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# Seminar on Electrical Impedance Mammography

СИМ -ТЕХНИКА

MODERN IMPEDANCE MEDICAL EQUIPMENT

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# Seminar on Electrical Impedance Mammography

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Method of electric impedance potential mammography has been implemented in clinic for several years. The authors offer a method for assessment and evaluation of electrical impedance images. There are determined the factors affecting an electrical impedance image. The data on electrical impedance measurements during the menstrual cycle are contributed. The sections covering diseases of the breast contain rich factual material. The method of electrical impedance potential mammography can be characterized as a method of histofunctional scanning. The diagnostic criteria for various forms of breast cancer are firstly introduced in the monograph. Formation of high-risk cancer groups is justified. The studies were carried out on the electric impedance computer mammograph “MEIK” v.5.6 developed and manufactured by PKF "SIM-Technika", in which backprojection method is used to reconstruct the image. The monograph is illustrated with electrical impedance mammograms, charts and tables.

It is intended for use by oncologists, mammalogists, surgeons, obstetricians, radiologists.

# Contents

# INTRODUCTION

In recent years breast deceases increasingly become the cause of women's visits to various medical specialists. Breast cancer incidence rate has increased in recent years - according to the Ministry of Public Health and Social Development of the Russian Federation the number of newly diagnosed women increased from 44.729 to 49.986. Breast cancer is high on the list of mortality and invalidization factors for women. Very often it affects women of working and childbearing age. The facts mentioned above lead to the necessity for finding methods of mammary glands examination, which would possess not only good diagnostic capabilities, but also would be safe, non-invasive, inexpensive, easy to repeat and to use.

Nowadays the X-ray mammogramphy is generally used for the diagnosis of breast diseases. However, it is well known that this method has some limitations: because of radiation exposure it is recommended only for the older age group, it cannot be used during pregnancy. The examination is recommended to be done every other year. There is no possibility to study the processes in dynamics. Moreover, certain histological features in the structure of mammary glands of some women limit the visualization of palpable abnormalites, which reduces the diagnostic capabilities of the method. Ultrasound examination of the mammary glands is recommended to use as an add-on to mammography, as well as a diagnostic method for younger age groups. However, there is no denying that both these methods are rather subjective in terms of data interpretation, because the results of the examination depend significantly on the class of equipment and staff training. Recently, such techniques as MRI and radionuclide methods are used more frequently. However, these methods also have some disadvantages and their use is justified only to clarify the diagnosis and extent of the process development. Therefore, the problem of finding new methods for mammary glands diagnostic without the disadvantages mentioned above remains a pressing issue.

And such a method, which is quite promising, was found. It is based on the differences in the electrical conductivity of healthy and altered tissues and it is called electrical impedance tomography. The method is one of the so-called radiation-free diagnostic techniques, i.e. it is safe both for patients and for personnel. Thus it makes possible to use it without any age restrictions and also for the examination of adolescents, pregnant women and parturients. Since the end of the last century EIT has been attracting the attention of scientists of all over the world. Active research conducted by our group was not an exception. In the monography you can find accumulated clinical data and results of electrochemical tests. Anatomical, histological and physiological features of the mammary gland during different periods of women's age are represented in accordance with the physical and chemical properties of constituent tissues. The peculiarities of electrical impedance images at different stages of breast diseases' pathogenesis are also described. This monography provides a large number of electrical impedance images of the mammary gland in normal condition as well as in cases of various benign and malignant lesions of the latter. It seems quite interesting to compare the images of the mammary gland acquired with the help of various diagnistic methods (X-ray mammography, ultrasound, impedance mammography). All the cases of breast cancer provided in the book were cytologically and histologically verified. Judging by our experience of electrical impedance mammography usage, we can recommend it for diagnosis of breast pathologies in the practice of doctors of various specialties and, above all, in practice of mammologist during primary reception, oncologist and gynecologist. Now it is possible to use electrical impedance diagnostic in order to monitore hormonal contraceptives taking and hormone replacement therapy in dynamic, and thus – to control treatment outcome as well.

The authors are deeply obliged to the management of the Municipal Health Care Institution Clinical Hospital 9 in person of Chief Doctor Mayorov M.I. , Chief of the radiology department A.Yu. Bulatov, Medical oncologist of Road Hospital N. I. Sotskova, Medical oncologist of Tutaev Central Regional Hospital Korotkov S.Yu. and all the staff of PKF "SIM-Technika". We hope that this book will be interesting and useful for a wide range of practitioners and medical researchers.

# Electric Current

# 1

### What is electric current?

ELECTRIC CURRENT is a directed flow of electric charge. The electric charge may be represented by electrons, ions, electron holes, etc.

### What is an electron?

ELECTRON (e-) is the first discovered elementary particle, a carrier of negative charge, equal to 1.6x10 (-19) C. It has a mass of 9.1x10 (-28) g, which is 1836 times less than the mass of a proton. Electrons perform a significant part in the formation of substances making up electron shells for the atoms of all chemical elements.

### What are ions?

IONS are electrically charged particles which come to being when atoms or groups of chemically combined atoms lose or acquire electrons. Positively charged ions are termed cations, while negatively charged ions are called anions. The separation of an electron from a particle requires energy consumption, the latter being called the ionization potential. The adjunction of the electron is followed by energy release.

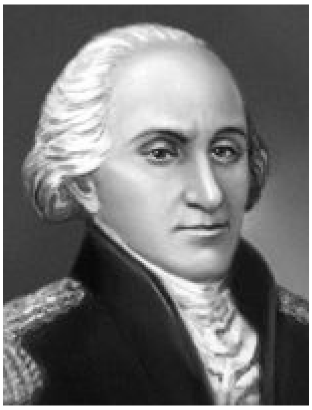
Directed flow of electrons takes place mainly in solids such as metals. Directed flow of ions occurs predominantly in fluids such as electrolytes.

**Volta, Alessandro (February 18, 1745, Como - March 5, 1827, Como), Italian physicist and physiologist.** He studied at Jesuit school. In 1774-79 he was a teacher of physics at high school in Como and in 1779 he became professor at the University of Pavia. In 1815 he became Director of the Faculty of Philosophy in Padua. Volta's works were on electricity, chemistry and physiology. Volta invented a number of electrical appliances (electrophorus, electrometer, capacitor, electroscope etc.). In 1800 Volta discovered the so-called voltaic pile - the first constant-current source, consisting of 20 pairs of circles made of two different metals, separated by layers of cloth or paper moistened with salt water or alkali solution. Volta discovered the mutual electrification of different metals when placed in contact (contact potential difference) and arranged them in a series according to the voltage developed between them. The unit of electrical potential, the volt, is named after him.

### What are electrolytes?

ELECTROLYTES are solid and liquid substances possessing ionic conductivity, i.e. conductors in which electric current is conditioned by the flow of ions.

Potential difference should be created in order to achieve directed flow of electric charge through an object.



**Coulomb**, Charles Augustin de (born June 14, 1736, in Angouleme; died Aug. 23, 1806, in Paris), French physicist, member of the Paris Academy of Sciences (1781). Between 1785 and 1789 he published seven volumes of memoirs in which he gave the law of interaction for electric charges and magnetic poles (Coulomb's law), showed that electric charges always lie on the surface of a conductor, and introduced the concepts of magnetic moment and polarization of charges etc. Experimental studies of Coulomb were extremely important for creation of an electromagnetic phenomena theory. The unit quantity of electric charge, the coulomb, was named for him.

### What is the potential difference?

POTENTIAL DIFFERENCE (voltage) is the difference in electric potential between two points or levels in an electric field. It is measured by work that has to be done to transfer a unit positive charge from one point to the other.

**Joule,** James Prescott (born Dec. 24, 1818, in Salford, Lancashire; died Oct. 11, 1889, in Sale, Cheshire), English physicist; member of the London Royal Society (beginning in 1850). He made important contributions to the study of electromagnetism and thermal phenomena, to the establishment of low-temperature physics, and to the justification of the law of conservation of energy. Joule found out (1841, published in 1843) that the amount of heat dissipated in a metal conductor carrying an electric current is proportional to the electrical resistance of the conductor and to the square of the current (Joule–Lenz law).

The charge, being able to move under the action of electric field, moves from higher potential to lower one. If one joule of work is required to move one coulomb of charge between two points in an electrical field potential difference between the two points is one volt. The potential difference is defined by:

$$V1 - V2 = A / q,$$

where A stands for the work expended on the movement of charge q. The SI unit of electric potential of the electric field (voltage) is the volt (V), which is set on the basis of the equation:

1 volt = 1 joule / 1 coulomb (V = J / C).

There are differences in the ability of various substances to pass electric current. This feature is called electrical conductivity (specific conductance).

### What is the electrical conductivity?

ELECTRICAL CONDUCTIVITY is a physical quantity which numerically characterizes the ability of a substance to pass the electric current under the influence of the electric field. The SI unit of electrical conductivity is Siemens (S).

Depending on the electrical properties of a medium all substances are divided into insulators and conductors. Metals, electrolytes, plasma are good conductors because they contain a large number of free electrons and ions per unit volume and therefore the charge flows easily. Insulators contain practically no mobile electrons so they cannot induce electric current under usual conditions.

### What is an insulator?

INSULATOR is a substance or material which does not conduct electric current under usual conditions. It is conditioned by the limitation of charge carrier mobility, charge carriers shifting slightly in reference to the initial positions inside the atom or molecule of a substance under the influence of the electric current. The electric conductivity of dielectrics (insulators) is very poor if compared to that of metals (Table 1-1).

Their specific resistance (r) is about $10^8 – 10^{17}$ Ohm/m, while metals possess a resistance of about $10^{-6} – 10^{-4}$ Ohm/m (Table 1-1).

**Table 1-1. Specific resistance of metals and insulators**

| Substance | Specific resistivity at 20°C, Ohm·m |
|---|---|
| **Metals** | |
| Aluminium | $2,8*10^{-8}$ |
| Iron | $9,8*10^{-8}$ |
| Gold | $2,4*10^{-8}$ |
| Copper | $1,7*10^{-8}$ |
| Mercury | $95,8*10^{-8}$ |
| Silver | $1,6*10^{-8}$ |
| **Insulators** | |
| Glass | $\approx 10^8$ |
| Mica | $\approx 10^{14}$ |
| Paraffin | $\approx 10^2$ |

## What is “Ohm's law”?

Due to different chemical constitution various conductors possess different capacities for the transmission of electric charges. German physicist Georg Ohm found out that the amperage (I) in a conductor is constant for a given conductor and is in proportion to the difference of potentials (V1-V2) between its ends under constant physical conditions (e.g. temperature):

$$R = (V_1 – V_2) / I \text{ or } I = V / R$$

Where constant R is termed as electrical resistance.

**Ohm,** Georg Simon (March 16, 1789, Erlangen, Bavaria — July 6, 1854, Munich) - German physicist. Ohm studied at the University of Erlangen (1805–06) and then worked as a teacher in Gottstadt (Switzerland, from 1806 to 1809). He prepared independently and defended his doctoral thesis at Erlangen in 1811. Ohm’s main works were on electricity, optics, crystal optics, and acoustics. In 1826, by carrying out a series of precise experiments, he established the fundamental law of electrical circuits (Ohm’s law) and in 1827 provided a theoretical foundation for it. In 1881 the name “ohm” was given to the unit of electric resistance (Ohm).

## What is current intensity?

AMPERAGE (current intensity, current strength) is a magnitude (I) which characterizes the ordered motion of electric charges and equals the quantity of the charge (Q) passing through the cross-section of the circuit within a unit of time (t).

$$I=Q/t,$$

where “t” stands for a period of time, expressed in seconds. The unit of current intensity is the Ampere: <u>1 ampere</u> is equal to 1 Coulomb per second.

**André-Marie Ampère** (January 20, 1775, Lyon – June 10, 1836, Marseille), French physicist and mathematician, who is generally credited as one of the founders of electrodynamics, member of the Academy of Sciences of Paris (1814). Ampère’s works in the field of physics have ranked him among the world’s most outstanding scientists. His research led Ampère to discover the mechanical interaction of electrical currents and establish the quantitative ratios for determining the force of this interaction (Ampère’s law).

## What is electrical resistance?

ELECTRICAL RESISTANCE is a quantity which characterizes the counteraction of an electric circuit (its unit) to the electric current and is measured in Ohms. The unit of electrical resistance is defined on the basis of the equation:

1 ohm = 1 volt/1 ampere (ohm = V/A).

1 ohm represents the resistance of a conductor, when if the voltage at the

ends of it equals to 1 V, the current intensity equals to 1 A.

In a good conductor a small difference of potentials (V) forms a heavy current (I), consequently a good conductor has low resistance (R). In a poor conductor a similar difference of potentials forms a low current which means that the resistance is high. Factors influencing the resistance of a conducting material include temperature, length and cross-section of the conductor. The temperature of the substance significantly affects its resistance in the following way: as a rule, for metal conductors temperature rise results in the reduction of resistance. On the contrary, increasing temperature of electrolytes leads to the decrease of resistance. Increase of the conductor's length or decrease of its cross-section also increases its resistance.

The quantitative evaluation of resistance in a circuit requires consideration of the electric current type, i.e. whether it is direct or alternating.

### What is direct current?

DIRECT CURRENT is a type of electric current which implies no change of its intensity or direction of flow in the course of time. Direct current is generated by the action of permanent voltage and can exist in a closed circuit only. The effective law of the direct current is Ohm's law ($I = U / R$) which establishes the dependence of amperage from voltage. When direct current is passed round the circuit, the electric resistance (R), as the law runs, is determined by the relation of the voltage to the amperage ($R = U / I$). Flow of direct, i.e. unidirectional current through, for example, biological tissues is accompanied by irreversible chemical reactions on the electrodes with the help of which the object is connected to the external electric circuit. Therefore, only alternating electric current of quite high frequency (typically above 1 kHz) is used in medical diagnosis purposes.

