci (bubbles of air) in the fetal lungs or bowel.

Contrast-Enhanced Ultrasound

Contrast-enhanced US (CEUS) is a noninvasive technique in which US is used to detect gas-filled microbubbles used as perfusion tracers. US contrast agents (microbubbles/gas) are true intravascular agents and do not cross the placenta. Intravascular rheological properties of these bubbles are similar to those of red blood cells and remain entirely within the intravascular space. They have been used effectively to evaluate pregnant patients requiring a contrast-enhanced examination and have a high diagnostic accuracy.[8] Currently, there are no official recommendations regarding US contrast administration during pregnancy as only a few small studies have explored potential harmful effects.[9] Studies in 2020 and 2021 by Geyer et al that aimed to monitor the safety of CEUS in nonobstetrical conditions in 5 pregnant patients reported no parental or fetal adverse effects.[10] Only a few studies regarding the use of CEUS in gravid patients have been reported, predominantly focusing on the evaluation of placental disorders (eg, uteroplacental blood flow or invasive placental conditions) or indeterminate hepatic lesions.[11]

CEUS has been used for years in many imaging applications (eg, liver, kidneys, and breast). In obstetrics, despite not yet being approved by the U.S. Food and Drug Administration (FDA) for clinical use, CEUS offers the opportunity to monitor the uteroplacental circulation and quantify the intervillous flow velocity. Microbubbles can result in potential cavitation foci when oscillated at their resonant frequencies.[12] To avoid the nonthermal effects of early destruction of microbubbles resulting in cavitation foci, studies in pregnant patients report using a low mechanical index to avoid early microbubble destruction. Geyer et al reported safe CEUS for the parent and the fetus with a mechanical index less than 0.2; moreover, no contrast enhancement of the fetus was observed.[10]

MRI

Clinical MRI is considered generally safe to the developing fetus. When diagnostic information cannot be acquired by US, or the US findings are equivocal, MRI can be performed in pregnant patients when benefits outweigh the theoretical risk, as determined by an attending radiologist and the referring physician, in consensus with the patient. It is the modality of choice for many indications as it provides highly detailed imaging without the use of ionizing radiation. According to ACR guidelines, MRI studies can be performed judiciously at 3T field strength or less during any trimester of pregnancy provided that the MRI cannot be postponed until the end of pregnancy, the information gained is likely to alter patient treatment, and the information cannot be obtained by other nonionizing imaging modalities.[13]

Research has shown no adverse effects on fetal growth in healthy neonates variably exposed in utero to 3T MR at any gestational age and no adverse effects on neonatal hearing in healthy neonates exposed to prenatal 3T MRI.[14]

The theoretical MRI tissue heating potential and secondary thermal damage (particularly during organogenesis) caused by energy deposition from radiofrequency pulse field(s) are directly influenced by the proximity to the scanner. In a pregnant abdomen, the heating effect is highest at the surface and almost negligible at the center, significantly lower than the levels known to cause harmful effects on the fetus.[15-17]

In general, a specific absorption rate (SAR) value < 2 W/kg is strictly recommended for the pregnant population to reduce the effects of tissue heating; this option is available as a default for most MRI scanners. Low SAR mode can be achieved by increasing the repetition time and reducing the flip angles, number of slices, and number of signals acquired; these modifications, though, may result in longer scan times.[18] Scan time can be improved through the optimization of MRI protocols while maintaining the SAR value < 2 W/kg.

MRI Contrast Material

The current standard of practice is to avoid gadolinium-based contrast agents (GBCAs) during pregnancy, owing to the unknown risk of fetal exposure.[19,20] The decision to administer a GBCA to pregnant patients should be made on a case-by-case basis by the responsible radiologist and referring physician, accompanied by a well-documented and thoughtful risk-benefit analysis discussion with the patient. This analysis should justify a decision to administer the contrast agent based on overwhelming potential benefit to the patient and/or fetus, outweighing the theoretical but potential risks of exposing the developing fetus to free gadolinium ions.

Studies in nonhuman primates have demonstrated that at least some of the GBCAs can pass through the placental barrier and enter the fetal circulation. While multiple small studies have not shown convincing evidence of adverse effects from fetal exposure to GBCAs, it is unclear what impact free gadolinium ion deposition into the developing fetus might have if they were to be released in any quantity in the amniotic fluid. The risk(s) to the fetus of GBCA remain unknown and may be harmful.[13,20]

A 2016 retrospective study from an Ontario, Canada, database of births including 397 pregnant patients exposed to GBCAs concluded that gadolinium exposure at any time during pregnancy was associated with an increased risk of a broad spectrum of rheumatological, inflammatory, or infiltrative skin diseases, and stillbirth or neonatal death. However, the hazard ratios for nephrogenic systemic fibrosis (NSF)-like outcomes and congenital anomalies to the exposed neonates were not increased compared with the control cohort. Findings were considered exploratory due to potential type 1 statistical error mentioned in the study limitations.[19]

The ACR Gadolinium Pregnancy Screening Statement from the 2022 Contrast Media Manual notes that because many questions regarding the study's methodology have not been independently confirmed, radiologists must exercise an abundance of caution due to uncertainty surrounding the harmful effects of a contrast-enhanced MRI examination on the fetus.[19,20] Therefore, intravenous administration of GBCAs is strongly discouraged (Table 1). The ACR statement emphasizes that because it is unclear how GBCAs affect the fetus, these agents should

Table 1. Risk Profiles for Iodinated Contrast vs Gadolinium-Based Contrast Agents

