POSTMORTEM MAGNETIC RESONANCE IMAGING IN THE DIAGNOSIS OF CONGENITAL PNEUMONIA

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Congenital pneumonia is one of the leading causes of neonatal deaths. In this work we assess the possibility of using postmortem magnetic resonance imaging for the diagnosis of congenital pneumonia. The study was conducted on 21 neonate bodies. Before the autopsy, MRI scanning was performed on the Magnetom Verio 3T system (Siemens, Germany) in T1 and T2 standard modes. The resulting images were used to analyze signal intensities of lung tissue, pleural fluid and air. Airiness index was computed as the ratio of pleural fluid signal intensity to lung tissue signal intensity. Then, the autopsy was performed. Based on the histological analysis results, the main and the control groups were formed. The bodies of 9 neonates who had died from congenital pneumonia were included into the main group; the control group consisted of 12 dead neonates with no signs of pneumonia. On T1-weighted images, the signal intensity from the lungs of the infants with congenital pneumonia was higher by 26.5 % in the left lung and 12.9 % in the right lung, compared to the controls (p >0.05). On T2-weighted images, the corresponding figures were 23.7 and 31.2 % (p >0.05). The sensitivity of the method is 77.8 %, specificity is 75.0 % and diagnostic efficacy is 76.2 %.

Keywords: congenital pneumonia, lung, postmortem magnetic resonance imaging, autopsy, airiness index

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Received: 17.08.2016 **Accepted:** 23.08.2016

ПОСМЕРТНАЯ МРТ ДЛЯ ДИАГНОСТИКИ ВРОЖДЕННОЙ ПНЕВМОНИИ

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Врожденная пневмония — одна из основных причин гибели детей в неонатальном периоде. В работе оценена возможность применения посмертной магнитно-резонансной томографии для диагностики врожденной пневмонии на аутопсийном материале. Исследовали тела 21 умершего новорожденного. До аутопсии проводили МРТ-исследование на аппарате 3T Magnetom Verio (Siemens, Германия) в стандартных T1 и T2 режимах. На томограммах анализировали интенсивность сигнала от ткани легких, плевральной жидкости и воздуха и рассчитывали показатель воздушности — отношение интенсивности сигнала от жидкости в плевральной полости к интенсивности сигнала от ткани легких. Затем проводили патологоанатомическое вскрытие и по результатам изучения гистологических препаратов все наблюдения разделили на две группы: в основную группу включили тела 9 новорожденных, умерших от врожденной пневмонии, в группу сравнения — тела 12 умерших новорожденных без признаков пневмонии. Интенсивность сигнала от ткани легких новорожденных с врожденной пневмонией была выше аналогичного показателя в группе сравнения: на 26,5 и 12,9 % в левом и правом легком соответственно на T1-взвешенных изображениях (p >0,05) и на 23,7 и 31,2 % — на T2-взвешенных изображениях (p >0,05). Чувствительность описанного метода составила 77,8 %, специфичность — 75,0 %, диагностическая эффективность — 76,2 %.

Ключевые слова: врожденная пневмония, легкое, посмертная магнитно-резонансная томография, аутопсия, показатель воздушности

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Статья поступила: 17.08.2016 **Статья принята к печати:** 23.08.2016

Congenital pneumonia is an acute inflammatory condition of the respiratory zone caused by an antenatal or/and intrapartum infection and manifesting itself clinically and radiographically within the first 72 hours after birth [1]. Improvements in diagnostic techniques and treatment approaches contribute to better survival of affected neonates, but death rate still remains relatively high. According to research data [2], congenital pneumonia is diagnosed worldwide in 10–38 % of stillborn and 20–63 % of liveborn babies who subsequently die. In Russia, congenital pneumonia accounted for 0.43 % of all intrauterine deaths and was also the primary cause of death of 8.7 % of infants in the early (0–6 days) neonatal period in 2010, as reported by the Federal Service for State Statistics [3]. In 2014, those figures were 0.35 % and 8.34 %, respectively [4].

The major technique for the postmortem diagnosis of congenital pneumonia is autopsy. However, morphological analysis is often impeded by false positive results of lung float test performed at autopsy and by a weak inflammatory response in premature babies or upon treatment with antibiotics [5, 6]. Here, radiography is usually an alternative.

