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REVIEW

Risks to the fetus from diagnostic imaging during pregnancy: review and proposal of a clinical protocol

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Abstract Every day, medical practitioners face the dilemma of exposing pregnant or possibly pregnant patients to radiation from diagnostic examinations. Both doctors and patients often have questions about the risks of radiation. The most vulnerable period is between the 8th and 15th weeks of gestation. Deterministic effects like pregnancy loss, congenital malformations, growth retardation and neurobehavioral abnormalities have threshold doses above 100–200 mGy. The risk is considered negligible at 50 mGy and in reality no diagnostic examination exceeds this limit. The risk of carcinogenesis is slightly higher than in the general population. Intravenous iodinated contrast is discouraged, except in highly selected patients. Considering all the possible noxious effects of radiation exposure, measures to diminish radiation are essential and affect the fetal outcome. Nonionizing procedures should be considered whenever possible and every radiology center should have its own data analysis on fetal radiation exposure. In this review, we analyze existing literature on fetal risks due to radiation exposure, producing a clinical protocol to guide safe radiation use in a clinical setting.

Keywords Diagnostic imaging · Fetal risks · Fetus · Pregnancy · Radiation

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Introduction

Medical practitioners frequently face the dilemma of exposing pregnant or possibly pregnant patients to radiation from diagnostic examinations [1–3]. In fact, irradiation of the fetus occurs more commonly than suspected [1], and one should be aware of the implicated risks [4].

There are many circumstances for fetal exposure to radiation. The most frequent one, especially during the first trimester, is accidental as the patient is not aware of the pregnancy [5–11]. To this, we add the rare need of an urgent medical diagnosis of the mother (at any given time during gestation) and exceptionally of the fetus (to confirm an abnormality or to provide further information, usually after ultrasound during the second and third trimesters). This irradiation during pregnancy more frequently results from diagnostic need in the mother and/or fetus, if no alternative to ionizing radiation is available [1]. Special consideration should be granted to pregnant radiology staff as the level of exposure is not negligible [6, 7, 11].

Important information regarding the effects of radiation exposure on the fetus comes from nuclear accidents in world history. Survivors of the atomic bombs of Hiroshima and Nagasaki have shown risks of fetal exposure to radiation, the most common one being microcephaly starting from 100 to 200 mSv [5, 12–14]. IQ changes were also observed among survivors (20–30 IQ points reduced per 100 rad; 25–31 IQ points reduced per Gy above 0.1 Gy) [12, 13, 15, 16], as well as growth retardation (permanent above 250 mSv, 25 rad or 0.25 Gy) [5, 13], teratogenesis (above 1 Gy) and childhood cancer (increased rate of leukemia) [13]. Studies on cancer after intrauterine exposure to the atomic bomb are inconsistent [17]. The Chernobyl reactor accident was also associated with increased rate of cancer [13]. Studies on children exposed to

radiation before 15 weeks of gestational age showed a higher susceptibility to these effects [12].

Ionizing radiation has been frequently used with the purpose of achieving a medical diagnosis since the discovery of X-rays [18] and is still a helpful tool. In recent years, there has been a greater focus on developing new techniques and methods to decrease the risk of radiation exposure to pregnant women as well as to the fetus [4, 19].

Both doctors and patients often question the risks of radiation. Therefore, creating a guideline is not only a useful tool for every medical practitioner, but also a necessity [1]. The main objectives of this systematic review are to analyze existing literature on the risks of radiation exposure and the safety of contrast agents. In addition, a clinical protocol is proposed to guide radiation exposure in a clinical setting.

Materials and methods

The present article is a systematic review that aims to analyze existing literature on the fetal risks from radiation exposure during pregnancy. An initial query was made on PubMed: "Diagnostic radiography in pregnancy AND radiation," with the limits "published from January 1st 1993 to December 31st 2013, in English or Portuguese." This research yielded 381 articles. Those that reflected the same objective as intended in this systematic review were analyzed according to their medical subject heading (MESH) terms. Gathering the most frequent MESH terms led to the final query: "((radiation) AND pregnancy) AND diagnostic imaging." On April 15, 2014, the total number of articles retrieved from this research on PubMed was 1,462. After applying the same restrictions based on publication date and language, 688 articles remained, 261 of them reviews. The same query and research limits were applied on SCOPUS, gathering an additional 245 articles (Fig. 1). After reading and analyzing the title and abstract, when available, 635 were excluded.

The main inclusion criteria considered were:

- Radiation doses absorbed by the fetus.
- Risks of radiation from diagnostic examinations to the fetus.
- Protection measures for diagnostic radiology examinations in pregnant women.

The following excluding criteria were also used:

– Studies on radiotherapy.
– Studies on occupational hazards of radiation.
– Risks of ultrasound.
– Discussion of ethical problems regarding radiation usage.