	IODINATED LOCM	GADOLINIUM-BASED CONTRAST AGENTS
Indication	Not routinely administered[a]	Administration strongly discouraged
	Do not withhold if medically indicated	Administer only if significant benefit to patient or fetus outweighs potential but unknown risk[b]
Mutagenic/teratogenic effects	None reported (in vivo tests)	Teratogenic at high and repeated doses in animal studies
		No evidence of mutagenesis or teratogenesis in humans
Fetal/neonatal effects	Neonatal TSH (short-term) not affected (the overall amount of excess iodide in fetal circulation is small and transient in usual clinical dose)	Increased risk of stillbirth or neonatal death
	No documented case of neonatal hypothyroidism from maternal intravenous injection of LOCM	Following administration of lowest possible dose when indicated, no neonatal testing is necessary
Postnatal follow-up	Check TSH levels at the time of birth; if normal, no extra attention	No known occurrence of neonatal nephrogenic systemic fibrosis
		Increased risk in childhood of rheumatological, inflammatory, or infiltrative conditions
Additional risk	Increases absorbed organ radiation dose	

Abbreviations: FDA = Food and Drug Administration; GBCA = gadolinium-based contrast agent; LOCM = low-osmolarity contrast material; TSH = thyroid-stimulating hormone.

[a]*FDA Category B*

[b]*FDA Category C*

be administered with caution in pregnant or potentially pregnant patients, and only if their usage is considered essential and information cannot be acquired without intravenous contrast or will alter clinical management. In each case, the potential benefits must justify the possible but unknown risk to the fetus. Facilities should have a standardized system of screening in place, including screening for unsuspected pregnancies. Patients of childbearing capability should be informed of the lack of certainty regarding the risk of fetal GBCA exposure.[20] A contrast-enhanced MRI may be essential in cases of parental malignancy and treatment planning if the benefit to the parent outweighs potential risk to the fetus. Bird et al found that most pregnant patients exposed to contrast-enhanced MRI examinations underwent brain MRI, followed by pelvic and abdominal MRI.[20,21]

Written informed consent should be obtained from the patient after discussion with the referring physician and, in situations for which intravenous use of GBCA cannot be avoided, then only macrocyclic agents should be administered at the lowest dose (0.1 mmol/kg) possible.[22]

For the above reasons, the FDA classified GCBAs as Category C drugs (ie, animal reproduction studies have shown an adverse effect on the fetus but there are no adequate and well-controlled studies in humans); potential benefits may warrant use of the drug in pregnant patients despite risks.[20] A prospective study evaluating the effect of antepartum gadolinium administration reported no adverse perinatal or neonatal outcomes among 26 pregnant patients who received gadolinium in the first trimester.[23]

The expected dose of paramagnetic contrast media absorbed by an infant from breast milk is extremely low and less than 0.0004% of the intravenous maternal dose. Scientific societies (ACOG, ACR) agree it is not necessary to pause breastfeeding following contrast administration.[22,24]

Emerging Off-Label Technique with Ferumoxytol

Recently, ferumoxytol has drawn increasing interest as an off-label MR contrast agent eliminating the safety concerns associated with GBCAs with respect to NSF and gadolinium deposition in the brain.[25] The concept of using ferumoxytol-enhanced ultrashort echo-time pulmonary MR angiography (FE-UTE-MRA) as an alternative to contrast-enhanced CT for detecting pulmonary embolism (PE) remains appealing, especially in patients for whom CTA is contraindicated or exposure to ionizing radiation is undesirable; 24% of patients have contraindications for CTA and pregnant patients may have particular challenges with breath-holding.[26]

A study by Knobloch et al concluded that the FE-UTE-MRA approach could be an attractive alternative for detecting PE under free-breathing, while simultaneously avoiding ionizing radiation and allowing for assessment of nonvascular structures. Authors concluded that further investigations with larger sample sizes are needed to determine the clinical utility of this approach in patients with known or suspected PE.[27] Ferumoxytol has been associated with a very small risk of anaphylaxis, which can be mitigated using slow injections of diluted agent; however, this limits its use in dynamic phase MRI. In the realm of MRI contrast agents, ferumoxytol stands out as the sole clinically available blood pool agent and is the most utilized gadolinium-free alternative. Advantages over GBCAs include lower required dosages, distinctive pharmacokinetics, bimodal imaging potential, and lack of nephrotoxicity.

Ionizing Radiation-Based Imaging (Radiography, Fluoroscopy, CT, and Nuclear Medicine/PET)

Examinations that expose the fetus to ionizing radiation may be required during pregnancy to aid clinical diagnosis and decision-making. With a few exceptions, radiation exposure through radiography, CT, or nuclear medicine imaging techniques are at doses much lower than exposures reported to be associated with fetal harm. When a study utilizing ionizing radiation is necessary to answer clinical questions in the pregnant patient (eg, suspected pneumonia, PE, trauma) or as an adjunct to nonionizing radiation studies (eg, US and MRI), it should not be withheld from a pregnant patient.[5]

Certainly, a benefit-risk assessment is required when caring for the ill or injured pregnant patient and one must adhere to the ALARA principle regarding the radiation dose.[28] It is important to carefully select the imaging modality that allows for minimized radiation dose to the fetus while maintaining satisfactory diagnostic information to answer clinical question(s) and decrease the need for reimaging.[5]

The International Commission on Radiological Protection 103 recommends justification of medical exposures in 3 ways: (1) overall use of radiation in medicine should do more good than harm, (2) a procedure is justified for a particular clinical indication if it will improve diagnosis or treatment, and (3) a medical procedure will do more good than harm by contributing to treatment management.