Computed tomography (CT) is considered the major radiographic technique used to diagnose pulmonary pathologies [7–9]. Postmortem CT is also quite effective in the assessment of lung conditions and determining cause of death in adults [10]. However, lungs of dead fetuses and neonates are not visible on unenhanced CT [11]. Parallel to CT, magnetic resonance imaging (MRI) is being increasingly used to detect pulmonary pathologies [12]. For example, bronchial pneumonia previously diagnosed during a CT scan was detected later by MRI in 21 out of 22 adults, and the efficacy of this technique was relatively high: sensitivity of 95 %, specificity of 88 %, positive prognostic value of 95 % [13]. MRI proved to be an effective diagnostic tool in the examination of 30 children (3–19 years of age) who had already been diagnosed with pneumonia based on the X-ray test [14]. The researchers concluded that MRI could be used as an alternative to X-ray or CT for the detection of pneumonia foci no smaller than 1 cm in size in the absence of calcification [13, 14]. Since MRI produces images in any projection and the patient is not exposed to radiation, it can be recommended for the dynamic assessment of pneumonia progression. Leutner et al. [15] demonstrated that MRI is more effective in diagnosing necrotizing pneumonia, compared to enhanced CT. MRI also proved highly effective in the differential diagnosis of causes of stillbirths and neonatal deaths [16, 17] and was successfully used to determine time of intrauterine fetal death by evaluating lung morphology [18, 19].

The aim of this work was to study a possibility of using postmortem MRI for diagnosing congenital pneumonia in autopsy material.

METHODS

We studied 21 dead neonates. Six to fifteen hours after infants had been pronounced dead but prior to autopsy, the bodies were scanned in standard T1 and T2 modes on 3T Magnetom Verio scanner (Siemens, Germany) set up to a field of view of 300 mm and a flip angle of 180°. T1-mode settings were as follows: slice thickness of 0.9 mm, repetition time of 1, 900 ms, echo time of 2.2 ms. T2-mode settings were as follows: slice thickness of 1 mm, repetition time of 3,200 ms, echo time of 410 ms. Using sagittal T1- and T2-weighted images, we measured signal intensity (SI) in the following regions of interest (ROI): the largest possible section of the right and left lung that did not contain big elements of the bronchovascular bundle, region of air in the area close to the anterior abdominal wall and in the pleural fluid. Then, an original airiness index (AI) was calculated for the right and left lungs as the ratio of the SI value of the pleural fluid to the SI value of the lung tissue. Because MR signal intensity within a given body region changes non-linearly and depends on a number of factors (distance from the scanner's isocenter, magnetic field homogeneity, physical properties of the surrounding tissues, etc.), to study its absolute value alone would be incorrect. We believe that airiness index allows minimizing or even eliminating measurement error related to the performance of an individual scanner.

After MRI scan, autopsy was performed followed by the analysis of hematoxylin- and eosin-stained histological slices. Based on the autopsy results, two groups were formed: group (the main experimental group) included bodies of 9 neonates who had died of congenital pneumonia 2 h 12 min to 36.5 days after birth; group II (the comparison group) included bodies of 12 neonates with no signs of pneumonia who had died 2 h 7 min to 24 days after birth. The bodies, the right lung and the left lung were weighted. The weight ratio of both lungs to the body was calculated.

Statistical processing was done using Statistica 8.0 software (StatSoft, USA). Mean values, standard deviations and a coefficient of variation were computed for each measured parameter. Differences were considered significant with $p < 0.05$. Using the obtained results, we calculated sensitivity, specificity and diagnostic efficacy of postmortem MRI in the diagnosis of congenital pneumonia.

The study was approved by the Biomedical Research Ethics Committee of Kulakov Research Center for Obstetrics, Gynecology and Perinatology (Protocol 25 dated June 22, 2012).

