CLINICAL TRAILS REPORT

Electrical Impedance Multifrequency Mammographer (MEM)

YAROSLAVL STATE MEDICAL ACADEMY

"APPROVED BY"

Rector of the Yaroslavl State Medical Academy, Professor

/Signature/ A.V. Pavlov

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Modern medicine has a huge arsenal of diagnostic methods. Nevertheless, the work on creating new ones and improving the existing methods of diagnostics continues. Currently, the diagnostics of mammary glands diseases is mainly focused on the mammography and the ultrasound examination. X-ray mammography method sensitivity is very high (71% -86.8%) when conducting the examinations of the mammary gland with a large amount of adipose tissue on the background of involution. And in young women with a glandular structure type, in the case of so-called radiographic "dense" mammary glands, the informativity is reduced, and sometimes it is doubtful. X-ray mammography method specificity is 37.8%. The reliable differential diagnostics for the differentiation between cysts and solid growths is not always possible, some cumulative signs of malignant growths stimulate a nonmalignant process. If there is a suspicion of intraductal process localization, it is necessary to supplement the mammography with the contrast-enhanced ductography. In addition, the X-ray mammography is performed once in 1 - 1.5 years; it is associated with the radiation exposure, and the use of the method without indications in women younger than 35 years is not recommended. Using the method in the dynamics for the evaluation of the mammary glands state in different phases of the menstrual cycle, in pregnant women, for the treatment effectiveness monitoring is not permitted. Another diagnostics method of mammary gland diseases - the ultrasound examination - today is very promising. Sensitivity of the ultrasound examination in the differential diagnostics of nonmalignant and malignant tumors is 98.4%, and specificity is 59%. But the accuracy of the diagnostics depends on the device technical specifications (ultrasound examination device class), the qualification of the examiner, the patient's age and hormonal status, the disease type and stage. Paracentesis with the cytologic material examination takes an important place in the mammary gland cancer diagnostics. Using this method, it possible to diagnose cancer in 89.4 - 97.3% of patients. But the frequency of errors in the cytologic diagnostics in patients with nonmalignant tumors of the mammary glands reaches 7%, and the cases of non-informative paracentesises - 18.6%. Significant disadvantages include unsuccessful paracentesises, small quantity or absence of the material, and insufficiently developed morphological criteria for the proliferative dysplasia cases and early forms of highly differentiated cancers. The use of other methods - NMR (Nuclear Magnetic Resonance), thermography, radioisotopic methods - is much less affordable due to the high examination cost. Therefore, many specialists conducting the diagnostics, treatment and rehabilitation of the patients with cancer and other mammary gland diseases face the task of finding a new and effective early detection method of the mammary glands pathology that differs from others in affordability, safety and informativeness.

At present, we have got an opportunity to visualize the mammary gland tissues with the use of the Electrical Impedance Tomography (EIT) - a method of obtaining an image of impedance distribution in tissues.

Until recently, there were known ways to obtain a tomographic image of a patient's body, based on the measuring the spatial distribution of the physical field or radiation, penetrating the object, and then by reconstructing the image using mathematical methods.

The operation of well-known tomographs is based on the use of X-ray radiation or nuclear magnetic resonance. They provide high resolution capabilities. However, the complex X-ray or nuclear magnetic resonance equipment used for the diagnostics is expensive and quite complicated in operation, the examination procedure is long enough, in addition, the radiation passing through the body is not harmless to the patient and care-taking personnel.

Specialists know about the method for obtaining a tomographic image of the body for the diagnostics in medicine, based on the use of electric current as a means of probing the object to be examined - the electrical impedance mammography. In this method, a series of contact electrodes is placed on the body surface, a current source is connected in series to the electrode pairs, potential differences are measured between each pair of remaining electrodes, and the body's conductivity spatial distribution image is reconstructed. However, the use of this method in the clinical practice until now has been hampered, in particular, by the unresolved problem of obtaining "static" images during performing the measurements on the human body. Existing tomographs allow to obtain only dynamic tomograms, which is poorly informative for clinical applications.

At the end of the 90s, the Moscow Institute of Radio Engineering and Electronics of the Russian Academy of Sciences developed a compact single-frequency electrical impedance tomograph that made it possible to obtain a qualitative body volume conductivity image with high sensitivity and satisfactory resolution capabilities, which allowed it to be used in the medical practice.

Clinical examination method of the mammary glands was developed on the basis of the Department of Obstetrics and Gynecology of the Yaroslavl State Medical Academy and Municipal Health Care Institution Clinical Hospital No. 9 in Yaroslavl. In the device licensing process, the clinical trials were conducted on the basis of the Russian Center of Roentgenology, as well as on the bases of functional diagnostic departments and radiology departments of out-patient clinics in Moscow. In addition, the developed technique was tested on the basis of the oncology department of the hospital in the state of Colorado, USA.

When working with a single-frequency tomograph, we came to the following conclusions:

1. The electrical impedance mammography method is simple, affordable, inexpensive, has no contraindications for the application, is not accompanied by the radiation exposure, non-invasive, allows not only to visually evaluate the received electrical impedance images, but also to quantify the

mammograms, which is very important in the differential diagnostics of various mammary gland conditions and their pathology.

2. It does not have any contraindications for the application and multiplicity limitations for examination procedures, which is important for the dynamic observation of women with the mammary gland pathology, for treatment monitoring, when using COCs (combined oral contraceptives) or HRT (hormone replacement therapy) drugs.

3. It gives an opportunity to carry out the examination of pregnant women and puerperas.

4. The created electrical impedance mammographer can be used in hospitals, out-patient clinics, women's health consultation clinics, doctor's offices and other medical and preventive facilities.

In recent years, the Institute of Radio Engineering and Electronics of the Russian Academy of Sciences has developed the multifrequency mammography program. Since 2005, on the basis of the Department of Obstetrics and Gynecology of the Yaroslavl State Medical Academy, the work has been carried out whose purpose is to evaluate the capabilities of the multifrequency electrical impedance mammography in the diagnostics of various mammary gland diseases and identify its differences from the single-frequency tomography.

Since January 2005, the examinations were carnied out for 2,340 women from 19 to 73 years old. We used the following diagnostics methods:

- ultrasound examination of the mammary glands, which was carried out for all patients from the 5th to the 9th day of the menstrual cycle on ultrasound device “Combison 530” with the use of 7.5MHz electronic linear sensor;
- X-ray mammography was performed from the 5th to the 9th day of the menstrual cycle in women over 35 years old on the X-ray apparatus "MAMMODIAGNOST UC". We used ACFA MAMORAY HDR film and KODAK min-R cassette;
- the electrical impedance mammography was performed for all patients using a multi-frequency 256-electrode electrical impedance mammographer (MEM) developed by the Institute of Radio Engineering and Electronics of the Russian Academy of Sciences, at frequencies of 10 kHz and 50 kHz from 3 to 10 and from 17 to 28 day of the menstrual cycle;
- the puncture biopsy was performed with the use of a special puncture needle according to the standard procedure after obtaining the results of ultrasound and X-ray examinations;
- the obtained examination results were subjected to statistical processing using the method of alternative variation with the calculation of the average value and the standard deviation.

Student's t-test was used to assess the reliability, the reliability value of which was determined from the table.

Age groups were selected taking into account the periods of age-related mammary gland structure rearrangement as follows:

- up to 34 years old - unchanged mammary glands;
- 35-40 years old - gradual loss of glandular structures;
- 41-45 years old - thickening of the cylindrical duct epithelium, thickening of the basal membrane and fibrous restructuring of the connective tissue;
- 46-50 years old- dilation, and sometimes the cystic dilatation of lactiferous ducts, clamped by the fibrous tissue;
- after 51 years old- a slow obliteration of lactiferous ducts, as well as small diameter vessels, and the adipose tissue formation.

In order to identify the multifrequency electrical impedance mammography technical capabilities in the diagnostics of the mammary gland diseases, the examination of women began with the use of the following well-known methods: the ultrasound examination and x-ray mammography examination (in women over 35 years old).

For the purpose of diagnosis verifying, the puncture biopsy was performed in the case of detecting the mammary gland pathology.

Examination results.

450 women, with the ultrasound examination signs listed below, comprised 1 clinical group (control group):

- correspondence of the ultrasound type of the mammary gland structure to the patient's age (juvenile, reproductive, premenopausal);
- correspondence of the ultrasound image to different physiological periods of the woman's life (the first phase of the menstrual cycle, the second phase of the menstrual cycle);
- clear differentiation of mammary gland tissues;
- parenchymatous tissue thickness- not more than 14 mm;
- absence of focal symptomatology, ductectasia, duct wall fibrosis;
- absence changes in regional lymph efflux zones.

The second clinical group consisted of 1,770 women with the mastopathy who, during the ultrasound examination, had the following signs:

- mismatch between the breast structure type and the woman's age;
- glandular tissue layer thickening to more than 14 mm in all cases of the diffuse mastopathy;
- fibrotic changes (fibrosis of duct walls, interlobular partitions);
- change in the parameters of the glandular tissue echolucency not corresponding to the patient's age;
- ductectasia, thickening of the walls, lumen enlarging, duct contour unevenness, pocket-like expansions along the main duct axis;
- presence of multiple cysts.

Women with the mastopathy from the second group were divided into two subgroups:

- 1st type Mastopathy – without a cystic component (960 people);
- 2nd type Mastopathy – with the presence of single or multiple cysts (810 people).

The third clinical group consisted of 98 women with the fibrous adenoma who, during the ultrasound examination, had the following signs:

- presence of a single, rarely multiple oval with hypehyperechogenic rechoic clear, even contours, a hypoechogenic heterogeneous growth structure with hyperechogenic inclusions of different sizes;
- presence of the "slippage" symptom - the tumor displacement in the surrounding tissues;
- pseudo-enhancement effect behind fibrous adenoma.

The fourth clinical group consisted of 23 women with focal lesions, among whom some of the following signs were found during the ultrasound examination:

- stellate shape;
- fuzzy uneven contours;
- solid, cystic-solid "complex" structure;
- nonhomogenous hypoechogenic internal structure with hyperechogenic inclusions inside;
- spreading inward (vertically), that is, П/ПЗ <1.4
- asymmetric dilatation of the lactiferous duct in the form of a hypoechogenic undisplaced structure;
- presence of the anechoic rim around the growth;
- acoustic shadows;
- pseudo-enhancement effect behind the growth.
- presence of lymph nodes in the lymph efflux regions.

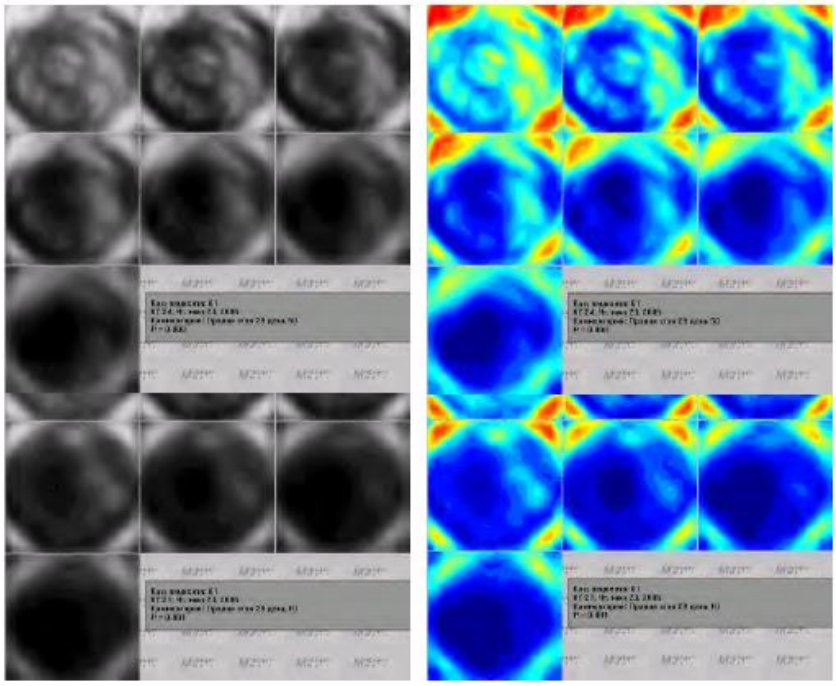
Electrical impedance images in the normal state

The electrical impedance image of the mammary gland is presented in the gray scale gradations with smooth transitions from dark (hyperimpedance) to light (hypoimpedance) regions, that is, from low electrical conductivity to high electrical conductivity regions. The anatomical structure complexity and the presence in the structure of tissues having close electrical properties explains the "mosaic" effect of the electrical impedance image. Nevertheless, on the tomograms, the electrical impedance anatomy corresponding to the normal structure of the mammary gland in different physiological periods of a woman's life is clearly traced. Additional color contrast enhancement helps to identify the anatomical landmarks.

When analyzing the images, it is necessary to consider the following factors:

- electrical impedance anatomy (Figure 1, 2, 3, 4, 5);
- correspondence of the electrical impedance image to the age type structure of the mammary gland(Figure 1, 2, 3, 4, 5);
- presence of the image contours deformation (Figure 5);
- architectonics abnormality of internal structures (Figure 5);
- presence of focal lesions and the nature of the contour around them (Figure 5);
- difference in the images, depending on the scanning position and side;
- symmetry of the electrical conductivity frequency distribution graph (Figure 1, 2, 3, 4).

Figure 1.Electrical impedance mammography.
Juvenile type. 19 years old. 50 KHz. 10 KHz.



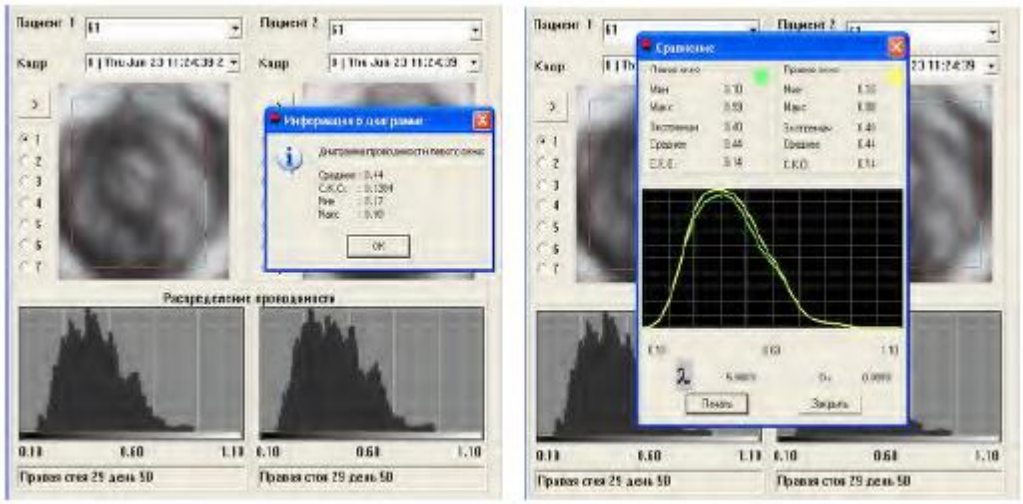


Figure 2.Electrical impedance mammography.

Reproductive type. 36 years old. 50 KHz. 10 KHz.