Radiation Effects

Information about the effects of radiation exposure is mainly derived from animal experiments and studies on the effect of the atomic bombings in Hiroshima and Nagasaki, together with industrial and medical (ie, radiation therapy) exposure of humans. The main radiation effects on the tissues have been divided into the deterministic/threshold effects and stochastic/nonthreshold effects.

Deterministic Effects (Threshold or Nonstochastic Effects)

Deterministic effects result from radiation doses above a threshold value, in the early weeks of pregnancy, and from accumulated dose during multiple consecutive examinations during the same pregnancy. A major concern of the deterministic/threshold effect of ionizing radiation on the conceptus is teratogenesis (Table 2). The magnitude of these effects is thought to be predictable based on dose and fetal gestational age, and are associated with cellular injury or death.[4,30]

During the first 2 weeks of pregnancy, cell damage usually results in miscarriage; if the pregnancy continues, a fetal radiation-induced injury is highly unlikely (the "all or none effect"). Organogenesis takes place predominantly between gestational weeks 2 and 15. In this period, embryonic exposure to ionizing radiation may induce potential injury to specific organs, including the developing brain and orbits, and/or causing intrauterine growth restriction. During the second and third trimesters, the major organs have formed and cell injuries are of lesser concern.

Risks of central nervous system malformation and intellectual deficit have only been reported at fetal doses higher than 100 mSv. Fetal doses from routine medical imaging are generally well below 100 mSv, and generally below 20 mSv.[30]

It should be noted that, when the fetus or the abdomen is outside of the study's field of view, the conceptus dose is negligible. In rare situations, in which the dose might exceed the level of 100 mGy (ie, multiphase examinations), patients should be informed about potential effects and individualized scan protocols should be applied.[18-2830,,31]

Stochastic/Carcinogenic Effects (Nonthreshold)

Stochastic effects have no known threshold value and are theorized to occur at any radiation dose level. The major concern regarding in utero radiation exposure is the increased lifetime risk of the fetus for developing cancer, with the most common childhood malignancies being leukemia and lymphoma.[30]

When calculating cancer risk from diagnostic imaging, the linear no-threshold (LNT) model is chosen not because it is most likely to be correct, but because it is the most conservative. When counseling patients, it is important to keep in mind there has never been a direct quantification of cancer risk to fetuses with doses delivered by CT.

Stochastic effects are late and nonpredictable (nonthreshold). They are the consequence of cellular damage at the DNA level, are independent of the radiation dose, and cause carcinogenesis or other germ cell mutation(s). The LNT model predicts that carcinogenic risk increases linearly with increased radiation dose and that there is no minimum dose below which there is no cancer risk.[4]

It has been reported that when a fetus is exposed to common medical examination doses (eg, a fetal dose of 20-50 mGy received

Table 2. Deterministic/Threshold Effects of Ionizing Radiation on the Conceptus

FETAL DOSE EXPOSURE (MGy)	SUSPECTED IN UTERO DETERMINISTIC EFFECTS
< 50 mGy	Negligible deterministic effects (ie, abortion or malformation)
50-100 mGy	Potential effects scientifically uncertain and potentially too subtle to be clinically detectable
> 100 mGy	Risk of fetal malformation increases with gestational age: • < 2 weeks: "all or none effect" (possible spontaneous abortion) • Weeks 3-8: possible malformations increase in likelihood as dose increases • Weeks 9-15: intrauterine growth retardation, increased sensitivity of central nervous system (CNS) (mental retardation, decreased IQ, microcephaly), risk of CNS effect increases in frequency and severity with increasing dose • Weeks 16-25: decreased sensitivity of radiation effects on CNS, IQ deficit not detectable at diagnostic dose • > 27 weeks: no malformation at diagnostic doses
No dose threshold[a]	Stochastic effects:[b] late risk of carcinogenesis from exposure at any dose of radiation during any trimester

[a]The baseline risk for unexposed fetuses is 1 in 1,500 or 0.067%. An absolute incidence of 0.0043% per mGy was observed for fetuses with radiation exposure in the second and third trimesters.[29]

[b]Data on the stochastic effects are inconsistent.

during pelvic CT), the risk of carcinogenesis increases by a factor of 2,[5,32] but remains low in absolute terms (< 1 in 250). According to the ACR, a dose of 20 mGy represents an additional projected lifetime risk of about 40 or fewer additional cancers per 5000, or about 0.8% (or 0.4% per 10 mGy).[18,28]

The French Academy of Sciences and the French National Academy of Medicine in their joint report argue against the validity of using LNT models for "evaluating the carcinogenic risk of low doses (< 100 mGy) and considers the effect of very low doses (< 10 mGy) even more trivial."

Instead, they support the model of radiation hormesis, which is defined as the beneficial stimulatory (biopositive) effect(s) caused by exposure to low doses of ionizing radiation known to have toxic (bionegative) effect(s) at higher doses.[33] They conclude that LNT assessment of carcinogenic risks induced by low doses, such as those delivered by diagnostic radiology or the nuclear industry, is not based on valid data.[34]

The relationship between the risk of carcinogenesis and gestational age at the time of radiation exposure is even more controversial. The Oxford Survey for Childhood Cancer (OSCC) study suggests that the risk of carcinogenesis is higher with exposure in the first trimester than with exposure in the second or third trimesters, with relative risks of 3.19, 1.29, and 1.30, respectively.[16,35] ACOG describes the risk of carcinogenesis due to fetal radiation exposure from diagnostic imaging during pregnancy as "very small," concluding that "abortion should not be recommended."[5] ACOG guidelines do not discuss what kind of information, particularly on cancer risk estimates, should be provided during parental counseling in such cases, if any.