RESULTS

Morphological analysis of autopsy material obtained from the comparison group established that left lung weight varied from 2.1 to 36.5 g (coefficient of variation was 95.4 %) and right lung weight varied from 0.3 to 24.2 g (coefficient of variation was 50.9 %) (table 1). Mean weight of the left, right and both lungs was 10.8 ± 10.8, 11.5 ± 6.1 and 22.3 ± 14.6 g, respectively. Histological samples of lung tissue had signs of hypoplasia (in bodies with congenital diaphragmatic hernia) (fig. 1A), atelectases and dystelectases.

In neonates who had died of pneumonia, the weights of the left and right lungs were 4.1 to 42.7 g (coefficient of variation was 44.9 and 40.1 %, respectively) (table 1). Mean weights were 19.6 ± 9.3 and 24.1 ± 10.2 g, respectively; mean weight of both lungs was 45.9 ± 17.7 g. This indicates that all values were 1.8–2.1 times higher than in the comparison group ($p < 0.05$). The weight ratio of both lungs to the body was 2.4 times higher in the experimental group ($p < 0.05$). Histological samples obtained from group I showed signs of pneumonia manifested as weak monocyte/macrophage infiltration. (fig. 1B).

Visual analysis of T1- and T2-weighted images obtained from both groups indicated almost identical signal intensity in both lungs, but T2-weighted images reflected the organ structure more clearly, compared to T1-weighted images (fig.2, 3). The signal from the lungs of neonates who had died of pneumonia was more intense in both scanning modes as compared to the signal from the lungs of neonates who had died of other pathologies. It was 26.5 and 12.9 % more intense for the left and right lungs, respectively, on T1-weighted images and 23.7 and 31.2 % more intense on T2-weighted images ($p > 0.05$) (table 2). Nonuniform signal intensity within one lung was occasionally observed in the comparison group as a result of a haemorrhage (fig.4); differences in tissue brightness in the right and left lungs were due to organ compression caused by diaphragmatic hernia (fig. 5).

Mean airiness index of the left lung calculated upon the analysis of T1-weighted images of neonates who had died of pneumonia was by 44 % lower in the experimental group than in the comparison group; with the right lung, it was by 1.1 % higher (table 2). The same index calculated upon the analysis of T2-weighted images was lower for both lungs in the experimental group: by 14.3 % for the left lung and by 5.7 % for the right lung. When airiness index was calculated in the right and left lung separately, differences were statistically insignificant ($p > 0.05$). However, if the index value obtained from T2-weighted images was less than 2.5 in both lungs of a newborn, it indicated a morphologically confirmed pneumonia in the vast majority of cases (77.8 %).

Sensitivity of the applied technique was 77.8 %, its specificity was 75.0 % and diagnostic efficacy was 76.2 %, which indicates its high diagnostic value.

Table 1. Clinical and morphological features of dead neonates

Group	Case	Sex	Gestational age	Age	Body weight	Weight of both lungs	Right lung weight	Left lung weight	Weight ratio of both lungs to the body
I	1	F	38	5 сут. 11 ч	2080.0	43.2	22.1	21.1	0.021
	2	M	33	28 сут.	2800.0	58.6	25.2	33.4	0.021
	3	м	24	5 сут. 15 ч	800.0	16.3	12.2	14.1	0.020
	4	F	33	7 сут. 14 ч	2674.0	52.6	29.3	23.3	0.020
	5	M	35	36 сут. 10 ч	3206.0	43.9	23.3	20.6	0.014
	6	M	39	3 сут. 4 ч	3980.0	65.3	42.7	22.6	0.016
	7	M	30	5 сут.	1942.0	62.7	33.7	29.0	0.032
	8	F	33	1 сут. 1 ч	2636.0	21.3	17.2	4.1	0.008
	9	F	27	2 ч	980.0	19.3	10.8	8.5	0.020
	M ± SD		32.4 ± 4.8	10 сут. 7 ч	2344.2 ± 1018.4	45.9 ± 17.7	24.1 ± 10.2	19.6 ± 9.3	0.019 ± 0.006
II	10	M	40	2 ч	2747.0	15.7	9.6	6.1	0.006
	11	F	36	23 сут. 15 ч	1820.0	46.5	24.2	22.3	0.026
	12	M	39	23 ч	3538.0	13.2	6.2	7.0	0.004
	13	M	35	3 сут. 2 ч	1391.0	12.6	9.4	3.2	0.009
	14	F	39	2 сут.	3740.0	17.0	14.5	2.5	0.005
	15	F	39	21 ч	4450.0	21.3	11.4	9.9	0.005
	16	F	37	16 ч	2310.0	10.1	7.8	2.3	0.004
	17	M	40	6 ч	4550.0	13.6	11.3	2.3	0.003
	18	F	37	19 ч	2853.0	11.5	9.4	2.1	0.004
	19	M	37	4 сут.	3182.0	36.0	17.5	18.5	0.011
	20	F	39	24 сут.	5164.0	53.1	16.6	36.5	0.010
	21	F	37	1 сут. 11 ч	3770.0	17.1	0.3	16.8	0.005
	M ± SD		37.9 ± 1.6	5 сут. 10 ч	3292.9 ± 1134.7	22.3 ± 14.6	11.5 ± 6.1	10.8 ± 10.8	0.008 ± 0.006

