Canadian Stroke Best Practices

CANADIAN STROKE BEST PRACTICE RECOMMENDATIONS

Acute Stroke Management during Pregnancy

Consensus Statement

Diagnostic Imaging

Ladhani NNN, Swartz R H, (Writing Group Chairs), Lindsay MP (Senior Editor)
on Behalf of the Canadian Stroke Best Practice Recommendations
STROKE IN PREGNANCY Writing Group and the
Canadian Stroke Best Practices and Quality Advisory Committees,
in collaboration with the Canadian Stroke Consortium

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Published Guidelines

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ACOG Committee Opinion No. 723 (October 2017) Interim update **Guidelines for diagnostic imaging during pregnancy. American College of Obstetricians and Gynecologists.** **Obstet Gynecol 2016;130(4):e210-216.**	Ultrasonography and MRI are not associated with risk and are the imaging techniques of choice for the pregnant patient, but they should be used prudently and only when use is expected to anser a relevant clinical question or otherwise provide medical benefit to the patient. With few exceptions, radiation exposure through radiography, CTs can or nuclear medicine imaging techniques is at a dose much lower than the exposure associated with fetal harm. If these techniques are necessary in addition to ultrasonography or MRI or are more readily available for the diagnosis in question, they should not be withheld from a pregnant patient. The use of gadolinium contrast with MRI should be limited; it may be used as a contrast agent in a pregnant woman only if it significantly improves diagnostic performance and is expected to improve fetal or maternal outcome. Breast-feeding should not be interrupted after gadolinium administration.
Patenaude Y, Pugash D, Lim K, Morin L, Bly S, Butt K, Cargill Y, Davies G, Denis N, Hazlitt G, Naud K. The use of magnetic resonance imaging in the obstetric patient. Journal of obstetrics and gynaecology Canada: JOGC= Journal d'obstetrique et gynecologie du Canada. **The Use of Magnetic Resonance Imaging in the Obstetric Patient** **J Obstet Gynaecol Can 2014;36(4):349–355**	**Summary Statements** 1. Fetal magnetic resonance imaging is safe at 3.0 tesla or less during the second and third trimesters. (II-2) 2. It is safe to continue breastfeeding after receiving a gadolinium contrast agent. (III) **Recommendations** 1. Use of magnetic resonance imaging during the first trimester of pregnancy should be restricted to maternal indications for which the information is considered clinically imperative. Inadvertent exposure to magnetic resonance imaging during the first trimester has not been associated with any long-term sequelae and should not raise clinical concern. (III-C) 2. Gadolinium contrast may be used in pregnant women when the benefits outweigh the potential risks. (III-C)
Thomsen HS, Morcos SK, Almén T, Bellin MF, Bertolotto M, Bongartz G, Clement O, Leander P, Heinz-Peer G, Reimer P, Stacul F. **Nephrogenic systemic fibrosis and gadolinium-based contrast media: updated ESUR Contrast Medium Safety Committee guidelines.** **European radiology. 2013 Feb 1;23(2):307-18. (selected)**	**Contrast agents with highest risk of Nephrogenic systemic fibrosis (NSF) (Gadodiamide, Gadopentetate dimeglumine and Gadoversetamide):** 1. (b) Contra-indicated in neonates and pregnant women. Level of evidence C, Class of recommendation 2B 1. (e) Lactating women should not breastfeed for 24 h after contrast medium and should discard the breast milk. Level of evidence C, Class of recommendation 2B. **Contrast agents with intermediate risk of NSF (Gadobenate dimeglumine, Gadofosvest trisodium, Gadoxetate disodium) and contrast agents with lowest risk of NSF (Gadobutrol, Gadoterate meglumine and Gadoteridol)** 2 (b). Can be used in pregnant women to give essential diagnostic information. Level of evidence C, Class of recommendation 2B. 2. (c) In lactating women the decision about whether to stop breast feeding and discard the breast milk for 24 h after