Another potential radiation-related risk during pregnancy is associated with the increased radiosensitivity of breast tissue in pregnant patients due to glandular proliferation. Parker et al concluded that the minimum radiation dose delivered to the breast of an average-sized patient during CT pulmonary angiography was 20 mGy, which exceeds the ACR standard recommendation of 3 mGy for 2-view mammography (2D only, not tomosynthesis).[36] The potential carcinogenesis effect of such radiation exposure remains unknown.

According to the seventh report of the Biological Effects of Ionizing Radiation study on the survivors of Hiroshima and Nagasaki, the background risk of cancer over the course of an individual's lifetime is 42%. Exposure to 100 mSv of ionizing radiation increases lifetime-attributable risk of cancer by 1%.[18]

CT

The use of CT during pregnancy has substantially increased in the United States and Ontario over the past 2 decades. CT examinations were performed in approximately 0.8% of pregnancies in the United States and 0.4% in Canada (Ontario) in 2016.[37]

Obtaining a CT examination is often quicker and easier than an MRI, and this may account for its expanding use in emergency situations such as suspected PE, trauma, brain aneurysm rupture, or for surgical abdominal conditions.

The main limitation of CT is it uses ionizing radiation at significantly higher doses than that of conventional x-rays. When the fetus is outside the field of the scanned area (eg, head, cervical spine, thorax, extremities), the estimated dose delivered to the conceptus is minimal (usually < 1 mGy).[31] The fetal dose for a CT head is 0 mGy and for a CT chest is 0.2 mGy or less, depending on the trimester of pregnancy. Shielding the gravid uterus does little to reduce the radiation dose to the fetus for CT.

Concern about the harmful effects of CT to the fetus only occurs when the gravid uterus is directly in the field of view. The typical fetal radiation dose for CT of the abdomen and pelvis is 25 mGy. With modern CT scanners that use automated exposure control, the dose is about 13 mGy. Low-dose (LD) CT protocols can result in doses on the order of 10-11 mGy.[38]

As such, doses used during standard CT examinations, including an abdomino-pelvic scan (single-phase), do not exceed the cutoff of 100 mGy (the minimum threshold level for which radiogenic malformations might occur and the individual probability of radiogenic cancer is very low).[31] Interestingly, in a recent study, the mean in utero doses at different stages of pregnancy were estimated with the use of an appropriate anthropomorphic phantom and were calibrated with volumetric CT dose index measurements and Monte Carlo simulation; they varied from 0.04 to 1.04 mGy for pulmonary angiography, 4.8 to 5.8 mGy for abdomino-pelvic CT, and 9.8 to 12.6 mGy for trauma CTs performed with 64-slice CT. Assuming that the fetus accounts for 9% (12 weeks), 37% (20 weeks), 56% (28 weeks), and 69% (38 weeks) of intrauterine volume, the maximum theoretical fetal doses would then have been 15.5, 7.5, and 0.8 mGy, for trauma, abdominal, and pulmonary angiography protocols, respectively. Again, all doses were substantially lower than the recommended threshold.[39]

Furthermore, major dose reductions can be achieved with LD and ultralow-dose CTs, which may potentially be used in pregnant women.[40]

Several additional technical improvements may optimize CT diagnostic performance. New CT scanners further decrease the dose level delivered to the parent and fetus by using advanced technologies such as tube current modulation, iterative reconstruction, or even deep-learning image reconstruction algorithms.[30,41,42] Dose reduction techniques should be applied when a pregnant patient requires a CT.[2,42]

Typical dose reduction techniques include lowering tube kilovoltage in accordance with the patient's weight, decreasing tube current time (mA-s), limiting image length (z-axis), increasing pitch, widening the beam collimation, selecting smaller areas to scan, and using a single acquisition.[30] Limiting image length and CT acquisitions seem the best ways to reduce fetal exposure. Position statements from the ACR, National Council on Radiation Protection and Measurements, American Board of Radiologists, Society for Pediatric Radiology, and Image Gently all recommend discontinuing gonadal and fetal shielding.[2]

Fetal Dose Estimation

When the expectant parent undergoes CT examination during the first 2 weeks of gestation, dose estimation may not be required given the all-or-none response to radiation. Beyond 2 weeks' gestation, accounting for the potential risk of carcinogenesis, more information and reassurance can be provided to the patient through consultation with a qualified medical physicist and communication between the patient, radiologist, and obstetrician. Radiologists and radiologic technologists are trained to prospectively optimize exposure of the pregnant patient; for some modalities such as CT, dose indexes are prospectively displayed when imaging parameters are inputted and act as an indirect surrogate for parental dose.

The radiation dose absorbed by the fetus cannot be measured directly. Fetal dose is best and most accurately determined by a medical physicist. There are methods for rough estimation of fetal dose such as multiplying the effective milliampere seconds (milliampere seconds per pitch) or volume CT dose index by 10.8 mGy/100 mAs for a 120 kVp abdominal examination.[43] For example, an effective 222 mAs for a CT scan of the pelvis would result in a fetal dose of 24 mGy (10.8 × 2.22). However, these methods are not substitutes for accurate estimation by a qualified medical physicist, who uses scan parameters and the patient's geometry for Monte Carlo calculations, the practice most widely used. If the estimated fetal dose is expected to exceed 50 mGy, consultation with a medical physicist is recommended. Fetal dose estimation can also be performed prospectively by placing the dosimeter at the level of the uterus, but this is not routine at many institutions.[42]

