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Radiotherapy and Pregnancy: Together or Alone?

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Organ malformations and mental retardation (the sensitivity is high from 2 to 8 weeks, and 8 to 25 weeks after conception, respectively) are the most serious results of fetal exposure to radiation that are observed after birth and probably arise above a threshold dose of 0.1–0.2 Gy. This threshold dose is not generally reached with curative radiotherapy during pregnancy, because most of the tumors are located sufficiently far from the fetus and that precautions have been taken to protect the unborn child against leakage radiation and collimator scatter.
Generally, pregnant women with malignant diseases are advised to delay the radiotherapy until after delivery. If a pregnant patient necessitates radiotherapy the physician should inform the risk of the fetus and the benefits of the mother. Subjects like week of pregnancy, stage of the disease and radiation safety must be discussed in details and the final decision should be taken by the patient. In this review, patients who were exposed to radiation during pregnancy because of radiotherapy and their fetal exposure were discussed.
Key Words: Radiotherapy; Pregnancy; Fetal Exposure.

Radyoterapi ve Hamilelik: Birlikte ya da Tek Başına?

Organ kusurları ve zeka gelişim bozukluğu (döllenmeden sonra sırasıyla 2-8. ve 8-25. haftalarda duyarlılık yüksektir) doğumdan sonra fetal radyasyon maruziyetine bağlı görülen en ciddi sorunlardır ve muhtemelen 0.1-0.2 Gy'lik eşik dozun üzerinde ortaya çıkar. Bu eşik doza hamilelik sırasında küratif radyoterapi ile genellikle ulaşılmaz çünkü tümörlerin çoğu fetüsten yeterince uzakta yerleşiktir ve doğmamış çocuğu korumak için sızıntı radyasyona ve kolimatör saçılmalarına karşı önlemler alınmıştır.
Genellikle malign hastalığı olan hamile kadınlara radyoterapinin doğum sonrasına ertelenmesi tavsiye edilir. Eğer hamile bir hastaya radyoterapi zorunluluğu olursa hekim fetüsün riskleri ve annenin faydaları konusunda bilgilendirmek zorundadır. Hamilelik haftası, hastalığın evresi ve radyasyon güvenliği gibi konular detaylı bir şekilde tartışılmalı ve son karar hasta tarafından verilmelidir. Bu derlemede hamilelik sırasında radyoterapi sırasında radyasyona maruz kalan hastalar ve fetal maruziyetleri tartışılmıştır.
Anahtar Kelimeler: Radyoterapi; Hamilelik; Fetal Maruziyet.

Introduction

The probability that a pregnant woman will be diagnosed with cancer is very low, with an incidence of about 1/1000 pregnancies[1]. Breast and cervical cancer, Hodgkin's disease, malignant melanoma, and leukemia are the most frequently diagnosed malignant disorders during pregnancy. The incidence of breast cancer, Hodgkin's disease, cervical cancer and malignant melanoma is 1/3000 to 10000, 1/1000 to 6000, 1/2000 to 10000, and 1/1000 to 10000 pregnancies, respectively[2-6]. The frequencies of brain and head and neck tumors are probably lower.

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Radiotherapy (RT) in pregnant cancer patients should be aimed at controlling the tumor while affording the fetus the best chance for normal development. If cancer is diagnosed during pregnancy and RT is planned and executed with special care treatment may not be delayed until delivery, there are concerns as to whether RT can be given safely. The radiation oncologist can advise on whether to give the patient RT before delivery. Because of the expected risks associated with fetal exposure to radiation, several commentators have stated that RT should be avoided in pregnant breast cancer patients and should be given after delivery.[1,7-9] Some clinicians recommend termination of pregnancy when doses higher than 0.05–0.10 Gy are to be received by the fetus.[10,11] The available information on radiation induced embryonic damage is derived from animal

studies and follow-up of individuals exposed to atomic bomb explosions in Japan.[12-15] The possible embryonic or fetal damage from radiation may be classified in two types; teratogenic (abnormal fetal development) and carcinogenic (induction of malignancy). As the probability of fetal exposure to radiation varies in relation to gestational age, the radiation dose, and possibly fractionation, it is important to calculate the fetal dose in each case. We reviewed published works on the risks of medical irradiation of pregnant women with malignant disorders and the fetal dose as a result of the RT.