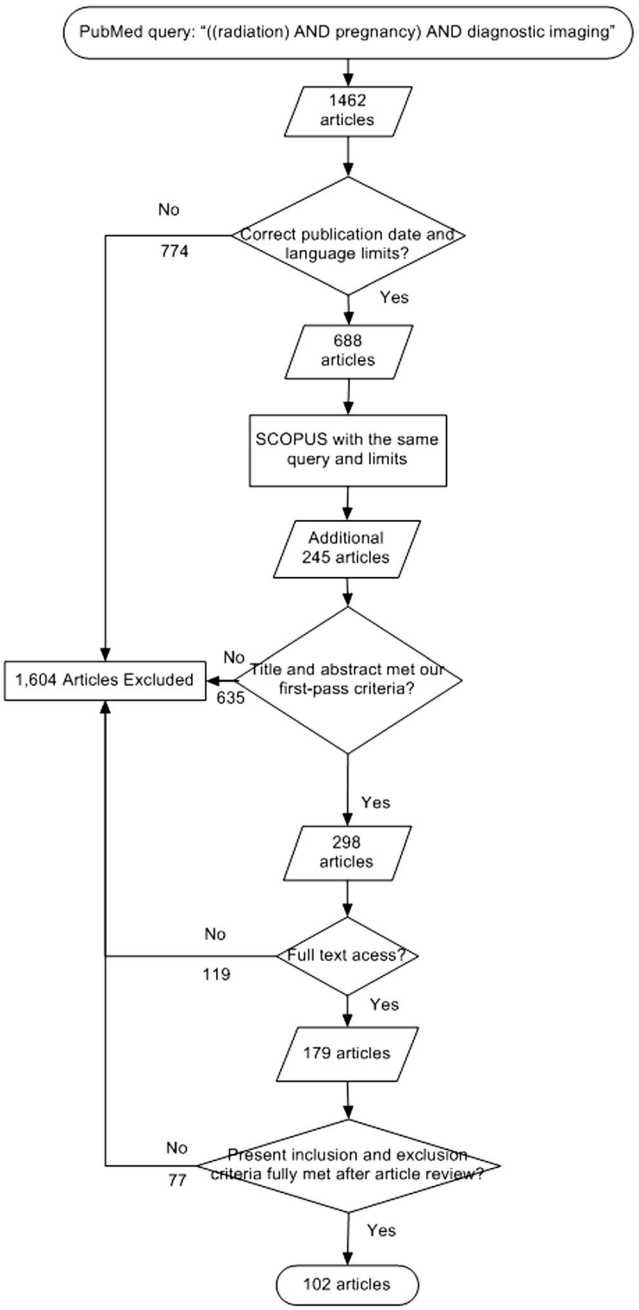

Fig. 1 Literature search strategy and results

– Molecular studies of radiation rather than clinical ones.
– Articles with an iconographic purpose.
– Studies on animals rather than humans.
– Studies with the objective of comparing diagnostic examinations for specific pathologies regardless of the risks for the fetus (for example: comparison of sensitivity and specificity of two different diagnostic examinations).

Of the 298 final articles, 179 allowed access to full text. Our institution had no access to the 119 articles excluded here

(all required payment) and the selected articles that appeared to meet the variables considered did not present a clear alternative access. The remaining articles were analyzed according to different variables: dosages of radiation absorbed by the fetus according to the irradiated area of the pregnant woman, effects and safety limits of radiation. For this, we used the inclusion and exclusion criteria once more, this time to evaluate the articles in full. Finally, a total of 102 articles were retained for use, including one regarding in utero exposure from atomic bombs to show the importance of these early studies (Fig. 1). Due to the time limits imposed, this kind of early article was not included in the initial PubMed research. The PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) statement was followed for the construction of this systematic review. As a result of our research from the literature, a protocol for medical use was designed.

Dosage of radiation to the fetus

Background radiation varies between 1.3 and 5.8 mSv/year [20] worldwide, with the average annual effective dose of about 3.6 mSv (0.36 rem) for an adult [3, 15, 21, 22] and 0.5-1 mSv or 1.1-2.5 mGy [23, 24] for a fetus during the entire period of gestation [3, 25–28]. The fetus is more radiosensitive than the mother [28, 29].

If a pregnant woman is in need of medical care and, to achieve diagnosis, requires the use of a diagnostic procedure that will expose her unborn child to radiation, we need to take into account not only the type of energy but also the quantity of photons, size of the patient and vulnerability of irradiated tissues. However, quantifying the dosage delivered to the fetus is not an easy task [21, 30].

In radiographic and fluoroscopic examinations, if the uterus is outside the field of view, the fetus is only exposed to scatter radiation in small doses [32, 32]. Therefore, the fetal exposure increases if the uterus is within the field of view. It appears that posteroanterior chest X-rays expose the fetus to less radiation than the anteroposterior projection [32] (Tables 1 and 2). The dosage applied to the fetus in radiography depends on the patient thickness, the direction of projection, the depth of the fetus from the skin surface and radiographic factors [25, 37].

Maximum exposure of the fetus to radiation comes from abdominal computed tomography (CT) [18, 25]. However, the dosage is small and the patient can benefit significantly from the examination [25] (Tables 1 and 2). If the abdomen is not in the field of view, the fetus is only exposed to scatter radiation [24]. The fetal radiation dose from a CT depends on kilovolt peak, milliamperes, slice thickness [38], gestational age, the depth of the fetus and proximity of the uterus to the field of interest [25, 34] (Tables 1 and 2).

The mean effective dose of radiation for each procedure to the mother, the fetal exposure, the fetal equivalent dose (Table 3) and the number of examinations needed to reach the accepted cumulative dose of fetal exposure (Table 4) are presented. The measurements vary extensively and each radiology department should be aware of its own statistics.

The absorbed dose of radiation relates to the energy deposited per unit mass of tissue for a given procedure and provides a means to assess the potential for biological effects. It is measured in gray (Gy) or rad (the latter being the oldest unit currently used) [9, 13, 37, 39]. The absorbed dose rate is the amount of energy deposited in a given period of time and is typically measured in units of milligrays per minutes or hours [37]. Roentgen-equivalent man (rem) is the equivalent unit of exposure or effective dose, therefore, the number of ions produced per kilogram of air [3, 13, 37, 39]. Exposure can also be expressed in coulombs/kg (C/kg) [3].

