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Review paper

Estimation and reduction of the radiation dose to the fetus from external-beam radiotherapy

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ABSTRACT

The appearance of a malignant disease during pregnancy is relatively rare. The use of external-beam radiation therapy is limited to non-pelvic tumors which are usually located above the diaphragm. However, supra-diaphragmatic radiotherapy unavoidably exposes the fetus to secondary radiation due to head leakage, scatter from the machine and scatter produced inside the patient. This fetal exposure may be associated with an elevated risk for the development of deterministic harmful effects and/or carcinogenesis. The decision about the administration of radiotherapy in a pregnant patient is influenced by the fetal dose which must always be estimated before the patient's treatment course. The methods employed for fetal dosimetry in external-beam radiotherapy are described in this review study. Direct dose measurements using thermoluminescent dosemeters or large ionization chambers placed on physical phantoms may be used. Monte Carlo simulations on computational phantoms may also provide accurate fetal dose calculations. The physical and/or computational phantoms need to simulate the full-scatter geometry of the pregnant patient. Typical fetal dose values attributable to radiation therapy for brain tumors, head and neck cancer, breast carcinoma and Hodgkin lymphoma at the first, second and third trimesters of gestation are presented. The effectiveness of different shielding devices for fetal dose reduction in radiotherapy is discussed. The effect of the dimensions and setup of the shielding material on the radiation dose received by the fetus is described. Moreover, practical methods for reducing the fetal dose by selecting the appropriate irradiation parameters are presented.

1. Introduction

The diagnosis of a malignancy during pregnancy is a relatively uncommon phenomenon with an incidence of approximately 1 in every 1000 gestations [1]. This incidence has increased considerably in recent decades due to the delay in child-bearing until later in life in developed countries [2]. The management of a pregnant patient with a malignant disease is a difficult procedure. This management should ensure the effective treatment of the mother and the safety of the fetus. The selection of the optimal treatment should be made by a multidisciplinary team including an obstetrician gynecologist, a medical oncologist, a surgeon, a radiation oncologist, a medical physicist, a pediatrician and a psychologist, taking into account the type and stage of the disease and the gestational age [3]. The selected treatment may be based on surgery, chemotherapy or radiation therapy [3].

The AAPM radiation therapy committee task group (TG) 36 previously reported that about 4000 pregnant patients need anticancer treatment in United States annually [4]. Many of these patients should be subjected to radiotherapy. Radiation therapy involves the use of high energy photon or particle beams to deliver high doses to the tumor site. The fetus is unavoidably exposed to ionizing radiation. The ICRP publication 84 noted that fetal doses of more than 100–200 mGy may lead to deterministic effects including fetal death, malformations, growth and mental retardation [5]. The probability of childhood cancer appearance also exists at all levels of dose absorbed by the conceptus. It has been established that pregnancy termination cannot be justified for fetal doses below 100 mGy [6]. Radiation therapy for specific malignant diseases at specific periods of pregnancy may result in fetal doses exceeding the above threshold value [7].

This study reviews the use of radiation therapy for the management of malignant diseases during pregnancy and presents the methods that can be used for estimating and reducing the radiation dose to the fetus.

2. Radiation therapy of pregnant patients

2.1. Pelvic tumors

The most common malignant diseases presented during pregnancy

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are melanoma, breast cancer, cervical cancer, Hodgkin lymphoma, leukemia, ovarian carcinoma and colon cancer [8]. Outside the context of pregnancy, radiation therapy might be considered as the treatment of choice for some pelvic tumors such as carcinoma of the uterine cervix. The pelvic treatment fields employed for the management of cervical cancer typically deliver a radiation dose to the tumor site of more than 45 Gy. For such a treatment, the fetus would be partly or entirely included within the treatment volume, and thus receive a radiation dose far in excess of the threshold of 100 mGy. This implies that pelvic radiotherapy during pregnancy may result in severe harmful effects or even lethal consequences for the developing fetus and, therefore, it cannot be applied in clinical practice. The modification of the standard treatment based on pelvic radiotherapy should be thoroughly investigated [1]. The delay of irradiation until delivery in combination with a close monitoring of the disease can also be an option for early stage cervical carcinomas [1].

2.2. Non-pelvic tumors

The role of radiation therapy during pregnancy is limited to tumors outside the pelvis region. Radiation therapy has been used for the management of several supradiaphragmatic malignancies in pregnant patients such as brain tumors [9–11], head and neck cancer [12,13], breast tumors [14,15] and Hodgkin lymphoma [16,17]. The fetus is always completely excluded from the above treatment fields and therefore receives only an out-of-field dose which is much lower than the dose to the tumor site. The fetal exposure from radiation therapy is due to scattered radiation and leakage through the head of the treatment machine. The fetal dose can be above or below the threshold of 100 mGy, depending on the tumor site and the gestational age at the time of irradiation [7]. The radiation dose to the fetus should always be estimated prior to the start of radiotherapy. This dose assessment allows the radiation oncologist and the medical physicist to examine the need and technical possibilities for fetal dose reduction either by using special shielding equipment or by modifying the irradiation parameters. The accurate knowledge of the fetal dose before the patient's treatment is a prerequisite for deciding whether the radiotherapy can be applied during pregnancy.