DISCUSSION

For this work, we selected pleural fluid and air as the most stable lung components with regard to their physical parameters. Signal intensity varied in the area containing pleural fluid and air. Since there were no signs of pleuritis at autopsy, such variability was probably related to different scanner settings used by different tomography specialists. The presence of fluid of non-inflammatory origin (transudate-like) in the pleural cavity is indicative of early nonspecific postmortem changes [20] and is observed in all deaths, as proved by the autopsy.

Differences between groups with regard to airiness index were statistically insignificant, which might be due to a relatively small sample size and a need to assess lung pathology in each individual case and not in the whole group. However, we believe that AI <2.5 registered simultaneously in both lungs on T2-weighted images indicates pneumonia. This pattern was observed in 7 out of 9 cases in the experimental group. In two other cases, a higher AI was a result of concomitant pathologies: pneumothorax in case 1 and the edematous form of hemolytic disease in case 7. In the comparison group, AI was >2.5 for both lungs in 9 out of 12 cases. In three cases with airiness index <2.5 for both lungs indicating pneumonia, we detected multiple congenital defects (case 11) and false congenital diaphragmatic hernia with compression of the lungs (cases 13 and 18).

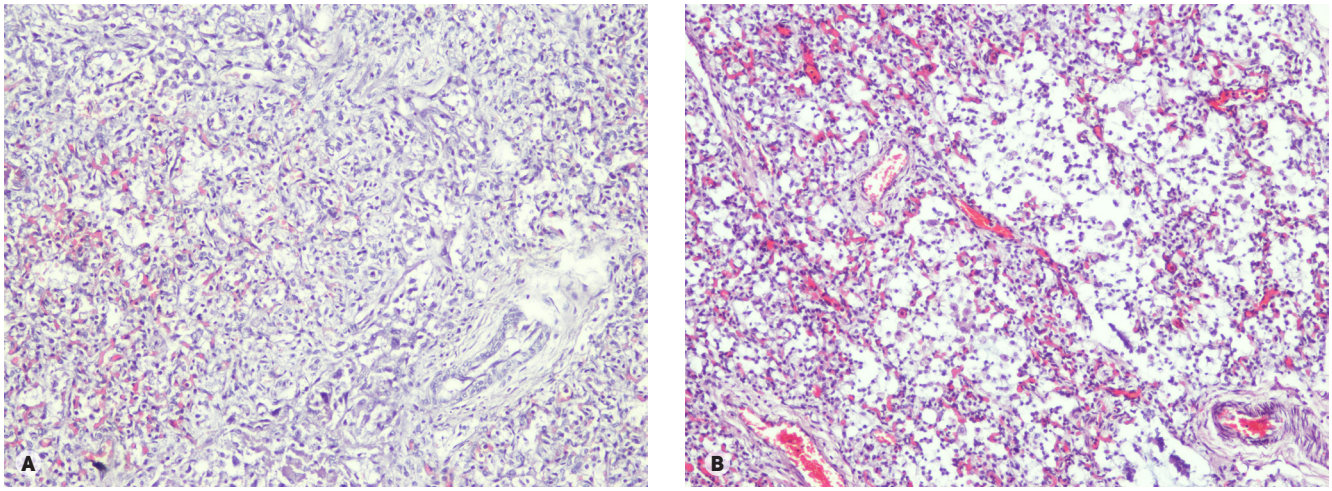

Fig. 1. Histological changes of lungs: **(A)** hypoplasia, **(B)** monocyte/macrophage pneumonia. Staining with hematoxylin and eosin, ×100