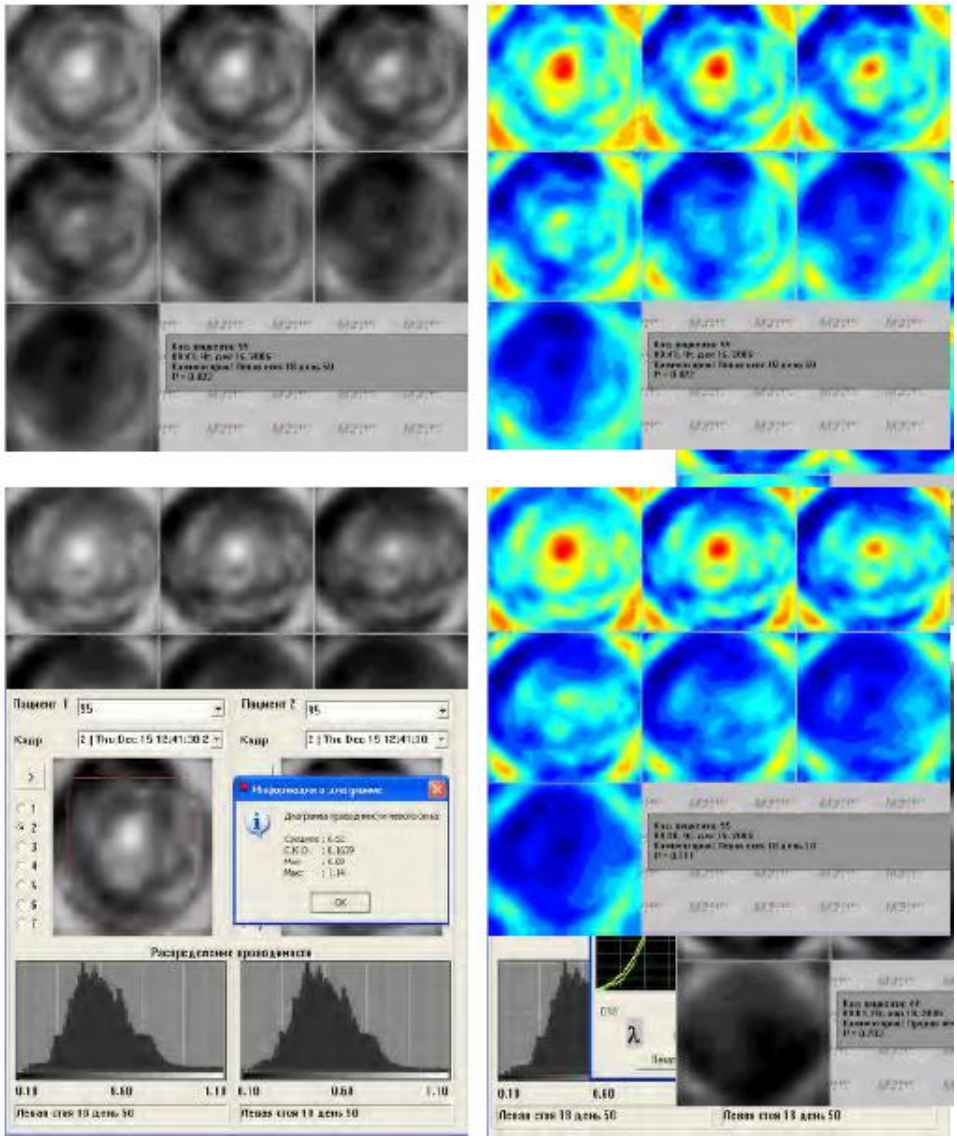


Figure 3.Electrical impedance mammography.

Premenopausal type. 48 years old. 50 KHz. 10 KHz.

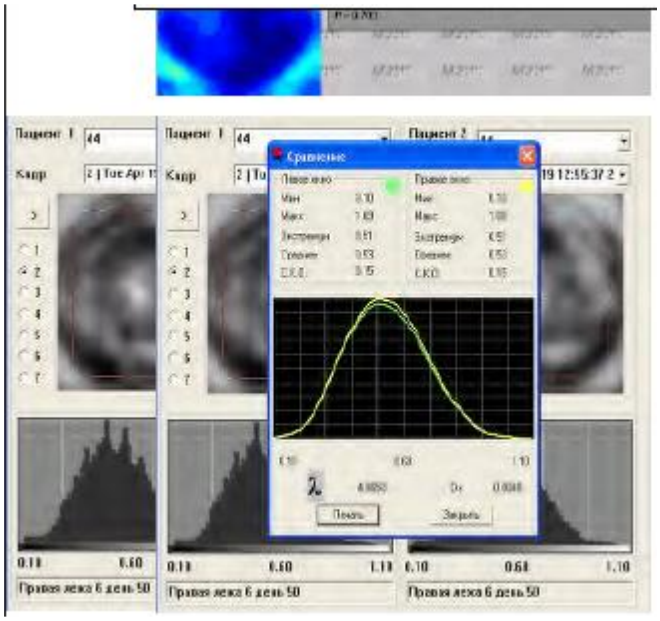


Figure 4.Electrical impedance mammography.

Postmenopausal type. 52 years old. 50 KHz. 10 KHz.

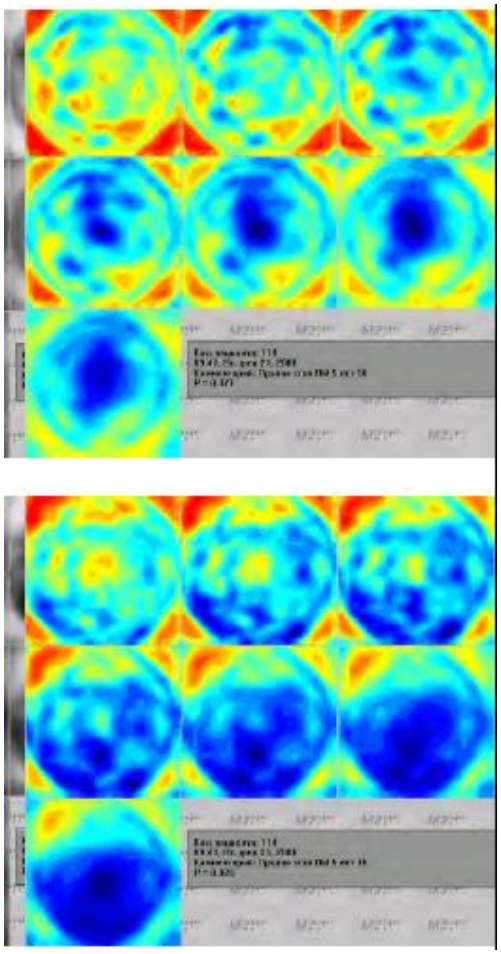
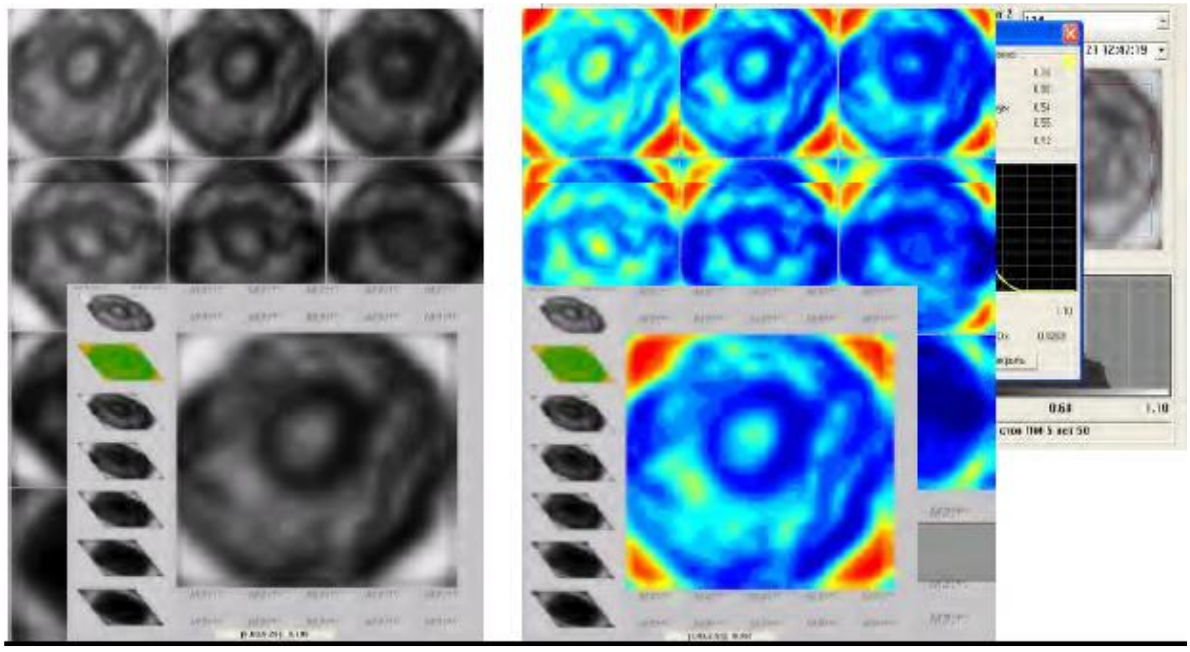


Figure 5.Electrical impedance mammography.

50 KHz. 10 KHz.



Quantification of electrical impedance images in the normal state

Absence of the deformation of image contours and displacement of internal structures, the absence of architectonics abnormality due to the proper anatomical structure, absence of focal lesions.

Experience of many years work has proved the absence of the statistically significant difference in the electrical conductivity parameters depending on the position during the examination (lying - standing) and the scanning side (right - left mammary gland). The percentage of the difference in the average electrical conductivity in the normal state between the right and left mammary gland, as well as in the lying and standing positions, does not exceed 7%. Behavior patterns of the change in the electrical conductivity are the same at all levels, respectively. Therefore, for the best visibility, it is recommended to use the average values from 2 scanning level (depth of 1.2 cm). In addition, taking into account the anatomical structure, the detection of all the tissues and structures of the mammary gland is possible at this depth. Table 1 presents the obtained results.

Electrical conductivity is expressed in relative value units.

Table 1. Average electrical conductivity of mammary glands in the normal state in different phases of the menstrual cycle and in the postmenopause in women of different age groups (10 kHz, 50 kHz)

	19 - 34 years old		35 – 39 years old		40 – 44 years old		45 – 50 years old		51 - 55 years old Postmenopause	
	50 KHz	10 KHz	50 KHz	10 KHz	50 KHz	10 KHz	50 KHz	10 KHz	50 KHz	10 KHz
Normal state 1 phase of MC	0.43±0.09	0.37±0.09	0.47±0.09	0.44±0.09	0.47±0.08	0.41±0.09	0.52±0.03	0.48±0.05	0.56±0.06	0.51±0.07
Normal state 2 phase of MC	0.43±0.09	0.39±0.08	0.48±0.03	0.43±0.04	0.48±0.03	0.43±0.03	0.53±0.05	0.48±0.05	0.56±0.06	0.51±0.07

Diagnostics of mammary gland diseases with the use of the electrical impedance mammography method

Dishormonal hyperplasia (mastopathy)

According to the definition of the WHO (World Health Organisation) (Geneva, 1984), the mastopathy is understood as the mammary gland dysplasia, fibrocystic-cystic disease characterized by a wide spectrum of proliferative and regressive changes in the mammary gland tissue with an abnormal ratio of epithelial and connective components. These changes are combined in different ways. Among a number of mastopathy classifications for the clinical practice, the most convenient is the one described in the methodological recommendations of the Ministry of Health of the Russian Soviet Federated Socialist Republic "Tactics of a comprehensive examination of women with the syndrome of diffuse changes in the mammary gland" (1985):

1. Diffuse fibrocystic mastopathy:

- with a predominance of the glandular component

- with a predominance of the fibrotic component

- with a predominance of the cystic component

- mixed form

2. Nodular fibrocystic mastopathy.

In practice, more often we have to deal with a mixed form of the diffuse mastopathy, in which all the above morphological changes are expressed to varying degrees. To determine the rational tactics of conducting the treatment of women with the dishormonal hyperplasia, it is expedient to divide the mastopathy into the non-cystic form and cystic form, since according to the morphologists' opinion, the incidence rate of hyperplasia and atypia cases is higher in the case of the non-cystic form than in the case of the cystic form.

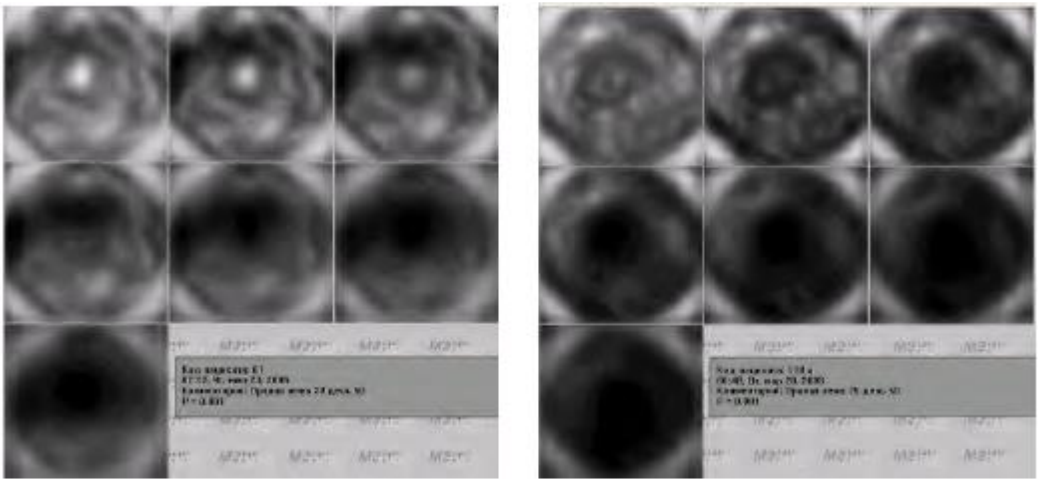
During a visual evaluation of electrical impedance images in the case of the mastopathy (Figures 6 - 26), we note the following:

- architectonics abnormality of the images due to a change in the ratio of the mammary gland tissues, and as a result - a mismatch of the electrical impedance image type (juvenile, reproductive, premenopausal, postmenopausal) to the age;
- increase in the number of hyperimpedance regions with the mastopathy on the images due to fibrotic changes in the adipose tissue, fibrosis of the duct walls and Cooper's ligaments;

- increase in the images of the average echogenicity zones due to the glandular tissue hyperplasia in case of adenosis;
- clear undeformed contours of the mammary gland;
- absence of displacements of internal structures;
- emergence of hypoimpedance inclusions with distinct contours corresponding to the cysts of the mammary glands or the expressed pocket-type widening of the ducts and the absence of hyperechogenic zones around the foci on the mammograms with the mastopathy;
- electrical conductivity of any hypoimpedance foci does not exceed 0.95 relative value units, starting from the second scanning level;
- hypoimpedance regions in women before the menopause onset usually occur against the background of reduced average electrical conductivity parameters. Hypoimpedance regions in women of postmenopausal period, as a rule, occur against the background of normal average electrical conductivity parameters.
- shift of the electrical conductivity frequency distribution graph to the left in comparison with the normal state;
- reduction of differences between electrical impedance images in the case of the mastopathy and the normal state in women of postmenopausal period, as well as the minimal discrepancy in the electrical conductivity frequency distribution graphs.

