ABSTRACT

The ventilation/perfusion (V/Q) single-photon emission computed tomography is the first method of diagnosis for pulmonary embolism in pregnant women. This study aimed to calculate the fetal absorbed dose and compare to recommended values in V/Q scan at three trimesters of pregnancy by Monte Carlo simulation (code MCNPX) using simulated phantoms, based on the adult female MIRD phantom. The collection of pregnant women phantoms (that of Stabin) was designed with changes in the MIRD phantom. Source organs were defined for each of the radiopharmaceuticals used in two scans, $^{133}$Xe and $^{81m}$Kr for the lung and bladder and technetium diethylene-triamine-pentaacetate ($^{99m}$Tc-DTPA) aerosol for lung ventilation scan. Also, technetium macroaggregated albumin ($^{99m}$Tc-MAA) for lung ventilation scan, lung, bladder, and liver. Fetal absorbed dose was calculated and evaluated for the administration radiopharmaceuticals using the MCNP simulation output. For 200 MBq $^{99m}$Tc-MAA, fetal absorbed dose was 1.01–1.97 mGy, which is higher than the values recommended by International Commission on Radiological Protection (ICRP). The same fetal absorbed dose was found for activities of 54 and 70 MBq in the third trimester. For $^{99m}$Tc-DTPA-aerosol, fetal absorbed dose as a ventilation tracer was within the permitted range. For $^{133}$Xe and $^{81m}$Kr, it was negligible. It is concluded that the fetus received the highest absorbed dose in the third trimester of pregnancy. For this reason, in this period of pregnancy, it is recommended to use the lower administration activity and her awareness must be done.

Keywords: Absorbed dose, fetus, Monte Carlo simulation, ventilation-perfusion scan

INTRODUCTION

Pulmonary embolism (PE) is a blockage in one of the pulmonary arteries in the lungs.[1] PE is a major cause of maternal mortality in the world.[2] The risk for PE is increased fivefold during pregnancy, and more than 50% of events occur in the first 20 weeks of pregnancy.[3] A clinical suspicion of PE always needs to be confirmed by an imaging test. Currently, ventilation/perfusion single-photon emission computed tomography (V/P SPECT)[3,4] or planar pulmonary scintigraphy[5] is recommended by different European guidelines as an initial imaging modality, based on its low radiation exposure, high sensitivity and specificity, as well as the possibility for follow-up examinations.

When assessing the risks and benefits of a diagnostic method for a pregnant woman, the fetal absorbed dose should be considered.[6] The estimation of the absorbed dose caused by scintigraphy to the fetus is a key factor in risk assessment. V/Q Scan is the most common diagnostic method for PE in pregnant women and consequently measurements of fetal absorbed dose and its comparison to recommended values are important.[7]
Using a low-activity perfusion protocol of 40 MBq technetium macroaggregated albumin ($^{99m}$Tc-MAA) and 600 MBq $^{81m}$Kr-aerosol gas in a 2-min rebreathing protocol, Nijkeuter et al.$^{[10]}$ reported a fetal absorbed dose of 0.11–0.20 mGy and 0.0001 mGy, respectively, without specifying the period of gestation. Cook and Kyrilou$^{[9]}$ reported a fetal absorbed dose of 0.12 mGy for perfusion scintigraphy, using low-activity perfusion imaging (50 MBq $^{99m}$Tc-MAA neither further technical details nor term of pregnancy were further specified). In publication 84, the International Commission on Radiological Protection (ICRP) published fetal absorbed dose estimations for early and late pregnancy using 200 MBq $^{99m}$Tc-MAA for the calculations.$^{[10]}$ A fetal absorbed dose of 0.4–0.6 mGy was estimated in early pregnancy, whereas in late pregnancy, an absorbed dose of 0.8 mGy was reported and for ventilation scintigraphy using 40 MBq $^{99m}$Tc-DTPA-aerosol, the fetal absorbed dose was estimated to be 0.1–0.3 mGy in early and 0.1 mGy in late pregnancy. The mean fetal absorbed doses of 0.21–0.3 mGy in early pregnancy were described by Hurwitz et al.$^{[11]}$ using 74 MBq $^{99m}$Tc-MAA, and the fetal absorbed dose by maternal ventilation imaging was calculated as 0.15 mGy in early pregnancy and 0.02 mGy in late pregnancy with 5-min maternal rebreathing of 370 MBq $^{133}$Xe. Russel et al.$^{[12]}$ reported mean fetal absorbed doses for different stages of pregnancy. Stabin et al.$^{[13,14]}$ reported (SAFs) for different stages of pregnancy.