### What is alternating current?

ALTERNATING CURRENT is a specific type of electric current, which varies over time. Alternating current is normally defined as a periodical current whose mean value within a period of amperage and voltage equals zero. More precisely, this current is called a sine wave, as the dependence of current on time is characterized by a sinusoidal

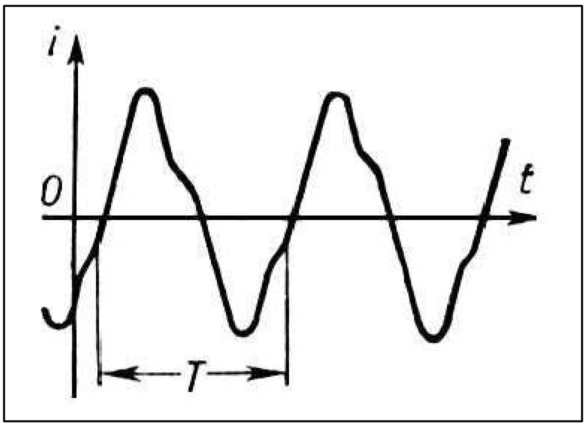



**Fig. 1-1.** Alternating periodical current diagram i(t).

graph (Fig. 1-1). Alternating current is defined by a complete period T which is the smallest interval (measured in seconds) within which amperage and voltage change once only, or linear frequency (*f*) which is defined as a number of cycles (periods) per second:

$$f = 1 / T,$$

measured in hertz, or angular frequency ($\omega$): $\omega = 2\pi/T$, measured in $sec^{-1}$.

**Hertz,** Heinrich Rudolf (February 22, 1857, Hamburg - January 1, 1894, Bonn) - German physicist. One of the founders of electrodynamics. Hertz' work in electrodynamics played an enormous role in the development of science and technology and was a basis for the development of wireless telegraphy, radio communication, television, and radar etc. The unit of frequency of oscillation has been named after him.

Alternating current is generated under the action of alternating voltage and can exist in an open circuit (provided the latter avails of electric capacity or inductivity), as opposed to direct current passing through closed circuit solely. With alternating current the electric resistance in a circuit is described by the equation $Z = \sqrt{r^2 + x^2}$, where "r" is active resistance and "x" is reactive resistance of the circuit. "Z" is a quantity termed as overall (total) electric resistance.

**What is active resistance?**

ACTIVE RESISTANCE is a quantity which characterizes the counteraction of an electric circuit to the alternating current. Active resistance is conditioned by an irreversible conversion of electric energy into other types (into heat energy, normally). Active resistance of a circuit unit depends on its shape, size and matter (substance) it is made of. Resistance between the two ends of the cylinder at a constant temperature is directly proportional to its length (L) and inversely to its cross-sectional area (S):

$$R = \rho(L / S),$$

where $\rho$ characterizes the (matter) substance of the conductor and is called resistivity (specific resistance), ohm-meter (ohm·m). Ohm's law for the effective current in the given circuit will be defined by the same equation as for the circuit of direct current: $I = U / r$, where r is the active resistance of the circuit.

**What is reactance?**

Reactive (capacitive/capacitance) resistance (reactance) - is a quantity which characterizes the resistance of the circuit capacitance to the alternating current. Reactive resistance (reactance) is a magnitude inverse to the current frequency and electric capacity:

$$1 / (2 \pi * f * C),$$

where "f" is the frequency of electric current, "C" stands for capacitance. Hence, the frequency increasing, the reactive resistance is reduced. When frequency values are extremely low, the reactive capacity is infinite. The reactive resistance also rises when the electric capacity of the circuit goes up. Capacitance is a physical characteristic of a condenser or capacitor, i.e. an appliance consisting of two and over conducting plates and an insulator between them. Capacitor is used to concentrate as many charges as possible. A capacitor stores the electric charge for a period of time depending on the resistance of the insulator. Capacitance of a capacitor is determined by the amount of electricity to be transferred from one plate to another in order to cause the voltage of one volt between them. Capacitance is determined by the formula:

$$C = \frac{Q}{E},$$

where "C" stands for capacitance of a capacitor, "Q" is the ratio of charge on a plate, "E" is the voltage between the plates. The SI unit for capacitance is the farad, which is established on the basis of the formula:

1 farad = 1 coulomb / 1 volt (F = C/V).

The total charge contained by the capacitor is limited and is determined by the quantity of electricity and the applied loss of voltage.

The concept of capacitive reactance includes such notions as polarization and permittivity.

**What is polarization?**

POLARIZATION is a term used to characterize the so called passive electric phenomena, i.e. phenomena connected with the passage of direct or alternating current through dielectrics (insulators). When a dielectric is placed in the electric field, electric charges are redistributed in such a way that the "centres of gravity" of positive and negative charges shift in relation to each other. Bound charges appear on the surface of the dielectric causing the formation of a reverse field which reduces the external electric field. This phenomenon is referred to as substance polarization.

In an alternating electric field, dielectric polarization develops as long as the dipoles have time to follow the change in the field, while the frequency of the field is lower than the natural oscillation frequency of elastically bound particles or the relaxation frequency of weakly bound particles. With increasing the frequency of electric current there is a pronounced dependence of the dielectric properties of matter on the frequency, which is accompanied by significant dielectric losses and heat release.

**What is a dipole?**

ELECTRIC DIPOLE (from Greek di – two and polos - pole) is an aggregate of two opposite point charges, equal in their absolute value and located at a distance from each other.

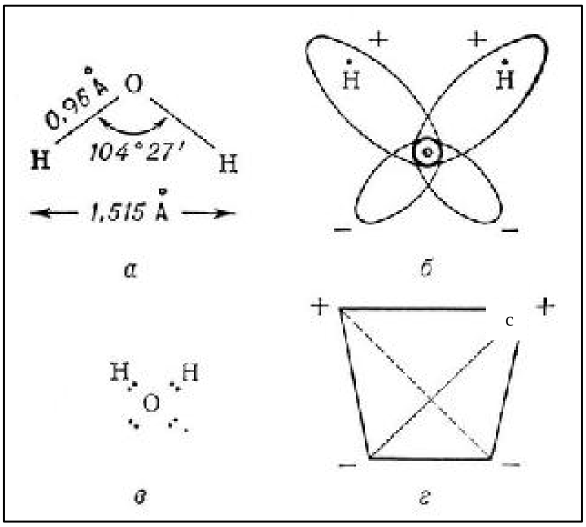



**Fig. 1-2. Structure of a water molecule:** (a) geometry of the $H_2O$ molecule (in the gaseous state), (b) electron orbits in the $H_2O$ molecule, (c) electron configuration of the $H_2O$ molecule (the unshared electron pairs are visible), (d) four charge poles situated at the corners of a tetrahedron in the $H_2O$ molecule.

Water is a typical representative of polar fluids. It consists of dipoles which, being placed in the electric field, are guided by the interaction of dipole charges and the field. This results in the emergence of dipole (orientation) polarization (Fig. 1-2).

Apart from polarization of dielectrics one can observe electrochemical polarization.

**What is electrochemical polarization?**

ELECTROCHEMICAL POLARIZATION is a change of potential on the boundaries of two phases conditioned by changes of the boundary (interfacial) layer structure. Electrochemical polarization is a part of numerous processes which take place in living bodies on different layers of their structural organization (molecular, sub-cellular, cellular, tissue, organic). On the boundary of phases which in the issue of various physical-chemical processes acquire charged particles or dipole molecules, a capacitor is formed – an electric double layer creating a difference of potentials on the phase boundary.

**What is permittivity?**

Permittivity is a physical quantity which describes the ability of a matter (substance) to reduce the electrodynamic forces in this matter as compared to the vacuum. Permittivity shows the extent to which the electrodynamic forces in a matter (substance) lower than in the vacuum. One can consider a capacitor with parallel plates of the area (A) separated by distance (d), with a dielectric substance between them. If the substance is represented by vacuum, the capacitance is $C_o$. If instead of vacuum there is some other insulator, the capacitance is C. The relation K = C / K is the so-called dielectric constant of the insulating substance.

$C_o$ is determined by the simple and well-known mathematical expression:

$$C_o = \varepsilon_o (A/d),$$

where $\varepsilon_o = 8.85 \times 10^{-12}$ F/m which is permittivity of free space (vacuum permittivity) or the electric constant. This enables to determine the dielectric constant using the previous equation:

$$C = K^*C_o = K^* \varepsilon_o (A/d) = \varepsilon(A/ d),$$

where ε is the dielectric constant of the insulator.

For instance, water sharply reduces interaction force of electric charges. If a charged body is moved from vacuum into water, the interaction force decreases 81 times. It means that the permittivity of water is anomalously high. The high value of permittivity determines a high degree of dissociation in water of various chemical substances as well as good solvability of salts, acids, bases and other chemical compounds. The environment able to maintain an adequate level of molecule ionization is essential for the development of life.

## Supplement

The value of permittivity characterizes the ability of a dielectric for polarization and depends on its molecular structure (Table 1-2).

**Table 1-2.** Electric permittivity values of various media in constant electric field at room temperature.

| | |
|---|---|
| White matter (alba)........................90 | Cow milk........................60 |
| Visual nerve.................................89 | Starch...........................12 |
| Gray matter..................................85 | Glass.........................6-10 |
| Whole blood.................................85 | Vegetable oil…..............2-4 |
| Water...........................................81 | Kerosene........................2 |
| Ovalbumin...................................72 | |

# Biological Object and Electric Current

# 2

### What is “electrical conductivity of biological objects”?

Conductivity of biological objects is the quantitative value characterizing the ability of the living objects (tissues) to conduct electrical current.

### Is it a “quantitative value”?

The coefficient of proportionality, which is known as the impedance of the system, can be determined when applying the same potential difference to different biological objects and measuring the intensity of a current (Fig. 2-1).

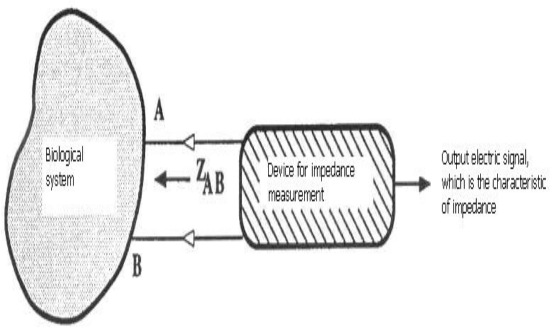



**Fig. 2-1.** Physiological processes cause impedance change between A and B (Biomedical Engineering, v24/is4-6, 1996)

Thus, impedance (Lat. impedire – to prevent) is a physical quantity, which characterizes the electrical opposition of the system. The electrical conductivity is inversely proportional to electrical impedance of the system.

### Structure of a biological system from the perspective of electricity

Biological objects, as complex systems, are characterized by the presence of numerous interface regions. In the living organism, this role is performed by various membranes, which from the molecular point of view can be regarded as virtually limitless two-dimensional surfaces. In biological tissue, electric current affects the components and structures that have a net electric charge and / or an electric dipole

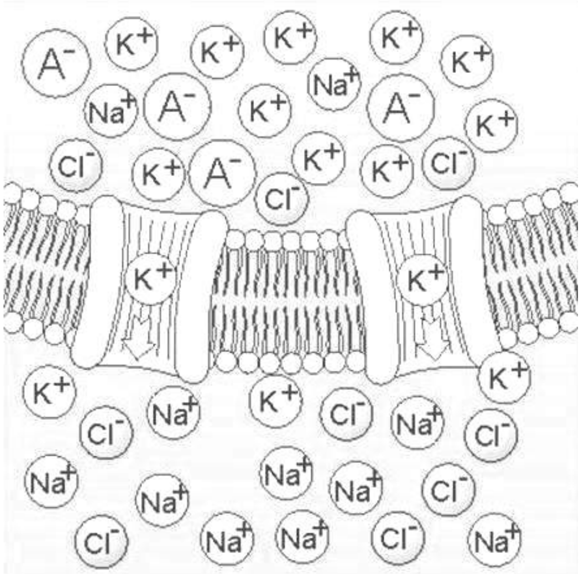



**Fig. 2-2.** Electric charges in the space surrounding the cell membrane (Biochemistry, D. Metzler, 1980).

moment. In the space surrounding cell membranes from both sides, the changes are carried by electric charges, mainly in the form of ions, and the sources of dipole moment in the form of polar water molecules and mobile polar macromolecules (Fig. 2-2). Moreover, the polarization ability of the cell membrane itself due to protein and lipid structures determines its exceptional electrical properties

**Extra-membranous electrical conductivity**

Extra-membranous conductivity is conditioned by electrons, ions, active polar molecules, the dipoles of water and dielectrics.

**Electrical equivalent of extra-membranous conductivity**

Electrical equivalent of extra-membranous conductivity is a cylindrical resistor. Resistance between the two ends of the cylinder with length (L) and area (A) can be determined by the formula:

$$R = \rho\ (L / A)$$

where ρ (ohm*cm) is the specific resistivity of the biological object. Changes of the biological object structure (modifying its chemical structure and geometrical parameters, such as its length or cross-sectional area) lead to change of its electrical resistance.

**Electrical properties of chemical compounds**

Electrical properties of chemical compounds are determined by several characteristics. The most significant of them are polarity, charge quantity and sign, molecular weight and mobility, ultimate composition.

**Polarity of chemical compounds**

Compounds can be polar and non-polar. Polarity should be understood to mean the presence in a chemical compound of polar or functional groups, in which electrons are shifted to one of the atoms (Fig. 2-3).The polarization phenomena which emerges due to that fact determines chemical and electrical

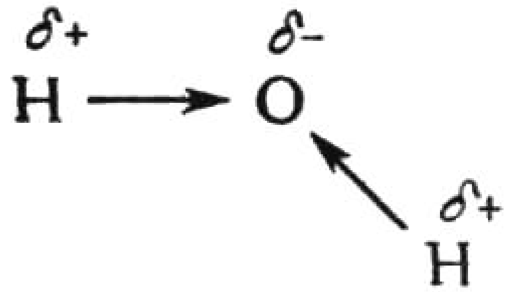



**Fig. 2-3.** The polar water molecule with polarized hydrogen bonds

properties of compounds. One distinguishes the following polar groups: -HO,-NH2,-NH,-SH,-CO. Thus, OH, NH2 and NH groups can donate a proton, while SB group accepts it relatively well. A special type of bond is formed – a hydrogen bond – it is particularly well pronounced in water molecules, where each oxygen atom is able to form hydrogen bonds with two other water molecules. In one chemical compound there can be from one to several positively or negatively charged functional groups (monopolar, bipolar and multipolar). Polar groups are the places of high activity. The presence of such groups determines the activity of a chemical compound in the electric field. Sugars and other compounds containing many polar groups are readily soluble in water. The solubility of sugar in water is determined by the ability of numerous hydroxyl groups of the compound to form hydrogen bonds with water molecules. In contrast, non-polar or hydrophobic groups such as -CH3-group, where the electrons are almost evenly distributed between the carbon and hydrogen atoms. The structures that have no functional groups are called non-polar compounds. The examples of such compounds in a biological organism are neutral fat and collagen - their molecules consist of nonpolar groups (Fig. 2-4). They are poorly water soluble and readily soluble in non-polar solvents. In the aqueous medium nonpolar groups tend

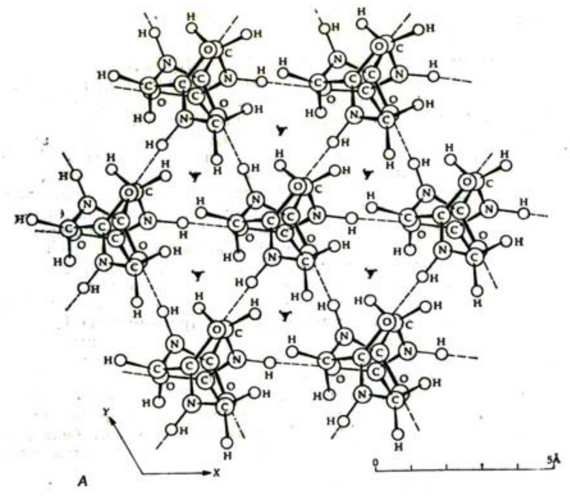


**Fig. 2-4.** Collagen - the main protein component of connective tissue, basement membranes and other structures Collagen contains 33% of glycine, 21% of proline+oxyproline, and 11% of alanine. The compound has no polar groups. (Biochemistry, D. Metzler, 1980)

to associate – this phenomenon is often referred to as hydrophobic interaction. At the same time, polar compounds are not able to associate. In an electric field, non-polar compounds behave as neutral particles or insulators.