The baseline risk of childhood cancer is approximately 1.0 to 2.5 per 1,000. Estimates of the additional risk of childhood cancer from a fetal radiation dose of 1000 mGy range from 0.022 (OSCC) through 0.028 (life span study of atomic bomb survivors) to 0.060 (expert statistical review).[43]

Parental counseling on the risks and benefits of a CT examination to fetal health and written documentation of informed consent are advised. According to the International Commission of Radiological Protection, counseling should take place after estimating the dose to the exposed embryo and comparing the radiation risk with other pregnancy risks, bearing in mind that there has been no direct quantification of cancer risk to humans from CT doses.[30]

Iodinated Low-Osmolarity Contrast Agents

Diagnostic doses of low-osmolarity contrast media have been shown to cross the placenta and enter the fetus. Both iodinated contrast materials and GBCAs cross the blood-placental barrier and enter the fetal circulation; they are then excreted into the amniotic fluid, swallowed by the fetus, and re-enter the fetal circulation. These pharmacokinetic properties result in a relatively long-term exposure of the developing fetus to the compounds of contrast agents. As such, ACR guidelines state that their use should be limited in pregnancy "since their effects on the human embryo or fetus are not completely understood."[44]

Oral iodinated contrast agents (eg, gastrografin) are not absorbed by the maternal intestine and, therefore, cause no real or theoretical harm.[5]

Iodinated contrast media intravenously or orally administrated are classified as FDA Category B drugs. This classification means that no mutagenic or teratogenic effects have been demonstrated in animal reproductive studies; however, there are no adequate data based on controlled studies in pregnant patients. The ACR does not recommend withholding intravenous iodinated contrast media in pregnant or potentially pregnant patients if it is medically indicated.[44] Iodinated media carry a low risk of anaphylactoid reactions and adverse effects to the pregnant patient such

as nausea, vomiting, flushing, and pain at the injection site.[45]

Recent data suggest that the presence of iodinated contrast media increases radiation absorption during CT scanning and may lead to an average 30% increase in absorbed organ dose.[46]

Neonatal hypothyroidism is not a concern associated with intravenous administration of iodinated contrast media as it does not affect short-term neonatal thyroid-stimulating hormone (TSH), possibly because the overall amount of excess iodide in fetal circulation is small and transient in routine clinical doses. Long-term adverse effects of the free iodide on the fetal thyroid gland are unknown. To date, there has been no documented case of neonatal hypothyroidism from the maternal intravascular injection of a water-soluble iodinated contrast agent. Based on the current available data and routine evaluation of newborns for congenital hypothyroidism by measuring TSH levels in the exposed neonates within the first week of life, ACR guidelines do not recommend any special attention to clinical doses of low-osmolarity iodinated contrast in pregnancy.[44]

Administration of iodinated contrast material is recommended only if clinically indicated and after careful investigation of the risks and benefits. Neonatal thyroid function should be checked soon after birth.[22]

Regarding breastfeeding, the level of iodinated contrast agent absorbed by the infant is exceptionally low and less than 0.01% of intravenous maternal dose; current guidelines support continuation of lactation.[22,45]

Radiography and Fluoroscopy Examinations

In general, conventional x-ray examinations that do not directly expose the gravid uterus to the x-ray beam do not require verified pregnancy status, and should not impact the decision to proceed with the examination as they result in negligible conceptus dose. Such examinations include chest radiography, extremity radiography (except the hips), mammography, and diagnostic examinations, including the head and neck. During such examinations, the only radiation to which the conceptus is exposed is scattered radiation, which characteristically results in a very low dose.[28,42]

Chest radiography in the third trimester is likely to expose part of the fetus to the direct x-ray beam, but this, too, can proceed when justified and optimized because the dose to the fetus remains very low and the fetus is less radiosensitive than in early pregnancy. Examples of optimization may be to limit frontal view examination and not perform the lateral view.

Mammography can also be performed safely at any time during pregnancy. Radiation exposure to a conceptus from a properly performed screening mammogram is expected to be inconsequential. Thus, proceeding with the examination should be based on clinical circumstances, not radiation risk.[28]

When an examination requires the fetus be included in the field of view, the parent should be reassured that "no single diagnostic x-ray has a radiation dose significant enough to cause adverse effects in a developing embryo or fetus." For almost all standard radiographs, including those of the pelvis and hips, estimated conceptus doses are considerably lower than the cutoff limit of 100 mGy. Caution should be taken if multiple radiographs are necessary (eg, in the setting of trauma) due to cumulative dose.

For radiological examinations, the highest radiation exposure to the conceptus occurs when the abdominal/pelvic region is exposed to the primary x-ray beam. Radiation exposure parameters may be reduced and a certain degree of compromise in image quality is acceptable; nevertheless, the quality cannot decrease beyond the level required for diagnosis. The exposure parameters should be determined prior to scanning by radiologists in collaboration with a qualified medical physicist.

In the few situations for which fluoroscopy is medically indicated, radiation-sparing maneuvers should be employed to lower the dose. These include minimizing the exposure time, decreasing the number of images acquired, keeping the lowest possible frame rate, optimizing collimation, and using image hold vs additional exposures when possible. Radiation monitoring with dose documentation in the medical record or the procedure report is important to help address potential future concerns regarding such exposures.[47]

For practical purposes, no specific counseling is required for patients undergoing diagnostic imaging with a predicted fetal absorbed dose of less than 10 mGy. This includes all x-ray and CT scanning not involving the abdomen and most nuclear scans. For potential exposure greater than 10 mGy, the patients should be counseled on a risk-benefit basis.