The relative effective dose or the equivalent dose is the product of the absorbed dose and the radiation weighting factor (a measure of the quality of the radiation, determined by the tissue or organs exposed as well as the type of radiation involved) and gives us the dose limits measured in sievert (Sv) or in rem [3, 13, 38–40]. The effective dose, in Sv, takes into account the location where the radiation is absorbed and attempts to estimate the whole-body dose that would produce the same risk as the radiology procedure [40].

Absorbed dose provides little information on biological effects since it lacks relation to the type of tissues involved. We can use it to compare the amount of radiation to which the body is exposed from the various diagnostic examinations. A more useful measure is the effective dose because it takes into account the weighting factor, specific for each kind of tissue [4].

The different units used in diagnostic examinations have the following conversions [3, 38, 39]:

$$1\ \text{Gy} = 100\ \text{rad} = 1\ \text{Sv} = 1,000\ \text{mGy} = 1\ \text{Joule}/\text{kg}$$
$$1\ \text{mGy} = 1\ \text{mSV}$$
$$1\ \text{rad} = 1\ \text{rem} = 1\ \text{cGy} = 10\ \text{mSV}$$

Risks to the fetus from radiation of diagnostic examinations

When using radiation, we have to consider two kinds of effects: deterministic and stochastic. Deterministic effects are those in which severity increases with the dose of radiation, having a threshold dose below which its effect is clinically irrelevant. For radiation to have an effect on the fetus, the threshold dose must be reached. Above this limit,

Table 1 Fetal exposure, fetal equivalent and effective doses for radiography and fluoroscopic examinations

		Fetal exposure (mGy)				Fetal equivalent (mSv)	Effective dose (mSv)		
Article exam		McCollough, Schueler et al. [25]	Toppenberg, Hill et al. [9]	Helmrot, Petterson et al. [33]	Damilakis, Perisinakis et al. [31]	Parmaksiz, Atac et al. [18]	Lockwood, Einstein et al. [21]	Goodman and Amurao [4]	Parmaksiz, Atac et al. [18]
Radiographic and fluoroscopic examinations									
Cervical spine (AP, lat)		<0.001				0			0.1 (0.007-0.2)
Extremities		<0.001	0.01						
Chest (PA, lat)		0.002	0.0007	0.001	0.0013-0.0138		0.06	0.02	
Chest (AP)				<0.001	0.0014-0.024	1.4 (0.001-8.7)			1.4 (0.1-4.3)
Thoracic spine (AP, lat)		0.003							
Abdomen (AP): patient thickness	21 cm	1	2.45	0.31-0.63	0.0021-0.036 (0.0006-0.107)	3.5 -7.6 (1.2-14)			1.6-4.5 (0.4-8.5)
	33 cm	3							
Lumbar spine (AP, lat)		1	3.59	0.91-1.75		0.9-2.7 (0.4-5.3)	2.1		0.4-0.9 (0.2-1.3)
Pelvis			2.5	0.66-0.72		1.8 (0.7-2.9)		0.6	1 (0.4-1.5)
Small bowel study		7					15		
Double contrast barium enema study		7	39.86	7.8			8.7	8	
Mammography							0.6	0.4	
Ventilation-perfusion scan			2.15				6.8		

AP anteroposterior, *Lat* lateral, *PA* posteroanterior

Table 2 Fetal exposure, fetal equivalent and effective doses for computed tomography – metanalysis of published results

Article Exam	Fetal exposure (mGy)					Fetal equivalent (mSv)	Effective dose (mSv)		
	McCollough, Schueler et al. [25]	Wieseler, Bhargava et al. [35]	Toppenberg, Hill et al. [9]	Hurwitz, Yoshizumi et al. [36]	Helmrot, Petterson et al. [33]	Parmaksiz, Atac et al. [18]	Lockwood, Einstein et al. [21]	Goodman and Amurao [4]	Parmaksiz, Atac et al. [18]
CT									
Head CT	0		0.5				1.8		
Chest CT routine	0.2	0.02			0.21	0.04 (0.03-0.06)	7.8		3.9 (2.3-5.4)
Chest CT pulmonary embolus	0.2	0.02		0.24-0.66					
Lumbar spine			35						
CT angiography of coronary arteries	0.1						10		
Abdominal routine	4	1.3	26			28 (7.3-98)	7.6		24.5 (4.3-86)
Abdominal/pelvis	25	13						21	
CT angiography of aorta (chest through pelvis)	34	13							
Abdomen/ pelvis, stone protocol	10	11	13.98	Early 1st T: 4–7.2 End 1st T: 8.5-11.7	13.8-15.8		44.1		