3. Fetal dose estimation

3.1. Dose measurements on physical phantoms

Simulation of the full-scatter geometry of the pregnant patient is of great importance. Dosimetry is often based on the use of commercially available tissue-equivalent anthropomorphic phantoms such as the RANDO phantom (Alderson Research Labs, Stanford, CA). These phantoms, which consist of a series of slices and represent average adults, have been broadly used for estimating the fetal dose at the first post-conception weeks [7,18,19]. However, the above phantom arrangements can not represent the real size of the abdominal region at advanced gestational ages. The absence of extra tissue material over the phantom's abdomen might introduce unknown inaccuracies in the fetal dose estimation. The replacement of the original phantom's slices by Lucite sections simulating the abdominopelvic region of a typical woman at 12 and 24 weeks of gestation has been previously reported [20]. The addition of specially constructed Lucite rings around the phantom's abdomen has also been used for simulating pregnancy at the second and third trimesters of pregnancy [21]. Humanoid phantoms may be also modified by coupling them with small-sized water tanks [12,17].

The dosimetry should provide data about the dose variation across the fetal volume. The fetal dose is usually measured at three different positions corresponding to the upper, middle and lower fetal levels [16,18,19]. The report from AAPM TG36 also proposed similar anatomical sites of fundus, umbilicus and symphysis pubis [4]. The above locations can be easily and safely determined by means of an ultrasound examination. This process needs to be repeated during the radiotherapy course to account for changes in fetal size and location. The fetal dose measurements at the first trimester of gestation may be limited to a single level based on the small size of the embryo at this stage.

The radiation dose to the fetus is usually measured by directly placing thermoluminescent dosemeters (TLDs) within the prefabricated holes of the anthropomorphic phantom slices. Fetal dosimetry has been performed either with lithium fluoride TLDs [9,22] or with calcium fluoride TLD crystals because of their high sensitivity [7,20]. The positioning of TLDs in different holes of each phantom slice may provide useful data about the fetal dose distribution. Large volume ionization chambers have also been employed for radiation dose assessments [16,17]. The use of this type of dosimeter is only feasible when the humanoid phantom abuts to a water or solid phantom for the accommodation of the chamber. The ionization chamber measures the radiation dose at a single point within the fetal volume. Bradley et al. [23] have also reported the use of film dosimetry for fetal dose determination.

3.2. Monte Carlo dose calculations

The Monte Carlo methodology can provide accurate calculations of the radiation dose received by critical sites located outside the collimated beam [24–26]. The application of these methods requires the detailed simulation of the head of the linear accelerator. The structural shielding components of the therapy machine should also be modeled in detail. The validity of the linear accelerator modeling needs to be verified against direct dose measurements before being employed for fetal dosimetry.

Stylized models of a pregnant patient at the end of the first, second and third trimesters of gestation have been previously implemented in the Monte Carlo environment for calculating the fetal dose from radiotherapy for breast cancer and Hodgkin lymphoma [27,28]. Voxel phantoms representing an average female patient together with her fetus at three different periods of pregnancy have also been developed [29]. These advanced models have been successfully employed for calculating the fetal doses associated with external-beam radiation therapy for various malignant diseases [30,31].

4. Fetal dose from radiation therapy

Fetal dose values from previous reports for several supradiaphragmatic malignancies, using typical irradiation techniques and 6 MV, are presented in Fig. 1 [7,18,19]. The tumor dose given in radiotherapy for brain tumors, head and neck cancer, breast cancer and Hodgkin lymphoma with typical field sizes was 60 Gy, 70 Gy, 50 Gy and 30 Gy, respectively. The fetal dose at the second and third trimesters of gestation corresponds to the value measured at the upper fetal level. For

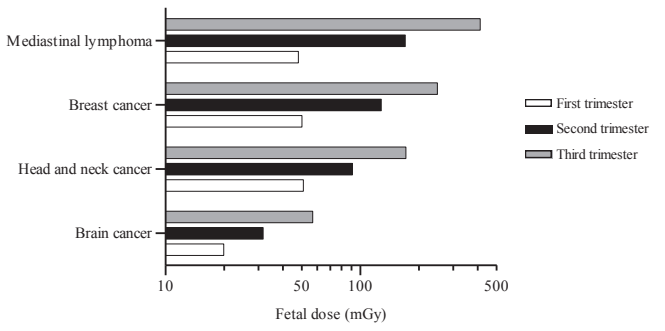

Fig. 1. Fetal dose from radiotherapy for brain tumors, head and neck cancer, breast carcinoma and mediastinal Hodgkin lymphoma during the entire pregnancy. The dose values at the second and third trimesters of gestation correspond to that received by the upper fetal level. Data were obtained from previous published reports [7,18,19].