Fetal exposure and risks

The developing fetus is radiosensitive throughout the prenatal period and this varies during the states of gestation. The fetal dose of radiation varies as a function of the disease requiring treatment, the size of the radiation field, the distance from the fetus to the edges of radiation field, the amount of radiation dose and the leakage from the radiation machine.

The risks of medical irradiation of pregnant women have been reviewed in two reports by the International Commission on Radiological Protection.[16,17] The study from which the risks were derived mentions results of animal studies, data from children exposed in utero to diagnostic X-rays, data from survivors of nuclear explosions, and data on children who were exposed to radiation from the Chernobyl accident in utero.[17] Also any imaging modality used in pregnant patient causes exposure to the embryo (Table 1), which can be reduced by radiologic techniques and taking precautions.[18]

Table 1. Average uterine/fetal exposed doses during imaging procedures.

Procedure	Uterine/fetal dose (mGy)
Chest X-ray	0.0004
Pelvic-lumbar spine X-ray	0.45-1.0
2-view mammogram	4
Chest CT scan	0.17
Abdominal-pelvic CT scan	18-25
Intravenous urography	45
Barium enema	36
ERCP	0.4
Tc99m-MDP bone scan	4.5 (1st trimester 2-4 (2nd trimester) 1.8-2.0 (3rd trimester)

The adverse effects of RT on embryos and fetuses include lethality, malformations, growth/mental retardation, cancer induction and genetic abnormalities.

As lethality attributable to radiation occurs in the preimplantation period (the first week after conception) radiation exposure often results in failure to implant or undetectable death.[16] Animal experiments have demonstrated that exposure to doses exceeding 0.1 Gy results in embryonic death 5% or more of the time.[10]

During early organogenesis, in weeks 2–8 after conception, the risks of malformations due to exposure to radiation increases, especially in the organs under development at the time of exposure. Data from animal studies, case reports on X-ray exposure during pregnancy, and survivors of nuclear explosion were used to determine threshold doses of radiation for the fetus.[17,19] Malformations might occur above a threshold dose of 0.1–0.2 Gy. Brent reported that malformations occurred frequently in neonates born to mothers who went abdominal irradiation in which the dose exceeded 0.5 Gy.[10]

During intrauterine period, the neural tissue of the embryo or fetus, especially the brain, seems to be the most sensitive organ to ionizing radiation. An association between radiation exposure and mental retardation was noted when the number of children born with severe mental retardation increased in population exposed to the atomic bombing of Hiroshima and Nagasaki.[20] During the 8–25 weeks after conception, the CNS is especially sensitive to radiation. In weeks 8–15 after conception, which is called 'window of cortical sensitivity', brain development is most sensitive to radiation damage and a fetal dose of 0.05-0.25 Gy can result in a verifiable decrease in IQ.[17,21,22] Much higher doses up to 1 Gy result in 40% probability of severe mental retardation during the same period.[22,23] A smaller shift in IQ is detectable after exposure to radiation from 16–25 weeks after conception. The effects of all doses are less striking from 25 weeks after conception onwards, and these effects have not been noted for other gestational periods.[16,17] The threshold dose for mental retardation for a fetus of 8–15 weeks of age is about 0.06 Gy and that for a fetus of 16–25 weeks of age is about 0.25 Gy.[22]

Growth retardation was also evident among the children of survivors of the atomic bomb explosions[24]. Growth retardation occurs when the fetus is exposed to radiation at 0.5 Gy or more during 2 to 15 weeks' gestation. The threshold value is estimated at approximately 0.1 Gy.[20]

Radiation exposure during the second and third trimesters is associated with a carcinogenic effect that may include an increased risk for the development of leukemia and other cancers. It is likely that late stage of fetogenesis is the period of highest radiosensitivity with

respect to cancer induction and the fetus is assumed to be as susceptible to the carcinogenic effects of radiation as a young child[17]. Stovall et al investigated the relationship between cancer in children and doses of radiation and showed that gestational exposure in Hiroshima and Nagasaki resulted in an increase in the occurrence of cancer when these individuals reached adulthood.[25] The spontaneous incidence of childhood cancer and leukemia is low at about 2–3/1000.[26] Prenatal irradiation with a fetal dose of 0.01 Gy will increase the incidence by 40% over this background risk (3–4/1000). A conservative estimate of the lifetime risk of radiation-induced fatal cancer at 0.01 Gy is about 1/1700 (0.06%)[27]. Without radiation exposure the lifetime risk of contracting cancer is about 33%; for fatal cancer the risk is about 20%.[16]