Figure 6.

Normal state. 19 years old. …



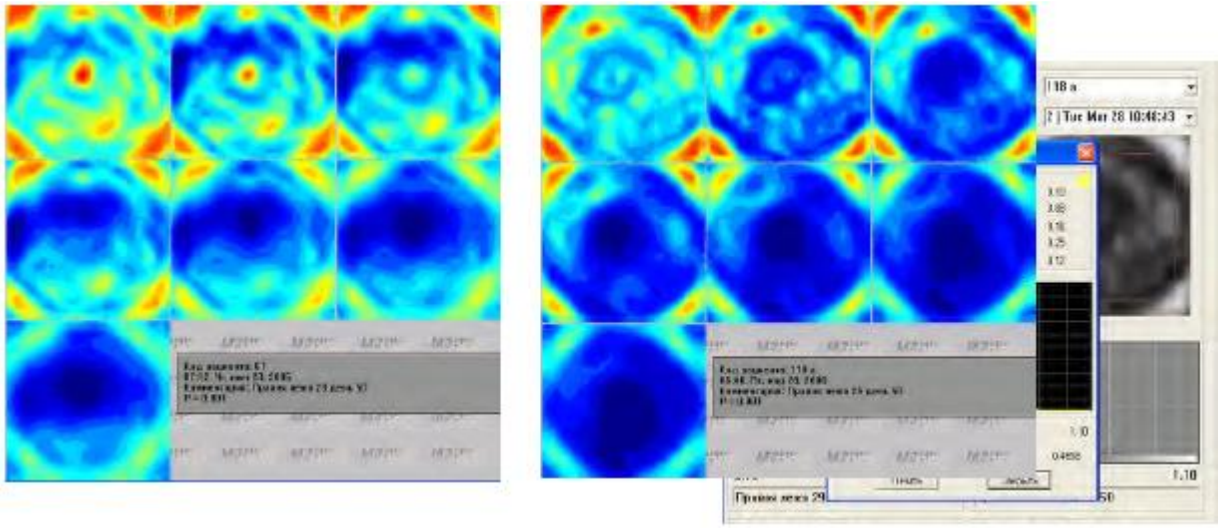


Figure 8.Electrical impedance mammography.
Normal state. 19 years old. 10 KHz.

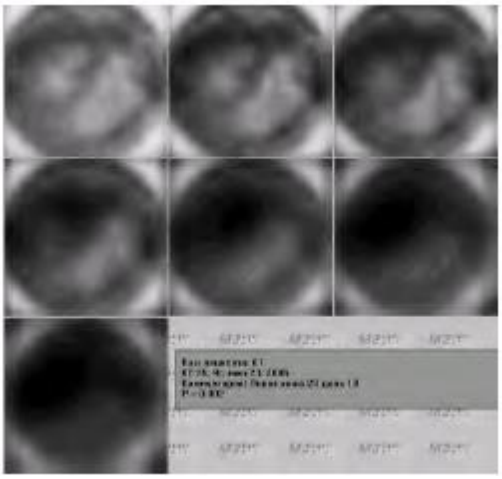
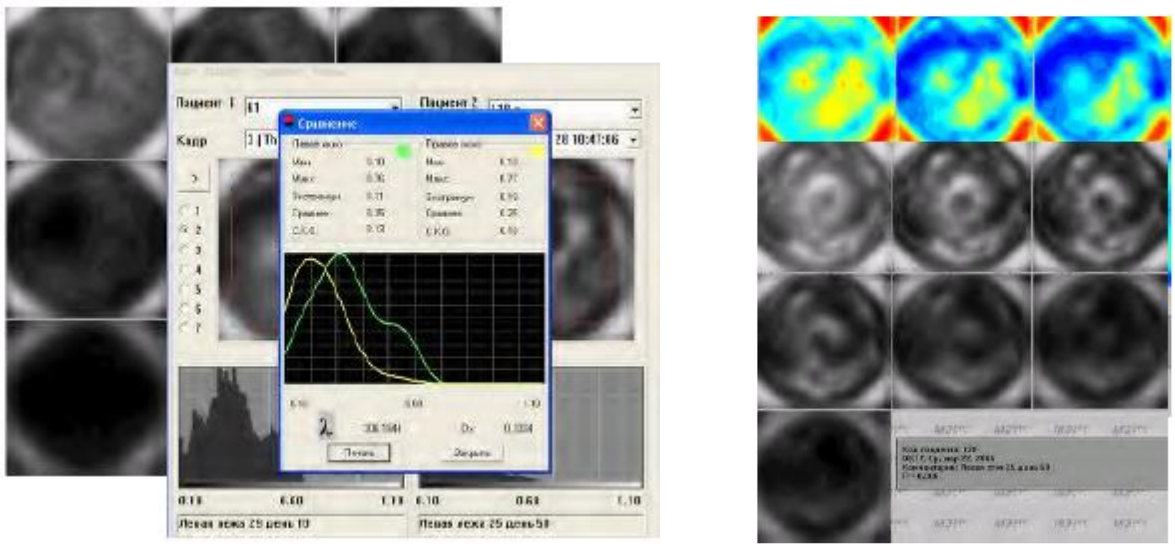
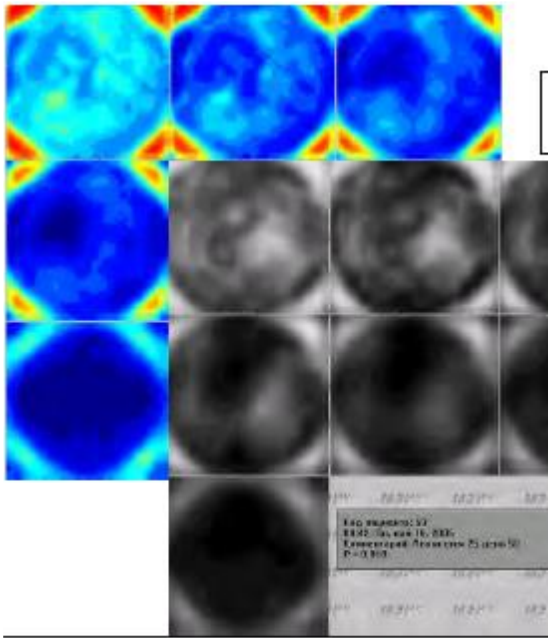


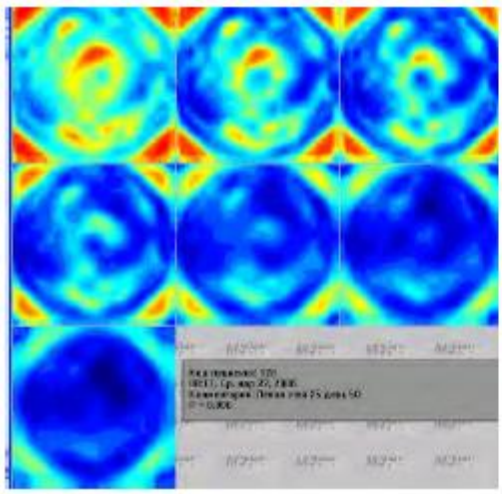
Figure 9.Electrical impedance mammography.
Mastopathy. 19 years old. 10 KHz.

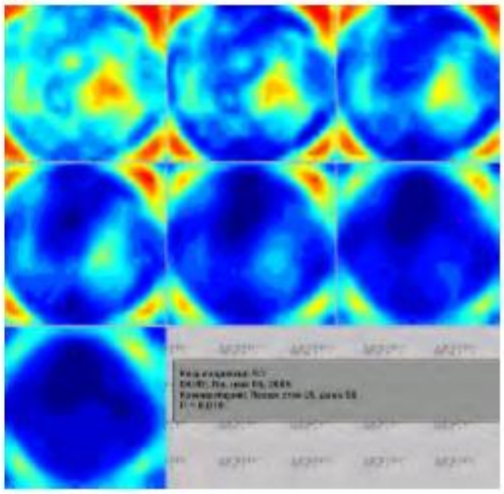


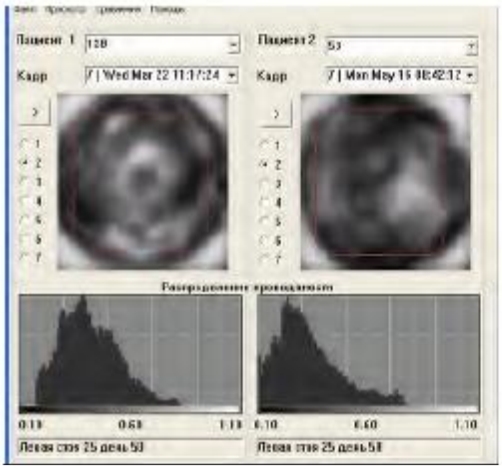
Figure…

Normal state...









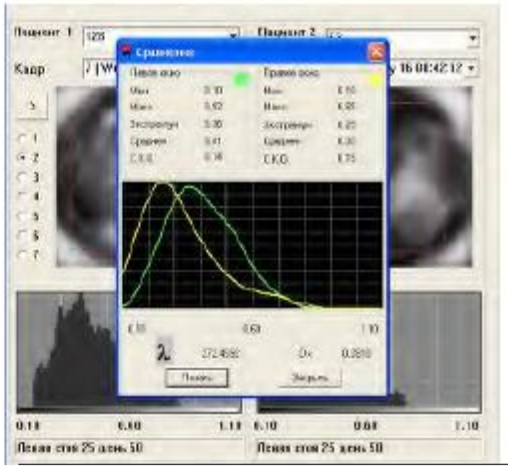


Figure 12.Electrical impedance mammography.

Normal state. 36 years old. 10 KHz.

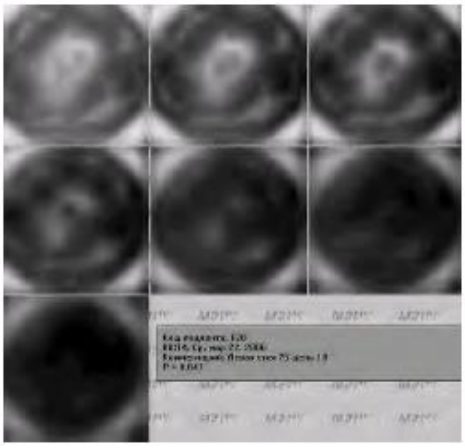
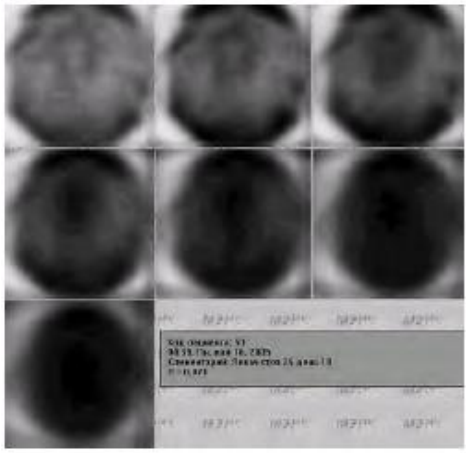
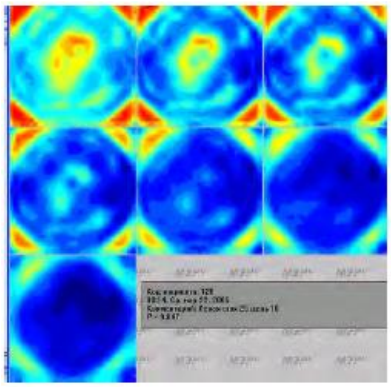
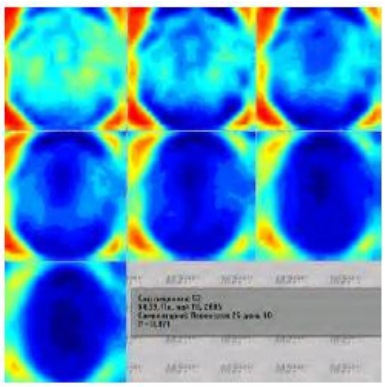


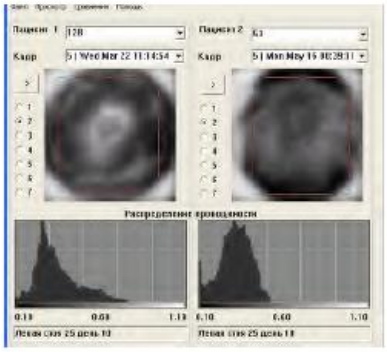
Figure 13.Electrical impedance mammography.

Mastopathy. 36 years old. 10 KHz.









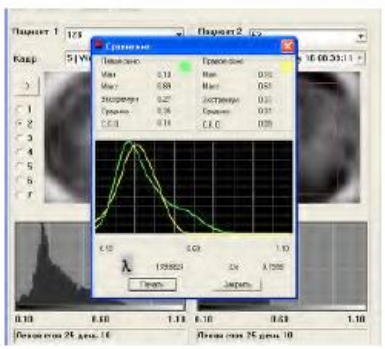


Figure 14.Electrical impedance mammography.

Normal state. 44 years old. 50 KHz.

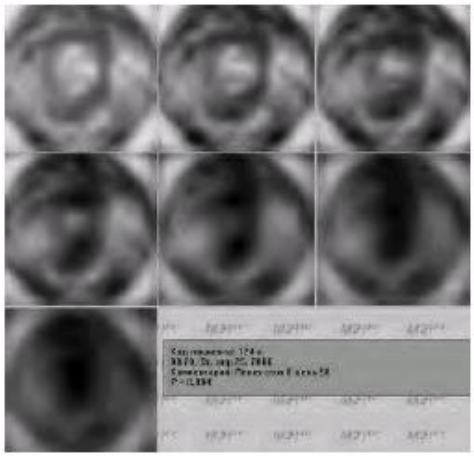
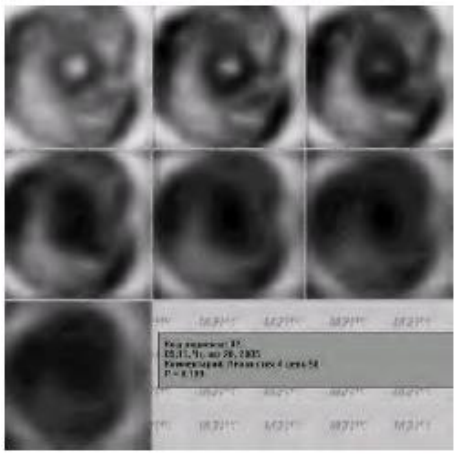
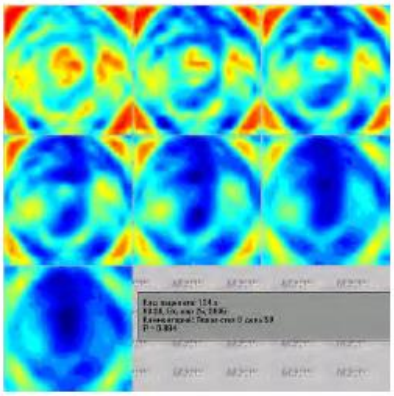
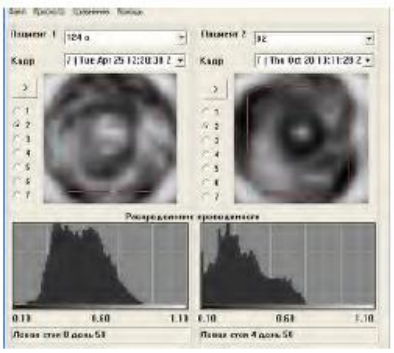


Figure 15.Electrical impedance mammography.