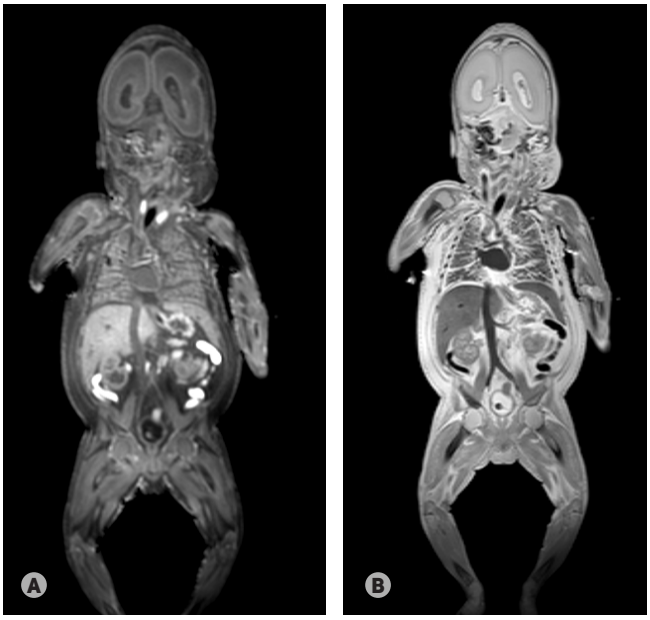

Fig. 2. Coronal MR-images of a dead neonate with congenital pneumonia (the experimental group): **(A)** T1-weighted image, **(B)** T2-weighted image

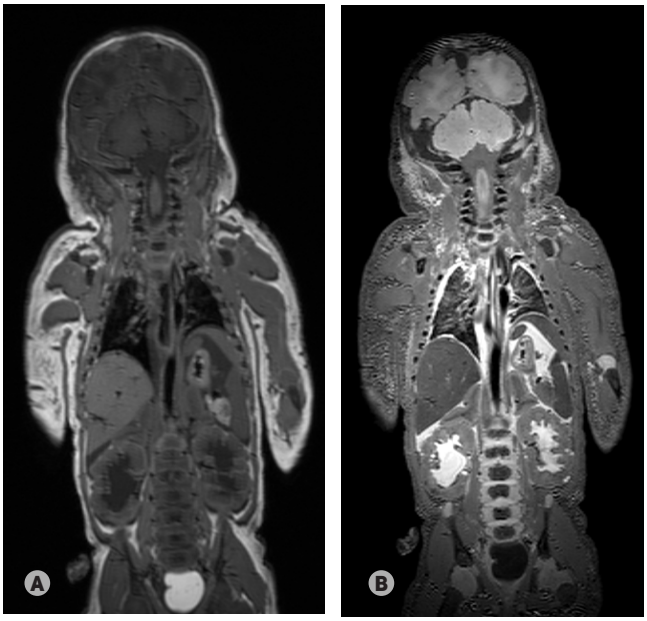

Fig. 3. Coronal MR-images of a dead neonate without lung pathology (the comparison group): **(A)** T1-weighted image, **(B)** T2-weighted image

