MEDICAL SCIENCES

CONTRAST ENHANCEMENT PATTERNS OF BREAST LESIONS IN DUAL-ENERGY CONTRAST-ENHANCED SPECTRAL MAMMOGRAPHY

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Abstract

BACKGROUND: Dual-energy contrast-enhanced spectral mammography (CESM) is a relatively new method for visualizing breast changes, which combines structural assessment and functional assessment of vascularization. According to the literature interpretation of contrast images is based only on the degree of contrast enhancement, but we propose a more detailed assessment of the structure of the hypervascular lesions by highlighting the contrast enhancement patterns.

PURPOSE: to evaluate the diagnostic perfomance of dual-energy contrast-enhanced spectral mammography (CESM) using the contrast enhancement patterns in malignant and benign lesions.

MATERIAL AND METHODS: 332 women were examined from August 2018 to June 2020. The mean age of the women was 50 years. Totally 428 lesions were revealed, 172 (40.2%) of them were malignant and 256 (59.8%) were benign. All lesions were histologically verified. During the analysis of our data 9 types of contrast enhancement patterns were proposed: reticular, granular, annular, diffuse-spherical, lacunar, cloud-like, heterogeneous-annular, point, cotton-like.

RESULTS: Using an additional diagnostic feature of contrast enhancement pattern increased the sensitivity of CESM from 79.7% to 94.8% (p = 0.26), specificity from 82.4% to 95.3% (p = 0.013), accuracy from 81.3 to 95.1% (p = 0.004) in comparison with using of only one feature of contrast enhancement intensity in the differential diagnosis of malignant and benign lesions.

CONCLUSION: thus, using contrast enhancement pattern allows to increase the efficiency of CESM in breast cancer detection.

Keywords: breast cancer, dual-energy contrast-enhanced spectral mammography, digital mammography, contrast enhancement patterns, benign breast lesions.

Introduction

Contrast enhanced spectral mammography (CESM) is a new promising imaging modality for detection pathological lesions in breast. It combines a standard mammographic examination and functional assessment of vascularization using intravenous contrast enhancement (1, 2). A great advantage of CESM in comparison with digital mammography (DM) is subtraction of the fibroglandular tissue, which makes it possible to differentiate pathological vascularization in a dense breast (3, 4, 5). In addition, numerous studies have shown that high density is an independent risk factor for the development of breast cancer and at the same time contributes to low detection rates of pathology (6, 7).

The experience of using CESM indicates that the modality is well tolerated by patients and provides similar information to magnetic resonance imaging with dynamic contrast enhancement (MRI with DCE) with the advantages that CESM is more accessible and can be performed in patients for whom MRI is contraindicated (8).

Nevertheless, the experience of using CESM is still limited, there are unresolved issues, both in the methodology of the study and its scientific justification (9), as well as in the interpretation of the images. It is necessary to conduct further studies on CESM in order to reveal the possibilities. At the moment the interpretation of subtraction images is based only on the assessment of the degree of the contrast enhancement (10), which usually is divided into 4 or 5 grades (11). At the same time, criteria for an assessment of lesions with integration with the BI-RADS system have not been developed yet. Greek scientists proposed the malignancy potential score (MPS), when all lesions are divided into four types according to the contrast enhancement (-1, 0, 1, 2) with conclusion to a final assessment BI-RADS category according to changes on a low-dose images (12). Hypervascular structures with a moderate and intense enhancement are naturally suspicious of malignancy, and the absence and weak enhancement may indicate a benign process (12).

The advantage of CESM is the acquisition of functional data in combination with data from routine mammographic examination, in particular the identification of grouped calcifications with malignant characteristics. In the Netherlands, a study was conducted on the effectiveness of the use of CESM in identifying suspicious calcifications. It turned out that with the accumulation of a contrast agent in a suspicious area, confidence in the malignancy of the process increases, but the absence of vascularization does not exclude the presence of a tumor and does not change the tactics of treatment and the volume of surgical intervention (13). At the same time, Yun-Chung Cheung and et al., reported that CESM does not significantly affect the accuracy of diagnostic conclusions in the detection of calcifications with malignant characteristics (14).

We proposed a new approach to the description of hypervascular lesions in CESM – to take into account the types of contrast enhancement. The aim of the proposed study was to determine the diagnostic possibilities of CESM using types of contrast enhancement by malignant and benign lesions.