1st T first trimester

Table 3 Mean and maximum of fetal exposure, fetal equivalent and effective doses

		Fetal exposure (mGy)		Fetal equivalent (mSv)		Effective dose (mSv)	
Radiographic, fluoroscopic and scintigraphic examinations							
Examination		Mean	Maximum	Mean	Maximum	Mean	Maximum
Cervical spine (AP, lat)		-	0.001	-	0	0.1	0.2
Extremities		0.0055	0.01				
Chest (PA, lat)		0.00281	0.0138			0.04	0.6
Chest (AP)		0.00685	0.024	1.4	8.7	1.4	4.3
Thoracic spine (AP, lat)		-	0.003				
Abdomen (AP): patient thickness	21 cm	0.99345	2.45	5.55	14	3.05	8.5
	33 cm	-	3				
Lumbar spine (AP, lat)		1.973	3.59	1.8	5.3	1.375	2.1
Pelvis		1.595	2.5	1.8	2.9	0.8	1.5
Small bowel study		-	7			-	15
Double contrast barium enema study		18.22	39.86			8.35	8.7
Mammography						0.5	0.6
Ventilation-perfusion scan		2.15	2.15			-	6.8
CT							
Exam		Mean	Maximum	Mean	Maximum	Mean	Maximum
Head CT		0.25	0.5			-	1.8
Chest CT routine		0.143	0.21	0.04	0.06	5.85	7.8
Chest CT pulmonary embolus		0.223	0.66				
Lumbar spine		-	35				
CT angiography of coronary arteries		-	0.1			-	10
Abdominal routine		10.43	26	28	98	16.05	86
Abdominal/Pelvis		19	25			-	21
CT angiography of aorta (chest through pelvis)		23.5	34				
Abdomen/pelvis, stone protocol		11.526	15.8			-	44.1

AP anteroposterior, *Lat* lateral, *PA* posteroanterior

the severity of the effect increases with the dose [3, 5, 13, 16, 32, 35, 38, 41–49]. Stochastic effects are those in which the probability of occurrence increases with the dose, not taking into consideration a threshold dose because the result is the same (acting on one single cell or a group of them). The severity of the effect is dose-independent [3, 5, 13, 16, 21, 32, 35, 38, 42–49]. The effects of radiation on the fetus depend on the stage of the pregnancy, radiation dose [5, 8, 11, 13, 15, 23, 32, 50–52] and fetal cellular repair mechanisms [25]; demographic factors (patient age and weight), medical history factors (coexisting diseases, genetic factors, medication use and radiation history) and procedure factors influence as well [3, 16, 23, 28, 45, 46, 53]. We can divide the fetal effects of radiation into:

1. Pregnancy loss.
2. Congenital malformations (teratogenesis) [21, 38].
3. Neurobehavioral abnormalities [13].
4. Fetal growth retardation [9, 41, 54].
5. Carcinogenesis [9, 21, 38, 41, 54, 55].

The risk is considered to be negligible at 50 mGy or less [3, 5, 8, 13, 15, 16, 23, 28, 43, 47, 56] and diagnostic examinations have lower doses [3, 23, 24, 42, 49, 52, 56, 57]. Deterministic effects have thresholds greater than 100–200 mGy (below are considered safe) [14, 32, 49, 58, 59] and the most crucial time to avoid radiation exposure is from the 8th to the 15th week of gestation [60]. Measuring the dosage of exposure is important to determine the risk to the fetus [28, 61].

Pregnancy loss

At the beginning of every pregnancy, the risk of spontaneous miscarriage is about 15% [3, 16, 24, 32, 41]. After conception and during preimplantation and preorganogenesis, the embryonic cells are omnipotential. This means that it is unlikely for malformations to occur due to the effects of ionizing radiation during these stages. Other cells can replace adjacent cells that have been deleteriously affected. This period is called “the all-or-none period” [11, 13, 14, 41, 53].

Table 4 Number of radiographic, fluoroscopic, scintigraphic and CT examinations needed to reach 50 mGy of fetal exposure (the accepted cumulative dose)

Radiographic, fluoroscopic and scintigraphic examinations				
Examination	Mean exposure dose	Number of examinations to reach fetal exposure of 50 mGy	Maximum exposure dose	Number of examinations to reach fetal exposure of 50 mGy
Cervical spine (AP, lat)	-	-	0.001	50,000
Extremities	0.0055	9,090.9	0.01	5,000
Chest (PA, lat)	0.00281	17,793.6	0.0138	3,623.2
Chest (AP)	0.00685	7,299.3	0.024	2,083.3
Thoracic spine (AP, lat)	-	-	0.003	16,666.7
Abdomen (AP) 21 cm patient thickness	0.99345	50.3	2.45	20.4
Abdomen (AP) 33 cm patient thickness	-	-	3	16.7
Lumbar spine (AP, lat)	1.973	25.3	3.59	13.9
Pelvis	1.595	31.3	2.5	20
Small bowel study	-	-	7	7.1
Double contrast barium enema study	18.22	2.7	39.86	1.25
Ventilation-perfusion scan	2.15	23.25	2.15	23.25
CT				
Exam	Mean exposure dose	Number of exams to reach fetal exposure of 50 mGy	Maximum exposure dose	Number of exams to reach fetal exposure of 50 mGy
Head CT	0.25	200	0.5	100
Chest CT routine	0.143	349.65	0.21	238.1
Chest CT pulmonary embolus	0.223	224.2	0.66	75.75
Lumbar spine	-	-	35	1.4
CT angiography of coronary arteries	-	-	0.1	500
Abdominal routine	10.43	4.79	26	1.9
Abdominal/Pelvis	19	2.6	25	2
CT angiography of aorta (chest through pelvis)	23.5	2.1	34	1.5
Abdomen/pelvis, stone protocol	11.526	4.3	15.8	3.2

The mean and maximum exposure doses were used to calculate the number of exams needed. None of the examinations presented reached the accepted level with one single exposure

AP anteroposterior, *Lat* lateral, *PA* posteroanterior

If the exposure to radiation exceeds 100 mGy or 100 mSv during the first 2 weeks after conception, the "all-or-none" phenomena can result in spontaneous abortion instead of a completely unaffected embryo [3, 5, 11, 14, 16, 20, 28, 38, 43, 48, 49, 52, 53]. From the 4th to 8th week of gestation, the threshold goes up to 150 mGy [46], 200 mGy [49] or 250 mGy and 500 mGy [41, 56]. After 26 weeks the risk of neonatal or fetal death rises with doses above 1Gy, with a threshold of 100 mGy [38, 39, 62].