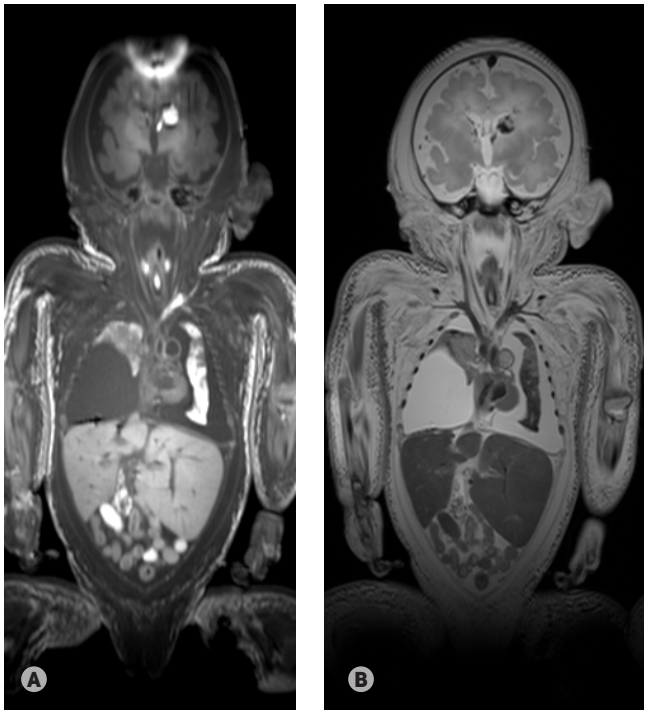

Fig. 4. Coronal MR-images of a dead neonate from the comparison group with hemorrhages in both lungs in the absence of pneumonia: **(A)** T1-weighted image, **(B)** T2-weighted image

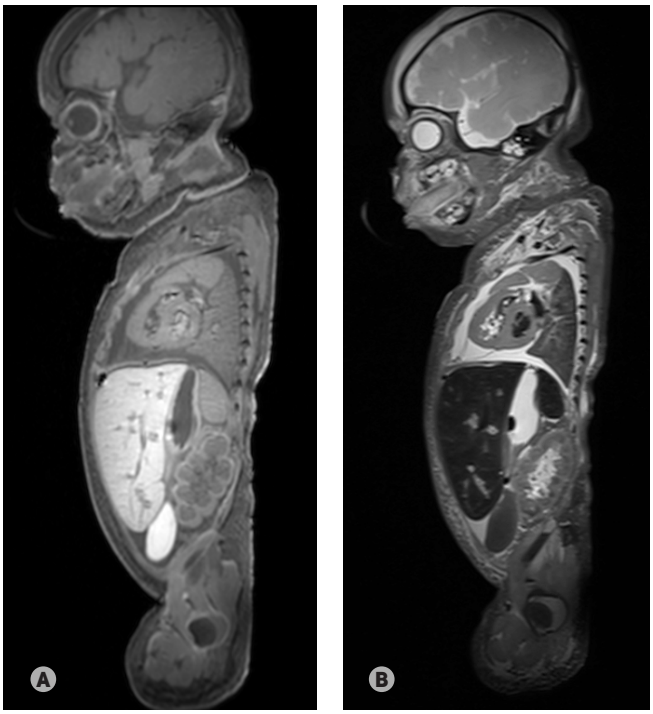

Fig. 5. Sagittal MR-images of a dead neonate from the comparison group with the intact left lung and right lung compressed by a diaphragmatic hernia

We think that airiness index allows for minimizing or eliminating measurement error related to the performance of an individual scanner and its settings.

Our results show a higher diagnostic efficacy of the applied technique as compared to the results obtained by Arthurs et al. [21], who demonstrated that sensitivity of the postmortem MRI in fetuses, newborns and children was 12.5 %, specificity was 92.6 % and the prognostic value of a positive result was 25 %. The reason here might be that the researchers visually assessed lung airiness and indurations to diagnose pneumonia. They also demonstrated that MRI diagnostic efficacy improves in older patients: the worst results (69.7 % of false negative results) were obtained for fetuses that had died before week 24 of gestation. On the one hand, MRI-based diagnosis of lung conditions, such as pneumonia, is a complicated clinical task; MR images of lungs are of low quality because of low proton density and a large amount of air-tissue gradients [22, 23]. On the other hand, back in the1990s Herold et al. [24] and Blum et al. [25] demonstrated moderate signal intensity on T1-weighted images and high signal intensity on T2-weighted images of immunocompromised patients with pulmonary aspergillosis. A definite MRI advantage is its ability to measure absolute and relative lung size that to some extent reflects progression of respiratory failure [26, 27].