Mastopathy. 44 years old. 50 KHz.







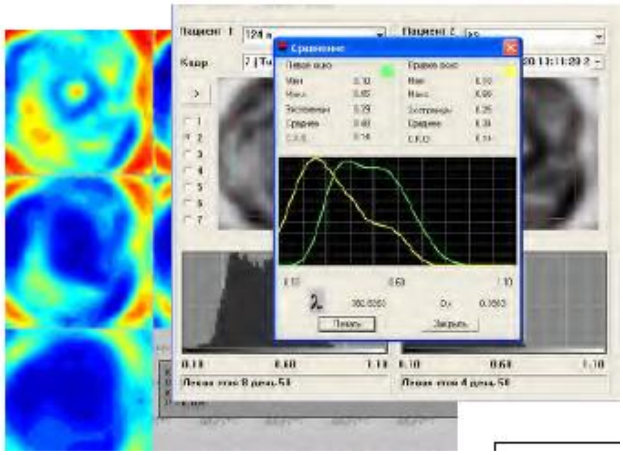
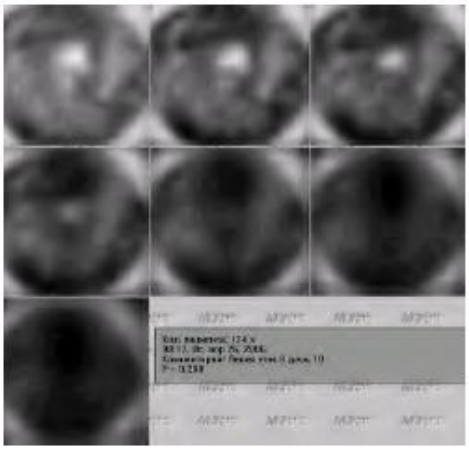
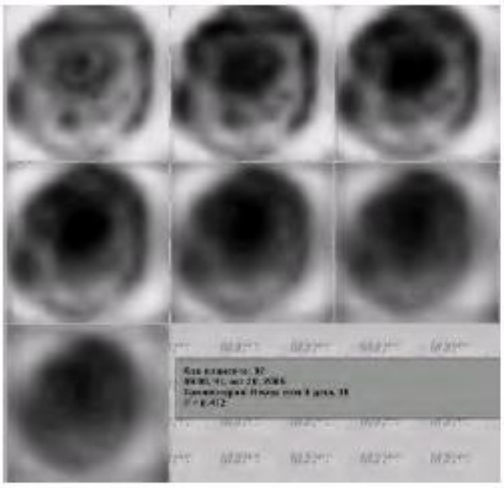
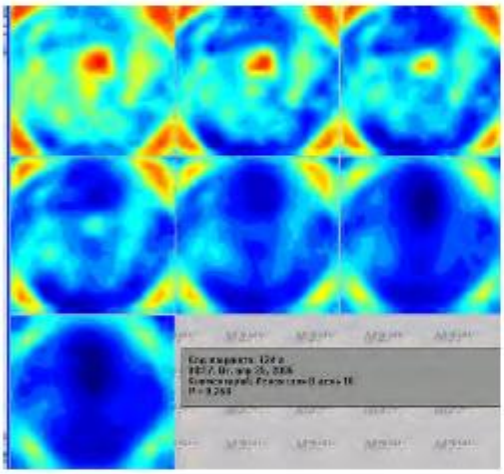


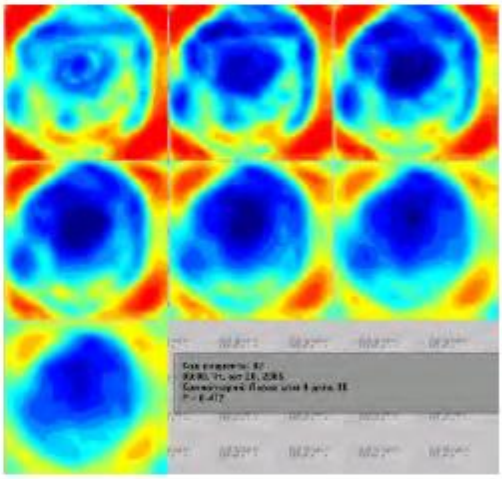
Figure …

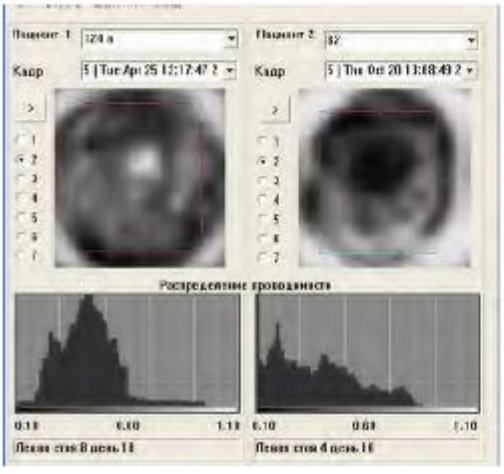
Normal state. 44 years old.










Распределение проводимости

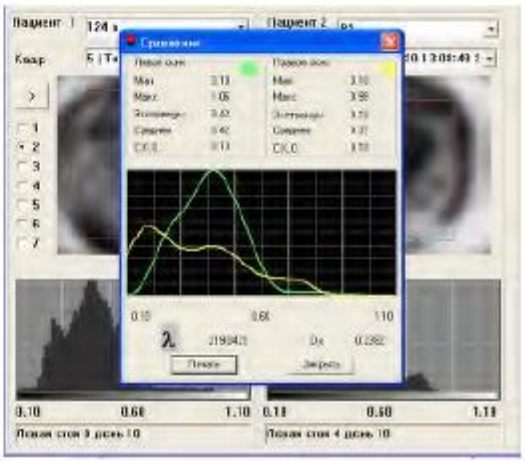


Figure 18. Electrical impedance mammography.
Normal state. 53 years old. 50 KHz.

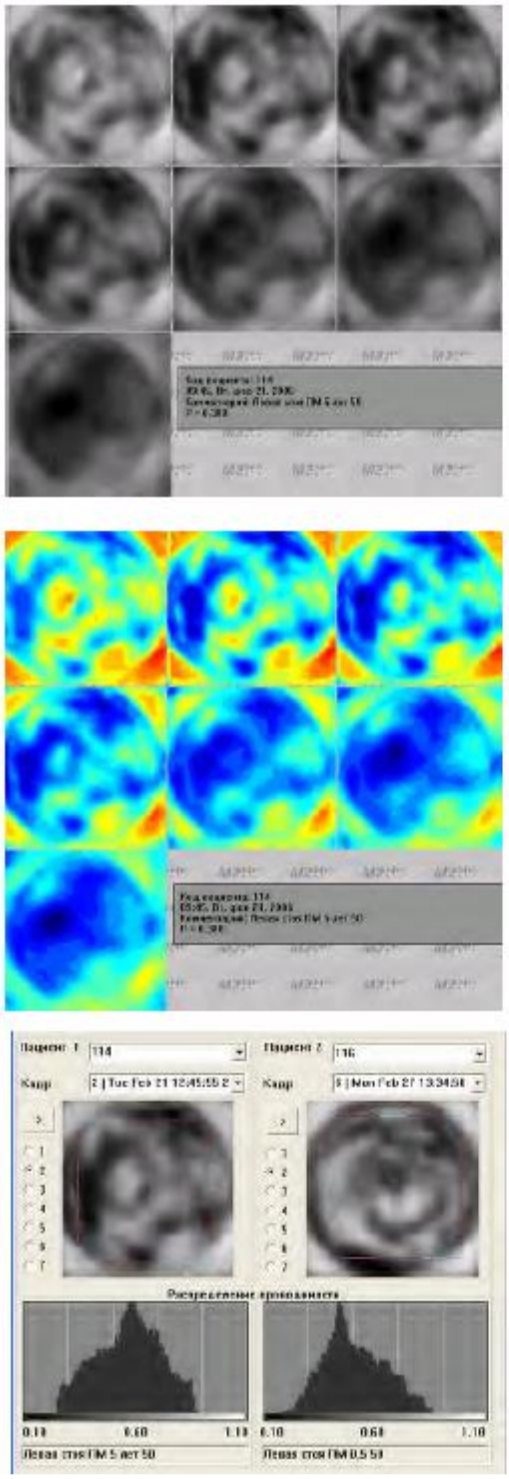


Figure 19. Electrical impedance mammography.
Mastopathy in the anamnesis. 55 years old. 50 KHz.

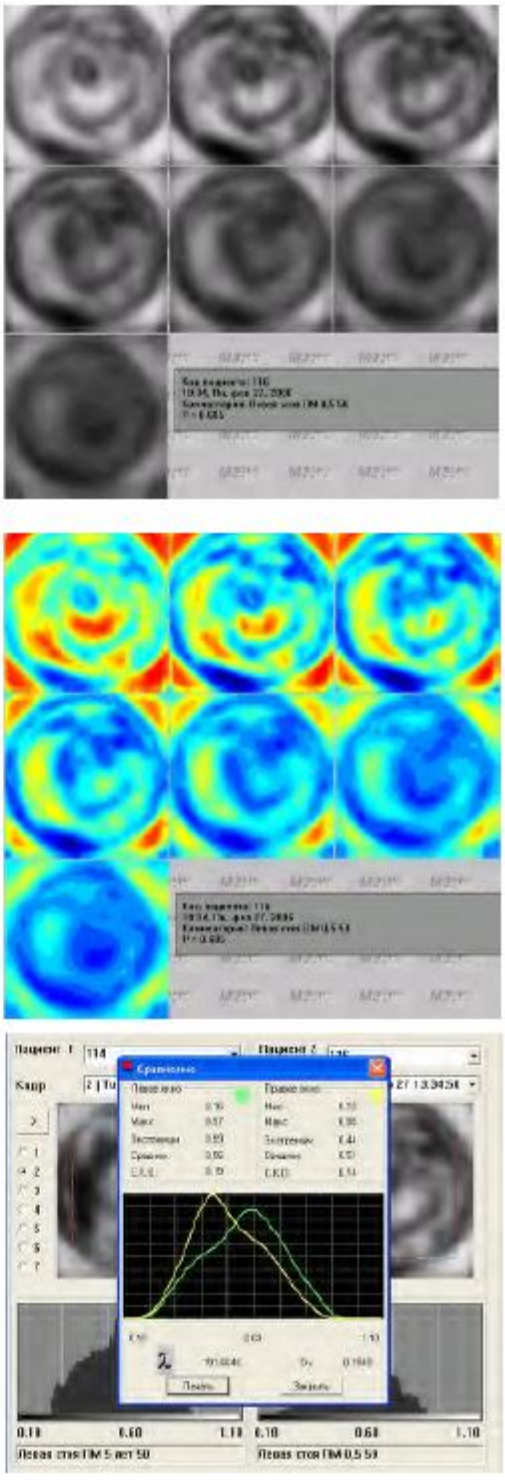
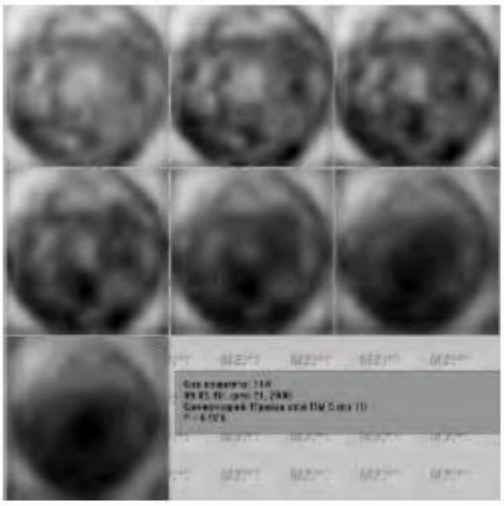
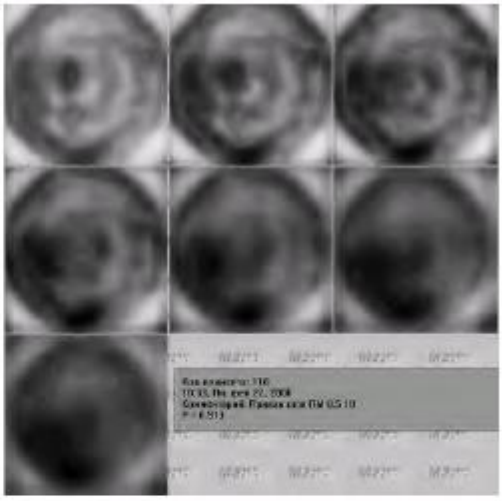
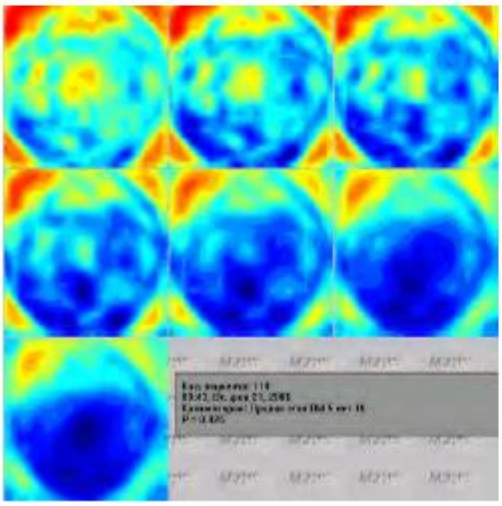


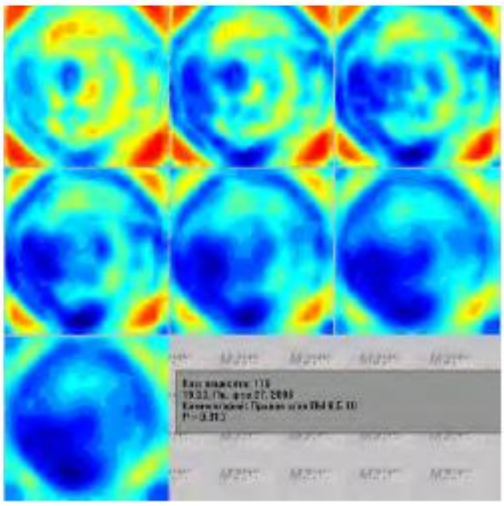
Figure …

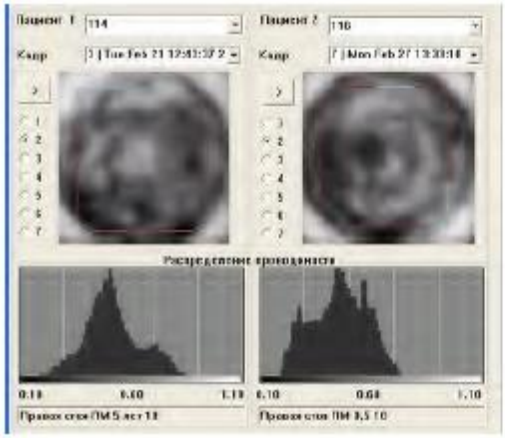
Normal state...