Exposure to less than 5 rad (50 mGy) has not been associated with increased fetal anomalies or pregnancy loss [25, 49, 50, 63]. The exposure to radiation on its own is not an indication for terminating the pregnancy [5, 9, 13, 25, 50] and should only be considered if the exposure dose is higher than 100 mGy, known as "The Danish rule" [7, 20, 24, 32, 44, 53, 59]. Some propose a limit dose of 150 mGy [8].

Congenital malformations

In every pregnancy, the background risk for birth defects is about 3% [3, 13, 16, 24, 32, 41]. The most sensitive period for malformations is from the 2nd to 8th week of gestation, during organogenesis [13, 21, 38, 54] and during the early fetal period (up to the 15th week) [11, 14], with a threshold of 100 mGy [15, 18, 23, 28, 32, 43, 52, 59, 64, 65]. Thresholds of 150 mGy [3, 8, 10, 25, 35, 66, 67], 200 mGy [3, 11, 15, 20, 41] or 250 mGy [25, 49] have been suggested. After 16 weeks, the threshold is about 500 mGy to 700 mGy [11, 49, 56]. During the last trimester, major organ malformations and functional anomalies are unlikely [13, 14]. There has been no evidence of congenital malformations at doses below 50 mGy or 5 rad, this being the accepted cumulative dose of ionizing radiation for the entire gestational period [11, 16, 20, 25, 32, 59, 61, 63]. No diagnostic examination exceeds this limit [9, 13]. The risk

of malformations is significantly increased above 150 mGy [13, 16, 26, 50]. When the dose of exposure exceeds 100 mGy, the probability of congenital birth defects increases 10% [68].

In the light of current knowledge, diagnostic radiographs, CTs or nuclear medicine procedures in isolation cannot be considered a risk for malformations [11, 20, 25, 26, 39].

Neurobehavioral abnormalities

The background risk for neurological development problems is about 1% [3, 24, 32] up to 6% [5]. The most sensitive stage for learning disability and microcephaly is from the 8th week to the 15th week of the gestation [3, 9, 11, 13, 15, 16, 41, 51, 65, 69]. Exposure prior to 20 weeks of development increases the risk of microcephaly and learning disability [13, 21]. However, from the 16th to the 25th week, the central nervous system is less radiosensitive [3, 13–15, 69]. After the 25th week, it becomes radioresistant [13].

Learning disability has a threshold of 100 mGy to 250 mGy [3, 13, 15, 16, 20, 25, 28, 43, 48, 49, 52, 63] or 120 mSv [18] and is not directly linked to microcephaly [13, 52]. Severe cases occur with higher doses: 350-500 mGy [16, 20, 41, 49] or even 1 Gy [20, 38], 120-230 mGy between the 8th and 15th weeks, 210 mGy between the 16th and 25th weeks [13]. The IQ loss is about 25 to 31 points per 1 Gy above 100 mGy of radiation [11, 15, 35, 49, 69] or 21-29 IQ points per Gy, 30 points for every Sv [13]. Eight weeks after conception, intellectual damage has not been demonstrated [65]. However, others have found that between 8 and 15 weeks, the incidence of severe learning disability establishes a linear connection without a threshold dose, with an increased risk of 40% per gray of radiation [9, 14, 15, 54, 69] or 40% per 100-200 mSv (200 mGy) [5]. After this period, the incidence is lower and doses from 20 mGy to 250 mGy may show cognitive loss [54], more common at higher doses (>=200 mGy) [58]. Between 16 and 25 weeks, the average IQ loss is approximately 13–21 points per Gy at doses above 700 mGy [13, 15, 69]. Microcephaly occurs at a threshold of 100 mGy [28], 200 mGy [52] or 350 mGy to 500 mGy [32, 41]. The different sensitivities during the gestational period with different threshold doses make it harder to understand which cases of neurobehavioral abnormalities occur due to radiation.

Based on the evidence seen so far, no diagnostic examination (radiographs, CT or nuclear medicine procedures) can cause neurodevelopment effects [20].

Fetal growth retardation

There is a 4% risk of growth retardation due to radiation exposure in all pregnancies [3, 16, 24, 32]. It occurs mainly during the first trimester, 14 days after conception [38]. Exposure to radiation during the first 20 weeks of development increases the risk of growth retardation [21]. It shows a dose threshold of 100 mGy to 250 mGy [16, 25, 48, 63], and in some studies up to 500 mGy [20, 41, 49, 56], 1 Gy [15] or 50–100 mSv [1, 15]. Growth retardation usually is not permanent and the fetus will recover [5].

