### Original Article

# Investigation of fetal absorbed dose in V/Q scan in three trimesters of pregnancy using Monte Carlo simulation

#### **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, <sup>133</sup>Xe and <sup>81m</sup>Kr for the lung and bladder and technetium diethylene-triamine-pentaacetate (<sup>99m</sup>Tc-DTPA) aerosol for lung ventilation scan. Also, technetium macroaggregated albumin (<sup>99m</sup>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 <sup>99m</sup>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 <sup>99m</sup>Tc-DTPA-aerosol, fetal absorbed dose as a ventilation tracer was within the permitted range. For <sup>133</sup>Xe and <sup>81m</sup>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.<sup>[1]</sup> PE is a major cause of maternal mortality in the world.<sup>[2]</sup> The risk for PE is increased fivefold during pregnancy, and more than 50% of events occur in the first 20 weeks of pregnancy.<sup>[3]</sup> 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)<sup>[3,4]</sup> or planar pulmonary scintigraphy<sup>[5]</sup> 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.<sup>[6]</sup> The estimation of the absorbed dose caused by scintigraphy to the fetus is a key factor in risk assessment. V/Q

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Scan is the most common diagnostic method for PE in pregnant women and consequently measurements of fetal absorbed dose and it comparison to recommended values are important.<sup>[7]</sup>

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Using a low-activity perfusion protocol of 40 MBq technetium macroaggregated albumin (99mTc-MAA) and 600 MBq<sup>81m</sup>Kr-aerosol gas in a 2-min rebreathing protocol, Nijkeuter et al. [8] reported a fetal absorbed dose of 0.11-0.20 mGy and 0.0001 mGy, respectively, without specifying the period of gestation. Cook and Kyriou<sup>[9]</sup> reported a fetal absorbed dose of 0.12 mGy for perfusion scintigraphy, using low-activity perfusion imaging (50 MBq<sup>99m</sup>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 MBq99mTc-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 MBq99mTc-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 of99mTc-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<sup>133</sup>Xe. Russel et al.<sup>[12]</sup> 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. 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 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.<sup>[13]</sup> 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.<sup>[13]</sup> 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 <sup>133</sup>Xe, 81mKr, and 99mTc-DTPA-aerosol for lung ventilation scan; lung, bladder, and liver for 99mTc-MAA for lung perfusion scan. The standard activity for each radiopharmaceutical is 40, 50, 74, and 200 MBq for 99mTc-MAA; 40 MBq for 99mTc-DTPA; 370 and 740 MBq for 133Xe and 600 MBq for 81mKr. 99mTc-MAA and 99mTc-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; 133Xe with an effective half-life of 5 min has gamma-ray with an energy of 81 keV and<sup>81m</sup>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]

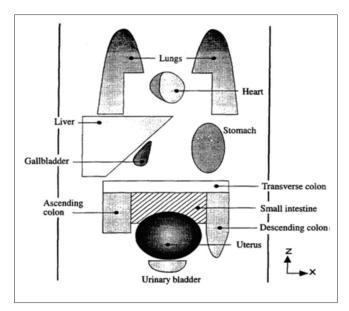


Figure 1: MIRD phantom of organs from the front view (A-P projection)

#### 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:

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

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 <sup>99m</sup>Tc-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

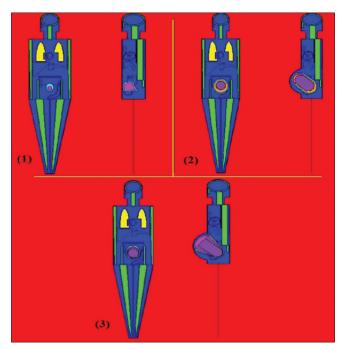


Figure 2: The patients' body phantom in: (1) the first trimester of pregnancy, (2) the second trimester of pregnancy, and (3) the third trimester of pregnancy

which are higher than the recommended limit (1 mGy) in the ICRP.<sup>[13]</sup> In the second trimester of pregnancy, for <sup>99m</sup>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 <sup>99m</sup>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<sup>99m</sup>Tc-DTPA, the amounts of fetal and maximum absorbed doses are below 1 mGy, and for<sup>133</sup>Xe and<sup>81m</sup>Kr, the amounts of fetal and maximum absorbed doses are negligible.

In Figure 4, the chart of the absorbed dose changes in the first half-life to the fifth half-life is shown separately for each radiopharmaceutical at the conventional activity.

As shown in the graphs, the <sup>99m</sup>Tc-MAA absorbed dose at a 200 MBq prescriptive activity is dangerous for the fetus.

#### **DISCUSSION**

PE occurs at different ages of pregnancy due to the inactivity of pregnant women, which is a serious risk to maternal health.