The fetus is at its most vulnerable stage in the first trimester of pregnancy and requires complete precaution for patients during this pregnancy period to perfusion scan so that as far as possible, activity 200 MBq should not be prescribed. The fetus receives the highest absorbed dose in the third trimester of pregnancy and needs to be diagnosed for patients in this period with the lowest possible prescriptive activity.

The results obtained by different methods are not available for all periods of pregnancy, and the lack of a more detailed study for all periods of pregnancy is felt by a reliable method using up-to-date data.$^{[15]}$ Internal radiation dosimetry in nuclear medicine is only possible through calculation and cannot be measured directly. MCNPX (MCNP eXtended) is a Fortran-90 (F90) Monte Carlo radiation transport computer code that transports all particles at all energies. The aim of this work is to calculate the fetal absorbed dose and compare to recommended values by Monte Carlo simulation (MCNPX code) using Stabin simulated phantoms$^{[13]}$ in three trimesters of pregnancy based on the Medical Internal Radiation Dosimetry (MIRD) adult female phantom.

**Materials and Methods**

In this study, a computer phantom (mathematical phantom) of a pregnant woman based on the Oak Ridge National Laboratory (ORNL) standard female phantom is used. This phantom is a modification of Stabin phantoms.$^{[13]}$ In this phantom, the fetus and all the displaced organs of the mother’s body were simulated using an adult female phantom.

**Phantom Specifications**

**ORNL Phantom**

The standard ORNL phantom used in the dosimetry computations is defined as follows:

In this coordinate system, the origin is at the center of the base of the elliptical cylinder representing the trunk of the phantom. The positive Z-axis is up, the positive X-axis is to the phantom’s left, and the positive Y-axis is toward the back of the phantom. Coordinates are given in cm.

The trunk contains the arms and the pelvic area, and the breasts are connected to the trunk from the outside. Volumes and weights are considered for the trunk, excluding the breast. Components of this phantom include the skeletal system (leg bones, arm, pelvis, spine, and skull [head and facial bone], chest, clavicle, scapula, and bone marrow), adrenal glands, brain, breasts, gallbladder, digestive tract (stomach, small intestine, lower colon, and upper colon), heart, kidneys, liver, lungs, ovaries, pancreas, skin, spleen, testicles, thymus, thyroid, bladder, and uterus.$^{[13]}$ A schematic of this phantom is shown in Figure 1.

**Schematic of Designed Pregnant Phantoms**

In Figure 2, the phantom image of the mother’s body is shown in the first, second, and third trimesters of pregnancy.

**Radiopharmaceuticals and Biokinetic Data**

Source organs were defined for each of the radiopharmaceuticals used in two lung ventilation and perfusion scans, including the lung and bladder for $^{133}$Xe, $^{81m}$Kr, and $^{99m}$Tc-DTPA-aerosol for lung ventilation scan; lung, bladder, and liver for $^{99m}$Tc-MAA for lung perfusion scan. The standard activity for each radiopharmaceutical is 40, 50, 74, and 200 MBq for $^{99m}$Tc-MAA; 40 MBq for $^{99m}$Tc-DTPA; 370 and 740 MBq for $^{133}$Xe and 600 MBq for $^{81m}$Kr. $^{99m}$Tc-MAA and $^{99m}$Tc-DTPA with effective half-lives of respectively 3 h and 106 min, both have two gamma-rays with energies of 140.5 and 142.6 keV. $^{133}$Xe with an effective half-life of 5 min has gamma-ray with an energy of 81 keV and $^{81m}$Kr with a half-life of 13 s has gamma-ray with an energy of 190 keV.$^{[12]}$ The administered activity distribution in source organs is taken from Russel et al.$^{[12]}$ Table 1 shows the distribution of the radiopharmaceuticals in each organ and the energy branching percentage for each radiopharmaceutical.$^{[12]}$
Fetal absorbed dose estimation
Monte Carlo calculations were performed using the MCNPX 2.6.0 code. Source organs are defined for each radiopharmaceutical. The phantom data input file is entered into the MCNPX code software. The energy remaining in the cell (MCNP treats problem geometry primarily in terms of regions or volumes bounded by first- and second-degree surfaces. Cells are defined by intersections, unions, and complements of the regions, and contained user-defined materials) is calculated by the F6 tally. Ten million histories were selected to run the program, which guarantees an error below 5%. The fetal absorbed dose was calculated for each of the radiopharmaceuticals using MCNP output data with the following basic unit conversion:

\[
\frac{\text{MeV}}{\text{gram}} \times \frac{1000 \text{ g}}{1 \text{ kg}} \times \frac{10^6 \text{ eV}}{1 \text{ MeV}} \times \frac{1.6 \times 10^{-19} \text{ J}}{1 \text{ eV}} = \frac{\text{J}}{\text{kg}} = \text{Gy}
\]