Materials and methods

This single-center prospective study was approved by the Institutional Ethical Committee. All patients signed a written informed consent. The study was performed in a group of 332 female patients (aged from 21 to 86; mean 50). A clinical and instrumental examination was conducted at N.N. Petrov National Medical Research Center of Oncology from February 2018 to June 2020.

Women were examined according to a unified algorithm for managing patients with breast pathology. All women underwent clinical and instrumental examination, including: physical examination, CESM, biopsy followed by pathomorphology studies, including immunohistochemistry. In women of reproductive age CESM was performed in the first phase of the menstrual cycle (from 5 to 12 days from the beginning of the cycle).

CESM was performed using a Senographe DS digital mammography system (General Electric, USA). System was equipped with an X-ray tube with a double molybdenum-rhodium anode track and a digital full-format flat-panel detector made of amorphous silicon with cesium iodide deposited on it. The resulting high-definition digital images were transmitted to the workstation. A special feature of the mammography system is a multilayer filter for the best visualization of the iodine contrast agent accumulation. This is done by adding a third filter made of copper and aluminum to the existing molybdenum and rhodium filters for high energy imaging. Also, a modification of the software was used to control the process of obtaining a series of two images with different exposure modes at CESM.

CESM was carried out after intravenous injection of a non-ionic iodine-containing contrast agent using power injector. The volume of contrast agent was calculated per body weight, 1.3 ml / kg with iodine concentration of 370 mg / ml and 1.5 ml / kg with iodine concentration of 350 mg / ml. Mammographic examination was performed with breast compression and included routine cranio-caudal (CC) and medio-lateral-oblique (MLO) views of the breasts. The latter displays tissue in larger volume and was performed at an angle of 45 degrees with simultaneous visualization of the axillary region and lymph nodes. Both breasts were examined regardless of the location of the suspicious lesion in order to timely diagnose clinically asymptomatic bilateral cancer (Fig. 1).

The diagnostic perfomance (sensitivity, specificity and accuracy) of CESM without taking into account contrast enhancement patterns (CESMnonep) and CESM with taking into account the contrast enhancement patterns (CESMep) was assessed. Negative and positive predictive values were also calculated. Pathomorphology was taken as the gold standard.

Results

Comparative analysis of CESMnonep and CESMep was performed in 332 women. There were 428 lesions identified, of which 172 (40.2%) were malignant and 256 (59.8%) were benign (Fig. 2). All lesions were histologically verified. Among malignant lesions invasive carcinoma of no special type were indentified in 152 (88.4%) patients, invasive lobular carcinoma in 3 (1.7%), lobular carcinoma in situ in 2 (1.2%), ductal carcinoma in situ in 8 (4.6%), mucinous carcinoma in 5 (2.9%), Paget's disease in 2 (1.2%). Among benign breast lesions fibroadenomas were found in 68 (26.6%) patients, intraductal papillomas in 16 (6.3%), cysts in 30 (11.7%), radial scar in 8 (3.1%), hamartoma in 15 (5.9%), benign phyllodes tumor in 3 (1.2%), localized adenosis in 72 (28.1%), lymphoceles in 12 (4.7%), oleogranulomas in 8 (3.1%), proliferative disease in 19 (7.4%) and inflammatory changes in 5 (1.9%). Of 322 lesions, 93 (28.9%) did not show contrast enhancement and 229 (71.1%) showed contrast enhancement.

By the grade of contrast enhancement, malignant tumors were distributed as follows: intense contrast enhancement was seen in 96 (55.8%), moderate - in 41 (23.8%), weak - in 30 (17.5%), no enhancement was observed in 5 cases (2.9 %). Benign lesions showed intense enhancement in 19 cases (7.4%), moderate - in 26 (10.1%), weak - in 89 (34.8%) and no enhancement in 122 (47.7%).