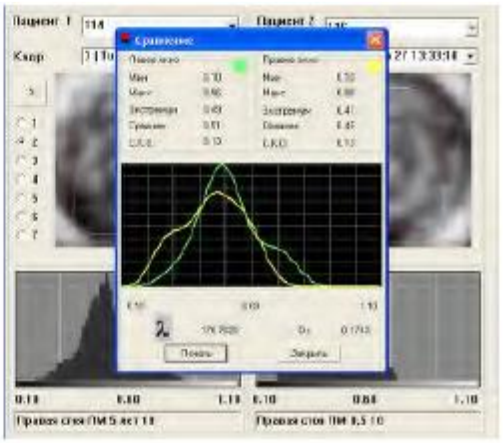
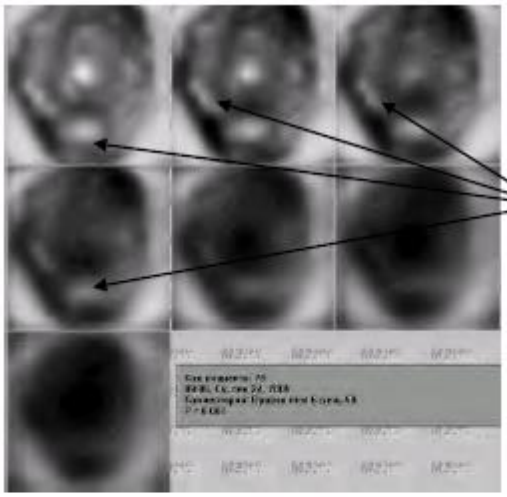
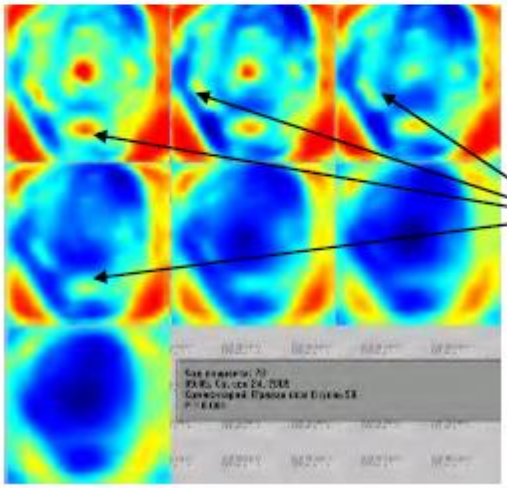


Figure 22.Electrical impedance mammography.

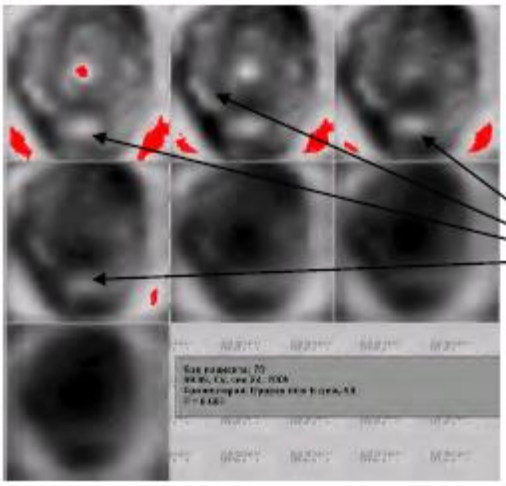
Mastopathy. 39 years old. 50 KHz.



Multiple cysts of the right mammary gland (mixed form of mastopathy).
They are visualized at 1, 2, 3, 4 scanning levels.



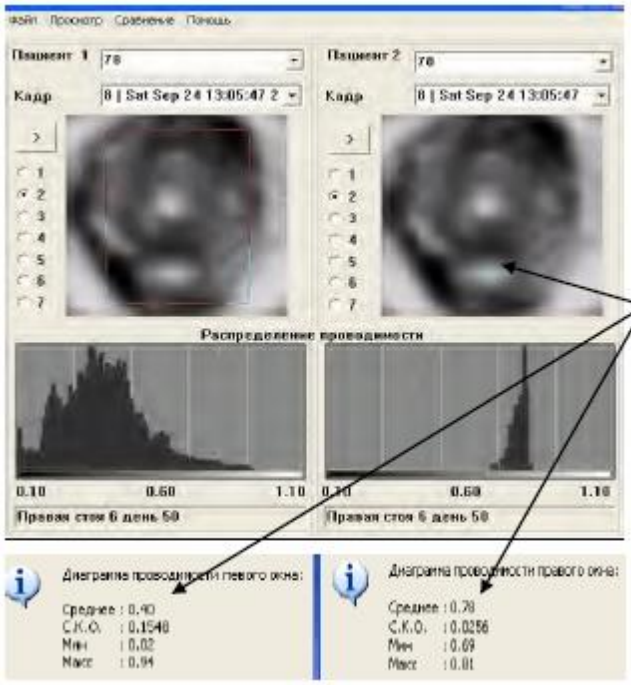
Multiple cysts of the right mammary gland (mixed form of mastopathy).
They are visualized at 1, 2, 3, 4 scanning levels.



With the additional contrast enhancement, the hypoimpedance regions corresponding to the mammary gland cysts are not colored in red in women of the reproductive period.

Figure 23.Electrical impedance mammography.

Mastopathy. 39 years old. 50 KHz.



Average electrical conductivity in the hypoimpedance zone is 0.78, against the background of a general decrease in the average electrical conductivity of 0.4

Figure.Electrical impedance mammography.

Mastopathy. 39 years old. 50 KHz.

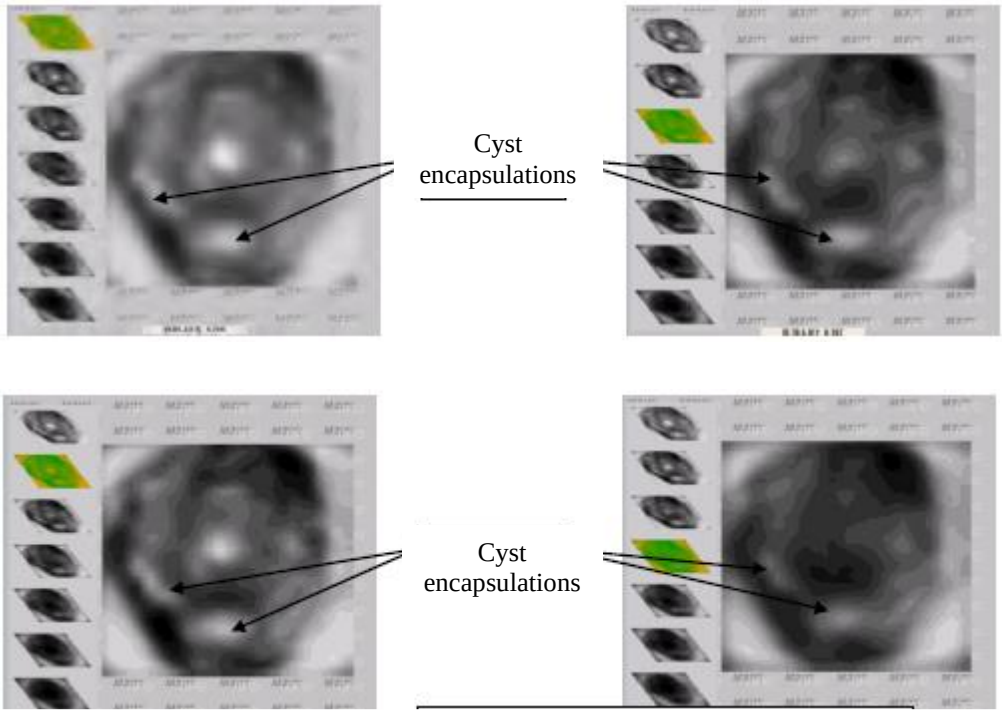
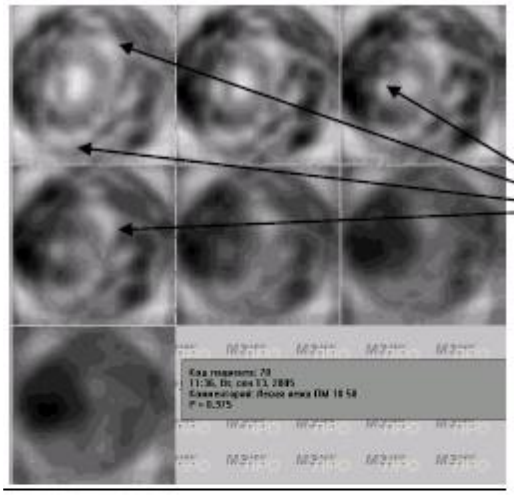
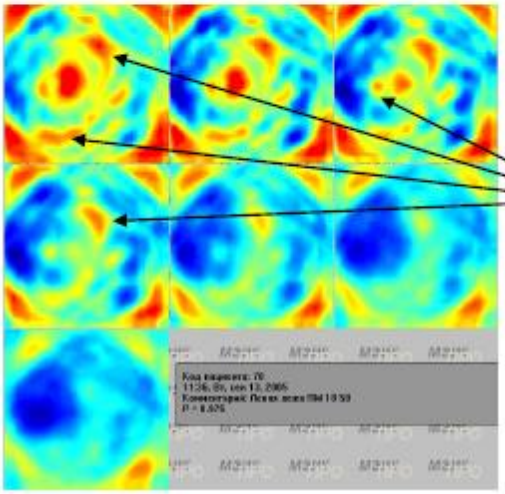


Figure 24.Electrical impedance mammography.

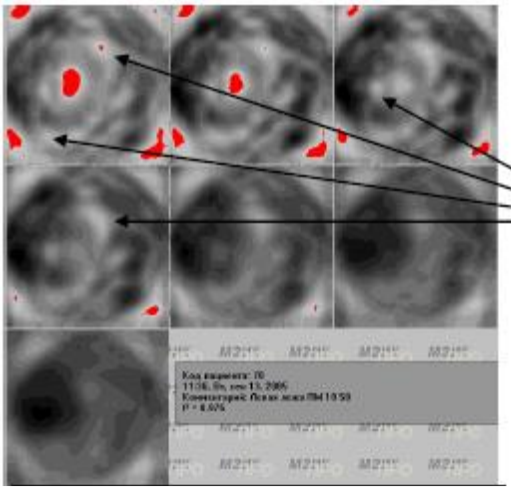
Mastopathy in the anamnesis. 70 years old. 50 KHz.



Multiple cysts of the left mammary gland (mixed form of mastopathy in the anamnesis).
They are visualized at 1, 2, 3, 4 scanning levels.



Multiple cysts of the left mammary gland (mixed form of mastopathy in the anamnesis).
They are visualized at 1, 2, 3, 4 scanning levels.



With the additional contrast enhancement, some hypoimpedance regions corresponding to the mammary gland cysts in women of the postmenopausal period can be colored in red.

Figure 25.Electrical impedance mammography.

Mastopathy. 39 years old. 50 KHz.

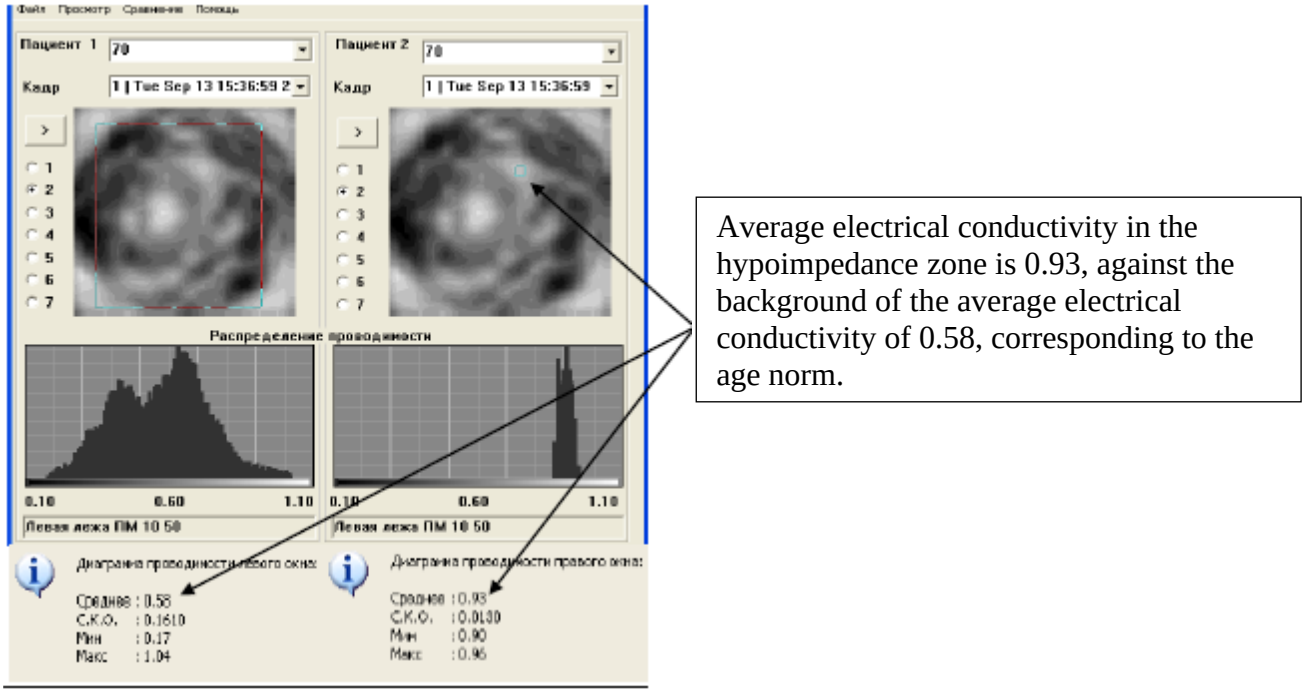
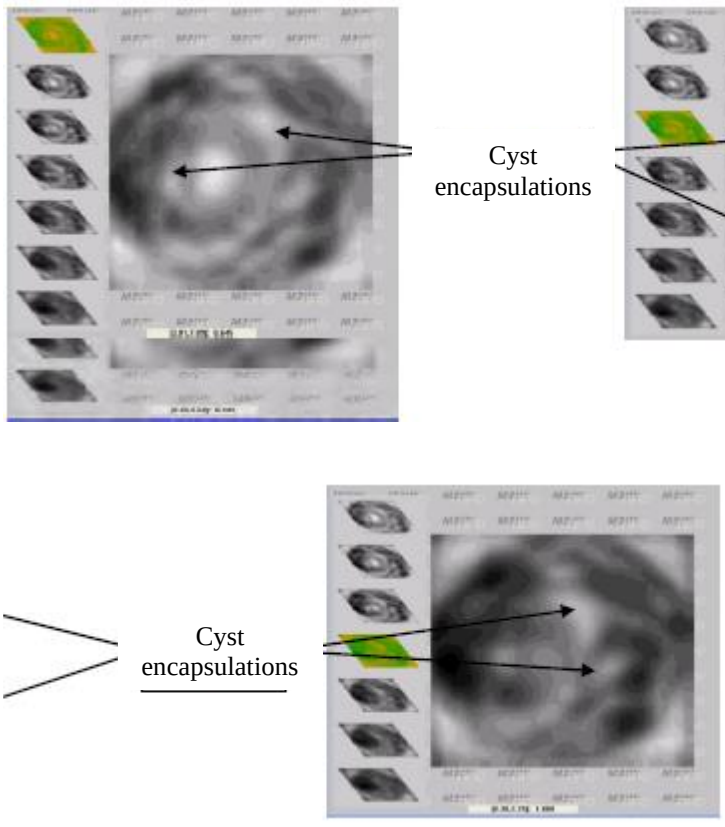