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)
99mTc-MAA	Lung	4.89			40
	Liver	1.04		1.4%—142.6	50
			3 h	98.6%—140.5	74
	Bladder	$2.17 \times 10^{-1}$			200
99mTc-DTPA aerosol	Lung	1.03		1.4%—142.6	
	Bladder	$7.48 \times 10^{-1}$	106 min	98.6%—140.5	40
<sup>133</sup> Xe					370
	Lung	$2.20 \times 10^{-2}$	5 min	36.9%–81	740
<sup>81m</sup> Kr	Lung	5.20×10 <sup>-3</sup>	13 s	65%—190	600

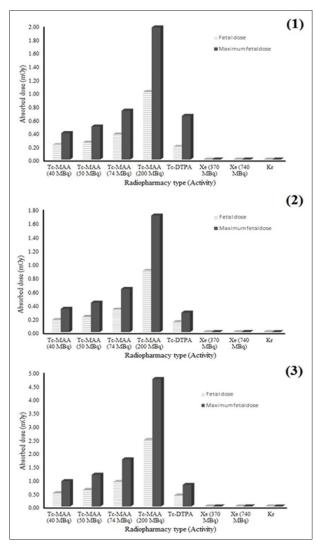


Figure 3: Amounts of fetal absorbed doses and maximum possible fetal absorbed doses for each activity (conventional prescription activities) for each radiopharmaceutical in (1) first trimester, (2) second trimester, and (3) third trimester

In the first trimester, for <sup>99m</sup>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

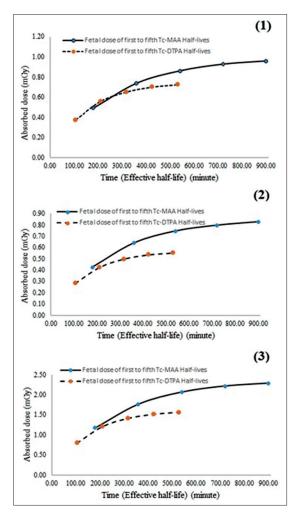


Figure 4: The fetal absorbed dose changes in the first half-life to the fifth half-life separately for each radiopharmaceutical at the conventional activity (50 MBq for 99mTc-MAA and 40 MBq for 99mTc-DTPA) in: (1) first trimester, (2) second trimester, and (3) third trimester

dose were 0.38 and 0.73 mGy, respectively. For other activities and three other radiopharmaceuticals, the absorbed dose value was not significant. For <sup>99m</sup>Tc-MAA with 200 MBq of activity, the fetal and maximum absorbed doses were higher than the recommended absorbed dose in ICRP<sup>[10]</sup> and this activity should not be prescribed.

In the second trimester, for <sup>99m</sup>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 <sup>99m</sup>Tc-MAA with 200 MBq of activity, the fetal absorbed dose was higher than the recommended absorbed dose in ICRP, <sup>[13]</sup> and this activity should not be prescribed.

In the third trimester, for <sup>99m</sup>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 74 and 50 MBq of activities, the maximum fetal absorbed dose is higher than the recommended absorbed dose in ICRP, and this activity should not be prescribed. For <sup>99m</sup>Tc-DTPA, the fetal absorbed dose and the maximum absorbed dose were 0.42 and 0.81 mGy, respectively. For <sup>133</sup>Xe and <sup>81m</sup>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 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.*<sup>[8]</sup> have worked on a low-activity perfusion protocol of 40 MBq<sup>99m</sup>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 <sup>99m</sup>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<sup>[9]</sup> reported a fetal absorbed dose of 0.12 mGy for 50 MBq<sup>99m</sup>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,<sup>[10]</sup> a fetal absorbed dose of 0.4–0.6 mGy was estimated in early pregnancy for 200 MBq<sup>99m</sup>Tc-MAA, whereas in late pregnancy, an absorbed dose of 0.8 mGy was reported, and for ventilation scintigraphy using 40 MBq<sup>99m</sup>Tc-DTPA-aerosol, the fetal absorbed dose was

prescription activities 2: The fetal absorbed doses (mGy) at three periods of pregnancy for each

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Radiopharmaceuticals	Prescription		This work		Publi	Publication 84 ICRP <sup>[9]</sup>	<b>RP</b> [9]	В	Russel et al.[12]	2]	Ŧ	Hurwitz et al.[11]	1]
	activity (mega	Third	Second	First	Third	Second	First	Third	Second	First	third	Second	First
	Becquerel)	trimester	trimester	trimester	trimester	trimester	trimester	trimester	trimester	trimester	trimester	trimester	trimester
99mTc-MAA	40	0.5	0.22	0.18	0.1		0.1-0.3						
	20	0.62	0.22	0.25									
	74	0.92	0.33	0.38									0.21-0.3
	200	2.47	0.89	1.01	0.8		0.4-0.6	9.0	0.75	9.0			
99mTc-DTPA aerosol	40	0.41	0.15	0.19				0.12	0.092	0.17			
	370	0.0013	0.0006	0.0002							0.02		0.15
<sup>133</sup> Xe	740	0.001	0.001	0.0004									
81mKr	009	0.003	0.00013	0.0001									
Radiopharmaceuticals	Pre	Prescription activity (Mega	_	Becquerel)			Nijkeuter et al.[8]	et al. <sup>[8]</sup>			Cook and	Cook and Kyriou <sup>[9]</sup>	
99mTc-MAA			40				0.11-0.20	0.20					
			50								0.12	12	
			74										
			200										
99mTc-DTPA aerosol			40										
<sup>133</sup> Xe			370										
			740										
81mKr			009				0.0001	101					