Guideline	Recommendations
	contrast medium should be made by the woman after discussion with the doctor. Level of evidence C, Class of recommendation 2B
Kanal E, Barkovich AJ, Bell C, Borgstede JP, Bradley WG, Froelich JW, Gimbel J, Gosbee JW, Kuhni-Kaminski E, Larson PA, Lester JW. **ACR guidance document on MR safe practices: 2013.** **Journal of Magnetic Resonance Imaging. 2013 Mar 1;37(3):501-30.** **(selected)**	a. Pregnant patients can be accepted to undergo MR scans at any stage of pregnancy if, in the determination of a level 2 MR personnel-designated attending radiologist, the risk–benefit ratio to the patient warrants that the study be performed. The radiologist should confer with the referring physician and document the following in the radiology report or the patient's medical record: 1. The information requested from the MR study cannot be acquired by means of nonionizing means (e.g., ultrasonography). 2. The data is needed to potentially affect the care of the patient or fetus during the pregnancy. 3. The referring physician believes that it is not prudent to wait until the patient is no longer pregnant to obtain this data. b. MR contrast agents should not be routinely provided to pregnant patients. This decision too, is on that must be made on a case-by-case basis by the covering level 2 MR personnel-designated attending radiologist who will assess the risk–benefit ratio for that particular patient.
Trembley E, Therasse E, Thomassin N et al. **Quality Initiatives Guidelines for use of medical imaging during pregnancy and lactation** **Radiographics 2012; 32: 897-911.**	**Iodinated Contrast Agents During Pregnancy** Considerations: • Data on fetal exposure to iodinated contrast agents are scarce • No malformation or side effects have been reported in newborns • Iodinated products given during pregnancy may induce neonatal hypothyroidism Recommendations: • Screening newborns for hypothyroidism during the 1st week of life is standard pediatric practice • Iodinated contrast agents must be essential for making the diagnosis • Informed consent as to the risk and benefits of the procedure is recommended • Use of topical iodine is contraindicated. **Iodinated Contrast Agents During Lactation** Consideration: • Dose of iodinated contrast agents in breast mild absorbed by the infant is 0.5% of the maternal dose • Breastfeeding after the injection of iodinated contrast agent is safe Recommendations: • Concerned mothers may be instructed to discard breast milk for 24 hours after injection to eliminate fetal exposure to contrast agent • Use of topical iodine is contraindicated because free iodine excretion may induce neonatal hypothyroidism **Gadolinium-based Contrast Agents During Pregnancy** Considerations: • Few studies have evaluated fetal exposure to gadolinium • There have been no studies on long-term risks in humans • Free gadolinium could potentially lead to neurotoxicity Recommendations: • Consensus is that gadolinium, should not be used during pregnancy unless the benefits outweigh the risk **Gadolinium-based Contrast Agents During Lactation**