As a result of the analysis 9 patterns of contrast enhancement were identified:

1. Reticular, characterized by the presence of rounded low-contrast areas in the structure, also a hypervascular centre may be visualized that contributes to a feeding vessel;

2. Granular, characterized by numerous oval and round hypervascular areas separated by hypovascular bridges;

3. Annular, characterized by uniformly enhanced margins of the lesion;

4. Diffuse-spherical, characterized by uniformly enhanced smooth margins and by smooth enhancement radial gradient from the center to the periphery;

5. Lacunar, characterized by the presence of hypovascular areas with irregular shape, the margins of kesionare indistinct and wavy;

6. Cloud-like type resembles cirrus clouds with separate filamentous margins;

7. Heterogeneous annular, characterized by enhanced margins with presence of a parietal hypervascular area;

8. Point, characterized by a displaced radial gradient of contrast enhancement, the lesion consists of multiple rounded hypervascular areas of various diameters;

9. Cotton-like, characterized by the presence of a large hypovascular area with undulating fuzzy margins.

Fig. 3 and Fig. 4 illustrate contrast enhancement patterns.

According to obtained data (Table 1), only benign lesions showed granular, reticular, point and annular patterns - 14.8%, 6.3%, 10.9% and 10.5%, respectively. The diffuse-spherical pattern was observed both in malignant (22.7%) and in benign lesions (4.3%). The lacunar (33.1%) and heterogeneous annular (15.1%) patterns predominantly were seen in malignant lesions, however, these patterns were also seen in large intraductal papillomas and lymphoceles, oleogranulomas, respectively. Cloud-like (26.2%) patterns were only seen in malignant lesions. The cotton-like pattern was detected during early postoperative changes (2.3%).

Based on the data obtained we made the following conclusions:

- if granular, reticular, point, annular, cotton-like enhancement patterns are detected, benign lesions are diagnosed, regardless of the contrast intensity grade;
- if a cloud-like pattern is detected, malignant lesion is diagnosed;
- if diffuse-spherical pattern is detected, it is necessary to determine its margins on low-dose images. When circumscribed margins with a radiolucent rim are visualized, a benign formation is diagnosed, when lesion is absent or has indistinct margins on low-dose images, then a malignant lesion is diagnosed;
- if a lacunar pattern is detected, a malignant lesion is diagnosed. However large intraductal papillomas showed this enhancement pattern in two cases and that did not allow to exclude intraductal papillary carcinomas;
- if heterogeneous-annular pattern is detected with no history of any invasive manipulations for a long time in the area of contrast enhancement, malignant lesion is diagnosed. Moreover, there were false positive results in two cases due to complex cysts and cysts with inflammation after puncture.

As shown in Table 2, malignant tumors were characterized by intense and moderate grades of contrast enhancement in 79.7% of cases. However, 20.3% of malignant tumors had weak or no contrast enhancement, which was characteristic for benign lesions. When enhancement patterns were included in the analysis, the percentage of false negative conclusions in our study was reduced to 5.2%.

Benign lesions were characterized by intense and moderate degree of contrast enhancement in 17.6% of cases, and in this cases false positive conclusions were made. When enhancement patterns were included in the analysis, number of false positive decreased to 4.7%.

In CESMnonep there were true positive mammographic results in 137 lesions (TP), false positive results (FP) were in 45 lesions. In 211lesions the results were true negative (TN) and in 35 lesions the results were false negative (FN).
In CESMep the frequency of TP results increased up to 163, and the frequency of FN decreased to 9 lesions. In 12 lesions there were FP conclusions. In 244 lesions results were true negative. Thus, in CESMep the number of FP results decreased and the number of TP increased by 33 cases and the number of FN conclusions decreased and the number of TN increased by 26.

Sensitivity, specificity and accuracy were 79.7%, 82.4%, 81.3% in CESMnonep and 94.8%, 95.3%, 95.1% in CESMep, respectively. Positive predictive values of CESMep and CESMnonep were 93.1% and 75.3%, respectively, and negative predictive values of CESMep and CESMnonep were 96.4% and 85.8%, respectively.

As it was shown in the analysis of diagnostic errors, FN results in CESMnonep were more often observed in women (30 cases) with a weak enhancement. In these cases, CESMep showed the following malignant patterns: cloud-like and lacunar. On the contrary, FP results in CESMnonep were observed in women with fibroadenomas with high mitotic activity, phyllodes tumor, phyllodes tumor (45 cases).

The main reason for the FN results in CESMep (7 cases), was ductal carcinoma in situ represented by grouped malignant calcifications (Fig. 5) and occult breast cancer (2 cases). The main reason for the FP results in CESMep were observed in intraductal papillomas (4 cases) with a lacunar pattern (Fig. 6).