Radiotherapy

In most cases where direct radiation to the fetus is not intended, the fetus is excluded from radiation field and is exposed only to leakage radiation from the accelerator, collimator dispersion generated from apparatuses other than the accelerator (e.g., lead block), scattered radiation from treatment table, back scatter and dispersion radiation from the mother. Internal scatter depends largely on the source of irradiation and on the size of the treatment fields and their proximity to the fetus.[16] While the exposure that occurs within the body of the mother cannot be controlled, radiation from the remaining sources can be reduced by a factor of two to four by proper shielding with, for example, four to five half- value layers of lead stacked over the patient's uterus.[16]

Less leakage of radiation, a lower target dose, smaller radiation fields, greater distance of the edges of the radiation fields from the fetus, and avoidance of lead wedges and other scattering objects (e.g. lead blocks), will all decrease the radiation dose to the fetus. A distance of over 30 cm from the field edges will limit the total exposure of the fetus to only 0.04-0.20 Gy.[25] Therefore, many areas remote from pelvis (head and neck, extremities, breast, brain) can be treated with radiation without significantly irradiating the embryo with a careful planning.[29] Cancers in the pelvis cannot be treated adequately with radiation during pregnancy without severe or lethal consequences for the fetus.[16]

Among various components of the fetal dose measured, head leakage was found to be the leading cause contributing 52%, followed by wedge scatter (31%), collimator scatter (14%) and internal scatter (13%).[30] Abdominal shielding can reduce fetal dose by 30-60%.[31]

Table 2 shows the total dose, fetal dose, and outcome of pregnant cancer patients undergoing radiotherapy.

Table 2. Treatment dose, fetal dose and outcome of pregnant cancer patients undergoing radiotherapy.

Total dose (Gy)	Fetal dose (Gy)	Pregnancy trimester	Delivery (n)
Breast cancer[29,33,35]			
50	0.160	3	Healthy boy (1)
50	0.14-0.18	3	*
46	0.039	1	Healthy boy (1)
Hodgkin'sdisease[5,28,36-38,40]			
35-40	0.014-0.55(6 MV)	1-3	Healthy babies (16)
	0.100-0.136 (cobalt)		
19	0.09-0.42, head 0.114	1	Healthy child at age 8 (1)
15-20	0.020-0.50	2-3	Healthy children at age 6-11 (7)
			Healthy babies (16)
35	<0.1	2	Healthy child (1)
35	0.12	1	Healthy child, growth lagging (1)
Brain tumors and head and neek cancers [30,36,47-49,51]			
64	0.027-0.086	2	Healthy baby (1)
45	0.020	1	*
25	0.0015-0.0031	3	*
30	0.003	2	Healthy boy at age 3 (1)
68	0.06	3	Healthy girl at age 2.5 (1)
78.2	0.030	3	Healthy girl at age 1.5 (1)
66	0.033-0.086	3	*

*: no information about the baby

The following sections discuss specific cancers complicating pregnancy that may require radiation therapy.

Breast cancer

Breast cancer during pregnancy is generally defined as that arising during pregnancy or within 1 year of delivery. If the embryo is in the true pelvis maternal breast or chest wall irradiation will expose the fetus to only 0.1–0.3% of the total dose for a typical regimen of 50 Gy (0.05–0.15 Gy).[32] Towards the end of pregnancy, the fetus lies closer to the radiation field and could receive more than 2 Gy for the same treatment course.[8,32] Van der Giessen published a data set to estimate the fetal dose as a function of stage of pregnancy. For 6–25 MV X-rays the maximal fetal dose ranged from 0.03 Gy at 8 weeks to 0.20 Gy at 24 weeks, to 1.43 Gy at 36 weeks of pregnancy.[33] For a breast cancer treatment course delivering 50 Gy to the tumor bed, a fetal exposure during the first trimester of 0.021-0.076 Gy using anthropomorphic phantoms was calculated. The corresponding dose ranges to the fetus during the second and third trimesters of gestation were 0.022-0.246 Gy and 0.022-0.586 Gy, respectively.[34]