Table 2 . Signal intensity and airiness index (AI) of lungs of dead neonates

Group	Case	T1-weighted images						T2-weighted images					
		Signal intensity				AI, RL	AI, LL	Signal intensity				AI, RL	AI, LL
		Right lung	Left lung	Air	Fluid			Right lung	Left lung	Air	Fluid		
I	1	128	664	6.0	515	4.0	0.8	120	330	3.0	880	7.3	2.7
	2	488	750	7.0	409	0.8	0.5	330	200	6.0	300	0.9	1.5
	3	538	517	9.0	379	0.7	0.7	416	345	4.5	735	1.8	2.1
	4	769	530	9.0	588	0.8	1.1	330	300	3.0	720	2.2	2.4
	5	566	492	6.0	293	0.5	0.6	380	290	1.0	523	1.4	1.8
	6	688	741	11	557	0.8	0.8	521	450	4.5	1122	2.2	2.5
	7	719	693	7.0	393	0.5	0.6	239	208	5.0	639	2.7	3.1
	8	479	595	12	444	0.9	0.7	446	453	6.0	920	2.1	2.0
	9	873	887	12	516	0.6	0.6	870	837	8.0	1120	1.3	1.3
	M ± SD	583.1 ± 217.2	652.1 ± 130.6	8.8 ± 2.4	454.9 ± 95.8	1.1 ± 1.1	0.7 ± 0.2	405.8 ± 209.8	379.2 ± 193.4	4.6 ± 2.1	773.2 ± 270.1	2.4 ± 1.9	2.2 ± 0.5
II	10	144	72	6.0	277	1.9	3.8	195	176	3.0	590	3.0	3.4
	11	938	871	9.6	736	0.8	0.8	552	465	4.0	996	2.1	2.1
	12	605	564	9.0	420	0.7	0.7	119	133	3.0	500	4.2	3.8
	13	624	585	7.0	430	0.7	0.7	363	365	3.0	672	1.9	1.8
	14	251	569	9.0	349	1.4	0.6	251	312	3.0	690	2.7	2.2
	15	477	384	10	340	0.7	0.9	265	237	3.0	598	2.3	2.5
	16	829	866	10	573	0.7	0.7	436	456	7.0	1140	2.6	2.5
	17	581	541	5.0	435	0.7	0.8	287	278	3.0	742	2.6	2.7
	18	524	388	7.0	261	0.5	0.7	279	396	4.0	583	2.1	1.5
	19	359	250	3.0	930	2.6	3.7	359	363	3.0	930	2.6	2.6
	20	504	678	3.0	341	0.7	0.5	446	323	2.0	926	2.1	2.9
	21	362	419	5.0	514	1.4	1.2	160	176	1.0	412	2.6	2.3
	M ± SD	516.5 ± 225.3	515.6 ± 232.8	7.0 ± 2.6	467.2 ± 197.5	1.1 ± 0.6	1.3 ± 1.1	309.3 ± 127.0	306.7 ± 109.6	3.3 ± 1.4	731.6 ± 220.5	2.6 ± 0.6	2.5 ± 0.6

Artifacts on MR images result from lung motion during aspiration and blood pulsations, especially in newborns [28]. They are not the case in postmortem MRI; however, we have to admit that there is a problem with accurate assessment of unspecific postmortem changes related to blood redistribution and autolysis [20, 29, 30]. To improve diagnostic accuracy and provide a possibility for differential diagnosis, some authors suggest histological analysis (apart from MRI) of lung tissue samples obtained percutaneously or endoscopically [31].

As postmortem MRI efficacy largely depends on the scanner type and its settings, special protocols should be elaborated considering scanner types, operating modes and corresponding software. Taylor et al. [32] inferred the necessity of using different protocols when analyzing the bodies of dead fetuses and infants.

CONCLUSIONS

Postmortem magnetic resonance imaging is effective in the detection of congenital pneumonia in stillborn babies and neonates who die shortly after birth. To verify the pathology, specific parameters of lung tissue on MR images are less important than a ratio of signal intensity in lung tissue to fluid signal intensity (pleural fluid in our case) on T2-weighted images. This ratio, or the airiness index, allows minimizing the impact of scanner settings on the procedure outcome. Differences in the airiness index between the studied groups of babies who died of congenital pneumonia and those who died of other causes were statistically insignificant because of a small sample size. A study with a larger sample may prove our hypothesis that airiness index less than 2.5 for both lungs on T2-weighted images can be used to diagnose congenital pneumonia.

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