Our results demonstrate an increase in the diagnostic efficiency of the CESM in the differential diagnosis of breast lesions.

Discussion

Modern radiology offers a wide range of methods for breast cancer visualization, but they are not flawless. Mammography has been the main method for detecting breast pathology for many years (15).

With the transition from analog to digital mammography, the sensitivity in detecting of breast cancer was increased and also it became possible to develop more advanced imaging technologies like tomosynthesis and CESM (16). Tomosynthesis is linear tomography at a qualitatively new level with the using of flat digital detectors, modern high-performance computers and methods of digital postprocessing and reconstruction.

The principle of tomosynthesis is a sequence of tomograms followed by the formation of three-dimensional images. In tomosynthesis the overlying layers of tissue are removed, which creates opportunities for a more accurate assessment of the structural features of the lesion. However, removal of the overlying structures may not be enough to detect of a malignancy, since the difference in attenuation coefficients between fibroglandular and tumor tissue varies from 4% at 15 keV to 1% at 25 keV (16). CESM is another technology which appeared after the introduction of digital mammography. The theory of CESM is based on the success of breast MRI with DCE, which is currently the most sensitive method of breast visualization with a sensitivity of up to 98% (17-18). Early diagnosis of breast cancer using MRI is based on the ability of DCE MRI to determine tumor vascularization. The main disadvantage of MRI study is the high cost, long duration, the complexity of implementation, the presence of contraindications. CESM can become a worthy alternative to functional visualization of breast lesions. Our results (19) and results the other research groups (20-23) demonstrate the high informativeness of CESM in the diagnosis of breast cancer. Accurate differential diagnosis of breast lesions allows choosing the correct treatment tactics for these patients and reducing the number of unnecessary invasive interventions.

Conclusion

CESM allows to combine analysis of mammographic structure and vascularization of breast lesions. CESM does not significantly increase duration of procedure, it allows to obtain important additional information that is easy to interpret. Comparing to MRI CESM is characterized by lower cost, short study time, ease of implementation and interpretation, especially for specialists with experience in mammography, it can be performed in patients with contraindications to MRI with DCE and with claustrophobia. CESM can increase the sensitivity of digital mammography in detecting minimal, multifocal, multicentric and bilateral breast cancer.

The method of differential diagnosis of breast cancer using an additional diagnostic feature of enhancement patterns increases the diagnostic perfomance of CESM, which is confirmed by a high percentage of coincidences with pathomorphological results. It was proved that using an additional diagnostic feature of the enhancement patterns in comparison with the analysis of only the enhancement intensity increased the sensitivity from 79.7 to 94.8% (p = 0.26), specificity from 82.4% up to 95.36% (p = 0.013), accuracy from 82.4% to 95.1% (p = 0.004) due to additional information of the structure of vascularization.

The use of CESM can significantly increase both the negative predictive values (from 85.8% to 96.4%, p = 0.098) and the positive predictive values (from 75.3% to 96.4%, p = 0.039) in the differential diagnosis of malignant and benign breast lesions.

Table 1.

Contrast enhancement patterns of breast lesions

Contrast enhancement patterns	Malignant lesions N=172	Benign lesions N=256
No enhancement	5 (2.9%)	122 (47.7%)
Reticular	0 (0.0%)	16 (6.3%)
Granular	0 (0.0%)	38 (14.8%)
Annular	0 (0.0%)	27 (10.5%)
Diffuse-spherical	39 (22.7%)	11 (4.3%)
Lacunar	57 (33.1%)	5 (2.0%)
Cloud-like	45 (26.2%)	0 (0.0%)
Heterogeneous-annular	26 (15.1%)	3 (1.2%)
Point	0 (0.0%)	28 (10.9%)
Cotton-like	0 (0.0%)	6 (2.3%)

Table 2.

Grade of contrast enhancement of breast lesions

Grade	Malignant lesions N=172	Benign lesions N=256
no enhancement	5 (2.9%)	122 (47.7%)
weak enhancement	30 (17.5%)	89 (34,8%)
moderate enhancement	41 (23.8%)	26 (10,1%)
intense enhancement	96 (55.8%)	19 (7.4%)

Table 3.