Guideline	Recommendations
	Consideration: • About 0.01% of the maternal gadolinium dose is excreted into breast milk • Breastfeeding after the injection of gadolinium-based contrast agent is safe Recommendations: • Concerned mothers may be instructed to discard breastmilk for 24 hours after injection to eliminate fetal exposure to contrast agent
Austin LM, Frush DP **Compendium of national guidelines for imaging the pregnant patient.** **American Journal of Roentgenology. 2011;197(4):W737-46.**	A compendium of resources representing national organization guidelines related to imaging of the pregnant patient, was compiled.
2009 Health Protection Agency, Royal College of Radiologists and College of Radiographers. Protection of Pregnant Patients during Diagnostic Medical Exposures to Ionising Radiation **http://www.who.int/tb/advisory_bodies/impact_measurement_taskforce/meetings/prevalence_survey/imaging_regnant_hpa.pdf**	1. The radiation dose to the embryo or fetus that is likely to result from any diagnostic procedure in current use should present no risk of causing fetal death, malformation, growth retardation or impairment of mental development. 2. For the majority of diagnostic medical procedures, giving fetal dose up to about a milligray, the associated risks of childhood cancer are very low (<1 in 10,000) and judged to be acceptable when compared to the natural risk (around 1 in 500). Consequently, all such examinations can be carried out on pregnant women, as long as they have been clinically justified and the dose is kept to a minimum consistent with the diagnostic requirements. The very low risks of childhood cancer from these examinations are certainly not sufficient to justify termination of the pregnancy (particularly in view of the associated risks to the health of the mother). 3. Exposure of pregnant women to higher dose procedures leads to fetal doses in excess of a few milligray, and-at the highest doses-may result in a doubling of childhood cancer risk compared to the natural rate. Consequently, such examinations should be avoided on pregnant women, if this can be achieved without serious detrimental effects to their health. However, if such examinations are considered to be clinical justified or are carried out inadvertently, the childhood cancer risk associated with them is still low in absolute terms (<1 in 200 and mostly <1 in 1000) and termination of the pregnancy would not be justified solely on the basis of the radiation risk to the unborn child. 4. For most diagnostic exposures in women in the first three to four weeks post conception when pregnancy is unrecognized, the risks of childhood cancer will be very small (and probably much smaller than if the exposure had occurred later in pregnancy). However, those few examinations yielding fatal doses in excess of about 10 mGy could involve levels of risk that should be avoided, if possible, even in unrecognized pregnancies. 5. Radiation doses resulting from diagnostic procedures in pregnancy present a negligible risk of causing radiation-induced hereditary disease in the descendants of the unborn. 6. Guidance is provided in the document on the practical implementation of the above advice in the everyday practice of diagnostic radiology and nuclear medicine.
American College of Radiology. ACR practice guideline for imaging pregnant or potentially pregnant adolescents and women with ionizing radiation. Reston, Va: American College of Radiology. 2008.	No specific recommendations. The guideline addresses the imaging of pregnant and possibly pregnant adolescents and adult women with X-rays (i.e., planar radiography, fluoroscopy, and computed tomography). It does not address issues for nuclear medicine, the lactating woman, or safety issues regarding the use of iodinated contrast or gadolinium contrast during imaging.

Guideline	Recommendations
Chen MM, Coakley V, Kaimal A, Laros RK **Guidelines for computed tomography and magnetic resonance imaging use during pregnancy and lactation** **Obstetric & Gynecology 2008; 112(2) Part 1: 333-40.**	**Key points:** 1. Teratogenesis in the fetus is not a major concern after diagnostic pelvic CT studies 2. Carcinogenesis in the fetus is a key concern after diagnostic pelvic CT studies; hence CT of the fetus should be avoided in all trimester of pregnancy unless absolutely necessary 3. It is exceptionally unlikely that any single diagnostic radiological study would deliver a radiation dose sufficient to justify pregnancy termination 4. Use of iodinated contrast seems safe in pregnancy and should be administered in the usual fashion. This is preferable to repeating a CT study because the initial examination was non-diagnostic due to lack of intravenous contrast administration 5. Although most studies evaluating MRI safety during pregnancy show no ill effects, it is good practice to avoid MRI during pregnancy, particularly for elective studies or during the first trimester. 6. Intravenous gadolinium is contraindicated in pregnancy and should be sued only if absolutely essential 7. Lactating women who receive iodinated contrast or gadolinium can continue breast-feeding without interruption 8. Computed tomographic pulmonary angiogram is the preferred modality for imaging of suspected pulmonary embolism
Amis ES, Butler PF, Applegate KE, Birnbaum SB, Brateman LF, Hevezi JM, Mettler FA, Morin RL, Pentecost MJ, Smith GG, Strauss KJ. American College of Radiology white paper on radiation dose in medicine. **American College of Radiology White Paper on Radiation Dose in Medicine** **J Am Coll Radiol 2007;4:272-284. (selected)**	**Measurement** 1. The ACR should adopt the policy of expressing quantitative radiation dose values as dose estimates and replace the term *dose* with *dose estimate* as ACR publications are revised. 2. The ACR should support the development of a national database for radiation dose indices to address the actual range of exposures for x-ray examinations. **Radiologists** 1. The ACR should support the current multiorganizational effort to improve radiology resident training in medical physics. 2. The ACR should include additional questions on radiation safety and patient dose in its Annual In-Training 3. Examination. 4. The ACR should request that the American Board of Radiology consider requiring at least 1 self-assessment 5. Module on patient safety, to include radiation dose, every 10 years as an integral part of the maintenance of certification. 6. The ACR should develop and implement maximum radiation dose estimate pass/fail criteria for the ACR CT 7. Accreditation Program. 8. The ACR should review and update the CT Accreditation Program's recommended scanning protocols on a routine basis and make them available on its Web site. 9. The ACR should create a prominent safety link on its Web site's home page to facilitate access to this information and to demonstrate the priority given to patient safety. 10. The ACR should include in its *Practice Guidelines and Technical Standards* additional considerations for special radiosensitive populations, such as children and **pregnant and potentially pregnant women.** 11. The ACR should encourage radiology practices to record all fluoroscopy times, compare them with benchmarks, and evaluate outliers as part of ongoing quality assurance programs.