### Charge quantity and sign

The electrical conductivity of biological fluids is proportional to the concentration of free ions in them. The major free positive charges in cells are ions of potassium ($K^+$) and magnesium ($Mg^{2+}$), the major negative ones - organic carboxylate ($COO^-$) and phosphate ($POO^-$) anions. As a result, the cell acquires total negative charge (Table 2-1). In extracellular space, the main positive charges are ions of sodium ($Na^+$), calcium ($Ca^{2+}$); the main negative

**Table 2-1.** Intracellular and extracellular free charges (Biochemistry, D. Metzler, 1980)

| **Cations** (meq/L) | extra-cellular | intra-cellular | **Anions** (meq/L) | extra-cellular | intra-cellular |
|---|---|---|---|---|---|
| $Na^+$ | 142 | 10 | $Cl^-$ | 103 | 4 |
| $K^+$ | 4 | 140 | $HCO_3$- | 24 | 10 |
| $Ca^{2+}$ | 5 | $10^{-4}$ | Protein- | 16 | 36 |
| $Mg^{2+}$ | 2 | 30 | $HPO_4^{2-}$ + $SO_4^{2-}$ +organic acids | 10 | 130 |
| $H^+$ | $4x10^{-5}$ | $4x10^{-5}$ | | | |
| Total | 153 | 180 | Total | 153 | 180 |

charges are represented by inorganic anions of chloride ($cl^-$).

### Molecular weight and mobility

With the increase of molecular weight of a chemical compound and its electrical properties change. Increasing molecular weight causes the increase of the number of functional or hydrophobic groups. In some cases, the increase of

| | |
|---|---|
| $H^+$ . . . . . . . . . . | 0,00326 |
| $OH^-$ . . . . . . . . . | 0,00180 |
| $Li^+$ . . . . . . . . . . | 0,00034 |
| $Na^+$ . . . . . . . . . | 0,00045 |
| $K^+$ . . . . . . . . . . | 0,00066 |

quantity of polar groups in complex molecules leads to the increase of the polarity of the molecule and its ability to dissolve in water, for example, hyaluronic acid. In other cases, the increase of quantity of hydrophobic groups imparts to the chemical compound the properties of an insulator, such as triglycerides.

The mobility of a chemical compound is also related to its molecular weight. Low molecular weight substances such as ions, possess much greater mobility than the high molecular weight compounds (Table 2-2). High molecular weight compounds have rotational and vibrational mobility. The nature of molecular motion depends on the molecular weight too: translational, rotational, vibrational, and electronic.

### Elemental composition

The presence of certain elements in chemical compounds gives the latter various electrical properties. The left side of the incomplete periodic table of elements (Table 2-3) shows the elements-metals, which are able to conduct electric current. This occurs because the electrons in their outer orbits (valence orbits) leave the atom and move freely on the atomic lattice structure. When a potential difference is applied to the metal, the set of free electrons provide electrical conductivity. Non-metal insulators are shown on the right side of the periodic table. They are single molecules without loosely held electrons, and therefore do not conduct electricity. In (R), known as active resistance of a biological object, depends on the chemical structure of the object, or, rather, on the chemical compounds that fill extra-membranous space.

**Tab. 2-3.** Simlified Periodic Table of Elements (Physics, G.Rowell, S.Herbert, 1994)

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 3<br>Li<br>6.94 | 4<br>Be<br>9.01 | 5<br>B<br>10.81 | 6<br>C<br>12.01 | 7<br>N<br>14.0 | 8<br>O<br>16.0 | 9<br>F<br>19.0 | 10<br>Ne<br>20.18 |
| 11<br>Na<br>22.99 | 12<br>Mg<br>24.31 | 13<br>Al<br>26.98 | [illegible]<br>Si<br>[illegible] | 15<br>P<br>30.97 | 16<br>S<br>32.06 | 17<br>Cl<br>35.45 | 18<br>Ar<br>39.95 |
| 19<br>K<br>39.10 | 20<br>Ca<br>40.08 | 31<br>Ga<br>69.72 | 32<br>Ge<br>[illegible] | [illegible]<br>As<br>74.92 | 34<br>Se<br>79.0 | 35<br>Br<br>79.9 | 36<br>Kr<br>83.8 |
| 37<br>Rb<br>85.47 | 38<br>Sr<br>87.62 | 49<br>In<br>114.82 | 50<br>Sn<br>118.7 | [illegible]<br>Sb<br>[illegible] | [illegible]<br>Te<br>[illegible] | 53<br>I<br>126.9 | 54<br>Xe<br>131.3 |
| 55<br>Cs<br>132.91 | 56<br>Ba<br>137.3 | 81<br>Tl<br>204.4 | 82<br>Pb<br>207.2 | 83<br>Bi<br>208.98 | [illegible]<br>Po<br>[illegible] | 85<br>At<br>210 | 86<br>Rn<br>222 |

extra-membranous space of a biological object, there are also the elements that determine the electrical properties of the medium. They are represented by the five essential elements that make up about 2% of body weight: sodium, potassium, magnesium, calcium and chlorine. Other chemical elements, which are insulators, form the firm basis for the body, its frame. They are represented by carbon, oxygen, nitrogen, phosphorus and sulphur, which together comprise 97.63% of body weight (Table 2-3).

**Principles of extra-membranous electricity**

Extra-membranous conductivity, which depends on ions, mobile polar molecules, the dipoles of water and insulators, is described by Ohm's law ($V = IR$). Where, proportionality coefficient

**What determines the active component of the impedance or resistance?**

If we compare extra-membranous space with a solution of chemical compounds, then in the solution containing ions, a small potential difference V forms high current I, therefore, this "conductor" has low resistance R. In the solution containing non-polar compounds such as triglycerides, the same potential difference forms low current and, consequently, the resistance of the "conductor" is high. Table 2-4 shows the collected values of this parameter for some biological tissues. Among the factors affecting extra-membranous resistance, one distinguishes temperature, the concentration of chemical compounds and the flow rate.

**Tab. 2-4.** Specific resistivity or conductivity of biological tissues (Biomedical Engineering, v24/is4-6, 1996)

| Substance | Specific resistivity (ohm-cm (1 ohm-in=2.54 ohm-cm)) | Species |
|---|---|---|
| Blood | 150[a] | Human |
| Plasma | 50-60 | Mammal |
| Spinal fluid | 65 | Human |
| Bile | 60 | Cow, pig |
| Urine | 30 | Cow, pig |
| Myocardium | 400 | Dog |
| Skeletal muscles (cross fibre) | 1600 | Dog |
| Skeletal muscles (longitudinal fibre) | 300 | Dog |
| Lungs | 1500 | Mammal |
| Kidneys | 370 | Mammal |
| Liver | 820 | Dog |
| Spleen | 885 | Dog |
| Spleen | 580 | Mammal |
| Fat | 2500 | Mammal |
| Sodium chloride | 14.9 (at 18 °C) | - |

## Temperature effect

The temperature of the substance affects its resistance significantly: as a rule, temperature increase leads to resistance decrease.

For example, the blood is an electrolyte, and electrical conductivity of the electrolyte solution increases by 2% for each Celsius temperature degree increase. This complex effect is the result of numerous factors, one of which is the change of the blood viscosity.

## Concentration effect

Electrolyte concentration increase is accompanied by resistance of the system increase (Fig. 2-5). For instance, despite the fact that blood is a suspension of plasma with red blood cells, white blood cells and platelets, plasma is still an electrolytic solution. Hematocrit volume increase is accompanied by the increase of total and specific resistance. Graphically, the resistance of blood $\rho$ in relation to the hematocrit volume can be represented by the graph all points of which descend on a straight line, the values of which are expressed by the following equation:

$$\rho = A [\exp (\alpha H / 100]$$

where H is hematocrit volume, A and $\alpha$ - empirical constants that depend on blood group. Interestingly, that the average electrical conductivity values of the northern mammals (human, dog, cow, horse, sheep, goat, cat) is 56.25 ohm*cm with standard deviation. 2.76;

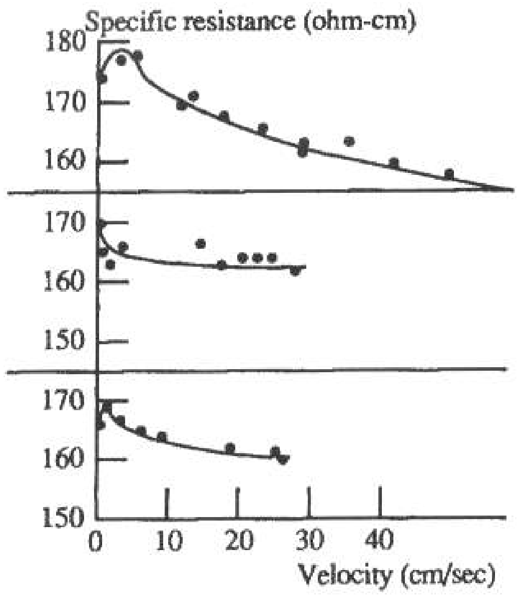



**Fig. 2-5.** Decrease of axial resistance in case of blood flow velocity increase expressed by Reynolds number (Biomedical Engineering, v24/is4-6, 1996)

68% of the values are between 53.73 and 59.25 ohm*cm.

**Flow rate effect**

The very unusual and unique behaviour of the circulating blood was first described in 1937 by Sigman et al. Here are his words: "We found that the electrical conductivity is altered when the blood is put in motion." They found out a clear decrease of resistance in blood samples collected from more than 50 cows, when the blood was put in motion. Fig. 2-6 illustrates this effect (using hematocrit value and the Reynolds number as independent variables).

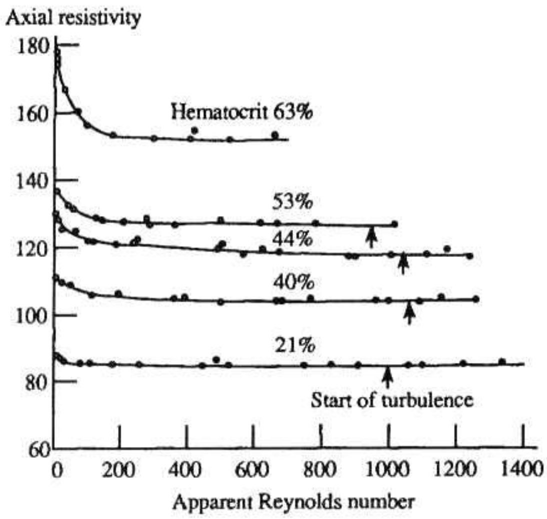



**Fig. 2-6.** Three examples of specific resistance alterations of cow blood depending on the blood flow velocity (Biomedical Engineering, v24/is4-6, 1996)

There is still no comprehensive explanation of this effect, but we can state that at least three phenomena, that clearly affect the resistance of blood, can be observed in a pulsating flow of blood:
- arterial lumen alterations
- alteration of cell orientation
- cell aggregation around the longitudinal axis of the vessel

**Membrane conductivity (dielectric permittivity)**

Biological cells, which size is usually at the range of 5-20 microns, include membranes, which control the movement of ions and molecules between intra- and the exo-cellular spaces. Membrane conductivity is conditioned by the structure of the membrane, namely by bilipid layer of 3-5 nm thickness, the molecules of the latter possessing hydrophilic and hydrophobic properties (Fig. 2-7). Polar heads are directed outward and the hydrophobic part is the inner part of the membrane. The second main component of the cell membrane is protein macromolecules, which are incorporated into the lipid bilayer. Thus,

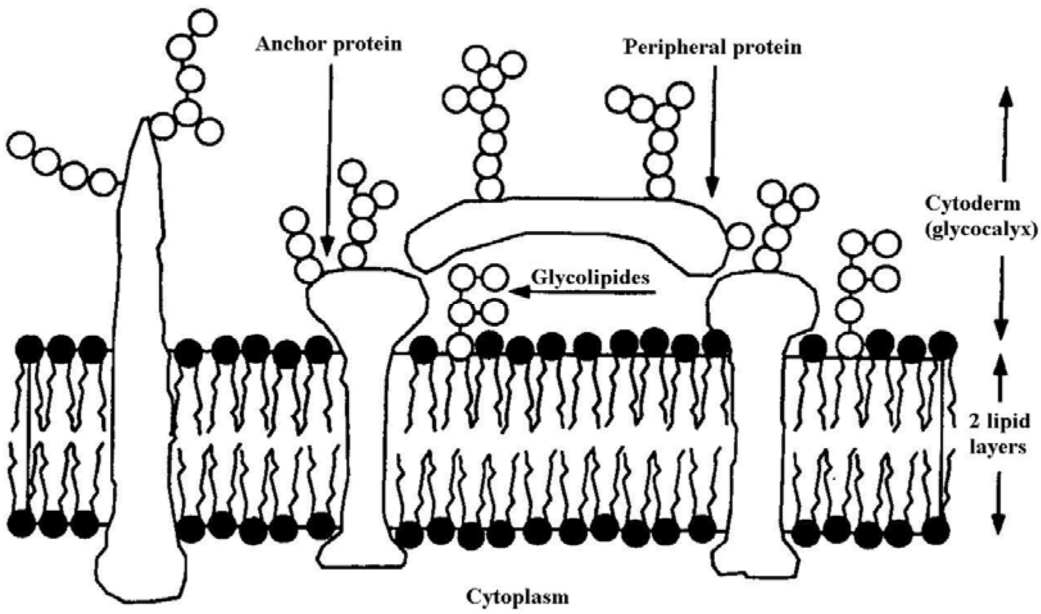



**Fig. 2-7.** The structure of the cell membrane (Biomedical Engineering, v24/is4-6, 1996)

these structures determine polarization properties of cell membranes.