Comparative analysis of CESM diagnostic performance without using patterns of enhancement and with using patterns of enhancement (number of lesions n=322)

Diagnostic modality	Number of lesions				Diagnostic performance, %				
	TP	FP	FN	TN	Sensitivity %	Specificity %	Accuracy %	Positive predictive value %	Negative predictive value %
CESMnonep	137	45	35	211	79.7	82.4	81.3	75.3	85.8
CESMep	163	12	9	244	94.8	95.3	95.1	93.1	96.4
P -value					0,26	0,013	0,004	0,039	0,098

TP – true positive
FP – false positive
FN – false negative
TN – true negative
CESMnonep – CESM without using patterns of enhancement
CESMep – CESM with using patterns of enhancement

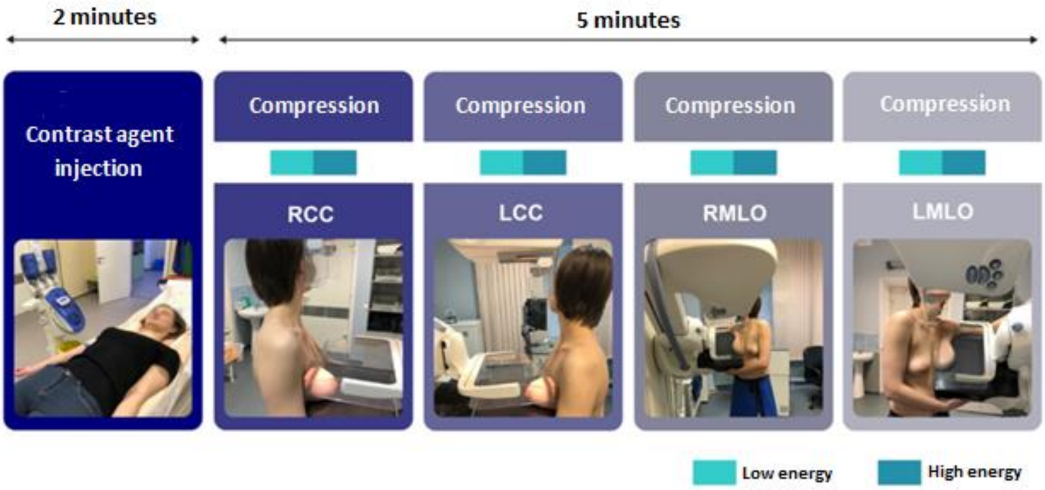

Figure 1. Scheme of implementation of CESM

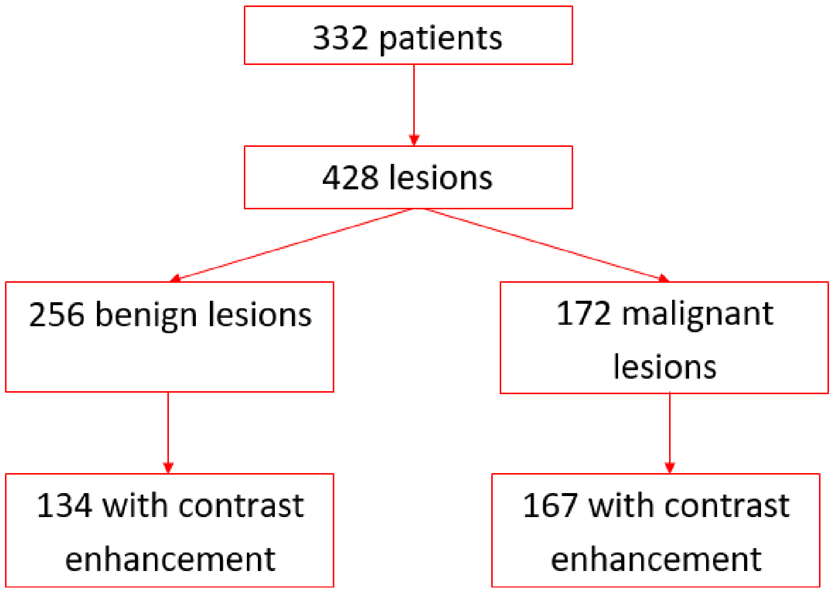

Figure 2. Study design

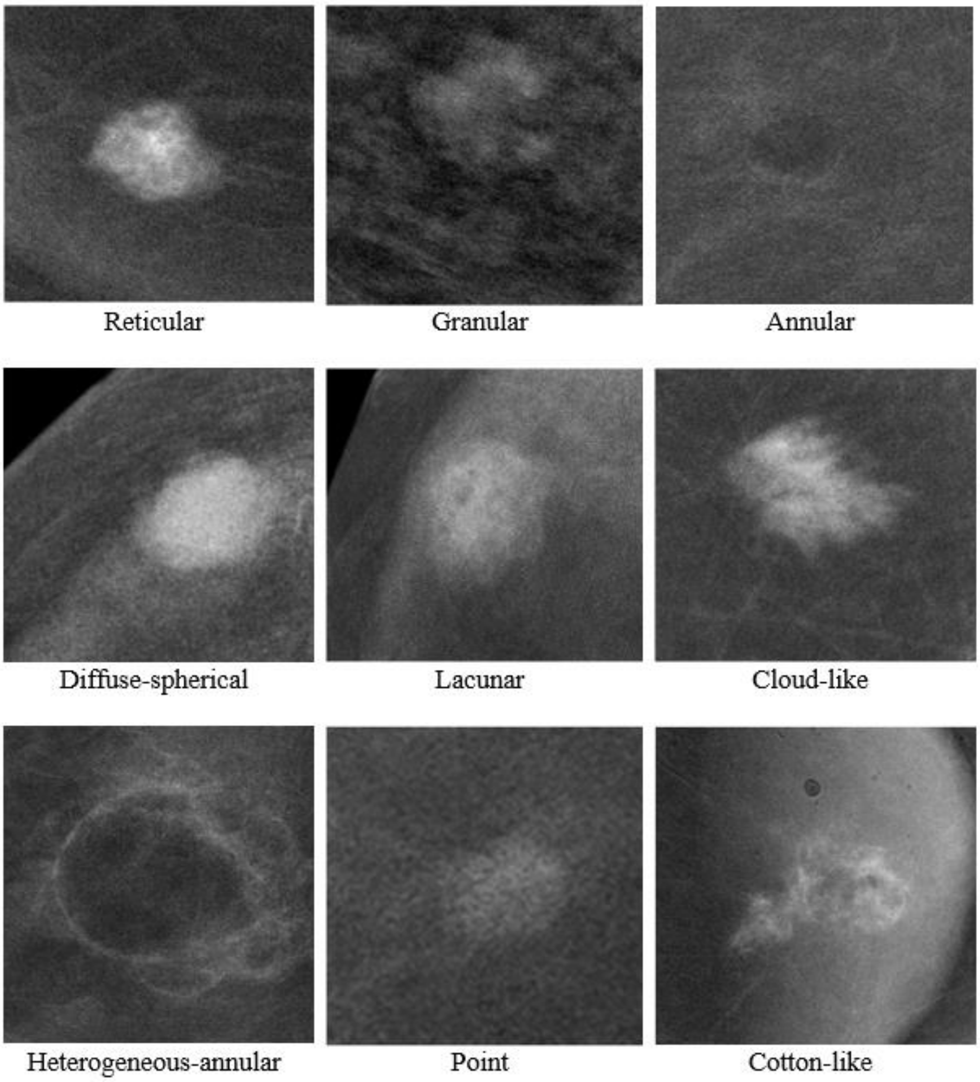

Figure 3. Contrast enhancement patterns

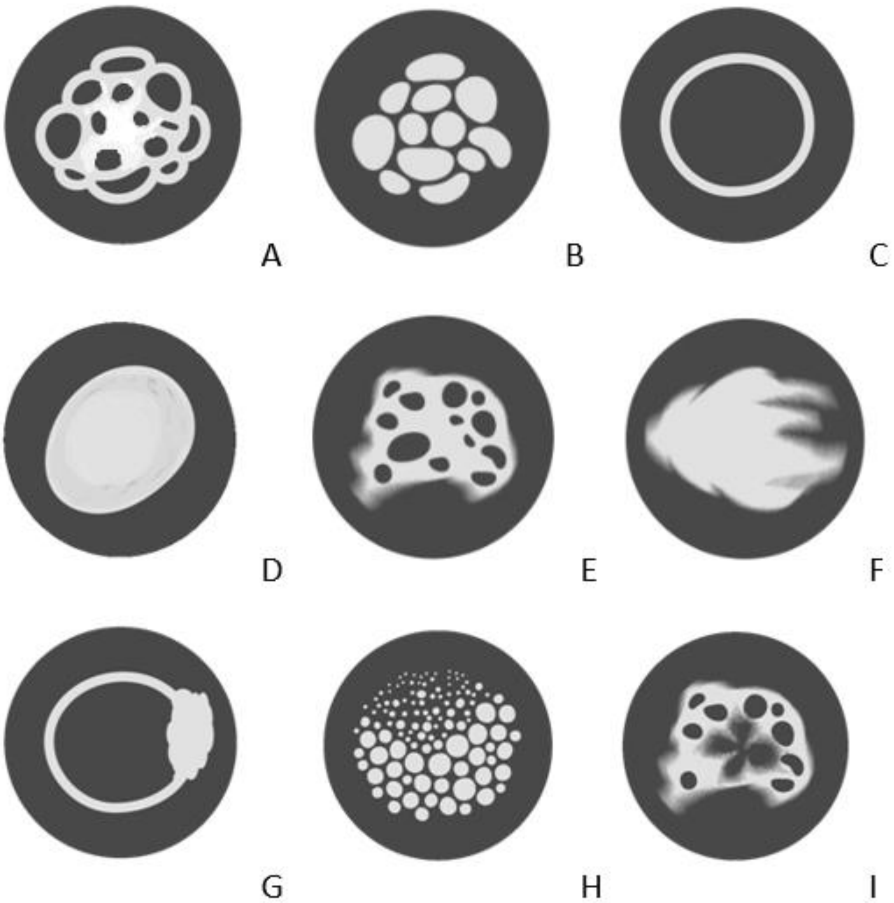