Successful breast cancer RT during pregnancy and birth of healthy children has been reported.[29,33,35] A patient in week 24 of her pregnancy was treated for a ductal carcinoma with 10 MV X-rays to a total dose of 50 Gy.[33] Lead shields of 4-cm thickness were used and the measured fetal dose was 0.16 Gy; without shielding the dose would have been 0.28 Gy. 3 months after treatment this patient gave birth to a healthy son. Ngu et al treated a patient in the third trimester with a total dose of 50 Gy to the breast with 6 MV photons[35]. With a lead shielding over the abdomen and a lead block inferior to the breast the estimated fetal dose was 0.14–0.18 Gy. Antypas and co-workers treated a patient in the first trimester with a total dose of 46 Gy. In vivo measurements were performed by inserting either a catheter with TLD or ionization chamber into the patient's rectum and phantom measurements were performed by simulating the treatment conditions on an anthropomorphic phantom. The measurements showed the fetal dose to be 0.036 and 0.038 Gy with shielding, respectively.[29]

RT to the breast or chest wall in pregnancy is not an absolute contraindication and is possible with fetal doses below the deterministic threshold if RT is mandatory. As adjuvant chemotherapy can be used safely in the third trimester, RT may also be delayed until after delivery.

Hodgkin's disease

Hodgkin's disease associated with pregnancy is not uncommon, occurring in approximately 1:6000 deliveries, while the incidence of pregnancy-associated non-Hodgkin's lymphoma is quite low.[1,18] The use of RT during pregnancy has been extensively investigated.[5,28,31,36-38] Mazonakis et al used a humanoid phantom to simulate first trimester of pregnancy and measure radiation doses to the embryo at a tumor dose of 40 Gy.[31] For neck-mediastinum and for mantle treatment, phantom measurements yielded doses to shielded embryos in the range of 0.028–0.186 Gy depending on the distance from the field isocenter and 0.042–0.245 Gy depending on the field size. Local-field irradiation in the regions of neck or axilla resulted in embryo doses of lower than 0.1 Gy. Therefore, local-field irradiations in the neck or axilla can be performed safely even without uterus shielding. For local field irradiation in the region of neck-mediastinum and for mantle RT, the extent of the irradiated area, the distance separating the embryo from the field isocenter, and the tumor dose are the factors determining whether the dose to the fetus can be reduced below 0.1 Gy.[31]

In another study of Mazonakis, anthropomorphic phantoms were used to simulate a pregnant woman at the 1st, 2nd, and 3rd trimesters of gestation. Phantom measurements were for the RT to lymph nodes in the neck, axilla, mediastinum, and neck-mediastinum. Irradiation with a tumor dose of 35 Gy in the regions of neck, axilla, mediastinum, and neck-mediastinum resulted in a conceptus dose of 0.011-0.087 Gy, 0.012-0.143 Gy, 0.037-0.577 Gy, and 0.051-0.918 Gy, respectively.[39]

Grossmann and co-workers treated a patient with Hodgkin's disease in her mediastinum. The patient underwent both chemotherapy and RT, and was incidentally found to be pregnant after completion of her treatment. The estimated fetal dose was 0.12 Gy. A healthy boy was delivered at term. At 2 years of age he remained in good health and his developmental milestones were normal; however, his growth was lagging, particularly his head circumference.[40]

Nuyttens and colleagues reported on a 26-year-old patient who presented with stage IIA Hodgkin's disease at 27 weeks of pregnancy[36]. A total dose of 19 Gy was delivered in 12 fractions. After the delivery, the treatment was continued. The dose to the fetus was in the range 0.09–0.42 Gy. As the fetus was in a head-down position, the head received an estimated dose of 0.113 Gy. 8 years after treatment, the child was healthy. Woo et al. described 16 patients received RT for supradiaphragmatic nodal disease during their pregnancies.[28] The range of reported doses to the fetus

was 0.014–0.055 Gy for treatment with 6 MV photons, and 0.100–0.136 Gy for cobalt-60 with lead shielding to the uterus. In all cases, the babies were born at term, without growth retardation, congenital anomalies, or subsequent childhood malignant disorders. Cygler et al reported that, the fetal exposure was restricted to below 0.1 Gy with shielding in a woman at 23 weeks' gestation receiving mantle-field RT to a dose of 35 Gy in 20 fractions.[38] A healthy infant was delivered at term. Nisce and colleagues reported on seven pregnant women who were irradiated at supradiaphragmatic sites with doses of 15–20 Gy during the second or third trimester.[37] The fetal dose ranged from 0.02 Gy to 0.50 Gy. All had full-term, spontaneous, healthy deliveries. The children were reported to be healthy at 6–11 years of age. Lishner et al did a historical-cohort study and compared 48 pregnant women with Hodgkin's disease (21 received RT during pregnancy) with matched controls.[5] The women who received RT during pregnancy gave birth to healthy babies without anomalies. There was no difference in 20-year survival between the two groups.