Nuclear Medicine Examinations

Nuclear medicine examinations are usually avoided during pregnancy and their effects depend on the physical and biochemical properties of the radioisotope, including patient uptake and excretion, passage of the agent across the blood-placenta barrier, and uptake from the conceptus. Technetium-99m (Tc-99m) is one of the most used isotopes and is used for brain, bone, renal, and cardiovascular scans. Its most common use in pregnancy is in ventilation-perfusion (V/Q) lung scanning for detecting PE. In

general, these procedures result in an embryonic or fetal exposure of less than 5 mGy, which is considered a safe dose in pregnancy. Its half-life is 6 hours, and it is a pure gamma-ray emitter, which minimizes the dose of radiation without compromising the image. All these facts support the safety of Tc-99m at 5 mGy when indicated during pregnancy.[18]

Not all radioisotopes can be used safely during pregnancy. Radioactive iodine (iodine-131) is contraindicated in pregnancy. It readily crosses the placenta, has a half-life of 8 days, and can cause deleterious effects on the fetal thyroid, especially if used after 10 to 12 weeks of gestation. Iodine-131 should not be used during pregnancy for diagnostic or therapeutic treatment purposes. If a diagnostic scan of the thyroid is essential, Tc-99m is the isotope of choice.[45]

The most frequent nuclear medicine examination in pregnancy is the V/Q scan, which is associated with a decreased dose to the breast when compared with pulmonary angiography. To minimize fetal exposure, the tracer dose is typically reduced by half, with a compensatory increase in imaging time. Absorbed dose to the fetus is estimated at 0.1 to 0.37 mGy.[42] Other nuclear medicine scans are rarely indicated in pregnancy.

F-18 fluorodeoxyglucose (FDG) PET/CT in a pregnant patient is discouraged due to fetal exposure to radiation and potential toxicity of the radiopharmaceutical, even though reported total absorbed fetal doses are below the threshold of 100 mGy.[18] If it is medically indicated, usually for staging purposes in pregnant patients with cancer, it may be performed after careful risk-benefit assessment. Absorbed fetal dose is proportional to fetal mass with higher doses in early gestation, which is explained by the smaller volume of the fetus and by the fetal body at this stage being composed of relatively undifferentiated and rapidly proliferating cells using more glucose and, therefore, concentrating FDG more effectively. Furthermore, the smaller size of the fetus is in closer proximity to the urinary bladder.[48] Even with the most conservative assumptions and the use of both PET and CT components, a full PET/CT scan is unlikely to deliver more than 15-20 mGy to the fetus.

In most institutions, images are acquired 45 to 60 minutes after injection. To reduce radiation exposure, patients should hydrate (orally and/or intravenously if needed) before and after the study, and void frequently. If not contraindicated, a bladder catheter can be used to drain radioactive urine to reduce photon exposure to the fetus.[48]

PET/MRI is the optimal PET procedure for imaging pregnant women as it provides detailed imaging without CT-related radiation for attenuation correction; however, its availability remains limited.[49] For PET/MR imaging, the value is more likely 5 mGy or less. Stochastic effects for these doses have never been demonstrated.[49]

Considerations in Lactating Patients Following a Nuclear Medicine Examination

Radionuclide compounds are excreted into breast milk in varying concentrations and for varying periods. In addition, excretion rates of the same compound can vary between patients. Because some specific nuclear materials excreted into breast milk can have deleterious effects (eg, iodine-131), consultation with experts on breastfeeding and nuclear medicine are recommended to ensure the breastfed infant is not exposed to radiation by proximity and through radioactivity in milk.

In 2002, the Nuclear Regulatory Commission stated that the dose to the infant in such cases should be less than 1 mSv. The recommended length of breastfeeding interruption for different pharmaceuticals should depend on the physical and biological half-lives of these agents. For instance, breastfeeding interruption after Tc-99m imaging depends on the radiopharmaceutical agent used, with 4 hours recommended for Tc-99m-pertechnetate imaging and 48 hours for Tc-99m-labeled leukocyte scintigraphy. During this period, the parent should be counseled to pump and store the milk for use after the radioactivity dissipates or discard it. As an alternative, if the imaging examination is not emergent, the parent may pump and store the milk before receiving the radiotracer to avoid interruption. Complete cessation of breastfeeding is advised after administration of ^{67}Ga citrate and procedures that use ^{131}I-NaI as more than 10% of the administered dose may be excreted in breast milk.[42]

Conclusions

In the pregnant patient, adherence to established guidelines and protocols is essential to safeguard parental and fetal health during radiological evaluations. However, the choice of imaging modality should be guided by a multidisciplinary approach involving obstetricians, radiologists, and other health care providers to ensure diagnostic efficacy while minimizing potential risks to the parent and fetus. Each modality offers distinct advantages and limitations. The ALARA principle should be followed with respect to the use of ionizing radiation. No examination should be withheld when an important clinical diagnosis is under consideration. Best practices require updates on available technologies and guidelines. The continual advancement in imaging technology and techniques promises

to further enhance the safety and diagnostic accuracy for parent-fetal dyads in the future.