Guideline	Recommendations
	12. The ACR should encourage radiology practices to define a surveillance mechanism to identify patients with high cumulative radiation doses due to repeated imaging.

Evidence Tables

Safety of Ionizing Radiation Associated with Diagnostic Tests during Pregnancy

Study/Type	Sample Description	Method	Outcomes	Key Findings and Recommendations
X-rays				
Rajaraman et al. 2011 **UK** **Case-control study**	2,690 cases from the UK Childhood Cancer Study, born 1976-96, aged ≥14 years, diagnosed between 1992-96, with a confirmed malignancy or tumour of the central nervous system. Median age was 5.7 years, 56% were male. 4,857 controls matched for age and sex from the same regions as the cases. Median age was 5.5 years, 55% were male.	Information related to social, occupational and medical histories was obtained from the parents or guardians of participating children through interview and/or review of medical records, including in utero and neonatal exposure to X-rays and ultrasound.	All cancers, Leukemia, Lymphoma, and cancers of the brain/CNS Models were adjusted for maternal age and birth weight.	There were 319 radiographic examinations conducted in utero; the most of which were pelvimetry (64% of all exams). All cancer: the odds were non-significantly increased in cases (4.46% vs. 3.81%, OR= 1.14, 95% CI 0.91-1.45). In sub group analysis by timing of exposure (T1, T2, T3), the odds of cancer given exposure to diagnostic radiation were not increased significantly Leukemia: the odds were non-significantly increased in cases (1.78% vs. 1.28%, OR= 1.36, 95% CI 0.91-2.02) Lymphoma: the odds were non-significantly increased in cases (0.60% vs. 0.62%, OR= 1.06, 95% CI 0.55-2.06) Brain/CNS cancer: the odds were non-significantly increased in cases (0.93% vs. 0.84%, OR= 1.06, 95% CI 0.64-1.77)
Wafeford 2008 **UK** **Review**	NA	A pooled estimate is provided using the results from 32 case-control studies, published from 1959-2005. These studies examined the association between antenatal exposure to diagnostic ionizing radiation (mainly X-rays of the abdomen) .and the incidence of childhood leukemia. Few details are provided of the cases/controls or the exposures of interest.	Incidence of childhood leukemia.	The total number of cases was 387. The risk of leukemia was increased significantly in 6/32 of the individual studies. Overall, the (unadjusted) risk of leukemia was increased significantly (RR=1.32, 95% CI 1.19-1.46).
Schulze-Rath et al. 2008	19 case-control and 6 cohort studies, published from 1990-2006 that examined	Data from each study including type of	Leukemia, Non-Hodgkin lymphoma, tumours of the	**Case-control studies** 8 case control studies investigated prenatal X-ray