Nowadays, however, the treatment regimen in Hodgkin's disease differs substantially from those mentioned above. Moreover, radiation treatment portals are now more restricted in size. We conclude that RT is an appropriate treatment if obligatory for supradiaphragmatic presentation of Hodgkin disease during pregnancy and the risk to the fetus appears to be minimal with special attention to shielding.

Brain tumors and head and neck cancers

An increase in the incidence of younger females with head and neck cancers and a departure from the traditional etiological factors of excessive smoking and alcohol, have been observed over the past two decades.[41,42] These epidemiological changes and the tendency for women to delay pregnancy until their late reproductive years, increases the likelihood of head and neck cancers presenting during pregnancy.[43,44]

Several groups of researchers have estimated fetal dose in the RT of brain tumors during pregnancy.[30,36,45-49] The fetal-dose estimate for RT of grade 3 astrocytoma without shielding was 0.022 Gy for a tumor dose of 54 Gy for a 6 MV Varian accelerator and 0.49–0.59 Gy for an Asea Brown Boveri accelerator at 8 MV and 16 MV[45]. For a treatment course delivering 65 Gy to brain tumors without shielding equipment, the calculated conceptus dose never exceeded 0.1 Gy.[46] Lead shielding lowered the dose from 26% to 71%, depending on gestational age, field size, and distance from the field isocenter.

For a pregnant woman with a pituitary macroadenoma, the dose to the fetus without shielding was 0.0199 Gy for a prescribed dose of 45 Gy.[30] A pregnant patient underwent gamma-knife-stereotactic radiosurgery for a solitary metastatic melanoma of the brain. The fetal in vivo dosimetry was measured using TLDs, which was placed at different positions on the patient, corresponding to different locations in the uterus and was in the range 0.0015–0.0031 Gy corresponding to approximately 0.01% of the maximum tumor dose of 25 Gy. Nine weeks after radiosurgery a healthy baby was delivered.[47] In another study for whole-brain irradiation for a solitary brain metastasis from lung cancer with a total dose of 30 Gy, the dose to the fetus was about 0.003 Gy.[48] A healthy boy was born and at of 3 years of age, the child showed normal growth and development. Nuyttens et al described a 29-year-old woman with a squamous cell carcinoma of the tongue.[36] She was 16 weeks pregnant at the time of surgery. Six weeks after surgery, she was given RT consisting of 64 Gy in 32 fractions. The dose to the fetus was in the range of 0.027–0.086 Gy. A healthy baby was delivered 7 weeks after the treatment.
Münter et al reported a 27-year-old pregnant with skull base chordoma.[50] As chordomas are radioresistant tumors, carbon-ion therapy is considered for the therapy. Maximum uterus dose was calculated <2 mSv. A healthy boy was born by cesarean section on the 38th week. At 1 year old, the boy was healthy, with normal cognitive and physical development appropriate to his age.

Podgorsak and co-workers assessed the fetal dose for a pregnant patient undergoing 66 Gy RT to head and neck region.[51] With no shielding, the total dose as determined from phantom measurements would have ranged from 0.133 Gy to 0.280 Gy, and with shielding the dose range was 0.033–0.086 Gy.

Sneed and colleagues reported on two patients treated for malignant brain tumors.[49] Fetal doses were 0.06 Gy for a tumor dose of 68 Gy and 0.03 Gy for a tumor dose of 78 Gy. Healthy babies were born and showed normal growth and development at the ages of 2.5 and 1.5 years. Ioffe et al. provided a reference to estimate the fetal dose from a cranial isocenter for pregnant patients undergoing gamma knife radiosurgery and found fetal dose ranged from 0.05 cGy/min to 0.27 cGy/min based on distance from the isocenter.[52]

These examples indicate that tumors of the brain and head and neck can be irradiated to high doses during pregnancy, resulting in fetal exposure of less than 0.1 Gy, a dose below the deterministic threshold.