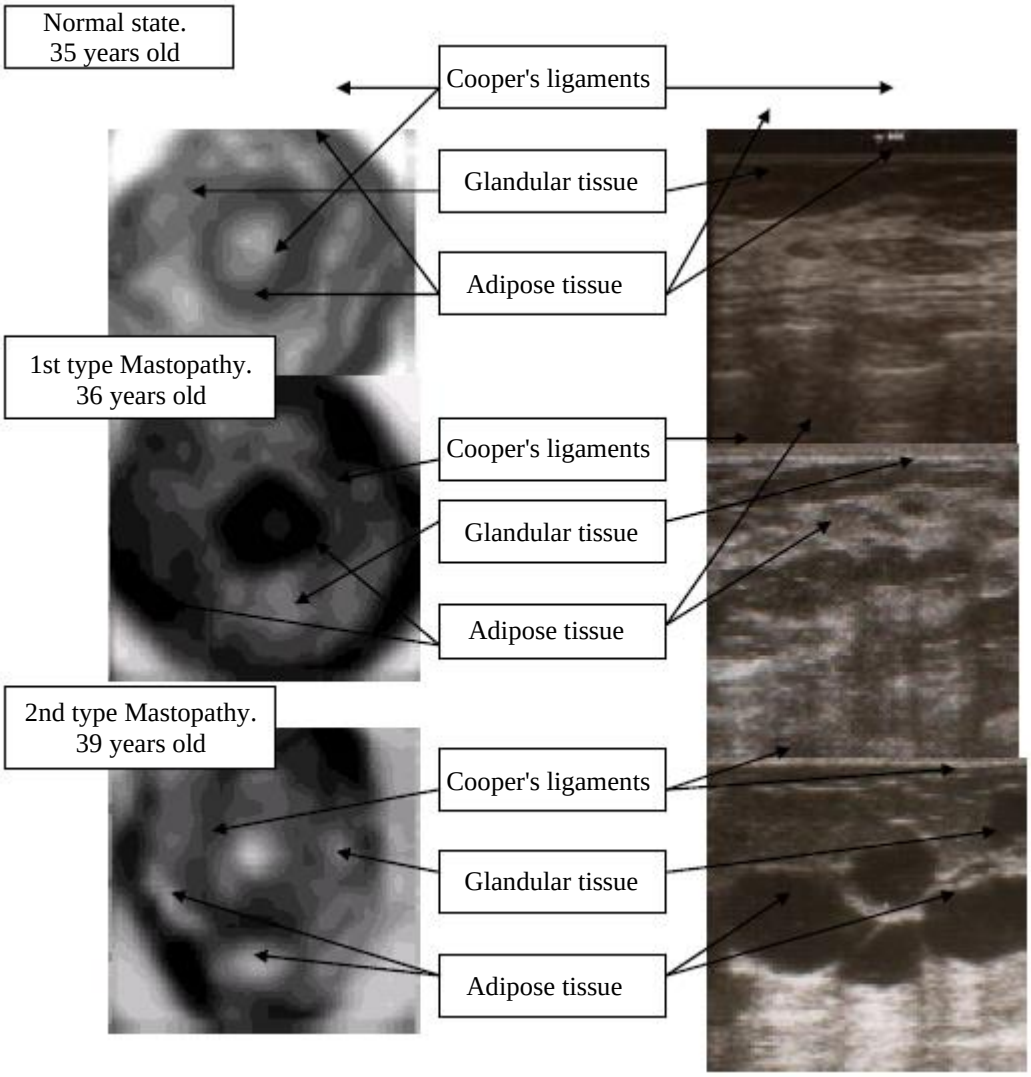
Figure 26.Electrical impedance mammography.

Mastopathy in the anamnesis. 70 years old. 50 KHz.



Visual changes in the structure of the mammary glands on the tomograms are confirmed by the ultrasound examination.

Figure 27. Electrical impedance and ultrasound images of the mammary glands in the normal state and in the case of the mastopathy (second scanning level, 50 kHz)



Note:

- 1st type Mastopathy - non-cystic form
- 2nd type Mastopathy - cystic form

Quantification of electrical impedance images in the case of mastopathy

When obtaining the parameters of the average electrical conductivity (from the second scanning level), please, not that:

- for any mastopathy form in menstruating women, the parameter deviation percentage of the average electrical conductivity should be at least 7%;
- a smaller percentage of a change in electrical conductivity is a variant of the normal state;
- in women of the postmenopausal period with a previously established diagnosis of "mastopathy", the percentage shift approaches the normal values.

The results of the change in the electrical conductivity as a percentage of mastopathy are presented in Tables 2 and 3.

Table 2. Percentage change in the parameters of the average electrical conductivity of mammary glands in the case of mastopathy in the first phase of the menstrual cycle and in the postmenopause in women of different age groups (10 kHz, 50 kHz)

	19 - 34 years old		35 – 39 years old		40 – 44 years old		45 – 50 years old		51 - 55 years old Postmenopause	
	50 KHz	10 KHz	50 KHz	10 KHz	50 KHz	10 KHz	50 KHz	10 KHz	50 KHz	10 KHz
Normal state / 1st type Mastopathy	30.3%	21.7%	34.1%	31.9%	19.2%	7.4%	27%	20.9%	1.9%	5.1%
Normal state / 2nd type Mastopathy	23.3%	21.7%	19.2%	22.8%	7%	7.4%	15.4%	25%	5.1%	7.9%

Table 3. Percentage change in the parameters of the average electrical conductivity of mammary glands in the case of mastopathy in the second phase of the menstrual cycle and in the postmenopause in women of different age groups (10 kHz, 50 kHz)

	19 - 34 years old		35 – 39 years old		40 – 44 years old		45 – 50 years old		51 - 55 years old Postmenopause	
	50 KHz	10 KHz	50 KHz	10 KHz	50 KHz	10 KHz	50 KHz	10 KHz	50 KHz	10 KHz
Normal state / 1st type Mastopathy	34.9%	30.8%	37.5%	32.6%	27.1%	16.3%	28.3%	23%	1.9%	5.1%
Normal state / 2nd type Mastopathy	23.3%	25.7%	25%	28%	16.7%	21%	13.3%	23%	5.1%	7.9%

Average electrical conductivity parameters for various types of mastopathy in comparison with the normal state are presented in Tables 4 and 5.

Table 4. Average electrical conductivity of mammary glands in the normal state in the first phase of the menstrual cycle and in the postmenopause in women of different age groups (10 kHz, 50 kHz)

	19 - 34 years old		35 – 39 years old		40 – 44 years old		45 – 50 years old		51 - 55 years old Postmenopause	
	50 KHz	10 KHz	50 KHz	10 KHz	50 KHz	10 KHz	50 KHz	10 KHz	50 KHz	10 KHz
Normal state	0.43±0.09	0.37±0.09	0.47±0.09	0.44±0.09	0.47±0.08	0.41±0.09	0.52±0.03	0.48±0.05	0.56±0.06	0.51±0.07
1st type Mastopathy	0.30±0.07	0.29±0.07	0.31±0.05	0.30±0.05	0.38±0.05	0.38±0.08	0.38±0.09	0.38±0.09	0.55±0.03	0.54±0.05
2nd type Mastopathy	0.33±0.03	0.29±0.03	0.38±0.07	0.34±0.07	0.44±0.09	0.38±0.06	0.44±0.03	0.36±0.07	0.59±0.02	0.47±0.03

Table 5. Average electrical conductivity of mammary glands in the normal state in the second phase of the menstrual cycle and in the postmenopause in women of different age groups (10 kHz, 50 kHz)

	19 - 34 years old		35 – 39 years old		40 – 44 years old		45 – 50 years old		51 - 55 years old Postmenopause	
	50 KHz	10 KHz	50 KHz	10 KHz	50 KHz	10 KHz	50 KHz	10 KHz	50 KHz	10 KHz
Normal state	0.43±0.09	0.39±0.08	0.48±0.03	0.43±0.04	0.48±0.03	0.43±0.03	0.53±0.05	0.48±0.05	0.56±0.06	0.51±0.07
1st type Mastopathy	0.28±0.05	0.27±0.07	0.30±0.07	0.29±0.07	0.35±0.05	0.36±0.06	0.38±0.09	0.37±0.09	0.55±0.03	0.54±0.05
2nd type Mastopathy	0.33±0.07	0.29±0.04	0.36±0.06	0.31±0.05	0.4±0.09	0.34±0.06	0.46±0.04	0.37±0.05	0.59±0.02	0.47±0.03

When analyzing the obtained results, it is necessary to pay attention to the following:

- electrical conductivity parameters in the case of mastopathy of any type increase with the age of patients in both phases of the menstrual cycle as in the normal state;
- electrical conductivity for both mastopathy types is statistically significantly lower in the corresponding age groups in menstruating women (up to 50 years old) than in the normal state and at a frequency of 50 kHz and at a frequency of 10 kHz in both phases of the menstrual cycle (in all cases, $p < 0.05$). In the postmenopause women (51-55 years old), the electrical conductivity in the case of mastopathy is not different or slightly higher than in the normal state (the difference is statistically unreliable, $p > 0.05$);
- in the case of 2 type mastopathy in both phases of the menstrual type and in the postmenopause period at a frequency of 50 kHz, the electrical conductivity is higher than for 1 type mastopathy;

- in the normal state and in the case of 2 type mastopathy, a clear statistically significant decrease in electrical conductivity is observed in both phases of the menstrual cycle and in the postmenopause period in the corresponding age groups at a frequency of 10 kHz (in all cases, $p < 0.05$);
- for 1 type mastopathy, there is no difference in the average electrical conductivity parameters at different frequencies in any of the studied groups.

Thus, despite the same behavior pattern of electrical conductivity changes in the normal state and the dysplasia cases with age, the electrical impedance mammography method makes it possible to clearly diagnose the mastopathy by the decrease of the electrical conductivity parameters in the corresponding age groups at different frequencies in menstruating women. The absence of a difference in electrical conductivity between the normal state and in the case of mastopathy in women of the postmenopausal period is confirmed by the fact that dysplasia cases are the consequence of the dysfunction in the ovary-mammary gland system, and not by an independent disease. An important advantage of the multifrequency electrical impedance mammography over the single frequency mammography is that it not only makes possible to diagnose the mastopathy, but also accurately isolates the non-cystic form due to the missing difference between the average electrical conductivity parameters in the respective age groups in both phases of the menstrual cycle.

Space-occupying lesions of the mammary glands

1. Cysts

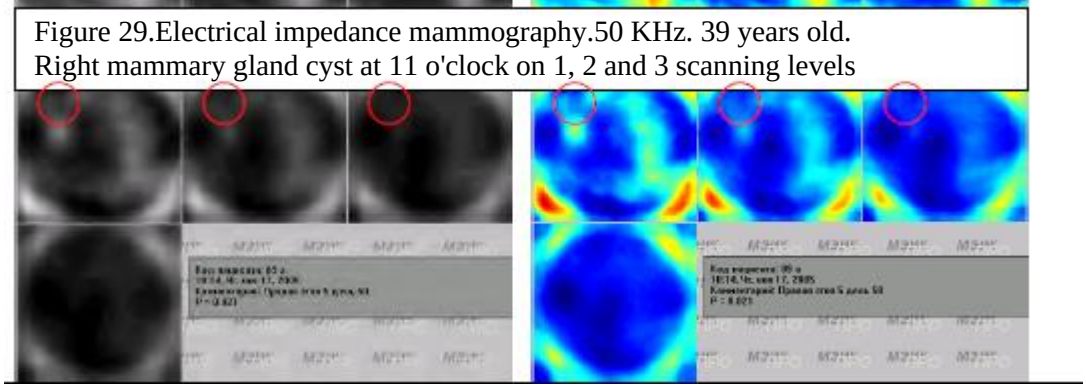
Cysts are the most common mammary gland disease. The age of menstruating women (35 - 50 years old) is typical for the emergence of cysts. With the menopause onset, the cysts usually regress, but they can appear and even increase in size against the background of the hormonal therapy with the use of estrogens, steroids, when taking the medications that reduce the blood pressure, and are the derivatives of digitalis. Cysts in their sizes can be from 3 mm to 5 - 6 cm. They can be single, multiple, one-sided, two-sided by their type. Closely located cysts tend to merge, unite into a single cavity. In the region of several closely located cysts, during dynamic observation, a multiocular ganglion cystic growth with septa will form. Subsequently, in connection with the septa lysis, the unicameral cyst is formed. The regression period of the septa usually lasts several months. Most often, cysts are formed in the terminal part of the lactiferous duct (III level galactophore). Small cysts are less likely to degenerate than larger cysts.

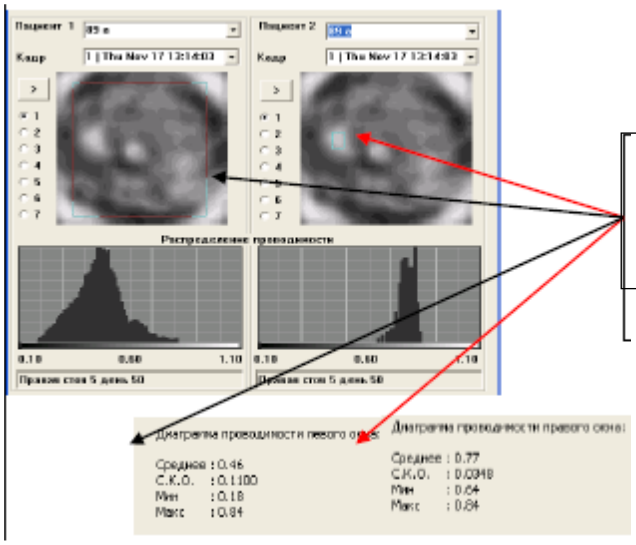
On electrical impedance tomograms in gray scale gradations, the cysts look like rounded hypoimpedance growths with slightly blurred contours and with an electrical conductivity of 0.6 to 0.85 relative value units starting from the second scanning level. With an increase in the scanning depth, the electrical conductivity decreases to 0.35-0.4 of relative value units. On tomograms with the colored contrast enhancement, the localization of the cysts is highlighted in orange-red color. Cysts can occur as an independent pathology, in which case the average electrical conductivity of the mammary glands will correspond to the age norm. If the cysts are a manifestation of cystic or fibrocystic mastopathy, the average electrical conductivity of the mammary glands will be lower than the age norm.