Figure 4. Figure of enhancement patterns of masses, architectural distortions, focal asymmetry in CESM: A – reticular, B – granular, C – annular, D – diffuse-spherical, E – lacunar, F – cloud-like, G – heterogeneous-annular, H – point, I - cotton-like

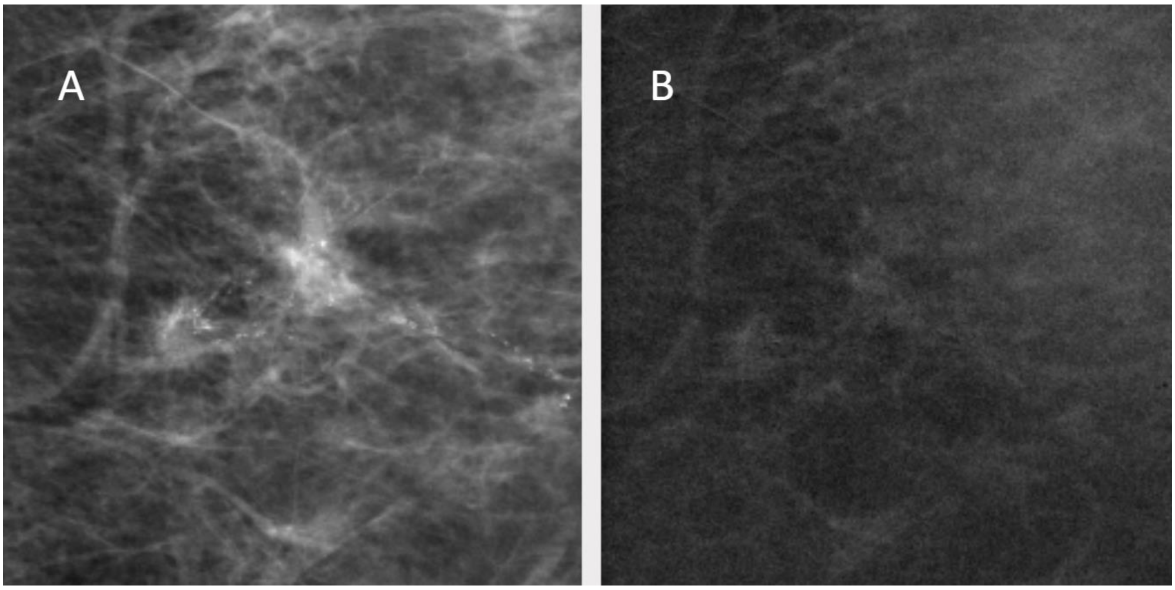

Figure 5. Ductal carcinoma in situ on CESM
A – low-dose image, cancer is visualized as grouped malignant calcifications;
B – subtraction image, no contrast enhancement was seen in this area