The maximum fetal absorbed dose that could be absorbed by the fetus for each radiopharmaceutical and its activity was calculated assuming that all the administered activities have been distributed within the cited organs.

RESULTS
In Figure 3, the fetal absorbed dose and the maximum possible fetal absorbed dose for each activity (conventional prescriptive activity) are shown separately for each radiopharmaceutical in the three periods of pregnancy.

In the first trimester of pregnancy, for $^{99m}\text{Tc}-\text{MAA}$ at an absorbed dose of 200 MBq, the fetal absorbed dose is 1.01 mGy and the maximum fetal absorbed dose is 1.97 mGy, both of which are higher than the recommended limit (1 mGy) in the ICRP. In the second trimester of pregnancy, for $^{99m}\text{Tc}$-MAA at a prescriptive activity of 200 MBq, the fetal absorbed dose was 0.89 mGy and the maximum absorbed dose was 1.70 mGy, that the maximum absorbed dose is above the recommended limit (1 mGy) in ICRP protocols. In the third trimester of pregnancy, for $^{99m}\text{Tc}$-MAA at a prescriptive activity of 200 MBq, the fetal absorbed dose was 2.47 mGy and the maximum fetal absorbed dose was 4.73 mGy. Furthermore, in the prescriptive activity of 74 and 50 MBq, respectively, the maximum absorbed dose was 1.75 and 1.18 mGy, all above the recommended limit (1 mGy) in the ICRP.

In each of the three gestational periods, for $^{99m}\text{Tc}$-DTPA, the amounts of fetal and maximum absorbed doses are below 1 mGy, and for $^{133}\text{Xe}$ and $^{85}\text{Kr}$, the amounts of fetal and maximum absorbed doses are negligible.

DISCUSSION
PE occurs at different ages of pregnancy due to the inactivity of pregnant women, which is a serious risk to maternal health.
In the first trimester, for $^{99m}$Tc-MAA with 200 MBq of activity, the fetal absorbed dose and the maximum absorbed dose were 1.01 and 1.97 mGy, respectively, and with 74 MBq of activity, the fetal absorbed dose and the maximum absorbed dose were 0.38 and 0.73 mGy, respectively. For other activities and three other radiopharmaceuticals, the absorbed dose value was not significant. For $^{99m}$Tc-MAA with 200 MBq of activity, the fetal and maximum absorbed doses were higher than the recommended absorbed dose in ICRP[10] and this activity should not be prescribed.

Table 1: Necessary data for dose calculations separately for each radiopharmaceutical

| Radiopharmaceuticals | Source organ | Radiopharmaceutical residence time in the body (h) | Effective half-life | Gamma energy-branching percentage (keV) | Prescription activity (Mega Becquerel) |
|----------------------|--------------|--------------------------------------------------|--------------------|-----------------------------------------|---------------------------------------|
| $^{99m}$Tc-MAA       | Lung         | 4.89                                              |                    | 1.4%–142.6                              | 40                                    |
|                      | Liver        | 1.04                                              |                    | 3 h                                     | 50                                    |
|                      | Bladder      | $2.17 \times 10^{-1}$                             |                    | 98.6%–140.5                             | 74                                    |
| $^{99m}$Tc-DTPA aerosol | Lung       | 1.03                                              |                    | 1.4%–142.6                              | 200                                   |
|                      | Bladder      | $7.48 \times 10^{-1}$                             | 106 min            | 98.6%–140.5                             | 40                                    |
| $^{133}$Xe          | Lung         | $2.20 \times 10^{-2}$                             | 5 min              | 36.9%–81                                | 740                                   |
| $^{81m}$Kr          | Lung         | $5.20 \times 10^{-3}$                             | 13 s               | 65%–190                                 | 600                                   |

Figure 3: Amounts of fetal absorbed doses and maximum possible fetal absorbed doses for each activity (conventional prescription activities) for each radiopharmaceutical in (1) first trimester, (2) second trimester, and (3) third trimester