Study/Type	Sample Description	Method	Outcomes	Key Findings and Recommendations
Germany **Systematic Review**	pregnant women and children <18 years who had been exposed to low doses of ionizing radiation for diagnostic purposes. The recruitment period ranged from 1936-1998.	diagnostic procedure, target organ, pre-and/or postnatal exposure, was compiled and the results pooled. Exposure ascertainment was assessed using hospital records or standardized interviews. Exposure was classified as X-rays yes vs. no and/or number of X-rays in most studies (n=23), while an estimation of organ dose was reported in 2 studies. Target organs were not reported or involved the pelvis or abdomen in the majority of studies.	CNS and solid tumours	exposure, while 8 investigated pre- and postnatal X-ray exposures. Most studies included 40 to 500 cases. The odds of leukemia were not increased significantly given prenatal exposure to X-rays (OR=0.99; 95% CI 0.87-1.13), using the results from 9 studies. Pooled results were not conducted for any of the other outcomes, although their odds were not increased significantly with X-rays exposure in any of the individual studies (Non-Hodgkin lymphoma n=3; tumours of the CNS n=4; and solid tumours n=3). **Cohort studies** No cohort studies examined the association between pre-natal X-rays and cancer incidence in childhood.
CT and MRI Scans				
Ray et al. 2016 **Canada** **Retrospective study**	1, 424,105 infants born in Ontario from 2003-2015 to mothers aged 16-50 years, of whom 5,654 were exposed to MRI during pregnancy (1,418,451 not exposed). Participants were assembled into 2 cohorts Cohort 1: All women who had an MRI during the first trimester of pregnancy (weeks 2-14) Cohort 2: All women who had a gadolinium-enhanced MRI during pregnancy (weeks 2 until 2 days before birth)	The safety of MRI during pregnancy was evaluated by comparing the pregnancy outcomes of women exposure to MRI with non-exposed women, using information contained in national databases. Adjustment for potential confounders was achieved through regression models using propensity scores.	**Cohort 1:** Stillbirth after 20 weeks' gestation or neonatal day within 28 days, any congenital abnormality, neoplasm, vision loss and hearing loss, assessed before 4 years of age **Cohort 2:** Nephrotic Systemic Fibrosis (NSF), or a broader outcome including rheumatologically, inflammatory and infiltrative skin conditions	5,654 women were exposed to MRI during pregnancy (rate of 3.97/1,000 pregnancies) **Cohort 1:** 1,737 of all MRIs occurred in the 1st trimester (rate of 1.2/1,000 pregnancies). The adjusted risk of neonatal deaths was not significantly increased in the MRI exposed group (10.9/1,000 MRI vs. 6.9/1,000 non-MRI, RR=1.68, 95% CI 0.97-2.90, adjusted risk difference=4.7/1,000, 95% CI -1.6-11.0 person-years). The risk of congenital abnormalities was not significantly increased in the offspring of women in the MRI-exposed group, who were followed for an average of 3.6 years (33.8/1,000 person-years, MRI vs. 24.0/1,000 person-years, non-MRI, HR=1.16, 95% CI 0.96-1.40, adjusted risk difference=3.8/1,000 person-years, 95% CI -1.0-9.6). The risks of hearing or vision loss were not increased significantly for the offspring of women in the MRI exposed group (adjusted HR=1.50, 95% CI 0.94-2.40