References

1) Lazarus E, Debenedectis C, North D, Spencer PK, Mayo-Smith WW. Utilization of imaging in pregnant patients: 10-year review of 5270 examinations in 3285 patients--1997–2006. *Radiology*. 2009;251(2):517-524. doi:10.1148/radiol.2512080736

2) Mainprize JG, Yaffe MJ, Chawla T, Glanc P. Effects of ionizing radiation exposure during pregnancy. *Abdom Radiol (NY)*. 2023;48(5):1564-1578. doi:10.1007/s00261-023-03861-w

3) ACR-SPR practice parameter for imaging pregnant or potentially pregnant adolescents and patients with ionizing radiation [Revised 2023 (Resolution 31)]. Accessed June 27, 2024. https://www.acr.org/-/media/ACR/Files/Practice-Parameters/Pregnant-Pts.pdf

4) Wieseler KM, Bhargava P, Kanal KM, et al. Imaging in pregnant patients: examination appropriateness. *Radiographics*. 2010;30(5):1215-1229. doi:10.1148/rg.305105034

5) ACOG'sCommittee opinion no. 723 summary: guidelines for diagnostic imaging during pregnancy and lactation. *Obstet Gynecol*. 2017;130(4):933-934. doi:10.1097/AOG.0000000000002350

6) Pellerito J, BromleyB, AllisonS. AIUM–acr–acog–smfm–sru practice parameter for the performance of standard diagnostic obstetric ultrasound examinations. *J Ultrasound Med*. 2018;37(11). doi:10.1002/jum.14831

7) Abramowicz JS. Benefits and risks of ultrasound in pregnancy. *Semin Perinatol*. 2013;37(5):295-300. doi:10.1053/j.semperi.2013.06.004

8) Wilson SR, Barr RG. Contrast-enhanced ultrasound: the ideal contrast imaging study for pregnant patients. *Abdom Radiol*. 48(11):3553-3553. doi:10.1007/s00261-023-04008-7

9) Sidhu P, Cantisani V, Dietrich C, et al. The EFSUMB guidelines and recommendations for the clinical practice of contrast-enhanced ultrasound (CEUS) in non-hepatic applications: update 2017 (long version). *Ultraschall Med*. 2018;39(2):e2-e44. doi:10.1055/a-0586-1107

10) Geyer T, Rübenthaler J, Froelich MF, et al. Contrast-enhanced ultrasound for assessing abdominal conditions in pregnancy. *Medicina*. 2020;56(12):675. doi:10.3390/medicina56120675

11) Poret-Bazin H, Simon EG, Bleuzen A, et al. Decrease of uteroplacental blood flow after feticide during second-trimester pregnancy termination with complete placenta previa: quantitative analysis using contrast-enhanced ultrasound imaging. *Placenta*. 2013;34(11):1113-1115. doi:10.1016/j.placenta.2013.08.002

12) Ajmal S. Contrast-enhanced ultrasonography: review and applications. *Cureus*. 2021;13(9):e18243. doi:10.7759/cureus.18243

13) Kanal E, Barkovich AJ, Bell C, et al. ACR guidance document on MR safe practices: 2013. *J Magn Reson Imaging*. 2013;37(3):501-530. doi:10.1002/jmri.24011

14) Chartier AL, Bouvier MJ, McPherson DR, et al. The safety of maternal and fetal MRI at 3 T. *AJR Am J Roentgenol*. 2019;213(5):1170-1173. doi:10.2214/AJR.19.21400

15) Ciet P, Litmanovich DE. MR safety issues particular to women. *Magn Reson Imaging Clin N Am*. 2015;23(1):59-67. doi:10.1016/j.mric.2014.09.002

16) Chen MM, Coakley FV, Kaimal A, Laros RK. Guidelines for computed tomography and magnetic resonance imaging use during pregnancy and lactation. *Obstet Gynecol*. 2008;112(2 pt 1):333-340. doi:10.1097/AOG.0b013e318180a505

17) Leyendecker JR, Gorengaut V, Brown JJ. MR imaging of maternal diseases of the abdomen and pelvis during pregnancy and the immediate postpartum period. *RadioGraphics*. 2004;24(5):1301-1316. doi:10.1148/rg.245045036

18) Bourgioti C, Konidari M, Gourtsoyianni S, Moulopoulos LA. Imaging during pregnancy: what the radiologist needs to know. *Diagn Interv Imaging*. 2021;102(10):593-603. doi:10.1016/j.diii.2021.05.003

19) Ray JG, Vermeulen MJ, Bharatha A, Montanera WJ, Park AL. Association between MRI exposure during pregnancy and fetal and childhood outcomes. *JAMA*. 2016;316(9):952-961. doi:10.1001/jama.2016.12126

20) ACR Commitee on Drugs and Contrast Media. ACR manual on conrast media. Gadolinium pregnacy screening statement. Accessed July 17, 2022. https://www.acr.org/-/media/ACR/Files/Clinical-Resources/Gadolinium-Pregnancy-Screening-Statement---FINAL.pdf

21) Bird ST, Gelperin K, Sahin L, et al. First-trimester exposure to gadolinium-based contrast agents: a utilization study of 4.6 million U.S. pregnancies. *Radiology*. 2019;293(1):193-200. doi:10.1148/radiol.2019190563

22) Members of Contrast Media Safety Committee of European Society of Urogenital Radiology ESUR guidelines on contrast agents, V.10. Accessed July 17, 2022. https://www.esur.org/wp-content/uploads/2022/03/ESUR-Guidelines-10_0-Final-Version.pdf

23) De Santis M, Straface G, Cavaliere AF, Carducci B, Caruso A. Gadolinium periconceptional exposure: pregnancy and neonatal outcome. *Acta Obstet Gynecol Scand*. 2007;86(1):99-101. doi:10.1080/00016340600804639

24) Perelli F, Turrini I, Giorgi MG, et al. Contrast agents during pregnancy: pros and cons when really needed. *Int J Environ Res Public Health*. 2022;19(24):16699. doi:10.3390/ijerph192416699

25) Fraum TJ, Ludwig DR, Bashir MR, Fowler KJ. Gadolinium-based contrast agents: a comprehensive risk assessment. *J Magn Reson Imaging*. 2017;46(2):338-353. doi:10.1002/jmri.25625