Table 3: Comparison between this work and Stabin's specific absorbed fractions ( $g^{-1}$ ) for three source organs (lungs, liver, and bladder) to the fetus (as target) for each trimester at this work's enerwiges (keV)

Source organs		Sta	bin	,	,	This	work	
	140.5	142.6	190	81	140.5	142.6	190	81
First trimester								
Lungs	$3.82 \times 10^{-7}$	$3.85 \times 10^{-7}$	$4.54 \times 10^{-7}$	$2.52 \times 10^{-7}$	$5.97 \times 10^{-7}$	$6.00 \times 10^{-7}$	$6.48 \times 10^{-7}$	$5.09 \times 10^{-7}$
Liver	$2.53 \times 10^{-6}$	$2.53 \times 10^{-6}$			$3.01 \times 10^{-6}$	$2.95 \times 10^{-6}$		
Bladder	$5.57 \times 10^{-5}$	$5.55 \times 10^{-5}$			$5.27 \times 10^{-5}$	$5.25{ imes}10^{-5}$		
Second trimester								
Lungs	$6.49 \times 10^{-7}$	$6.52 \times 10^{-7}$	$7.05 \times 10^{-7}$	$4.81 \times 10^{-7}$	$1.29 \times 10^{-6}$	$1.27 \times 10^{-6}$	$1.15 \times 10^{-6}$	$1.39 \times 10^{-6}$
Liver	$4.29 \times 10^{-6}$	$4.28 \times 10^{-6}$			$7.09 \times 10^{-6}$	$7.81 \times 10^{-6}$		
Bladder	$2.24 \times 10^{-5}$	$2.23 \times 10^{-5}$			$3.94 \times 10^{-5}$	$3.89 \times 10^{-5}$		
Third trimester								
Lungs	$8.17 \times 10^{-7}$	$8.19 \times 10^{-7}$	$8.54 \times 10^{-7}$	$6.53 \times 10^{-7}$	$3.18 \times 10^{-6}$	$3.16 \times 10^{-6}$	$2.86 \times 10^{-6}$	$3.32 \times 10^{-6}$
Liver	$5.13 \times 10^{-6}$	$5.12 \times 10^{-6}$			$1.99 \times 10^{-5}$	$1.97 \times 10^{-5}$		
Bladder	$2.11 \times 10^{-5}$	$2.10 \times 10^{-5}$			$3.08 \times 10^{-5}$	$1.10 \times 10^{-4}$		

estimated to be 0.1–0.3 mGy in early and 0.1 mGy in late pregnancy.

Russel *et al.*<sup>[12]</sup> reported 0.6 mGy for the first trimester, 0.75 mGy for the second trimester, and 0.6 mGy for the third trimester and for ventilation scintigraphy using 40 MBq<sup>99m</sup>Tc-DTPA-aerosol. They reported a fetal absorbed dose of 0.17 mGy in the first trimester, 0.092 mGy in the second trimester, and 0.12 mGy in the third trimester of pregnancy using 200 MBq<sup>99m</sup>Tc-MAA. Their results are consistent for ventilation scan, but for perfusion scan, the estimated absorbed dose in the mentioned studies is significantly different from those obtained.

Hurwitz *et al.*<sup>[11]</sup> reported a fetal absorbed dose of 0.21–0.3 mGy for 74 MBq<sup>99m</sup>Tc-MAA. For 370 MBq<sup>133</sup>Xe, they reported a fetal absorbed dose of 0.15 mGy in early pregnancy and 0.02 mGy in late pregnancy. In the present work, for 74 MBq<sup>99m</sup>Tc-MAA, the fetal absorbed dose was obtained 0.38 mGy for the first trimester; and for 370 MBq<sup>133</sup>Xe, 0.0002 mGy for the first trimester, 0.0006 mGy for the second trimester, and 0.0013 mGy for the third trimester.

The SAF values at the energies used in this work were compared to the Stabin's for data validation as indicated in Table 3.

The two data differ by about 5% for the bladder and at two energies, the difference is <20% in the first trimester. For the rest of the data, the difference is >20%. Such differences can be related to the method of SAF estimations. Besides, it can be said that a great portion of differences takes part in one of the two following reasons:<sup>[1]</sup> cases in which there exist minor photon histories in the target organ.<sup>[2]</sup> Cases in which the source or the target geometry changes concerning the Stabin's phantom.<sup>[16]</sup>

The fetal absorbed doses for <sup>99m</sup>Tc-MAA and <sup>99m</sup>Tc-DTPA were higher than <sup>133</sup>Xe and <sup>81m</sup>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 <sup>99m</sup>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 the ventilation scan, the fetal absorbed dose for <sup>133</sup>Xe and<sup>81m</sup>Kr was negligible and no special attention is required, but for the <sup>99m</sup>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.

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#### **Conflicts of interest**

There are no conflicts of interest.

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