Carcinogenesis

Cancer and hereditary effects after radiation exposure occur without a threshold dose [9, 17, 24, 25, 32, 53, 56, 67, 70] and appear at the same age as spontaneous ones [54], making it harder to understand which ones occur due to radiation. The risk of this occurrence is constant throughout the whole pregnancy [15, 28, 38, 52] except for the first two/three weeks of pregnancy when the risk is low [55, 65]. After radiation exposure to the fetus, there is an increase in risk for all cancers [14, 26, 30, 32, 34, 71] (including solid tumors [11, 16]) and leukemia, especially acute myeloid leukemia. However, this is not statistically significant [71].

After pelvic procedures like barium enema or CT, the carcinogenic risk is similar to the natural incidence of fatal carcinogenic risk before age 15 [14]. If the absorbed dose is 5 rad, the risk of childhood cancer is 0.3% (0.2-0.8%) – the same value as the natural risk for fatal childhood cancer [14–16, 51, 65]. The risk can be 0.06% per 10 mSv or 10 mGy [1, 28, 44] or 0.06% per 1 rad [51], 5% per Sv (100 rem) [5] (Table 4). Others say that 100 mGy of radiation increases the risk for childhood cancer by 0.1% [56]; a dose of 10 mSv during the last trimester increases the risk of leukemia by 40%. Ten mSv at any stage of the pregnancy increases the risk of leukemia by a multiple of 1.5. Doses above 10 mSv increases the risk coefficient 6% per Sv [5]. The most common attitude, by consensus, is to consider a risk slightly higher than the general population [49].

Most of the articles included in this review mention leukemia as the most common carcinogenic phenomenon associated with in utero radiation exposure [9, 32, 42, 46]. However, leukemia associated with radiation exposure is not more severe than a spontaneously occurring leukemia [41]. The background risk is about 3.6 per 10,000; after an exposure, this increases to 5 per 10,000 [9]. In utero exposure of 0.01 Gy slightly increases the risk of cancer in the first and second decades of life from 0.03% to 0.04% [42].

Some studies report that radiation exposure at all gestational ages increases the risk of childhood leukemia [21, 72], but others find that there is little evidence of any increased risk of childhood acute lymphoblastic leukemia associated with maternal radiographs during pregnancy [73]. In some cases, an excess of maternal X-ray exposure has been documented among children with acute lymphoblastic leukemia, but the statistical analyses and experimental data were reassuring and do not support this link [72].

Carcinogenesis associated with diagnostic radiation is a dose-independent event, but the risk seems relatively low with doses less than 50 mGy [35], 100 mGy [3, 14, 16, 35, 40, 42, 46] or 10 mSv [22, 40]. Although perfusion scanning examinations do not pose a risk for deterministic effects, they can be linked to cancer or genetic effects regardless of the dose [68].

Complementary use of contrasts

ntravenous contrast is discouraged during gestation, except in highly selected patients where there is no other alternative to obtain important diagnostic information [74]. These contrast agents are used in CT and magnetic resonance imaging (MRI) to detect, characterize and stage diseases [75]. There are two main contrast agents: iodine or gadolinium-based.

Iodinated contrast crosses the placenta [3, 8, 35, 44, 50, 76] so we have to consider the possible risk of hypothyroidism and thyroid cancer induction to the fetus, contraindicating iodine's use during pregnancy [3, 20, 23, 24, 26, 38, 70, 77]. However, insufficient human studies are available on fetal thyroid depression due to iodinated contrast [39, 50] and no deleterious effects have been observed during pregnancy [28, 44]. Evidence of mutagenic or teratogenic risk does not exist, but there is a lack of human studies [3, 23, 24, 42, 52, 57, 70]. It is considered generally safe during pregnancy and therefore iodinated contrast could be used during pregnancy after assessing the risk-benefit ratio [7, 8, 24, 44, 53, 77, 78]. If the mother received iodinated contrast material during her pregnancy, the thyroid function of the newborn should be evaluated in his first week of life [23, 26, 35, 42, 53, 57, 76].

Gadolinium-based contrast crosses the placenta, enters the fetal circulation and is excreted into the amniotic fluid, where it remains for some time [3, 35, 44, 70, 79, 80]. It appears there are no teratogenic or mutagenic effects in humans when using these agents [3, 35, 44, 50, 57, 70, 75, 78], but gadolinium's safety has not been established [3, 23, 38, 42, 77, 80]. Apparently nephrogenic systemic fibrosis and dissociation of toxic-free gadolinium are some of the effects being discussed [50]. At higher doses than the ones used in human studies, gadolinium has been associated with growth retardation and congenital anomalies [26]. Gadolinium should be contraindicated during pregnancy, only used when the benefits outweigh the risks and, even so, with extreme caution [8, 27, 28, 44, 51, 53, 77, 78, 81].

Barium sulphate is used during fluoroscopic examinations and appears to be safe for the fetus. Barium sulphate is either swallowed or used in enema and is poorly absorbed by the gastrointestinal tract [82]. Therefore, no deleterious effects are expected to the fetus.

Computed tomography

Computed tomography (CT) examinations on pregnant women are usually in areas away from the uterus, so the fetus is not directly exposed to radiation. The risk in these cases is due to scatter radiation that only hits low levels of radiation, thus posing a small risk to the fetus [29].

CT of maternal head and chest has negligible fetal exposure. Maternal pelvic CT may increase the risk of cancer [39]. CT pulmonary angiogram exposes the fetus to similar or lower doses of radiation as ventilation-perfusion (V/Q) scans [83]. Helical CT has an average fetal exposure dose smaller than ventilation-perfusion lung scanning [84].