26) Si G, Du Y, Tang P, et al. Unveiling the next generation of MRI contrast agents: current insights and perspectives on ferumoxytol-enhanced MRI. *Natl Sci Rev*. 2024;11(5):nwae057. doi:10.1093/nsr/nwae057

27) Knobloch G, Colgan T, Schiebler ML, et al. Comparison of gadolinium-enhanced and ferumoxytol-enhanced conventional and UTE-MRA for the depiction of the pulmonary vasculature. *Magn Reson Med*. 2019;82(5):1660-1670. doi:10.1002/mrm.27853

28) ACR-SPR practice parameter for imaging pregnant or potentially pregnant adolescents and women with ionizing radiation. Accessed July 17, 2022. https://www.acr.org/-/media/ACR/Files/Practice-Parameters/pregnant-pts.pdf

29) Chaparian A, Aghabagheri M. Fetal radiation doses and subsequent risks from X-ray examinations: should we be concerned?. *Iran J Reprod Med*. 2013;11(11):899-904.

30) Goldberg-Stein SA, Liu B, Hahn PF, Lee SI. Radiation dose management: part 2, estimating fetal radiation risk from CT during pregnancy. *AJR Am J Roentgenol*. 2012;198(4):W352-W356. doi:10.2214/AJR.11.7458

31) IRCP. Pregnancy and medical radiation. ICRP Publication 84. Ann. ICRP 30 (1); 2000.

32) Chen MM, Coakley FV, Kaimal A, Laros RKJ. Guidelines for computed tomography and magnetic resonance imaging use during pregnancy and lactation. Obstet Gynecol. 2008;112(2):333-340. doi:10.1097/AOG.0b013e318180a505

33) Luckey TD. Radiation hormesis: the good, the bad, and the ugly. *Dose Response*. 2006;4(3):169-190. doi:10.2203/dose-response.06-102.Luckey

34) Tubiana M. Dose–effect relationship and estimation of the carcinogenic effects of low doses of ionizing radiation: the joint report of the académie des sciences (paris) and of the académie nationale de Médecine. *Int J Radiat Oncol Biol Phy*. 2005;63(2):317-319. doi: 10.1016/j.ijrobp.2005.06.013

35) Chen J, Lee RJ, Tsodikov A, Smith L, Gaffney DK. Does radiotherapy around the time of pregnancy for Hodgkin's disease modify the risk of breast cancer? *Int J Radiat Oncol Biol Phy*. 2004;58(5):1474-1479. doi:10.1016/j.ijrobp.2003.09.018

36) Parker MS, Hui FK, Camacho MA, et al. Female breast radiation exposure during CT pulmonary angiography. *AJR Am J Roentgenol*. 2005;185(5):1228-1233. doi:10.2214/AJR.04.0770

37) Kwan ML, Miglioretti DL, Marlow EC, et al. Trends in medical imaging during pregnancy in the United States and Ontario, Canada, 1996 to 2016. *JAMA Netw Open*. 2019;2(7):e197249. doi:10.1001/jamanetworkopen.2019.7249

38) Sadro CT, Dubinsky TJ. CT in pregnancy: risks and benefits. *Appl Radiol*. 2013;6-16. doi:10.37549/AR2026

39) Kelaranta A, Mäkelä T, Kaasalainen T, Kortesniemi M. Fetal radiation dose in three common CT examinations during pregnancy - monte carlo study. *Phys Med*. 2017;43:199-206. doi:10.1016/j.ejmp.2017.09.120

40) Beregi JP, Greffier J. Low and ultra-low dose radiation in CT: opportunities and limitations. *Diagn Interv Imaging*. 2019;100(2):63-64. doi:10.1016/j.diii.2019.01.007

41) Raman SP, Johnson PT, Deshmukh S, et al. CT dose reduction applications: available tools on the latest generation of CT scanners. *J Am Coll Radiol*. 2013;10(1):37-41. doi:10.1016/j.jacr.2012.06.025

42) Tirada N, Dreizin D, Khati NJ, Akin EA, Zeman RK. Imaging pregnant and lactating patients. *Radiographics*. 2015;35(6):1751-1765. doi:10.1148/rg.2015150031

43) Coakley FV, Cody DD, Mahesh M. The pregnant patient: alternatives to CT and dose-saving modifications to CT technique. *Image Wisely Web Site*. 2010.

44) ACR Committee on Drugs and Contrast Media. ACR manual on contrast media; 2022.

45) ACOG committee opinion no. 723. Guidelines for diagnostic imaging during pregnancy and lactation. *Obstetrics and Gynecology*; 2017.

46) Mazloumi M, Van Gompel G, Kersemans V, de Mey J, Buls N. The presence of contrast agent increases organ radiation dose in contrast-enhanced CT. *Eur Radiol*. 2021;31(10):7540-7549. doi:10.1007/s00330-021-07763-7

47) Thabet A, Kalva SP, Liu B, Mueller PR, Lee SI. Interventional radiology in pregnancy complications: indications, technique, and methods for minimizing radiation exposure. *RadioGraphics*. 2012;32(1):255-274. doi:10.1148/rg.321115064

48) Stabin MG. Radiation dose concerns for the pregnant or lactating patient. *Semin Nucl Med*. 2014;44(6):479-488. doi:10.1053/j.semnuclmed.2014.06.003

49) Zanotti-Fregonara P, Laforest R, Wallis JW. fetal radiation dose from ^{18} f-FDG in pregnant patients imaged with PET, PET/CT, and PET/MR . *J Nucl Med*. 2015;56(8):1218-1222. doi:10.2967/jnumed.115.157032