Cervical cancer

The incidence of pregnancy-associated cervical cancer is approximately 1/2000 pregnancies.[6] RT for treatment of cervical cancer may be necessary during pregnancy, but the timing of treatment should be adjusted taking gestational age into consideration. Unlike most pregnancy-related malignancies, preservation of fetal life is not compatible with treatment of cervical cancer (unless neoadjuvant chemotherapy is chosen).[53] Therefore, when the tumor is detected in an early trimester, the medical staff and the patient have to decide whether to initiate treatment or to postpone it. As most of the tumors are identified in early stages, delay might be considered while expecting fetal maturity.[54] Patients in whom cervical cancer at advanced stage is diagnosed in the first or second trimester are not good candidates for delay of treatment and often necessitate external RT with the fetus in situ. Usually, miscarriage takes place after a few days and intracavitary radiation can be added. Late second or early third trimester pregnancies should be allowed to continue to 35 weeks, unless there is evidence of rapidly growing tumor.[55] For patients for whose treatment can be postponed until after delivery, vaginal delivery should be avoided because of the risk of tumor implantation in the episiotomy site.[56]

Termination of pregnancy

Termination of pregnancy is always an emotional topic and no less so if radiation exposure is involved. Termination after radiation exposure is always an individual decision and many factors need to be taken into consideration. For fetal doses of less than 0.1 Gy, there is no medical justification for termination as at this level there is a 97% probability the child will not have a malformation and 99% probability it will not have cancer.[16,57] The dose of 0.1 Gy is derived from studies in animals and from the data on survivors of the nuclear explosions in Japan who were exposed to single doses at a high dose rate. In clinical practice, the total fetal dose will be given over a long overall treatment time with very low fractional doses. Therefore, in clinical practice, for fetal doses of less than 0.2 Gy, termination of a pregnancy might not be justified. Fetal doses in excess of 0.2 Gy are rare for cancers that are remote from the pelvis and for which proper shielding has been applied. At fetal doses above this value resulting from accidental exposure or RT without shielding fetal damage might occur. If the fetal dose is high, (in excess of 0.5 Gy), and it was incurred during the stage of organogenesis, there is a substantial chance of central nervous system effects and growth retardation.[26] Such a dose in later pregnancy is less likely to result in birth defect. Although the fetus might survive doses in this range, the parents should be informed of the high risks involved. In the dose range of 0.2–0.5 Gy, the risk of IQ reduction must be seriously considered if the fetus was exposed at a gestational age of 8–15 weeks. In such cases treatment requires discussion between the woman, the oncologist, and the obstetrician on the relative benefits early delivery followed by the treatment versus starting therapy, while continuing the pregnancy. Termination is recommended in patients in whom cancer is diagnosed at a late stage (stage III or IV) during the first trimester (requiring immediate treatment), in cases involving aggressive primary tumors, or in cases in which survival may be shorter than needed to complete pregnancy.[58]

Conclusions

RT during pregnancy exposes the fetus to risks which depend on gestational age and dose. The use of supplemental shielding can considerably reduce the fetal exposure. During planning, angle of the beams should be carefully arranged by using non-coplaner beams that output of the beams should not directly affect uterus or organs related with the fetus. Pretreatment dose measurements by a qualified medical physicist are essential for reliable prediction of side-effects and, thus, sufficient provision of information to parents. For supradiaphragmatic Hodgkin's disease, brain tumors, head and neck, and breast cancers with proper shielding, the dose to the fetus will be lower than the threshold doses for deterministic effects. The risk of radiation-induced stochastic (genomic damage that might lead to secondary cancers) effects of childhood cancer and leukemia is somewhat higher than the spontaneous incidence of 2–3 per 1000, with a relative risk of 1.4 at 0.01 Gy.[27] We can say that RT during pregnancy carries serious risks for the embryo/fetus but can be applied, if obligatory, in patients with supradiaphragmatic Hodgkin's disease, brain tumors, head and neck, and breast cancers with adequate shielding. The decision to give RT to pregnant women with cancer should be taken by the patient after the radiation oncologist has informed her adequately.

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