Magnetic resonance imaging

Nonionizing diagnostic tools should be considered whenever possible [26, 46, 47, 60, 85, 86]. In fact, MRI should be the second-line examination, after US, since it is an expensive, more complex and less available examination [6, 50, 78, 81, 87–89].

MRI can be performed at any stage of the gestational period, but safety during the first trimester has not yet been established [16, 50, 53, 79, 80]. The major concerns are thermal effects of radiofrequency pulses and effects of acoustic noise on the fetus [6, 26, 35, 51, 53, 77, 89–91]. Thermal heating can cause biological damage, related to cell migration, proliferation and differentiation, and may lead to miscarriage [77, 87, 91]. The central nervous system is especially sensitive to heat. A 2°C rise over 24 h can result in abnormalities like neural tube and craniofacial defects [6, 90, 91]. Some say MRI should be avoided in the first trimester to avoid excessive heating and high fetal exposure; however, after 24 weeks (when fetal hearing is developing) it is not easy to provide the fetus with additional protection from acoustic noise [3, 35, 92]. Acoustic damage appears to be a more theoretical risk and not a significant practical issue [8, 53].

No harmful effects of MRI on the fetus were reported under 1.5 T [7, 18, 26, 28, 35, 44, 53, 93], considered generally safe for use in pregnancy [50, 78, 85]. In some radiology centers, higher field strengths are used with no apparent risk to the fetus. The use of 3-T equipment is gradually being introduced in clinical practice. Field strengths above 2.5 T should however be avoided for now [3, 26, 35, 92]. Safety of the fetus is overestimated because the effect of heat dissipation by convection in the amniotic fluid is overlooked. Further studies on this issue are still needed [93].

To date, no evidence of conclusive harmful effects to the fetus from MRI exists [3, 8, 35, 51, 79–81, 87, 89, 91].

Measures to diminish the risks of radiation

Accurate imaging helps achieve a definitive diagnosis, find effective treatment, and avoid complications and unnecessary interventions [78, 81]. Withholding proper diagnostic imaging care can result in significant harm to the mother and, by extension, to the fetus, and is considered an irresponsible medical action [58]. Protection in radiology follows some basic principles: There should be no risk without benefit, prescribed limits should not be exceeded and, at all times, the ALARA concept (as low as reasonably achievable) should be observed [21, 23, 26, 35, 43, 45, 46, 50, 56, 94]. Therefore, measures to reduce the dosage to the fetus should be implemented.

Screening for pregnancy

The first step to take is screening for pregnancy [2, 43, 45, 49, 79, 80]. The "10 day rule" states that, in women of childbearing potential, nonurgent radiography examinations that involve pelvic irradiation should be restricted to the first 10 days of the menstrual cycle [55, 62, 64, 65]. Hence, avoiding irradiating the fetus before the mother knows she is pregnant [55] and avoiding the risk of pregnancy loss [64].

Recently, the accepted interpretation is that if the patient's menstruation started fewer than 10 days before the procedure, the chance of an existing pregnancy is very low and no cause for concern [62]. Most radiology departments no longer follow this principle [64].

In all situations, informed consent should be acquired, if the patient is stable [43, 45, 80].

General measures

Ionizing radiation should be avoided especially during the first trimester. Whenever possible, throughout the whole pregnancy, US and MRI should be used instead, if at all possible [26, 35, 60, 78, 86]. Special care is needed between 10 and 17 weeks' gestation due to the risk of central nervous system teratogenesis. In this period, nonurgent examinations should be postponed [9, 51].

Additionally, all radiologic equipment should be well-maintained and periodically inspected for radiation safety [2]. It is important to monitor the radiation dose of every examination [5, 45].

For all diagnostic examinations, it is important to minimize exposure time [2, 34, 48, 50, 61, 65, 94–97]. In general terms, protraction and fractionation of exposures of ionizing radiation to the embryo decreases the magnitude of the deleterious effects of deterministic effects [41]. Measures that apply to radiography, fluoroscopy and CT should apply the following caution measures:

- Use of lead shielding whenever possible [5, 8, 14, 16, 23, 24, 28, 35, 43, 45, 47, 61, 78, 94].
- Collimate the beam [3, 5, 23, 28, 35, 50, 52, 61, 94, 98, 99].
- Minimize the number of acquisitions [2, 23, 35, 46, 52, 61, 63].
- Scan the minimum body area needed to provide sufficient guidance [3, 24, 32, 35, 46, 61, 100, 101].

Specific technicalities adopted in radiographic, fluoroscopic and CT examinations are detailed in the clinical protocol section.

Clinical protocol

Every female patient in reproductive age should be screened for pregnancy before undergoing diagnostic radiation examinations. If pregnancy is a possibility, the risks of radiation to the mother and fetus need to be weighed against the benefit of the examinations.

Deterministic effects like pregnancy loss, congenital malformations, growth retardation and neurobehavioral abnormalities have threshold doses greater than 100–200 mGy [14, 32, 49, 58, 59] (Table 5), and are considered to be negligible at 50 mGy or less [3, 5, 8, 13, 15, 16, 23, 28, 43, 47, 56]. No diagnostic examination exceeds these values [3, 23, 24, 42, 49, 52, 56, 57] (Fig. 2). Moreover, the most crucial time to avoid radiation exposure is from the 8th to the 15th week of gestation [60]. The risk of carcinogenesis is slightly higher than in the general population and should be taken into consideration throughout pregnancy [49].

Intravenous contrast is relatively contraindicated during pregnancy, except in highly selected patients where there is no other alternative to obtain important diagnostic information [74].