Figure 28.Ultrasound examination. 39 years old.
Right mammary gland cyst at 11 o'clock

- oval shape
- absence of reflections from internal content
- distal enhancement
- clear differentiation of the outer and inner contours
- bright posterior wall
- symmetrical lateral acoustic shadows

Figure 29.Electrical impedance mammography.50 KHz. 39 years old.
Right mammary gland cyst at 11 o'clock on 1, 2 and 3 scanning levels





Electrical conductivity of the cyst is 0.77 against the background of the average electrical conductivity of 0.46, which corresponds to the age norm

Figure 30.Ultrasound examination. 38 years old. Multiple cysts of the left mammary gland at 15 - 17 o'clock

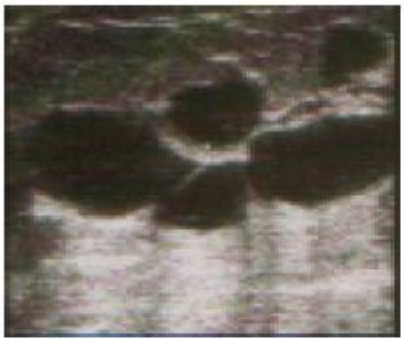


Figure 31.Ultrasound examination. 38 years old. Multiple cysts of the right mammary gland at 7 - 9 o'clock

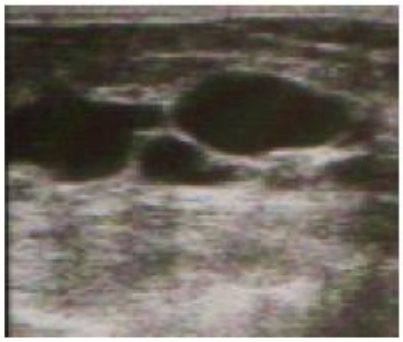


Figure 32.Electrical impedance mammography.50 KHz. 38 years old. Multiple cysts of the left and right mammary glands on 1, 2 and 3 and 4 scanning levels

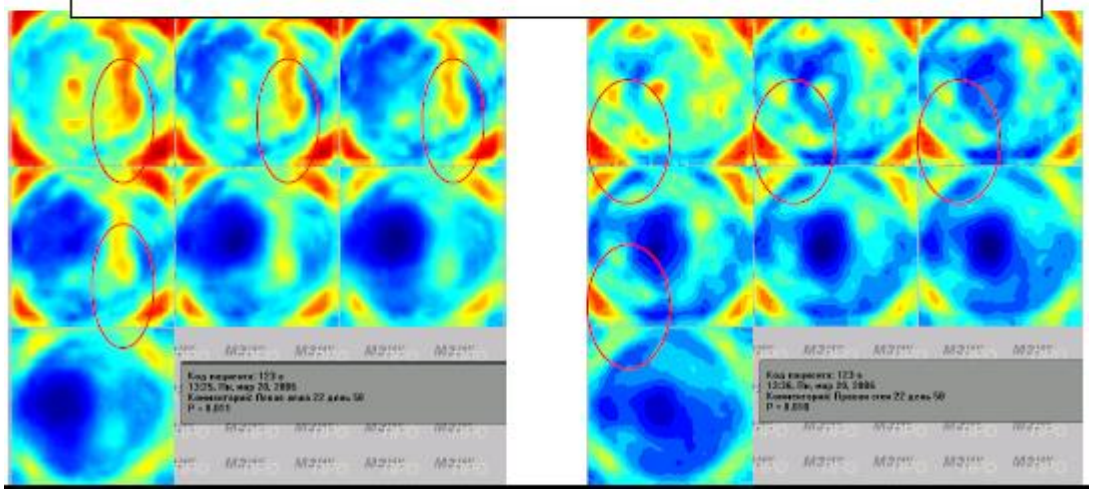


Figure 33.Electrical impedance mammography.50 KHz. 38 years old. Multiple cysts of the right mammary gland

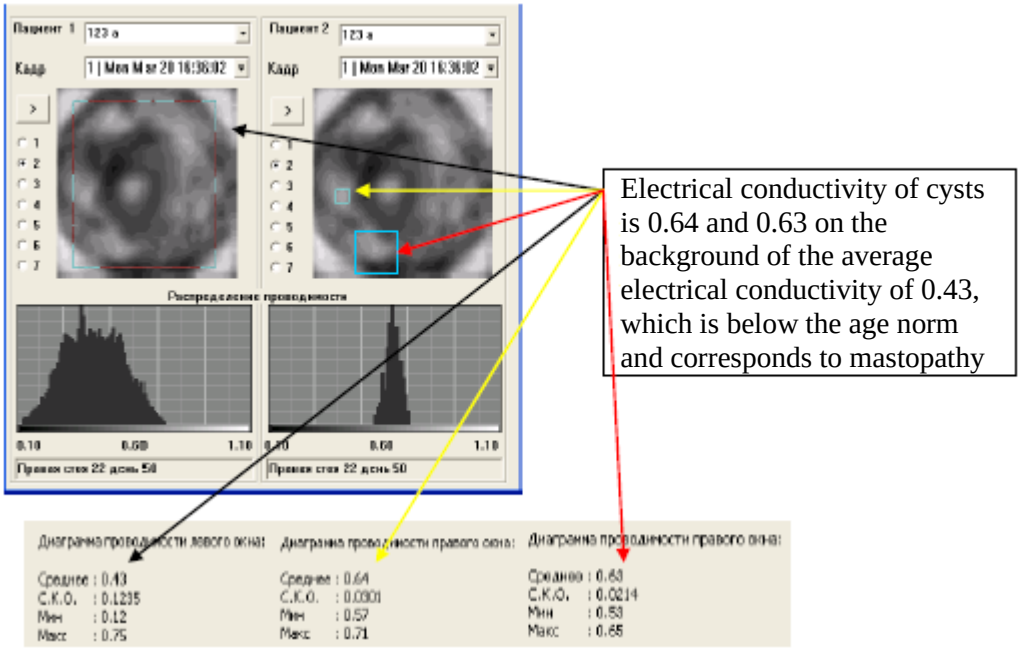
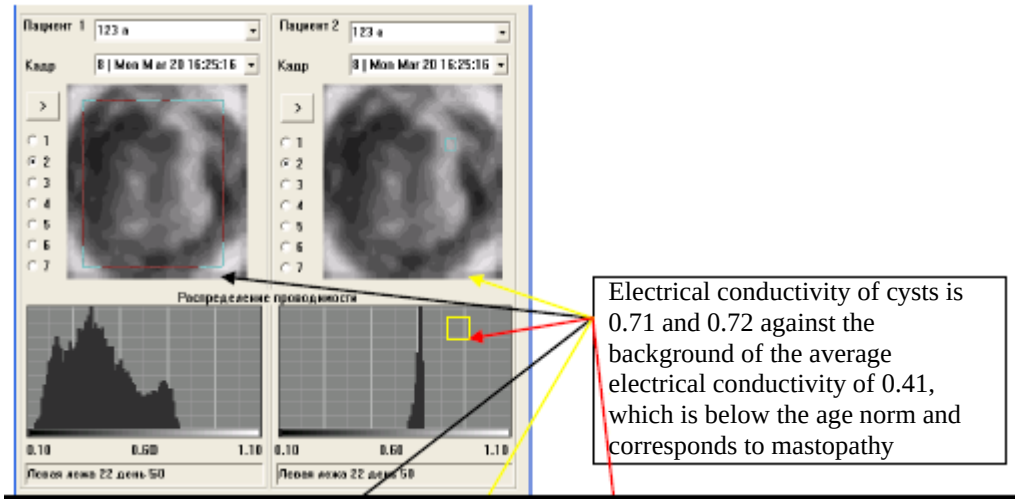


Figure 34.Electrical impedance mammography.50 KHz. 38 years old. Multiple cysts of the ... mammary gland



2. Fibrous adenoma

It makes 95% of all nonmalignant mammary gland tumors. It is the most common between the ages of 15 - 45 years. It is the result of improper development of the glandular tissue. Long-existing fibrous adenomas undergo the involution, calcination and hyalinization. Since the formation of the fibrous adenoma is associated with the estrogenic stimulation, the development and growth can occur in the perimenopausal period, as well as against the background of the hormone replacement therapy. More often the fibrous adenoma is a single growth, but it can also be multiple. Its dimensions usually do not exceed 2 - 3 cm. It is located more often in the upper external quadrant. On electrical impedance tomograms in gray scale gradations, the fibrous adenoma looks like rounded hypoimpedance growths with slightly blurred contours and with an electrical conductivity of 0.5 to 0.65 relative value units starting from the second scanning level. With an increase in the scanning depth, the electrical conductivity decreases to 0.35-0.4 of relative value units. On tomograms with the colored contrast enhancement, the localization of the cysts is highlighted in yellow-orange color. Impedance characteristics of fibrous adenomas are similar in value to the normal parenchymatous tissue parameters. This explains the difficulty of detecting the fibrous adenomas of small sizes.

Figure 35.Ultrasound examination. 33 years old.
Left mammary gland fibrous adenoma at 14 o'clock

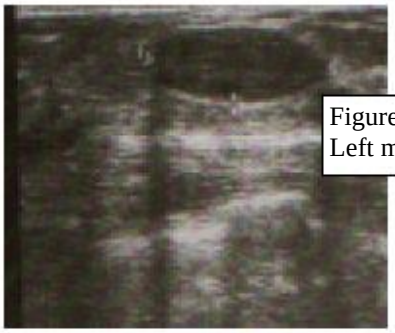
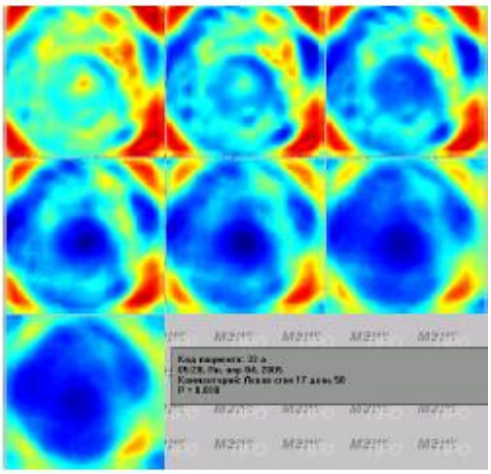
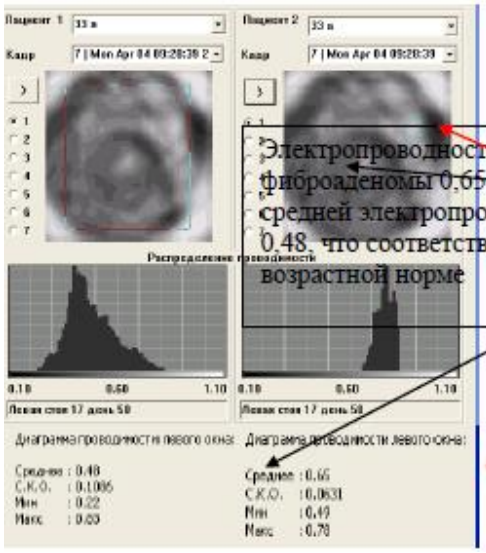


Figure 36.Electrical impedance mammography.50 KHz. 33 years old.
Left mammary gland fibrous adenoma on 1, 2 and 3 scanning levels

- hypoechogenic inclusions of different sizes
- distal pseudo-enhancement effect behind fibrous adenoma.





Electrical conductivity of the fibrous adenoma is 0.65 against the background of the average electrical conductivity of 0.48, which corresponds to the age norm

3. Malignant mammary gland tumors

Mammary gland cancer is a disease with which all nonmalignant mammary gland processes are differentiated. Most lesions of the mammary glands are detected in the upper external quadrant. This, apparently, is connected with the concentration of lactiferous ducts in these segments.

Mammary gland cancer can be of two types: in the diffuse form type (edematous-infiltrative cancer) and the nodal form type. The nodular mammary gland cancer type can be in the form of a single node, multinodular, have a multicentric arrangement and be two-sided.

Infiltrative cancers

Cancers, having a stellate configuration, regardless of the type (infiltrative, ductal, lobular) have a scirrhous structure. Most often in the center of such tumors, we see the predominance of fibrotic regions, sometimes vitreous stromas. On the growth periphery, we see the locations of the complexes of epithelial nature turmor cells. A uniform distribution of the parenchymatous tissue and stroma in the turmor node is observed less frequently. The turmor boundaries are always fuzzy due to the expressed infiltration of the surrounding tissues. The stellate shape is caused by the pressure of the tumor by Cooper's ligaments.

Nodular forms of cancers with expansive growth (well-localized)

Nodular forms of well-localized cancers include medullar, mucinous, papillary, some ductal type cancers and sarcoma (which constitutes a small percentage of malignant mammary gland tumors). Although these tumors squeeze the surrounding tissues during their growth, they practically do not cause or do cause the minimal fibrotic changes in the surrounding structures.

Medullar cancers have a round or a lobular shape, cystic and solid structure, they are well-localized from the surrounding tissues, and they do not have capsules. As the tumor grows, the necrosis regions form with the segments of existing and fresh hemorrhages. In the case of large sizes, the tumor is fixed to the anterior thoracic cage wall and can ulcerate. Tumors of small sizes resemble fibrous adenoma. They rarely occur after the menopause.

Colloid carcinomas are slowly developing tumors, the cells of which produce a mucous secretion. They occur at the age of 50 - 60 years. Their shape can be round or oval, the borders - from well-localized to fuzzy. The detection of calcification is possible.

Cavity and intracavitary carcinoma is a rare form of malignant mammary gland tumor. Histologically, it is a papilliferous carcinoma that emerges from the cyst wall.

Diffuse cancer form (edematous-infiltrative)

Edematous-infiltrative cancer form is a consequence of the infiltration of the mammary gland lymphatic vessels by tumor cells.

Other malignant processes of mammary glands

Metastatic lesions into the mammary glands are responsible from 1 to 6% of all malignant processes of the mammary glands. They can be single or multiple type, have a rounded shape. They are localized in the subcutaneous regions.

The primary focus can be localized in the lungs, gastrointestinal tract, pelvic organs, bladder, thyroid gland or in the contralateral mammary gland. Melanomas, lymphomas, sarcomas, leukemia, leukemias, erythroid myeloma can also cause the mammary gland damages.

According to the international histological classification (WHO, 1981), the epithelial tumors of the mammary gland are divided into:

A. Nonmalignant.

B. Malignant:

1. Noninvasive:

a) ductal carcinoma,

b) lobular carcinoma.

2. Invasive:

a) invasive ductal carcinoma,

b) invasive ductal carcinoma with prevalence of intraductal component,

c) invasive lobular carcinoma,

d) mucosal,

e) medullar,

f) papillary,

g) glandular,

h) adenoid cystic,

i) secreting (juvenile),

j) apocrine,

k) carcinoma with metaplasia:

- squamous type,

- spindle-cell type,

- mixed type,

l) other.

3. Paget's disease of the mamilla.

On the electrical impedance tomograms, the hypoimpedance regions of high electrical conductivity appear at the probable tumor locations, extending to several scanning planes. When using the additional contrast enhancement, the regions with high electrical conductivity are colored in red. In the color contrast enhancement mode, the regions with electrical conductivity ≥ 0.95 are also highlighted in bright red color. In most cases, in the case of malignant growths of the mammary glands, the deformation of the contours, architectonics abnormality, shift of internal structures are detected on the tomograms.

High electrical conductivity of the tumor is attributable to the pathological angiogenesis and atypia of cells.