Figure 4: The fetal absorbed dose changes in the first half-life to the fifth half-life separately for each radiopharmaceutical at the conventional activity (50 MBq for $^{99m}$Tc-MAA and 40 MBq for $^{99m}$Tc-DTPA) in: (1) first trimester, (2) second trimester, and (3) third trimester
In the second trimester, for $^{99m}$Tc-MAA with 200 MBq of activity, the fetal absorbed dose and the maximum absorbed dose were 0.89 and 1.70 mGy, respectively and with 74 MBq of activity, the fetal absorbed dose and the maximum absorbed dose were 0.33 and 0.63 mGy, respectively. For other activities and three other radiopharmaceuticals, the absorbed dose value was not significant. For $^{99m}$Tc-MAA with 200 MBq of activity, the fetal absorbed dose was higher than the recommended absorbed dose in ICRP, and this activity should not be prescribed.

In the third trimester, for $^{99m}$Tc-MAA with 200 MBq of activity, the fetal absorbed dose and the maximum absorbed dose were 2.47 and 4.73 mGy, respectively. For 74 MBq of activity, the fetal absorbed dose and the maximum absorbed dose were found to be 0.92 and 1.75 mGy, respectively, and for 50 MBq, the fetal absorbed dose and the maximum absorbed dose were 0.62 and 1.18 mGy, respectively. For $^{99m}$Tc-MAA with 200 MBq of activity, the fetal absorbed dose was higher than the recommended absorbed dose in ICRP, and this activity should not be prescribed. For $^{99m}$Tc-DTPA, the fetal absorbed dose and the maximum absorbed dose were 0.42 and 0.81 mGy, respectively. For $^{133}$Xe and $^{81m}$Kr, the amount of fetal absorbed dose is greater but still negligible.

Many researchers have reported the values of fetal absorbed doses using different radiopharmaceuticals. From a point of comparison view, the results of the present work with the other relevant studies are shown in Table 2. In a study, Nijkeuter et al. have worked on a low-activity perfusion protocol of 40 MBq $^{99m}$Tc-MAA. They have found the fetal absorbed dose of 0.11–0.20 mGy for the third trimester and were lower than that of this work. Furthermore, they obtained the fetal absorbed doses of 0.50 and 0.62 mGy for the third trimester using $^{99m}$Tc-MAA at low prescription activities of 40 and 50 MBq, indicating that the calculation of the mentioned study absorbed dose was probably for the early stages of pregnancy.

Cook and Kyriou reported a fetal absorbed dose of 0.12 mGy for 50 MBq $^{99m}$Tc-MAA, which in this study was 0.25 mGy for the first trimester, 0.22 mGy for the second trimester, and 0.65 mGy for the third trimester. Since the pregnancy period is not specified in the mentioned study, the reported absorbed dose is probably for one of the early pregnancy stages.

In publication 84 ICRP, a fetal absorbed dose of 0.4–0.6 mGy was estimated in early pregnancy for 200 MBq $^{99m}$Tc-MAA, whereas in late pregnancy, an absorbed dose of 0.8 mGy was reported, and for ventilation scintigraphy using 40 MBq $^{99m}$Tc-DTPA-aerosol, the fetal absorbed dose was
The fetal absorbed doses for $^{99m}$Tc-MAA and $^{99m}$Tc-DTPA were higher than $^{133}$Xe and $^{81m}$Kr, which is due to the more half-life and uptake of technetium than xenon and krypton in organs, which is due to the ratio distribution of these radiopharmaceuticals.

**CONCLUSION**

In perfusion scans with 200 MBq activity of $^{99m}$Tc-MAA, the fetal absorbed dose for all three pregnancy periods was exceeded the recommended level by the ICRP. This indicated that in the case of perfusion scans for 200 MBq activity and higher, fetal health is at risk. If a lung scan in PE is considered as an emergency scan for a pregnant woman, the mother should be informed. Furthermore, for 50 and 74 MBq activities in the third pregnancy trimester, the fetal maximum absorbed dose was higher than the recommended absorbed dose, where lower activity should be prescribed. In the case of ventilation scan, the fetal absorbed dose for $^{133}$Xe and $^{81m}$Kr was negligible and no special attention is required, but for the $^{99m}$Tc-DTPA aerosol, if higher absorbed doses are required, the fetal absorbed dose should be checked and considered.