Study/Type	Sample Description	Method	Outcomes	Key Findings and Recommendations
				and HR-1.04, 95% CI 0.75-1.45, respectively). The risk of any neoplasm was not increased significantly for the offspring of women in the MRI exposed group (adjusted HR=0.53, 95% CI 0.08-3.67). **Cohort 2:** 397 gadolinium-enhance MRIs occurred in any trimester (rate of 0.3/1,000 pregnancies). The rate of stillbirth/neonatal death was significantly higher in the gadolinium MRI group (17.6 vs. 6.9/1,000 person-years, adjusted RR=3.70, 95% CI 1.55-8.85, risk difference= 47.5, 95% CI 9.7-138.2 person-years). The rate of NSF-like conditions was not increased significantly in the gadolinium MRI group (3.3 vs. 1.8/1,000 person-years, adjusted RR=1.00, 95% CI 0.33-3.02). The rate of broader rheumatologically, inflammatory and infiltrative skin conditions was significantly higher in the gadolinium MRI group (125.8 vs. 93.7/1,000 person-years, adjusted RR=1.36, 95% CI 1.09-1.69, risk difference= 45.3, 95% CI 11.3-86.8 person-years).
Choi et al. 2015 **Korea** **Case series**	15 consecutive women who had undergone an MRI within the first trimester of a pregnancy that they were unaware of, at the time the test was conducted. Two women received gadolinium as a contrast agent. Mean age was 30.4 years.	Women were followed until delivery	Any malformations	Mean gestational age at the time of exposure was 3.8 weeks. Location of scans was head (n=5), cervical spine (n=4), lumbar spine (n=4), pelvis (n=1) and knee (n=1). 15 babies were delivered spontaneously (mean 38.8 weeks' gestation). Birth weight, length and head circumference were within normal limits. There were 2 cases of major birth defects, a male baby born without a kidney not visualized on ultrasound examination and a female born with an overlapping toe on the right foot.
Brass et al. 2007 **USA** **Narrative**	NA	NA	NA	Recommendations on using head MRI and CT in pregnancy: 1. Discuss and documents indications, risks, and benefits and alternatives with patients 2. Involve and inform the radiologist and obstetrician when deciding CT and MRI in the pregnant

Study/Type	Sample Description	Method	Outcomes	Key Findings and Recommendations
Review				patients; some CT and MRI examinations can be modified to provide diagnostically critical information while exposing the embryo or fetus to as little risk as possible 3. MRI is thought to be preferable to CT, although conclusive data to this effect are not available 4. During head CT examination of the mother, the fetus is exposed only to radiation that is scattered through the body; therefore, shielding of the abdomen does not significantly reduce the minimal fetal radiation dose, but may help alleviate maternal anxiety 5. Delay elective MRI until after pregnancy 6. Avoid MRI in the first trimester unless no alternative exists. 7. Iodinated contrast is rated by the FDA as a category B drug 8. Avoid gadolinium in pregnancy unless no alternative exists – gadolinium is rated by the FDA as category C drug. Effect of irradiation (or medical radiation) during fetal period of development: unlikely to result in gross malformation, mild microcephaly may occur, risk of mental retardation 4 times greater in the 8-to-15 week period than in the 15-to-25 week period, dose threshold of ~12 to 20 rad, below which excess incidence of mental retardation is not likely to be seen, increased risk of childhood cancer, specifically leukemia among children exposed to as little as 1 to 2 rads in utero, increased risk is dose-dependent, measuring 6% per 100 rads For children of patients who have to go diagnostic neuroimaging procedure during pregnancy, there is an extremely small added risk; multiple CT scans of the lumber spine would only minimally increase the natural risk of childhood cancer. Estimated fetal radiation dose (rad): Head CT - <0.01 Lumbar spine CT 0.28-2.4 (depending on whether fetus is directly irradiated) Exposure due to background radiation during entire gestation (for comparison) – 0.225

Study/Type	Sample Description	Method	Outcomes	Key Findings and Recommendations
				Exposure during round-trip cross-country trip (for comparison) – 0.005
Contrast Agents				
De Santis et al. 2007 **Italy** **Prospective Study**	26 women who had been exposed to gadopentetate during the first trimester of pregnancy, who had undergone an MRI. Mean age was 31 years.	All patients were followed by phone interview during pregnancy and one month after delivery	Pregnancy outcome	There were 2 miscarriages, 1 elective abortion and 23 term deliveries. There were no preterm deliveries MRI exposures were CNS (n=17). Pelvis (n=2), spine (n=5), thorax (n=1) and abdomen (n=1). Six patients were exposed to X-rays, including one to whole body CT. Two pregnancies were complicated by low birth weight infants. There were no neonatal complications. Mean birth weight was 3,219 g.

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