**Electrical equivalent of extra-membranous conductivity**

A cell membrane acts as an insulator and resembles two parallel condenser disks having an area **A** separated by the distance **d** with the insulator between them possessing dielectric permittivity which is close to that of lipids. The capacitance of this structure is described by the following equation:

$$Cm = \varepsilon_m \varepsilon_0 / d \quad (\mu F/cm^2)$$

where $\varepsilon_m$ is the relative permittivity of a cell membrane; $\varepsilon_0$ - vacuum permittivity ($\varepsilon_0$=8.854*$10^{-14}$ F/cm) and **d** – membrane thickness.

**The capacitance of a membrane and relaxation**

The capacitance of a cell membrane is about 1 ɥF/$cm^2$. When applying an alternating electrical field the charges of ions move and accumulate on both sides of the membrane. Usually, this effect is observed when using the AC of low frequency, when the period of

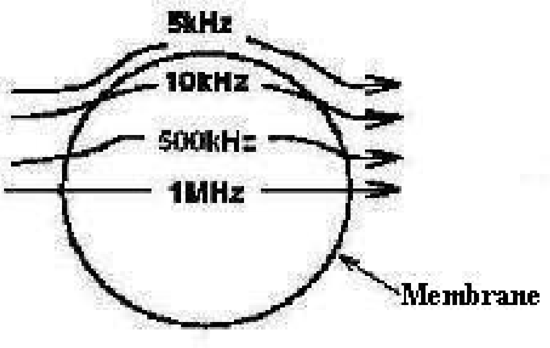



**Fig. 2-8.** Cell membrane permittivity depending on the frequency of electric current (J.Jossinet The Physician who Introduced Bioimpedance Analisys. Proceedings of ICEBI XII-EIT V. 2004)

charge alteration is long enough, so that it allows charging and discharging the membrane. At the current frequency of several kilohertz the capacitance of the membrane decreases and the polarization relaxation of the membrane occurs: the occupied capacitance of the membrane cannot follow changes of the electric field of high frequency (Fig. 2-8).

**Principles of the membranous electricity**

Membranous electrical conductivity, conditioned by the presence of a bilipid layer, is determined by the reactance of a biological object and described by the formula:

$$R = \frac{1}{2\pi * F * C},$$

where R stands for reactance (in ohms); F is the frequency of the electric current (in Hertz); C stands for capacitance (in farads); $\pi$= 3.1428.

The above equation shows that the reactance is inversely proportional to the frequency of the current and to capacitance.

Consequently, when increasing the frequency of the electric current, the reactance decreases.

**Dispersion**

Electrical properties of tissues are a direct consequence of their structure. In biological tissues, electric current affects those components which possess either net electric charge (mainly, ions), or electric dipole moment (mainly, cell membranes and water molecules). The movement of these charges induces the phenomenon of conductivity in the material, as well as the polarization of various dipoles as a result of the phenomenon of dielectric relaxation. These properties of biological tissues which are determined by a combination of electrical conductivity, $\sigma$, and dielectric constant, $\varepsilon_t$, showed their dependence on the frequency - dispersion.

## Dispersion of electrical conductivity

When the frequency of the applied current increases, the electrical conductivity of tissues increases from the low values, which depend on the volume of extracellular fluid (typical conductivity of high water content tissues is 0.1-2 S / m), forming a plateau at 10-100 MHz frequency. Then, at the microwave frequency, electrical conductivity rises rapidly, mainly due to dielectric relaxation of water (Fig. 2-9).

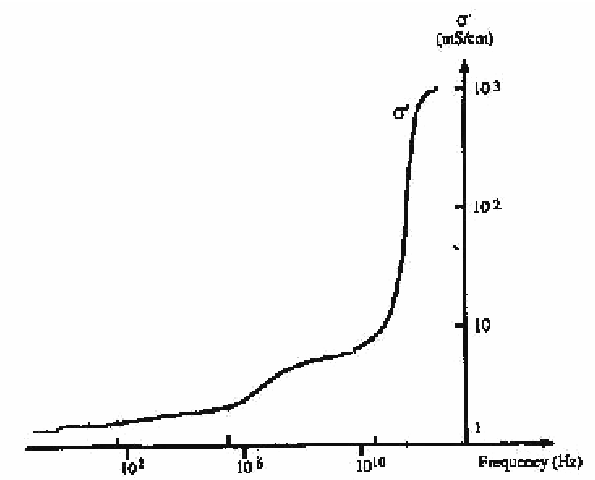



**Fig. 2-9.** Dependence of biological tissues conductivity on the frequency of electrical current (Biomedical Engineering, v24/is4-6, 1996)

## Dielectric dispersion

The electrical behaviour of biological tissues reveals that at high frequencies dielectric parameters of the object situated in the path of the electric current should depend on polarization and relaxation phenomena.

## Polarization

The term "polarization" is used to characterize the so-called passive electrical phenomena – the phenomena which are associated with direct or alternating electrical current passing through compound substances. It is mainly applied to dielectrics and capacitance.

Polarization is the phenomenon of bound charges emergence on the surface of a material (dielectric, capacitor) and the appearance of the corresponding reversed field, which diminishes the external electric field. The polarization of the matter is the result of molecular strain in one case and molecular orientation in other cases. The equation, which enables to find the relation between the applied electric field and polarization, is the following:

$$P = (\varepsilon_t - \varepsilon_0)E,$$

where P stands for polarization; εt is the dielectric permittivity of the material; $\varepsilon_0$ stands for vacuum permittivity ($\varepsilon_0$=8.854*$10^{-14}$ F/cm); E is the electric field strength.

## Types of polarization

There are several types of polarization. Electronic polarizability is conditioned by the displacement of the electron shells with respect to atomic nuclei in a field; ionic polarizability (in ionic crystals) derives from the displacement of ions of opposite signs from the equilibrium process and in opposite directions; atomic polarizability is due to the displacement of atoms of different types in a molecule.

## Polarizability and the frequency of electric current

When the frequency of an alternating electric field is low, the polariza-

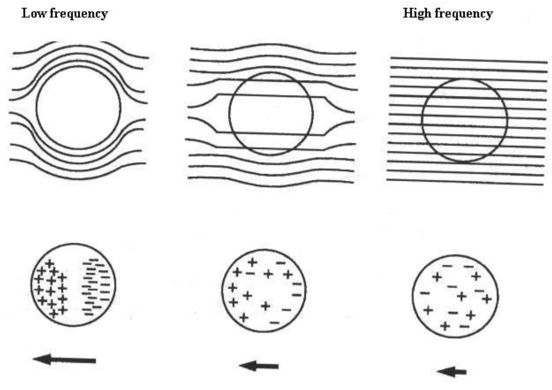



**Fig. 2-10.** Diagrammatic representation of dipole orientation depending on the frequency of electric current (Biomedical Engineering, v24/is4-6, 1996)

tion of dielectrics develops in the same way as in a direct electric field, that is, until the dipoles have time to follow the changing field, the field frequency change is lower than the natural frequency of elastically coupled particles or the relaxation frequency of weakly bound particles. In case of the increase of the electric current frequency, the orientation polarizability follows the change of electric field with time lag increasing. At very high frequencies, the dielectric does not "feel" the presence of a field and polarizability does not occur. As a result, the decrease of dielectric permittivity occurs. It is accompanied by significant dielectric losses, which is associated with conductivity increase. Thus, oscillations of various charges depend on the relaxation process and on the electric field frequency (Fig. 2-10).

## Relaxation phenomenon

Relaxation is a gradual transition of the system from a nonequilibrium state caused by external influences in a state of thermodynamic equilibrium. Electric relaxation means the establishment of the equilibrium dielectric polarizability. Various charges make different oscillations related to the frequency of electric current. At frequencies below 10 GHz there are three relaxation types: dipole, polarization and spatial. Dipole relaxation is conditioned by the dipole polarization. It covers high frequencies such as 10 MHz. Polarization relaxations are observed in heterogeneous materials. It occurs at frequencies around 10 kHz or higher (up to tens of MHz). Spatial relaxation is observed at low frequencies about 1 kHz in substances containing bonds and having the dipole oscillation for each half-period current.

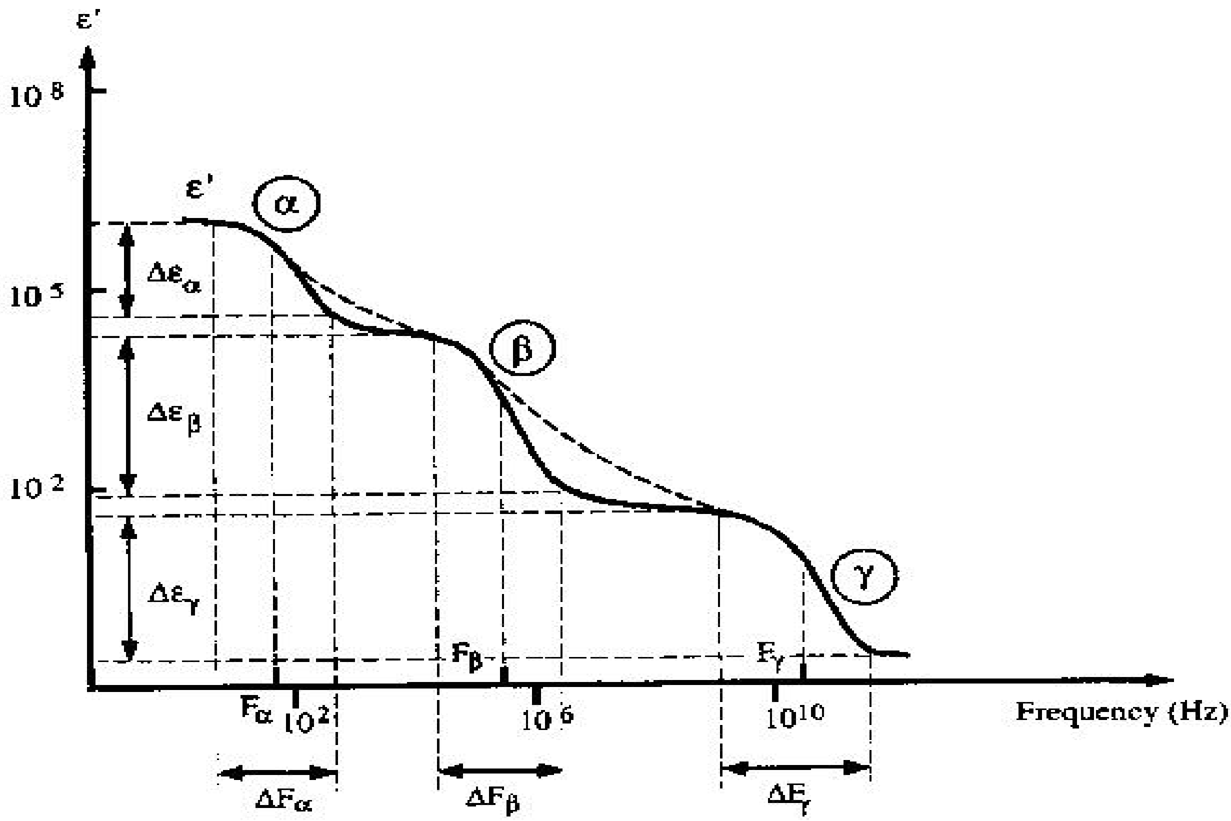



**Fig. 2-11.** Permittivity of biological tissues is represented as a function of frequency of electric current. Three large dispersions: $\alpha$, $\beta$ and $\gamma$ are characterized through the relaxation frequency, F, and the dielectric permittivity alteration $\Delta\varepsilon$ (Biomedical Engineering, v24/is4-6, 1996).

**Dielectric dispersion in biological tissues**

With increasing frequency of electric current the increase of conductivity is associated with the decrease of the dielectric constant in three main steps: α, β and γ. Each step is characterized by a specific type of relaxation that takes place at a specific frequency range and is typical for all types of tissues (Fig. 2-11).

**α-dispersion of dielectric permittivity**

α-dispersion dominates in the range from 10 Hz to several kilohertz. At low frequencies the period of charge alteration is short enough so that it allows membrane charging and discharging. Current passes only through the extracellular space. Calculated electrical conductivity is the electrical conductivity of the extracellular space. α-dispersion is usually associated with a number of cell membranes in the tissue, which has a large capacity and high dielectric permittivity. α-dispersion is conditioned, on the one hand, by the accumulation of charge with the formation of electrochemical double layer in membrane, and by the limitation of the ionic conductivity, on the other hand. α-dispersion is related to the dipole relaxation of large dipoles, which form the cell membrane and cause the accumulation of opposite sign charges on each side of the membrane in an electric field. Thus, α-dispersion is a near-surface phenomenon and does not provide information about the cell contents.

**β-dispersion of dielectric permittivity**

β-dispersion can be found in the so-called “radio frequency”: from 10 kHz to 1 MHz. The dielectric permittivity of soft tissues, associated with β-dispersion, is in the frequency range from 103 - 104 Hz, relaxation frequency is about 500 kHz. β-dispersion is conditioned by the change of the capacitance of cell membranes. The increase of electrical current frequency causes cell capacity (reactance) to decrease. This effect induces an increased flow of current passing through the intracellular space and thus increases the electrical conductivity of the tissue. In case of high frequency, part of β-dispersion is also determined by the dipole reorientation of the protein and tissue organelles that behave like electric dipoles.