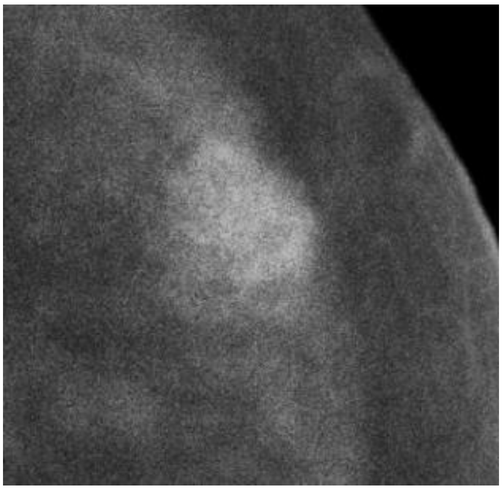

Figure 6. CESM, subtraction image. Intraductal papilloma with an intense lacunar enhancement pattern

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EFFICACY OF HIGH-CONCENTRATED OXYGEN INHALATIONS ADDING CAMOMILE OIL AT PATIENTS WITH VIRAL PNEUMONIAS

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Abstract

The aim - to study the clinical manifestations, capillary blood saturation, frequency of respiratory failure in patients with complicated forms of viral pneumonia.

Materials and methods. The study included 45 patients with viral pneumonias (mean age was 46.5±9.2 years). Patients observed were randomized into 2 groups. In group 1 (n=20), the only basic therapy was prescribed. In group 2 in addition to the basic therapy the inhalations with high concentrated oxygen with Camomile Oil were used.

The results of the study. It is proved that the use of highly concentrated oxygen with camomile oil in the inhalation treatment regimen significantly reduces the duration of local respiratory symptoms ($p<0.001$) and symptoms of general intoxication ($p<0.001$), prolonged hospital stay decreases by an average of 5 days ($p<0.001$). The relief of symptoms of RF in group 2 was noted for 10 days of hospitalization with an increase in capillary blood saturation (SatO2,%) to 95.2±2.91. Absolute therapeutic efficacy (absolute efficacy) of the correction of RF during complex treatment with the addition of highly concentrated oxygen was 85.0% versus 40.0% in group 1. Relative efficacy (relative efficacy) was 0.47 [0,27-0,83], with Odds Ratio (OR) – 0.12 [0,03-0,54]; $p<0.05$.

Conclusions. High-concentrated oxygen inhalations adding camomile oil is effective in complex treatment at patients with viral pneumonias.

Keywords: viral pneumonias, complications, oxygen inhalation.

Introduction. Regardless of the etiology of viral pneumonias (parainfluenza, adenovirus, respiratory syncytial, rhinovirus, reovirus, coronavirus infection and more than 200 pathogens), they are characterized by a short incubation period, generally a short fever, intoxication and damage to various parts of the respiratory tract [1].

Clinical differentiation of respiratory infections is difficult due to similar symptoms and clinical conditions [2, 3]. In case of damage and malfunction of the epithelium due to dryness, contamination, excessively high or excessively low temperature of the inhaled air, a change in the mucous membrane due to the use of some intranasal agents, the penetration of viruses into tissues is greatly facilitated [4, 5, 6].

According to studies, more than half of patients admitted for treatment in a hospital with complications of acute respiratory viral infections have hypoxemia and an increase in the partial pressure of blood carbon dioxide (pCO_2) above 45 mm Hg at the time of the initial examination. 20 % of patients with hospitalization due to exacerbation of the disease have respiratory acidosis [7, 8, 9]. Lesions of the lower respiratory tract (bronchitis or pneumonia) with acute respiratory viral infections can lead to the development of decompensated hypercapnia, which is most often the cause of the development of respiratory acidosis [10, 11, 12].

Nowdays, the question of the effectiveness of inhalation of highly concentrated oxygen, in particular, the use of pocket spray in these patients, is not sufficiently studied.

The aim - to study the effecticacy of highly concentrated oxygen inhalations with the addition of