Overall, it is concluded that the fetus received the highest absorbed dose in the third trimester of pregnancy. For this reason, in this period of pregnancy, it is recommended to use the lower administration activity and her awareness must be done.

**Acknowledgments**
The authors thank all persons who helped in this work.

**Financial support and sponsorship**
This work was financially supported (Grant No: 397555) by Isfahan University of Medical Sciences, Isfahan, Iran.
Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Bourjeily G, Paidas M, Khalil H, Rosene-Montella K, Rodger M. Pulmonary embolism in pregnancy. Lancet 2010;375:500-12.
2. Grüning T, Mingo RE, Gosling MG, Farrell SL, Drake BE, Loader RJ, et al. Diagnosing venous thromboembolism in pregnancy. Br J Radiol 2016;89:20160021.
3. Bajc M, Olsson B, Gottsäter A, Hindorf C, Jögi J. V/P SPECT as a diagnostic tool for pregnant women with suspected pulmonary embolism. Eur J Nucl Med Mol Imaging 2015;42:1325-30.
4. Bajc M, Neilly JB, Miniati M, Schuemichen C, Meignan M, Jonson B, et al. EANM guidelines for ventilation/perfusion scintigraphy: Part 1. Pulmonary imaging with ventilation/perfusion single photon emission tomography. Eur J Nucl Med Mol Imaging 2009;36:1356-70.
5. Konstantinides SV, Torbicki A, Agnelli G, Danchin N, Fitzmaurice D, Galie N, et al. 2014 ESC guidelines on the diagnosis and management of acute pulmonary embolism: The task force for the diagnosis and management of acute pulmonary embolism of the European society of cardiology (ESC) endorsed by the European respiratory society (ERS). Eur Heart J 2014;35:3033-80.
6. Niemann T, Nicolas G, Roser HW, Müller-Brand J, Bongartz G. Imaging for suspected pulmonary embolism in pregnancy--what about the fetal dose? A comprehensive review of the literature. Insights Imaging 2010;1:361-72.
7. Hendriks BMF, Schnerr RS, Milanese G, Jeukens CRLPN, Niesen S, Eijsvogel NG, et al. Computed tomography pulmonary angiography during pregnancy: Radiation dose of commonly used protocols and the effect of scan length optimization. Korean J Radiol 2019;20:313-22.
8. Nijkeuter M, Geleijnse J, De Roos A, Meinders AE, Huisman MV. Diagnosing pulmonary embolism in pregnancy: Rationalizing fetal radiation exposure in radiological procedures. J Thromb Haemost 2004;2:1857-8.
9. Cook JV, Kyriou J. Radiation from CT and perfusion scanning in pregnancy. BMJ 2005;331:350.
10. Mattsson S, Johansson L, Leide Svegborn S, Liniecki I, Nolke D, Riklund KA, et al. Radiation dose to patients from radiopharmaceuticals: A compendium of current information related to frequently used substances. Ann ICRP 2015;44:7-321.
11. Hurwitz LM, Yoshizumi T, Reiman RE, Goodman PC, Paulson EK, Frush DP, et al. Radiation dose to the fetus from body MDCT during early gestation. AJR Am J Roentgenol 2006;186:871-6.
12. Russell JR, Stabin MG, Sparks RB, Watson E. Radiation absorbed dose to the embryo/fetus from radiopharmaceuticals. Health Phys 1997;73:756-69.
13. Stabin M, Watson E, Cristy M, Ryman J, Eckerman K, Davis J, et al. Mathematical Phantoms and Specific Absorbed Fractions of Photon Energy in the Nonpregnant Adult Female and at the End of Each Trimester of Pregnancy. TN (United States): Oak Ridge National Lab; 1995.
14. Rafat Motavalli L, Hoseinian Azghadi E, Miri Hakimabad H, Akhlaghi P. Pulmonary embolism in pregnant patients: Assessing organ dose to pregnant phantom and its fetus during lung imaging. Med Phys 2017;44:6038-46.
15. Tester J, Hammerschlag G, Irving L, Pascoe D, Rees M. Investigation and diagnostic imaging of suspected pulmonary embolism during pregnancy and the puerperium: A review of the literature. J Med Imaging Radiat Oncol 2020;64:505-15.
16. Hakimabad HM, Motavalli LR. Evaluation of specific absorbed fractions from internal photon sources in ORNL analytical adult phantom. Radiat Prot Dosimetry 2008;128:427-31.