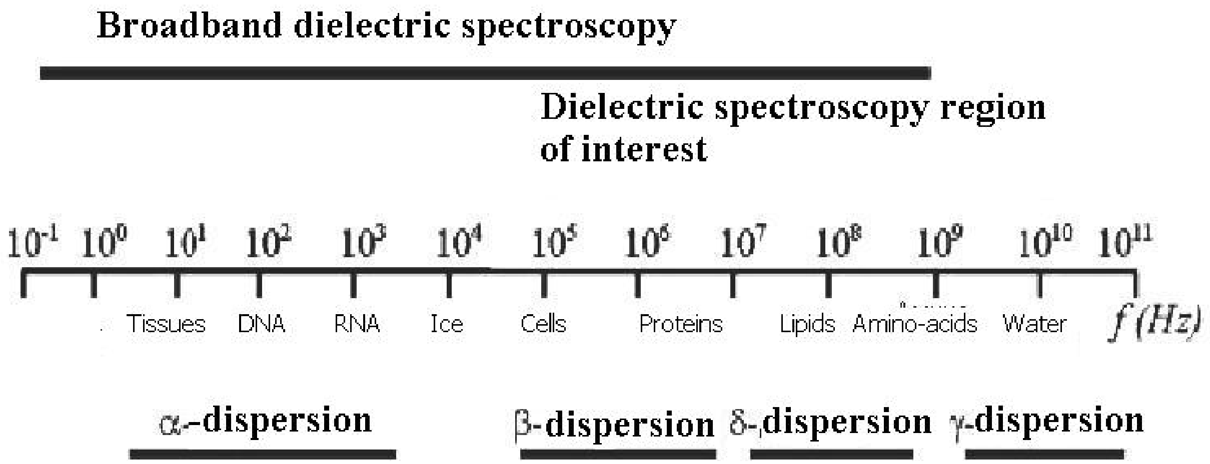



**Fig. 2-12.** Main types of electrical dispersion in biological tissues (Y.Feldman at all. Dielectric Spectroscopy of Biological.Systems; from Aminoacids to Cells. Proceedings of ICEBI XII-EIT V. 2004)

### γ-dispersion of dielectric permittivity

γ-dispersion dominates in the spectrum of high frequency (the so-called microwave frequency), when the capacities of the membrane are "short-circuited". Thus, an electrically "silent" membrane is formed. Dielectric permittivity decrease, and the consequent increase of the electrical conductivity at frequencies above 1 GHz can be associated with the polar properties of the tissue containing free water molecules, possessing the relaxation frequency about 25 GHz. γ-dispersion is a result of the reorientation of electric dipoles, which form water molecules, representing over 80% of soft tissue volume.

At very high frequencies of electrical current tissues lose their electrical properties and behave like electrolytes, because their dielectric permittivity is dominated by the relaxation mechanism of free water. It was found out that at very high frequencies dielectric constant correlated with free water content (Shepps and Foster).

### δ-dispersion of dielectric permittivity

Some authors have considered that the frequency range from 1 GHz to 10 GHz of δ-dispersion (corresponding to the rotation of the amino-acids, partial rotation of the charged groups of proteins and the relaxation of the protein-bound water and free water) is the feature of γ-dispersion (Fig. 2-12).

# Electrical Impedance Scanning Concept

# 3

## Historical background

The founders of impedance tomography are B. H. Brown and D. C. Barber from the University of Sheffield (UK). In 1982 they published their work on electrical impedance tomography and introduced the first electrical impedance tomogram of a hand, thus B. H. Brown and D. C. Barber opened a new area of research.

The word "tomography" in the name of the method is used mainly for historical reasons. Strictly speaking, the method is not tomographic, since there are no natural (physical) methods of layer-imaging "slice by slice", although mathematical methods can provide cross-sectional slices of conductivity. This is due to the fact that electrical current (as opposed to X-ray radiation) is impossible to focus in a specified plane – it always propagates throughout the area under investigation.

Currently, a variety of electrical impedance diagnostic systems is used both in academic studies and in clinical practice. A significant part of such systems employs electrodes which reside in a single plane and two-dimensional mathematical conductivity reconstruction algorithms in the plane of the electrodes. Such systems are a compromise between accuracy and processing speed (or the price of the hardware).

## The major task of electrical impedance tomography (EIT)

When conducting electrical impedance research, an array of electrodes is positioned on the surface of an object (Fig. 3-1). Part of the electrodes is used as inducers (i), another part as measuring electrodes ($\Delta$v). Typically, a source of current is used as an inducer, and the potential differences are measured between measuring electrodes, although sometimes other options are considered. Thus, all the measurements are made on the surface of the object under investigation. The main objective of EIT is to reconstruct the three-dimensional electrical conductivity distribution of the object basing on the results of electrical measurements on its surface.

## The inverse problem of EIT

From the viewpoint of mathematical physics, the main objective of EIT belongs to a class of the so-called *inverse problems*. A distinctive feature of inverse problems is the fact that they restore the physical causes of the observed phenomena (in this case, conductivity distribution of the tissue) using its external effect (surface conductivity of the object). Inverse problems are the most difficult problems in mathematical physics, because all inverse problems contain a considerable part of uncertainty - there are many alternative answers, most of which turn out to be meaningless in terms of physics. In the case of EIT various volume conductivity

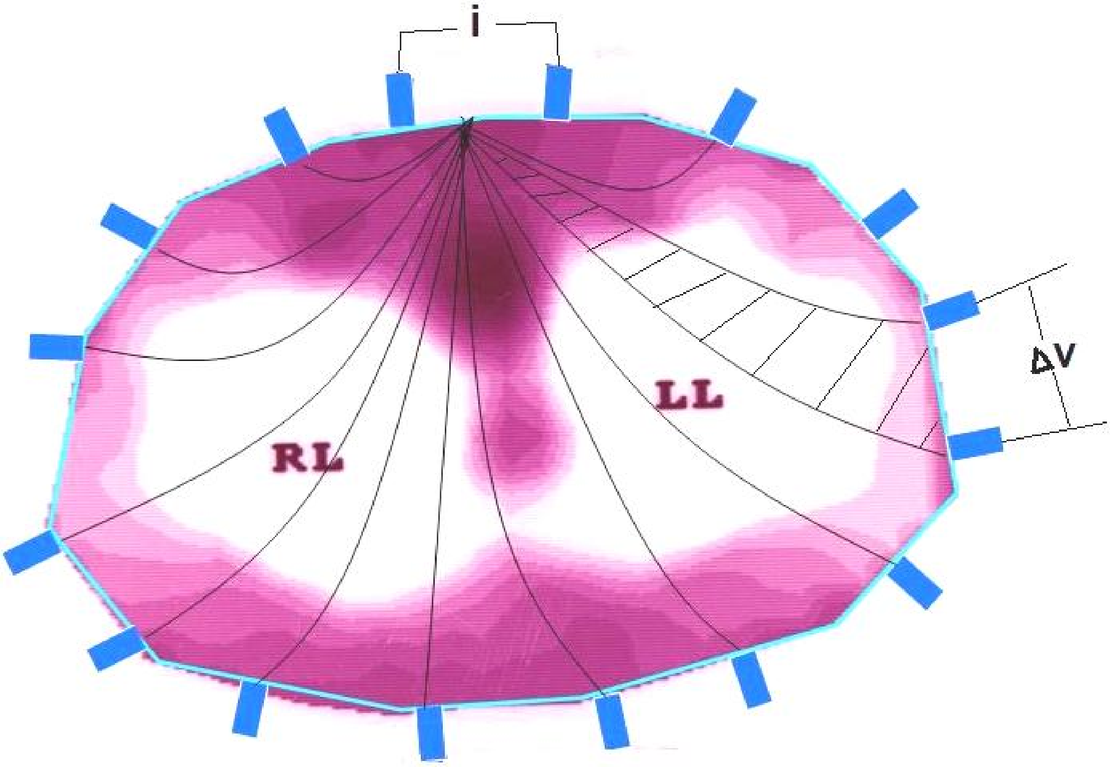



**Fig. 3-1.** The array of electrodes is positioned on the surface of an object. I - electrodes inducing current, Δv - measuring electrodes. The crosshatched region represents the equipotential surface.

distributions may give patterns of surface conductivity, which are slightly different from each other. In this case, the problem is called *incorrect*. However, an incorrect problem should not be understood as an insoluble - a whole area of mathematical physics occupies with the solution of incorrect problems. Successful solution of incorrect problems always requires prior information on the expected properties of the solution.

The term "discernibility", meaning the ability of a given configuration of the induced currents to generate different patterns of surface voltage in case of different volume conductivity distributions of tissues, is widely used to describe the properties of the inverse problem of EIT. The most recently developed methods are using the optimal configuration of inducing currents. Optimal configuration of currents causes considerable changes of surface voltage for a given heterogeneous distribution of volume conductivity in comparison with a homogeneous distribution. Methods employing optimal configuration of inducing currents require the possibility of simultaneous usage of each electrode, both as an inducer and as a measuring electrode. This fact considerably complicates the hardware implementation.

### Inverse problem solution methods

The most popular solution methods for the main EIT problem are the following: the backprojection method, the perturbation method and the method based on the usage of the Newton-Raphson iteration process. Historically, the backprojection method was first used in X-ray tomography, where it represents a natural generalization of early hardware solutions.

### Application of the back projection method in X-ray tomography

The two-dimensional section on the left of Figure 3-2 shows a simplified diagram of tomographic projections ***R (s, φ)*** acquisition for three directions: ***φ1, φ2, φ3***. Orange arrows indicate the direction of scanning radiation. Red spots represent the heterogeneities of

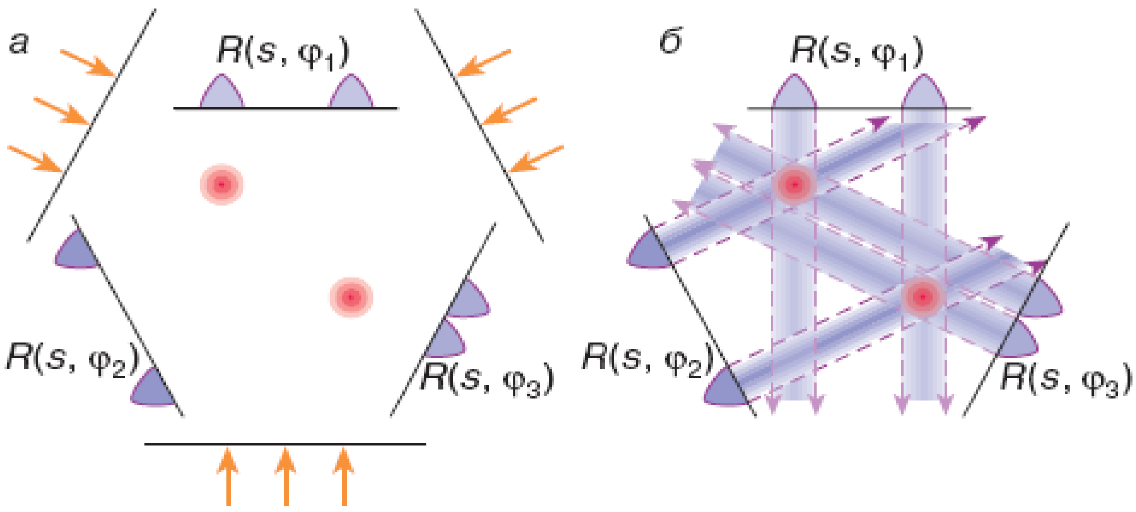



**Fig. 3-2.** Image reconstruction procedure using the back projection method.

the object. Blue graphs are the acquired tomographic projections. The same figure on the right shows the process of image reconstruction with the help of backprojection method.

A backprojection for each projection is formed by projecting in the opposite direction - smearing each projection back into the object region along the direction in which the projection was acquired. The image of heterogeneities within the object is obtained at the intersection of backprojection "rays". Apparently, the image acquired outside the intersection of rays is a "noise" image unrelated to the structure of the object. In case of a small number of directions a kind of a "striped" image is acquired with clearly visible backprojection "rays". In case of numerous directions, noise images reduce reconstructed image sharpness.

## Application of the back projection method in electrical impedance tomography

Historically, the back projection method is the first technique applied in order to reconstruct conductivity distribution in electrical impedance tomography. Initially, the back projection method was developed as an empirical method based on rectilinear propagation of scanning radiation in tissue (i.e. on the presence of “rays”). However, there are no rays in EIT acting as rectilinear directions of radiation propagation, thus when transferring the method one has to employ the so-called "pseudorays". The concept of "pseudorays" can be introduced due the following fact:

**change of surface potential difference (compared with the homogeneous case), caused by the presence of local heterogeneity in the object, is mainly concentrated in the area which is a projection of heterogeneity on the surface of the object along the equipotential lines (or surfaces) of the field.**

Thus, the method of back projection may be transferred to the EIT case, if instead of rays there are used the electric force lines, calculated for the case of homogeneous conductivity distribution.

The easiest way to illustrate the application of the method is a two-dimensional example. On the left of Figure 3-3 the system of equipotential lines for the two injecting electrodes **i(A)** and **i(B)** is represented. Here we have in mind the case when a pair of injecting electrodes is located diametrically opposite, but the reference electrode which is opposite to the injecting one is

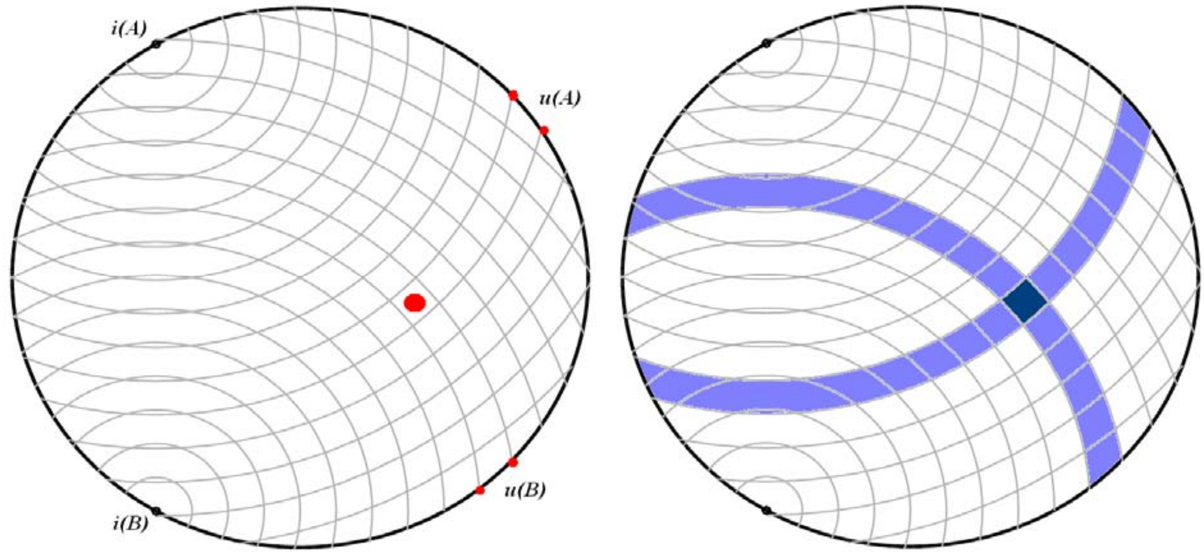



**Fig. 3-3.** Equipotential lines – "pseudorays" and image reconstruction.

not shown in the figure. Red spot represents the heterogeneity of the object. Red spots on the surface of the object indicate the pairs of measuring electrodes, where the potential differences ***u(A)*** and ***u(A)*** bear the strongest difference from the case of a homogeneous conductivity distribution.