For radiography and fluoroscopy

- Increase peak kilovoltage to the highest peak possible that results in acceptable image contrast, allowing more beam penetration and shorter exposure, thus reducing the dose [37].
- Use lead shielding whenever the abdomen or pelvis is not being imaged to protect the uterus from external scattered radiation [5, 14, 16, 28, 43, 45, 47, 61, 78, 94]. If a specifically designed shield is not available, lead aprons should be reserved specifically for this task [102].
- Minimize fluoroscopy time [2, 48, 61, 65, 94–96] and the number of images acquired during digital subtraction angiography and cinematic acquisitions [2, 61, 63].
- Magnify only if necessary [35, 61].

Table 5 Minimum and maximum threshold doses for deterministic effects on each gestational period

Gestational period	Effect	Minimum threshold (mGy)	Maximum threshold (mGy)	What to tell the patient in case of inadvertent exposure
First 2 weeks	Pregnancy loss	100	-	If the exposure was greater than the threshold, spontaneous abortion may happen. Smaller doses do not justify terminating the pregnancy.
2nd to 8th	Fetal growth retardation	100	1000	Most sensitive period. Usually reversible.
	Congenital malformations	100	250	Most sensitive period.
4th to 8th week	Pregnancy loss	150	500	Doses below threshold do not justify terminating the pregnancy.
8th to 15th week	Congenital malformations	100	250	Most sensitive period.
	Mental retardation	100	250	Most sensitive period.
	Microcephaly	100	500	Most sensitive period.
	Fetal growth retardation	100	1,000	Usually reversible.
After 16th week	Congenital malformations	500	700	Lower probability.
	Mental retardation	200	700	Less radiosensitive.
After 24th week	Pregnancy loss	100	-	Doses below threshold do not justify terminating the pregnancy.

- Perform pulsed fluoroscopy at the lowest pulse rate that provides sufficient image quality [35, 61, 94].
- Maximize the distance between the X-ray source and the receptor and minimize the distance between the patient and the receptor [45, 61, 94].
- Use collimators [5, 28, 35, 52, 61, 94].
- Use filtration [5] with copper [94].
- Avoid taking radiographs during fluoroscopy [94].
- Increase tube voltage [94].
- Use posterior-anterior projection rather than anterior-posterior projection [18, 28].

Generally, protraction and fractionation of exposures of ionizing radiation to the embryo decrease the magnitude of the deleterious effects of deterministic effects [41].

For CT

- Use lead shielding if it does not affect the image result, ideally with circumferential shielding [5, 8, 23–25, 35, 47, 99, 100, 103].
- Reduce kilovoltage peak [3, 4, 23, 24, 34, 35, 46, 56, 97, 99, 101], milliampere-second setting [4, 35, 46, 97, 101], the length of the scan [34, 50, 97] and the number of acquisitions [23, 35, 46, 52, 61].
- Center the patient in the CT gantry [100].
- Use a low tube current-time product for all acquisitions after the preliminary scan [3, 23, 24, 46, 47, 52, 56, 61, 76, 99].
- Scan the minimum body area needed to provide sufficient guidance [3, 24, 32, 35, 46, 61, 100, 101].
- Increase the pitch [3, 23, 35, 46, 61, 98, 99].
- Limit Z axis [23, 34, 99].

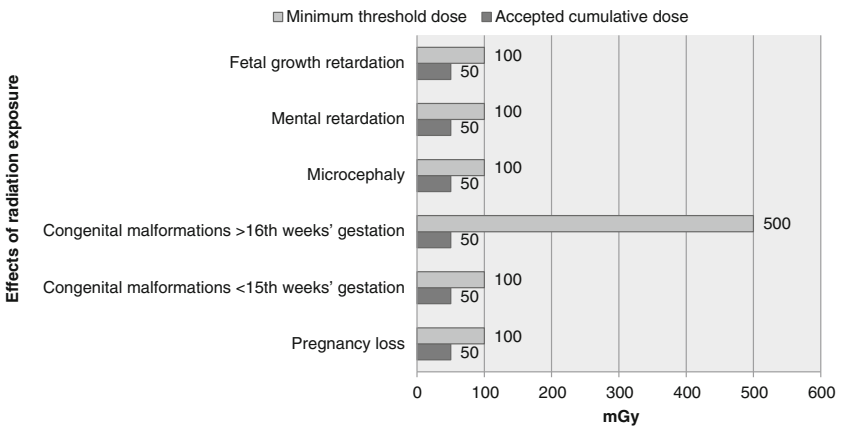

Fig. 2 Identified minimum threshold ionising radiation dose and accepted cumulative dose linked to causation, by adverse outcome

- Customize protocols to patient size and clinical indication [99].

Since CT scans are associated with higher radiation exposure dosage than other medical examinations, their use should be restrained [21, 78]. Here, the alternatives (US and MRI) have to be considered and offered to the patient if the benefit is higher than the risk [9, 21, 43].

Every radiology center should have its own data on fetal radiation exposure in order to determine the risks [28, 61].

Conclusion

When using radiation to achieve a diagnosis, one has to balance the welfare of the mother and of her unborn child, weighing the risks and benefits. However negligible the radiation exposure might be, one should refrain from performing unnecessary examinations at all times. Whenever possible, radiation should be avoided and modalities that use nonionizing techniques like US and MRI should be considered and offered to the patient first. Ideally, every radiology center should have their own data on fetal radiation exposure produced with their own equipment to determine the risks.

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