Figure 37.Ultrasound examination. 73 years old.
Left mammary gland cancer on 12 o'clock, 19 × 20 × 16 mm

- irregular shape
- fuzzy contours
- hypoechogenic heterogeneous structure
- hypoechogenic inclusions of different sizes
- acoustic shadows

Figure 38.Electrical impedance mammography.50 KHz. 73 years old.
Left mammary gland cancer on 1, 2 and 3 scanning levels

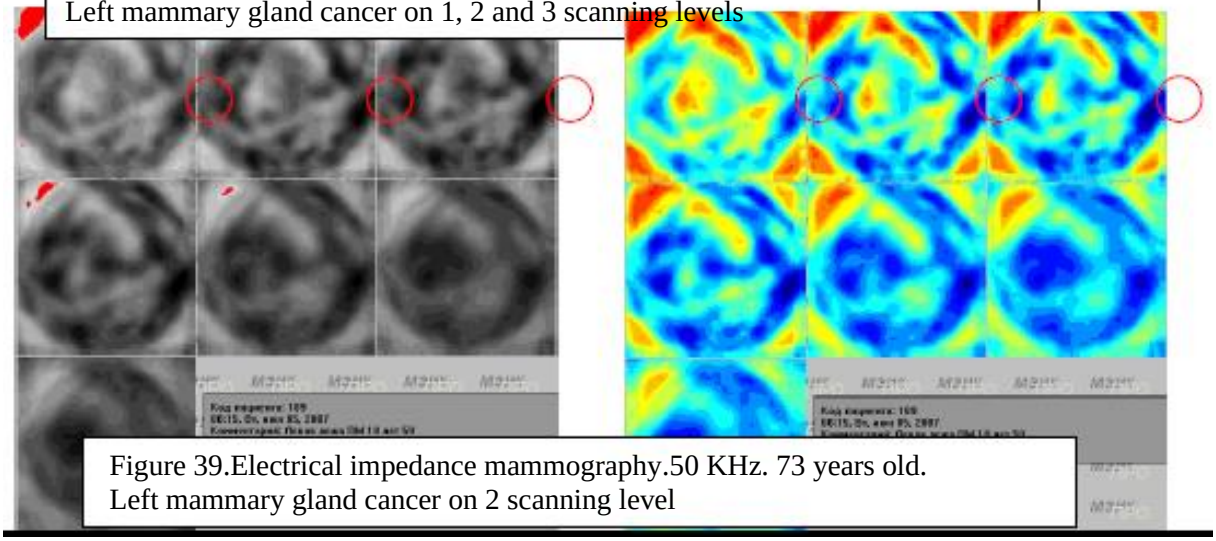
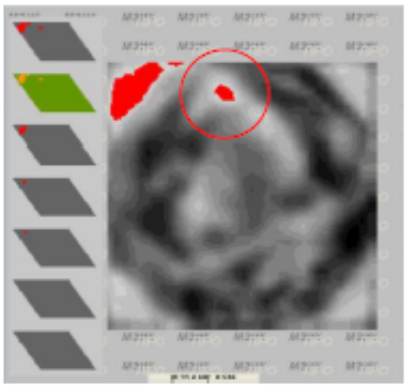


Figure 39.Electrical impedance mammography.50 KHz. 73 years old.
Left mammary gland cancer on 2 scanning level



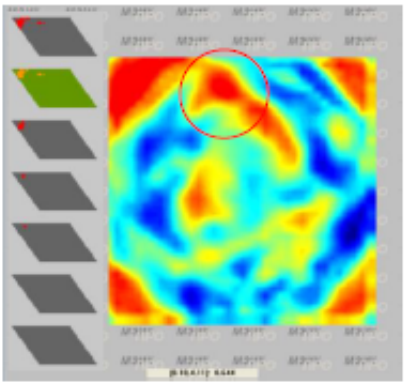
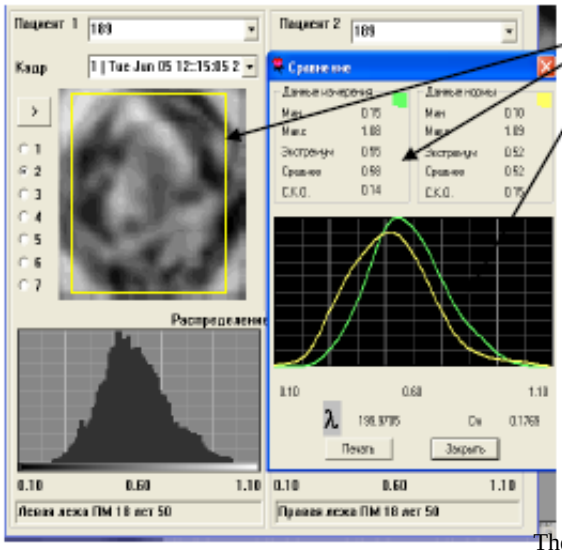
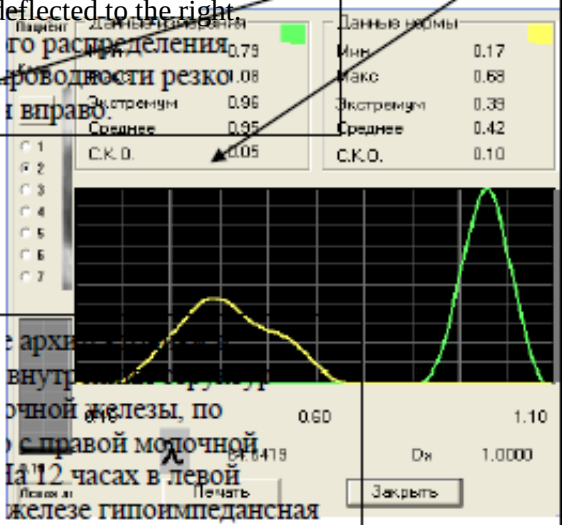


Figure 40.Electrical impedance mammography.50 KHz. 73 years old.
Left mammary gland cancer on 2 scanning level



Average electrical conductivity of the left mammary gland is 0.58, which corresponds to the age norm.

Electrical conductivity in the malignant tumor localization region is 0.96. Electrical conductivity frequency distribution graph is sharply deflected to the right.



The change in architectonics and the shift of internal structures of the left mammary gland compared with the right mammary gland. At 12 o'clock in the left mammary gland, a hypoimpedance ...

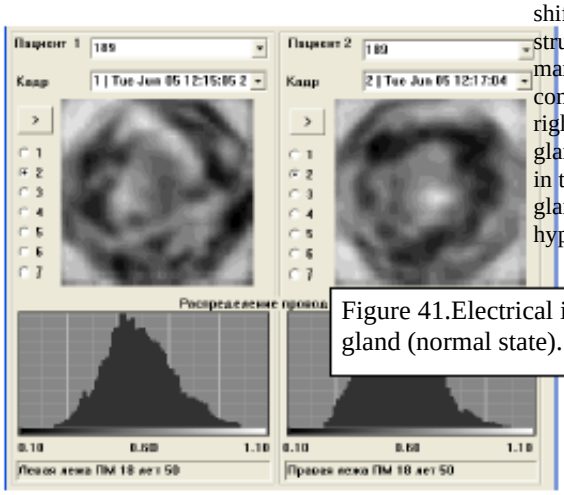
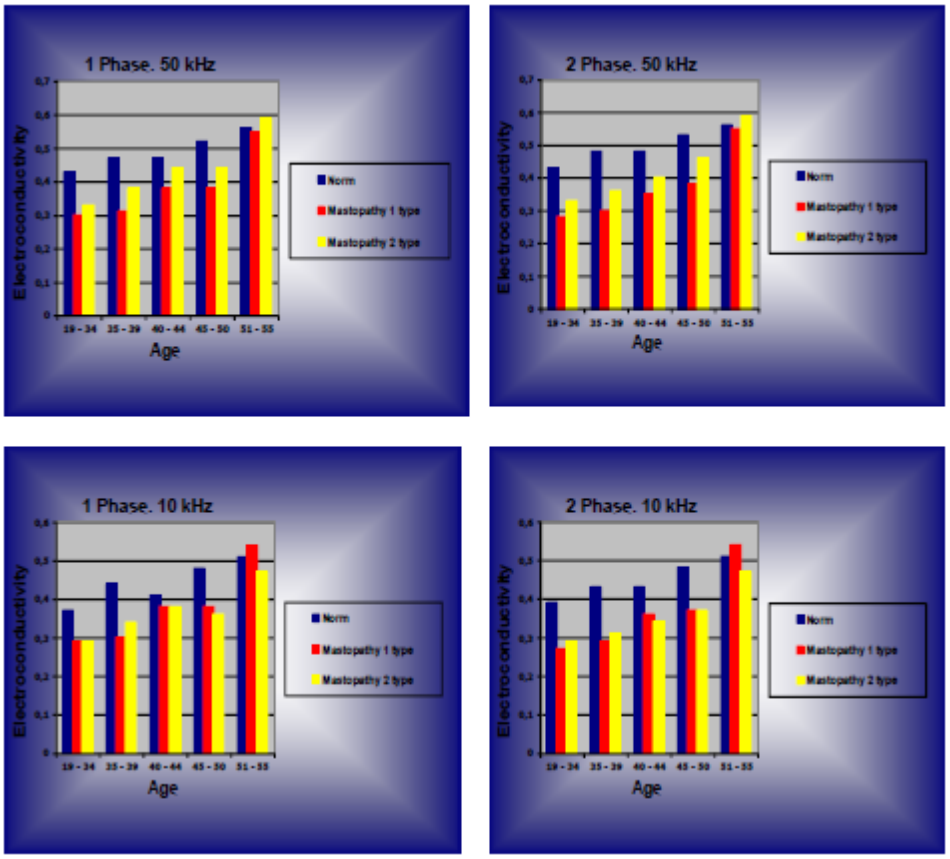


Figure 41.Electrical impedance mammography.50 KHz. 73 years old.Right mammary gland (normal state). Left mammary gland cancer at 12 o'clock 2 scanning level

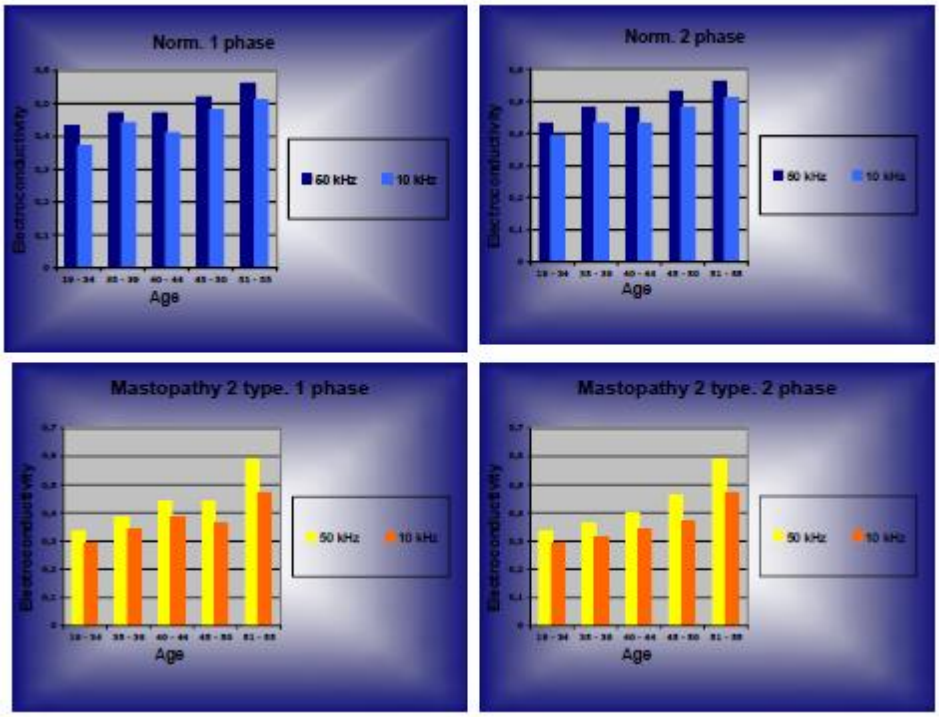
Conclusion

1. The multifrequency electrical impedance mammography method improves the quality of the diagnostics of the mammary gland dishormonal diseases.

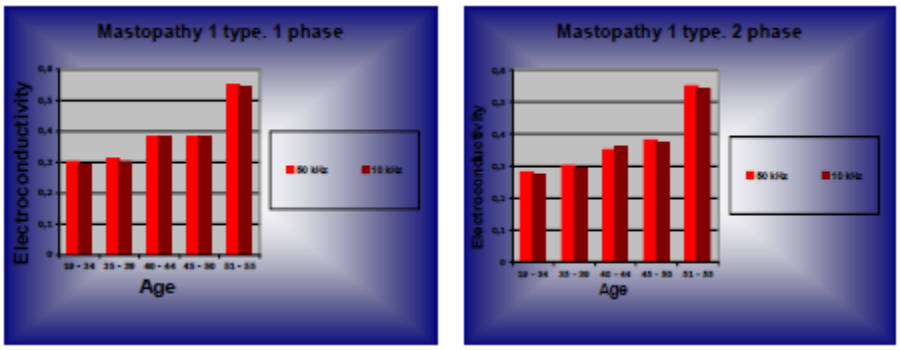
- electrical conductivity for both mastopathy types is statistically significantly lower in the corresponding age groups in menstruating women (up to 50 years old) than in the normal state and at a frequency of 50 kHz and at a frequency of 10 kHz in both phases of the menstrual cycle (in all cases, $p < 0.05$). In the postmenopause women (51-55 years old), the electrical conductivity in the case of mastopathy is not different or slightly higher than in the normal state (the difference is statistically unreliable, $p > 0.05$);



- in the case of 2 type mastopathy in both phases of the menstrual type and in the postmenopause period at a frequency of 50 kHz, the electrical conductivity is higher than for 1 type mastopathy;
- in the normal state and in the case of 2 type mastopathy, a clear statistically significant decrease in electrical conductivity is observed in both phases of the menstrual cycle and in the postmenopause period in the corresponding age groups at a frequency of 10 kHz (in all cases, $p < 0.05$);



- for 1 type mastopathy, there is no difference in the average electrical conductivity parameters at different frequencies in any of the studied groups.



Thus, an important advantage of the multifrequency electrical impedance mammography over the single frequency mammography is that it not only makes it possible to diagnose the mastopathy, but it also accurately isolates the non-cystic form due to the missing difference between the average electrical conductivity parameters in the respective age groups in both phases of the menstrual cycle. In the morphologists' opinion, the occurrence frequency of hyperplasia and atypia cases with this type of dysplasia is higher than with the cystic form, therefore it is possible to single out an increased risk group of the mammary gland cancer developing for a more careful monitoring.

2. Electrical impedance mammography method is very effective for the diagnostics of nonmalignant and malignant mammary gland growths. Sensitivity (the proportion of patients, among whom the symptom of the disease or the occurrence frequency of the symptom was detected) is 76%, the specificity (the absence of the symptom in healthy people) is 75%. For comparison: the sensitivity of

the X-ray mammography method is 71% - 86.8%, the specificity of the method is 37.8%. Sensitivity of the ultrasound examination in the differential diagnostics of nonmalignant and malignant growths is 98.4%, and specificity is 59%.