On the right of Figure 3-3 the image reconstruction from the measurements on two injecting electrodes is shown. Blue stripes represent the noise areas of the reconstructed image. The dark blue intersection is the reconstructed image of the heterogeneity. When reconstructing the image from measurements employing a large number of injecting electrodes, the higher quality of the reconstructed image can be ensured.

On the right of Figure 3-4 there is a typical result of the conductivity model reconstruction (shown on the left) based on measurements employing 16 electrodes. Smoothing and the usage of subpixel algorithms make it possible to acquire an image of better quality.

The difference between a three-dimensional case and a two-dimensional one is in the following:

- equipotential surfaces are spheres centered in the injecting electrode;
- the projection of a point heterogeneity along the equipotential surfaces on the object surface is a circumference centered in the injecting electrode having the radius equal to the distance from the injecting electrode to the heterogeneity;
- the change of surface potential difference (compared with the homogeneous case) is mostly focused in the circle described above, but decreases when the point on the circumference is moving away from the heterogeneity.

Thus, in case of three dimension imaging the back projection method is a normal projection of the changes of surface potential difference (compared with the homogeneous case) inside the object along the equipotential surfaces, but with the weight depending on the distance between the projected point and the point in which the conductivity is reconstructed.

The rigorous substantiation of the applicability of the back projection method as the EIT problem is not known, but the fact that the method gives acceptable results, at least for the distribution of conductivity, which is not very different from the homogeneous distribution, was established experimentally. However, even in the case of beam tomography, this method provides the images of very poor resolution and it is clearly the worst of known techniques in the sense of image resolution.

Currently, the method of back projection is practically not applied in the two-dimensional EIT systems, but it is widely used in three-dimensional systems. The fact of the matter is that in the case of three-dimensional systems, the back projection method is a reasonable compromise between image quality and computational complexity. More sophisticated techniques require an extremely large amount of computation, making them difficult to use for acquiring three dimensional images.

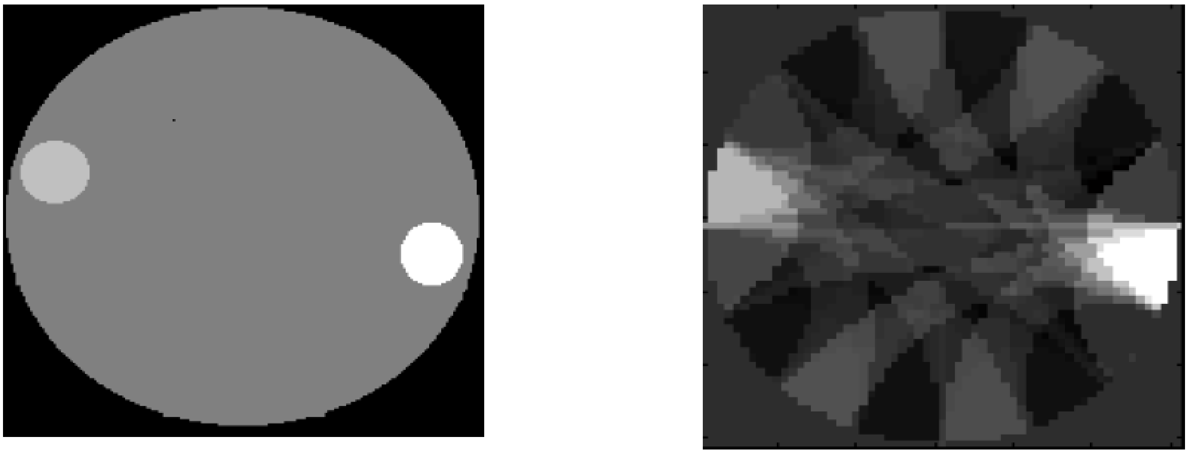


**Fig. 3-4.** The result of the conductivity model reconstruction (shown on the left) based on measurements employing 16 electrodes (shown on the right).

### Other methods of the EIT problem solving

*Newton-Raphson method*

The so-called Newton methods for the EIT problem solving reside in direct solution of equations relating surface conductivities with the volume distribution of conductivity with the help of the Newton-Raphson numerical method. It is established experimentally that the Newton methods have the best convergence, but are sensitive to errors in the data. Practical use of the Newton methods requires the employment of the so-called *regularization methods (smoothing methods)*, which turn the solution of an incorrect problem to the solution of the well-set problems sequence. The Newton methods are widely used in two-dimensional EIT systems: moreover when appropriate regularization methods are employed, the Newton methods provide the best image quality and convergence rate available to date.

*Perturbation method*

The perturbation method was adapted to the X-ray tomography from geophysics, where it was applied for electrical impedance soil analysis. The method consists of the successive alteration of the solution (volume distribution of conductivity) so that the acquired surface conductivity values are gradually getting closer to those measured. Although the perturbation method is not currently in use, it served as a basis for a wide class of optimization methods based on direct minimization of the model surface voltages deviation from the measured voltages. These methods have slower convergence rate than the Newton ones, but do not require usage of specific regularization methods.

# Anatomy, Histology and Physiology of Mammary Gland

# 4

Every diagnostic procedure demands from a researcher extensive and thorough knowledge of the subject under investigation. Such knowledge takes shape in the process of comprehension of the anatomic peculiarities of the subject, the histological structure of the tissues under analysis, the structure of hormones and their interaction with the hormone-dependent and hormone-sensitive cells and tissues of the organ under investigation. In order to be able to interpret the electrical impedance images of the mammary gland, one should notice the following aspects of anatomy, histology and physiology of the mamma.

## Anatomy

The mammary gland is a glandular organ with excretory function. Macroanatomically, the structure of this gland includes the following: a capsule, a stroma, a parenchyma, a reservoir for the accumulation of secretion (Fig. 4-1).

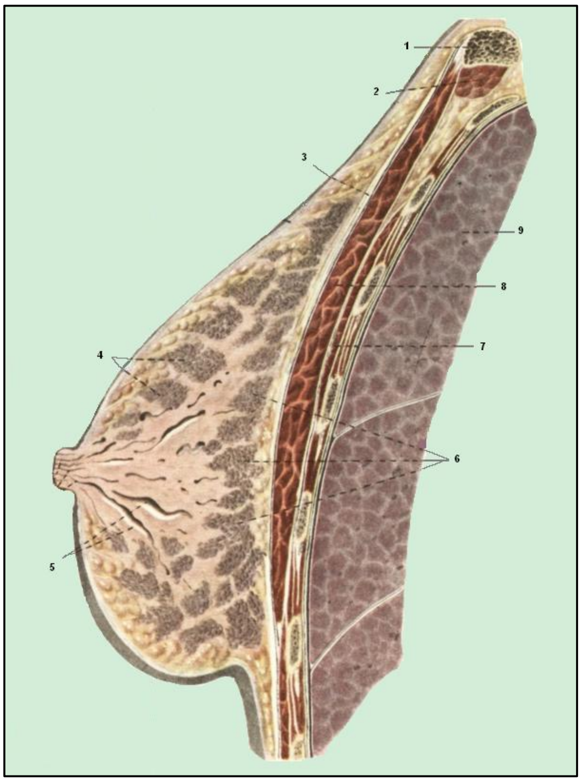



**Fig. 4-1.** Female breast, mamma (sagittal section). 1-clavicula; 2-M. subclavius; 3-Fascia pectoralis; 4-Lobi glandulae mammariae; 5-Sinus lactiferi; 6-Corpus mammae; 7-M. pecto-ralis minor; 8-M. pectoralis major; 9-Pulmo dexter. (R.D.Sinelnikov "Atlas of Human Anatomy", volume 2, Moscow, 1973, p. 225, amended).

### *Capsule*

The mammary gland is located between the leaves of the superficial fascia and is surrounded by the subcutaneous fat. The fatty tissue forms the adipose capsule of the mamma (capsula adiposa mammae). The pre-glandular layer of the fatty tissue is interrupted in the post-areolar area which houses the final sections of the lactiferous ducts. The post-glandular layer of the fatty tissue is composed of retromammary adi pose tissue and friable connective tissue.

### *Carcass*

The mammary gland is found in the connective tissue capsule which forms septa between the lobes of the mamma. The number of lobes vary from 6-8 (in smaller breasts) to 20-24 (in bigger breasts).

<u>*Parenchyma*</u>

The dimensions of the lobes fluctuate from 1-2 cm lengthways and 1-2 cm breadthways to 5-6 cm lengthways and 3-4 cm breadthways (Fig. 4-2). The lobes have radial location against the nipple and can overlap. Every lobe has a conic shape with its top at the nipple and is surrounded by friable connective tissue and a small amount of fatty tissue. The lobe consists of numerous lobules formed of repeatedly branching lactiferous ducts which are separated from each other by connective tissue. Each lobe has a complex system of lactiferous ducts (intralobular, interlobular and intralobar) which, on the one hand, make up the excretory duct and, on the other hand, end in glandular alveoli.

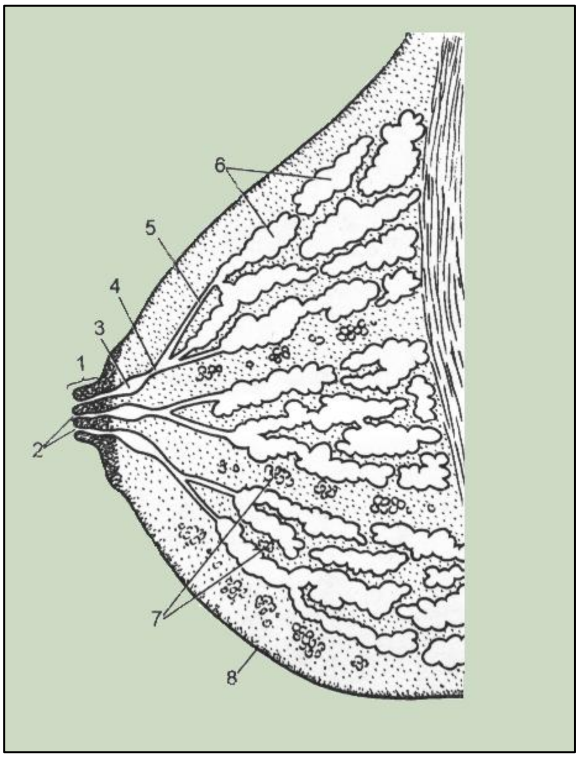



**Fig. 4-2.** Breast schematic diagram.
1-nipple; 2-excretory ducts; 3-lactiferous sinuses; 4-lactiferous ducts; 5-lactiferous tracts; 6-alveoli; 7-layers of loose connective tissue with adipocytes; 8-skin. ("Histology", edited by Yu.A. Afanasyev, N.A. Yurina, Moscow, 2002, p. 722).

<u>*Reservoir*</u>

Immediately before the outlet the lactiferous duct forms a lactiferous sinus which serves as reservoir in the process of lactation.

<u>*Blood circulation*</u>

Blood circulation in the mamma is furnished chiefly by the branches of the internal thoracic artery, the lateral thoracic artery and the intercostal arteries (Fig. 4-3). The lateral thoracic artery (a. thoracica lateralis) diverges from the axillary artery either singly or together with its branches and passes along the outside edge of the minor pectoral muscle and along the external surface of the front serratus muscle Sometimes a double or even a triple lateral thoracic artery can be found. The diameter of the lateral thoracic artery varies considerably and depends on the age as well as on the method of its deviation from the axillary artery, i.e. whether it moves away singly or with its branches. The lateral thoracic artery of adults is between 1.3 and 3.7 mm in diameter, 1.6-2.5mm in the majority of cases. The internal thoracic artery (a. thoracica interna) is found on the internal surface of the front thoracic cage. It develops from the subclavian artery and passes along the edge of the breast bone (at a distance of 4 to 20 mm). It can however have a winding or arched direction. The distance between the internal thoracic artery and the edge of the breast bone increases top-down,

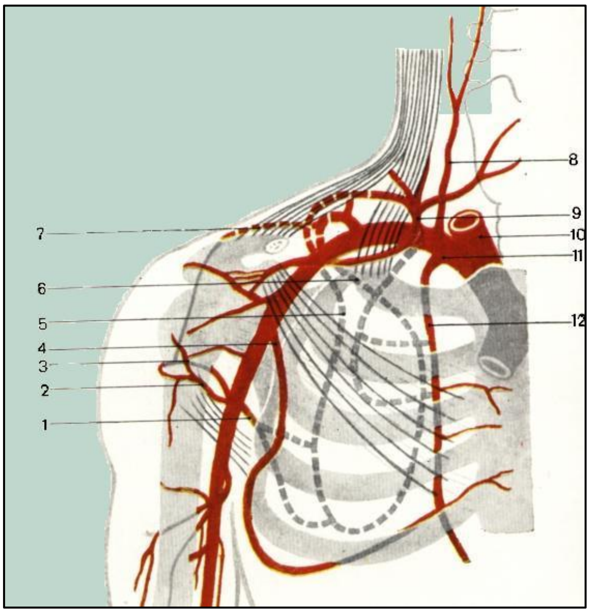



**Fig. 4-3.** The arteries of the shoulder joint area. 4-a.thoracica lateralis; 12-a.thoracica interna. (V.V. Kovanov, T.I. Anikina "Surgical anatomy of human arteries", Moscow, 1974, p.65, amended).

the left internal thoracic artery being located 2-6 mm farther from the breast bone edge than the right one. The internal thoracic artery is 1.9-2.9 mm in diameter. Among the branches of the internal thoracic artery one should distinguish the front perforating arteries (rr. perforantes a. thoracicae internae), reaching the upper-internal quadrant of the mammary gland. They penetrate into the external surface of the thoracic cage through the intercostal space close to the edge of the sternum. Women's front perforating arteries are 1.2-1.5 mm in diameter, the latter increasing to the utmost extent in the second and fourth intercostal spaces.

## Histology

Mammary glands originate from cutaneous perspiratory glands and represent the group of excretory or exocrine glands. . These glands are multicellular and consist of two parts: the secretory section or the acine and the excretory ducts. However, there is a difference. While perspiratory glands belong to simple tabular glands with an unbranched acine, mammary glands are compound alveolar-tabular glands with branching acini (Fig. 4-4).

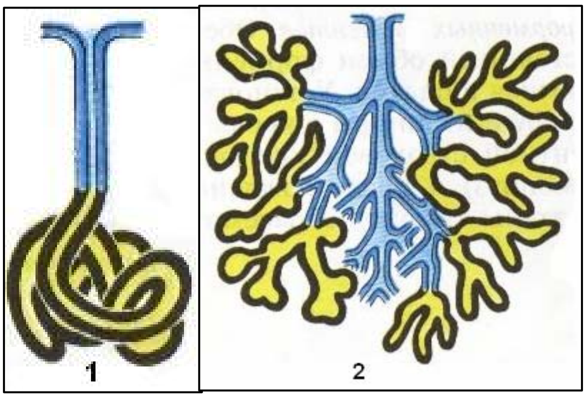



**Fig. 4-4.** The types of exocrine glands.
1 - simple terminal unbranched alveolar gland; 2- compound alveolar-tubular gland with branched acini (excretory ducts are highlighted with blue, secretory part - with yellow). ("Histology", edited by Yu.A. Afanasyev, N.A. Yurina, Moscow, 2002, p. 155, amended).

The mammary gland is composed of a number of tissues, performing various functions and filling the anatomical structures: epithelia, connective tissues, the neural tissue, blood and lymph.

*Capsule*

The capsule of the mamma consists of adipose tissue. The adipose tissue consists of adipocytes, capable of voluminous accumulation of spare fat. Adipocytes make up groups or else, accumulated in big amounts, form the adipose tissue. Each adipocyte has a cellular membrane; still, the central part of the cell is occupied by a large single drop of neutral fat (the non-polar triglyceride, $CH_2OCOR_1$-$CHOCOR_2$-$CH_2OCOR_3$).

*Carcass*

Septa of the mammary gland are of connective tissue origin. The intercellular substance of the connective tissue contains collagen and elastic fibers which form the septa. Collagen fibers define the strength of the connective tissue. They are slightly extensible and easily swell in water. Collagen fibers ($\{RCH\ (NH2)\ COOH\}_n$) are chemical compounds which consist of proline and glycine, possessing the properties of non-polar compounds.

*Parenchyma*

The parenchyma of the breast consists of the amorphous component of the intercellular substance of connective tissue and of the cellular components of epithelial tissue, which forms a system of ducts. The amorphous component of the intercellular substance is a jelly-like matter surrounding the cellular and fibrous structures of the connective tissue, the nerve and vascular components. Hyaluronic acid is its main constituent. It gives the intercellular substance its specific electronegative charge ($[C_6H_5(OH)_3CH_2OHNHCOCH_3$-$C_5H_5(OH)_4COO-]_n$). The cellular component is represented by the superficial epithelium of the mammary gland which forms a system of ducts: alveolar lactiferous ducts, lactiferous ducts proper, milk sinuses, excretory ducts. One should distinguish two main types of epithelia: single-layered and stratified. The smaller branches of the lactiferous ducts are lined with single-layered cubic or prismatic (columnar) epithelium, all the cells of which are attached to the basic membrane (Fig. 4-5). In excretory ducts

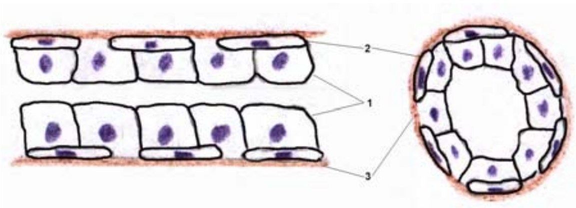



**Fig. 4-5.** Alveolar lactiferous duct (1 - epithelial cells, 2 - myoepithelial cells, 3 - basal membrane).

the epithelium becomes stratified, only the bottom layer of the cells, being attached to the membrane. The double-layered cell membranes of the epithelium play a role of the selective semipermeable barrier separating the intracellular space form the extracellular one. Moreover, they possess the properties of capacitance (reactance).

## Physiology

The mammary glands are susceptible to cycling effect of hormones and bioactive substances (Fig. 4-6). For each of the age period certain features endocrine statuses are inherent, they affect the changes in the structure of breast tissue.

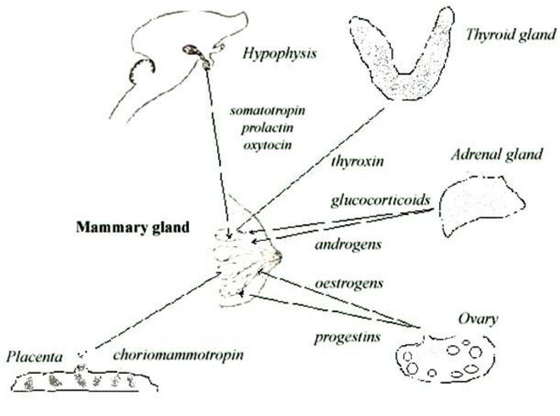



**Fig. 4-6.** Factors influencing mammary gland development and function.

*Neonatal period*

The mammary gland of the baby measuring 1.5 x 1.5 cm has a thin capsule and a poor ligamentous apparatus. The gland consists of lobules – vesicles, cylindrically shaped as a rule. The lobules are located at a distance from each other and transform into excretory ducts without a distinguished boundary (Fig. 4-7). The number of excretory ducts varies between 8 and 10. Connective tissue prevails over epithelial tissue. All newborn babies, regardless of their sex, experience a short secretory activity of the mammary glands, which morphologically exhibits in the extension of lactiferous ducts and the appearance of secretion in their lumen. The gland's stroma becomes friable and is enriched with cellular elements: lymphocytes, histiocytes (macrophages), myeloblasts, myelocytes and even normoblasts. Circulation of the mother's hormones in the baby's blood underlies this phenomenon. After the secretory activity comes to an end the mammary glands deflate, the connective tissue slightly thickens and the vasculature reduces.

*Prepubertal period*

In childhood estrogens are secreted in such a small amount that they do not induce the development of the genitals. This amount is sufficient to inhibit the secretion of gonadotropins on the level of the central nervous system (CNS). The growth and development of mammary glands are blocked. The excretory ducts formed in the period of in-

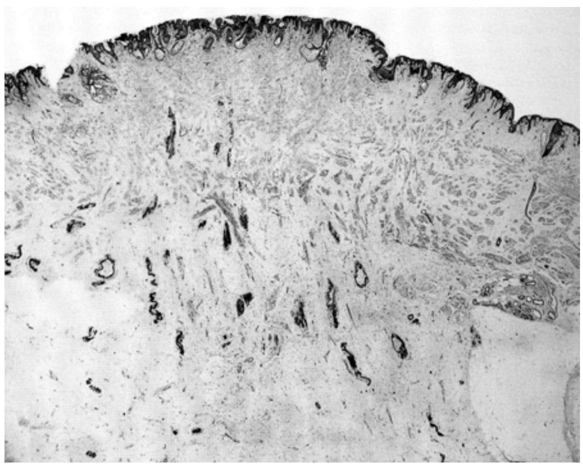


**Fig. 4-7.** Mammary gland during the neonatal period (the excretory ducts are visible).

trauterine growth possess an ability to increase in size and branch. However, it happens only under favourable hormonal conditions, for example, in the pubertal period.

*Pubertal Period*

The pubertal period is characterized by incipient secretion of gonadotropins. Intensive production of estrogens as well as androgens encourages the growth and maturation of skeletal bones,

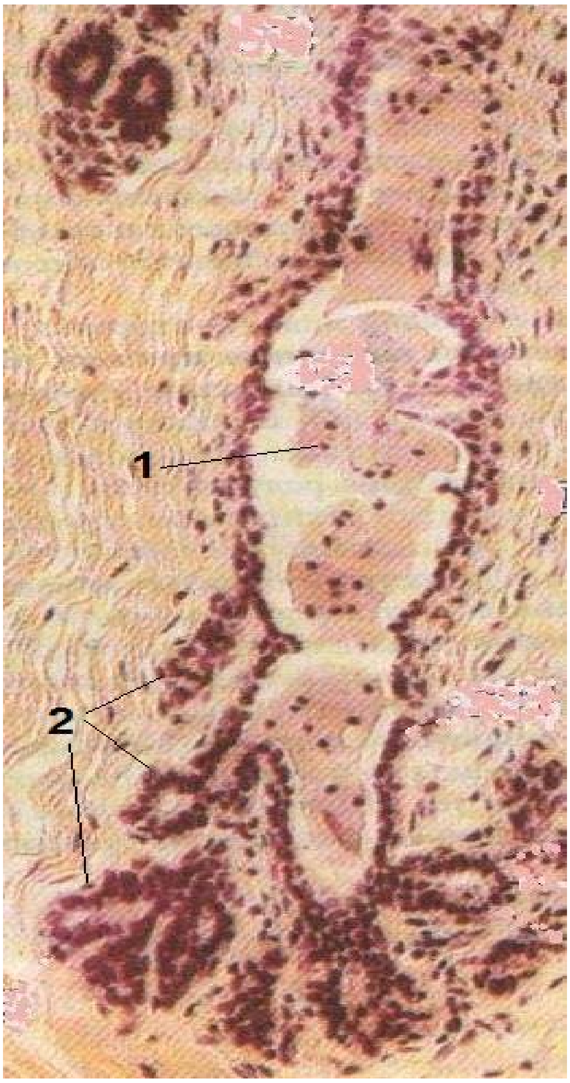



**Fig. 4-8.** Mammary gland during the pubertal period (1 – an excretory duct, 2 - the rudiments of the alveoli).

the enlargement of the externalia, the appearance of axillary and body pilosis. However, the growth of the mammary glands is conditioned exclusively by the activity of estrogens. Estrogen excretion in female organisms is characterized by gradual intensification with an apparent rise at the age of 12-13. The evolution of estrogen production in the organisms of adolescents with a steady menstrual cycle is different from that in the body of adult women. The difference lies in higher excretion of estrogens in the secretory phase of the cycle, which creates favourable conditions for the stimulation of proliferation processes in the genitals, including the mammary gland On the contrary, the release of pregnandiol in the second phase of the cycle, typical of young women (about 2 mg), does not reach the parameters characteristic of adult women (over 3 mg) even in ovulatory cycles. During puberty under the influence of estrogens, progestins and the prolactin there occurs initial differentiation of the mammary gland epithelium into ductal and glandular. The growth hormone, glucocorticoids, insulin and thyroid hormones intensify this effect. Estrogens initiate the growth and branching of ductal epithelium and sensitize the epithelial cells to the activity of progestins and the prolactin. The latter take part in the formation of alveolar glandular epithelium. However, unlike estrogens and androgens, progesterone and prolactin play a minor part in the processes of pubescence. In the pubertal period the tissue of the mammary gland is dominated by ductal epithelium that prevails over connective tissue. The end-ductal alveolar epithelium is poor being represented by thin tubules with blind ends – alveolar lactiferous ducts. Alveolar cells are potentially fit for lactation and do not function as lactocytes. However, being glandular epithelium cells, they perform a secretory function (Fig. 4-8). They undergo periodical changes determined by the menstrual cycle. On the average, the development of the mammary gland finishes by the age of 17.

*Pregnancy and lactation*

As placenta continues to grow and becomes differentiated, it begins to secrete more estrogens and progesterone. The main estrogen secreted in this

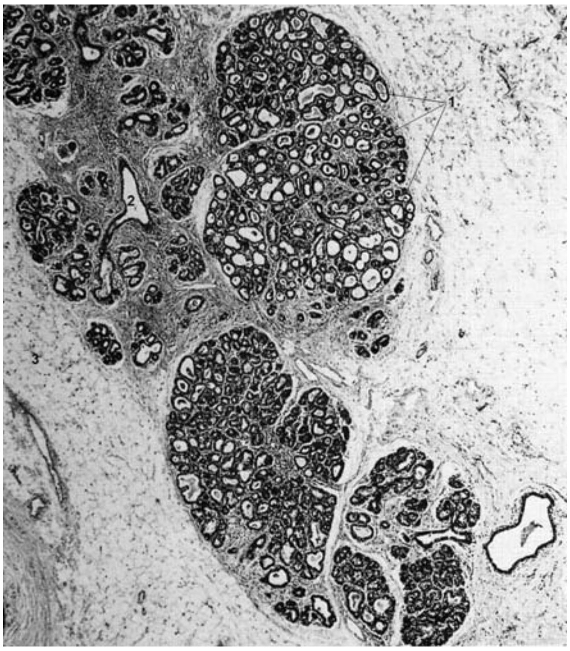



**Fig. 4-9.** Mammary gland during pregnancy (1 – the alveoli enlarged with secretion, 2 - extended excretory duct, 3 – the layers of connective tissue).

period – oestriol – reaches its maximum concentration, which is 1000 times higher than in the organism of a non-pregnant woman. During pregnancy progesterone secretion rises tenfold: from 25-50 mg per day in the first trimester to 180-565 mg per day at pregnancy end. Estrogens and progesterone assist in the growth and further differentiation of mammary glands, the former being conducive to the progressive growth of the glands. Stimulating the cell growth of duct epithelium they influence the development of the mammary gland duct system. Progesterone activates the maturation and differentiation of glandular epithelium cells, thus facilitating the formation of new glandular elements. Functioning jointly to block the influence of prolactin over the mammary glands, estrogens and progesterone prevent lactation during pregnancy. Pregnancy conditions the next stage in the development of mammary glands (Fig. 4-9). This is the period of enhanced growth and development of the active form of the gland alveolar epithelium which is capable of synthesizing specific milk factors. Along with progesterone an important part in the pre-lactation period is performed by choriomammotropin 4-10). It encourages the development of glandular epithelium and the formation

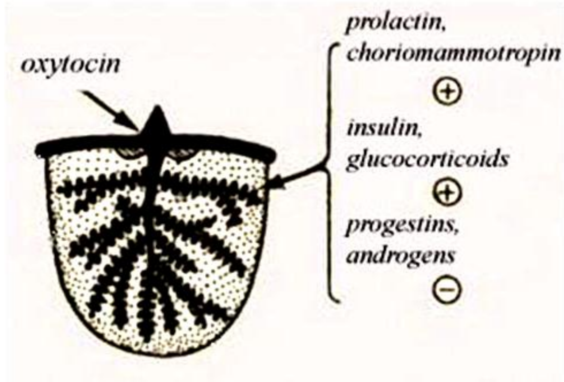



**Fig. 4-10.** Hormone-dependent formation of the lactating gland during pregnancy and during the postpartum period. V.B. Rozen, “Fundamentals of Endocrinology”, Moscow, 1980, p. 294, amended).

of alveoli. Thus, the second stage in the mammary gland differentiation is completed; the glands now acquire an ability to actively lactate under the influence of specific hormones (Fig. 4-11). After childbirth the concentration of progesterone and estrogens drops abruptly, making the glands secrete prolactin. Prolactin takes part in the processes of the mammary glands’ secretory activity, causing the transformation of transferase catalyzing the reaction of N-acetyllactosamine formation into lactosynthetase catalyzing the reaction of lactose generation. Moreover, prolactin

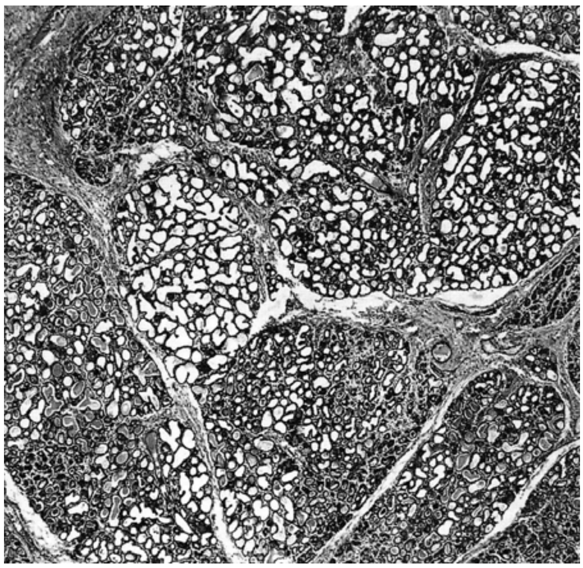


**Fig. 4-11.** Mammary gland during lactation (the alveoli enlarged with secretion are visible).

participates in the synthesis of hormone-dependent milk factors: casein, α-lactalbumin, β-lactoglobulin (Fig. 4-12). 3-4 months after childbirth the concentration of prolactin in plasma does not

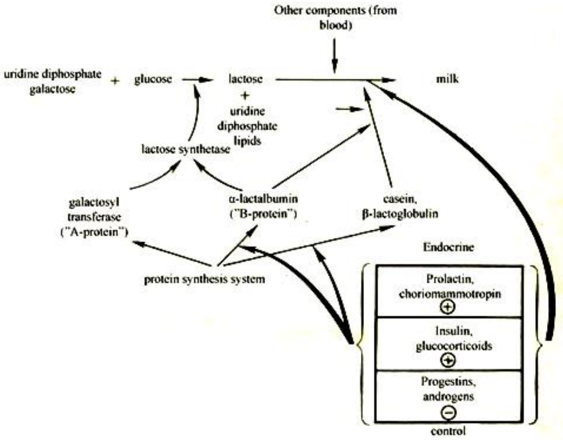



Fig. 4-12. Scheme of lactose and other milk components biosynthesis and their regulation in the lactating mammary gland. V.B. Rozen, "Fundamentals of Endocrinology", Moscow, 1980, p. 294, amended).

increase to any considerable extent despite the on-going process of breast-feeding. Upon the completion of the lactation period the overgrown alveolar tree of the mammary gland undergoes significant involution. The hormone-sensitive cells require an incessant supply of the balanced amount of hormones which is essential to maintain the normal functioning of the gland. This is called "the equilibrium position". However the discrepancy emerging between the alveolar cell mass ("the critical cell mass") and the concentration in blood of steroid sex hormones, progesterone in the first place, leads to the loss of a part of glandular epithelium with its further substitution for connective tissue. Upon the completion of the lactation period the overgrown alveolar tree of the mammary gland undergoes significant involution. Part of alveoli formed during pregnancy is preserved.

*Childbearing age (no-pregnancy period)*

In the period of approximately 35 years the production of estrogens, progestins and prolactin in a female body undergoes cyclic changes (Fig. 4-13). Starting from 15 years of age and finishing with 45 the average time of the menstrual cycle incessantly decreases. This is entirely conditioned by the shortening of the follicular phase of the menstrual cycle. The length of the lutein phase remains unchanged. During the menstrual cycle the mammary glands are affected by sex hormones. The development of gland tissue structures is ensured by the equilibrium of proliferation, differentiation and apoptosis. At childbearing age the mammary gland epithe-

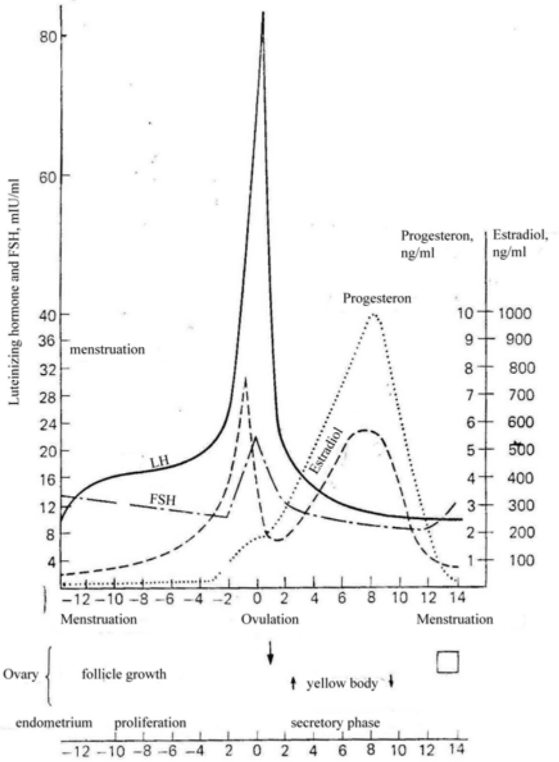



**Fig. 4-13.** The concentration of hormones in the blood during the structural and functional changes in the ovaries and endometrium during the menstrual cycle in humans {Speroff L., Van de Wiele R.L. (1971) Am. J. Obstet. Gynecol. 109, 234}

lium exposes itself to cyclic cell proliferation and apoptosis both being secondary to the cyclic function of the ovaries.

The cells are differentiated under the influence of estrogens but do not produce any secreta until they are repeatedly stimulated by progesterone. Encouraged by estrogens, the proliferation processes in the duct epithelium are observed throughout the menstrual cycle. The indications of the glandular epithelium secretion maintained by progesterone appear on the 20th day of the menstrual cycle. The histological analysis of the mammary gland (carried out by F. Longacre and co-authors) shows the presence of small lobules with 8 – 40 ducts in each in the proliferation phase of the cycle. The epithelium displays scarce figures of mitosis, a small amount of lymphocytic and plasmatic infiltrates are observed in the stroma. In

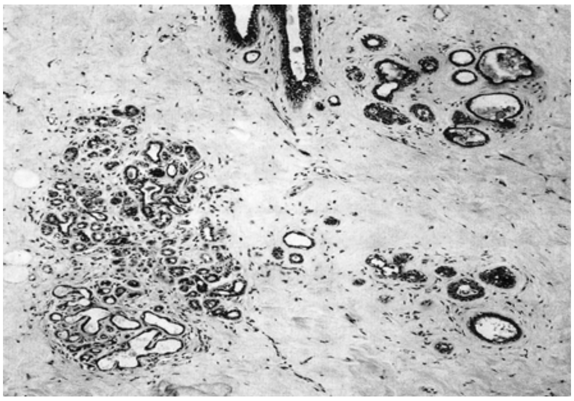


**Fig. 4-14.** Mammary gland during peri- and menopausal periods (involution of lobules).

the lutein phase of the menstrual cycle the number of terminal ducts and lymphocytic infiltrates in the lobules goes up, the vacuolization of basal epithelium is strongly pronounced, the stroma is oedematous, and the mitotic activity is heightened. In the post-menstrual period the lobule tissue lessens, the intercellular collagen thickens and hyalinizes. The epithelial cells display neither mitosis forms nor vacuoles. Hyperplasia of elastic fibers occurs. During menses fatty drops and cast-off epithelium appear in the lumen of glandular ducts, larger ducts see the appearance of erythrocytes. These substances are accumulated in the lactiferous sinus zone. As far as the tissue elements of the mammary gland are concerned, terminal duct alveolar epithelium prevails over duct epithelium in the mamma of women at childbearing age. The post-lactation loss of glandular structures causes their substitution for the connective tissue whose properties are defined by a varied correlation of tissue elements: cells, ground intercellular substance, fibers and adipose lobules.

*Peri-and Postmenopause period*

As the female organism gets older the number of primordial follicles in the ovaries goes down. Age-related disorders of the menstrual cycle result from non-cyclic ejection of follicle-stimulating and luteinizing hormones. This causes the appearance of anovulatory cycles, the arrested development of follicles and

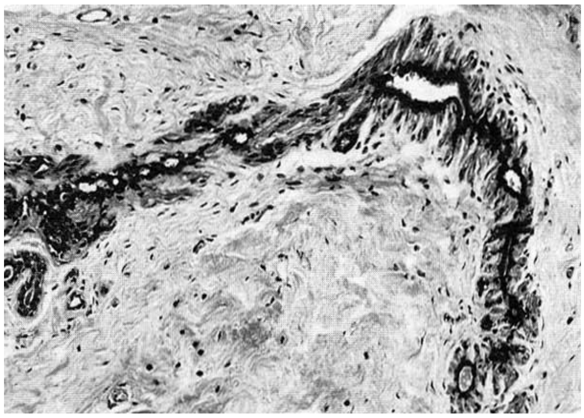


**Fig. 4-15.** Mammary gland during peri- and menopausal periods (involution of ducts).

finally, the total cessation of the process. The production of estrogens by the ovaries during the anovulatory cycles remains level to such during the normal menstrual cycle. However, the amount of progesterone does not rise in the second half of the cycle. In the postmenopausal period there occurs a permanent decrease in the content of estrogens in blood as well as their urinary excretion. The ovaries secrete increas-

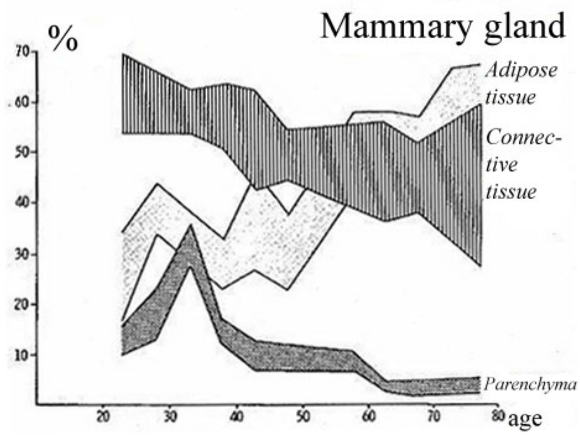



**Fig. 4-16.** Age involution of the parenchyma, connective and fatty tissues of the mammary gland (Page D.L., Anderson T.J. Stages of breast development. In: Diagnostic histopathology of the breast. Churchill Livingstone, New York 1987).

ingly less estradiol, its concentration in blood drops to extremely low measures: less than 20 pg/ml, the average amount for young women being 120 pg/ml. Since the ovaries contain no follicles in the advanced post-menopausal period, nearly all estrogens are generated from the androgens found in the peripheral tissues.

The progressive fall in the secretion of estradiol leads to a decline in the processes of proliferation of the mammary gland duct epithelium as well as gradual thickening of the duct epithelium and the basal membrane, followed by the obliteration and cystic dilatation of lactiferous ducts (Fig. 4-14, 4-15). The terminal-duct alveolar epithelium is substituted for the connective tissue with a varied correlation of tissue elements. 4-16).

# Electric impedance imaging of the mammary gland

# 5

## Anatomic and histological aspects

Macroanatomically, the structure of the mammary gland includes the following: *a capsule, a stroma, a parenchyma, a reservoir for the accumulation of secretion, a nipple and an areola.* The macroanatomical structures are the most demonstrable during the period of maximum functional activity of the organ.

*Capsule*

The capsule of the mamma is formed by the leaves of the superficial fascia and is surrounded by the subcutaneous fat. Between the fascial capsule of the gland and the fascia of breast itself there are retromammary adipose tissue and friable connective tissue. The figure shows the electrical impedance tomogram. Retromammary adipose tissue 5-1 is visualized on $6^{th}$ and $7^{th}$ scans as a hyperimpedance homogeneous formation of irregular shape with the electrical conductivity index less than 0.1 conventional units (cu), located in the center of the mammogram.

Adipose tissue intimately covers the body of the breast (capsula adiposa mammae). The front layer of the capsule is interrupted in the post-areolar area which houses the final sections of the lactiferous ducts. The figure 5-1 shows the electrical impedance tomogram, where the adipose tissue on the periphery of the breast is presented as the hyperimpedance areas demonstrating low conductivity values – less than 0.2 cu. Low conductivity values of adipose tissue can be explained by high intracellular impedance due to a drop of neutral fat, which occupies the entire volume of adipocyte. Neutral fat is composed of nonpolar triglycerides, which are insulators.

*Carcass*

The mammary gland is enveloped in a connective-tissue capsule wherefrom septa pass into the depth of the gland. The septa are made up of tender fibrillar tissue and are located between the glandular elements.

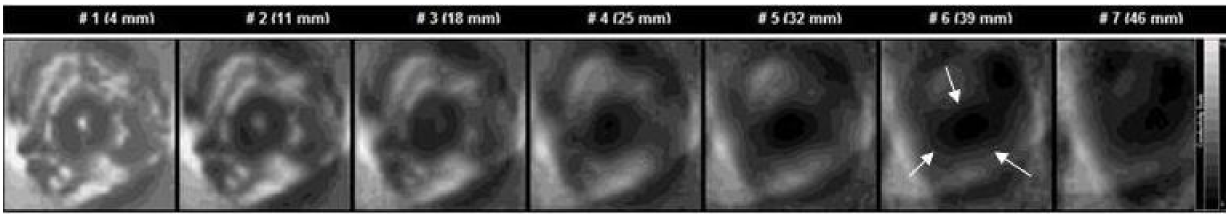



**Fig. 5-1.** Electrical impedance mammogram of the breast (EIM). Seven scan planes. Retromammary adipose tissue is visualized on $6^{th}$ and $7^{th}$ scans.

The figure 5-2 shows the electrical impedance mammogram, in which the low conductivity areas are marked with the help of contrasting.

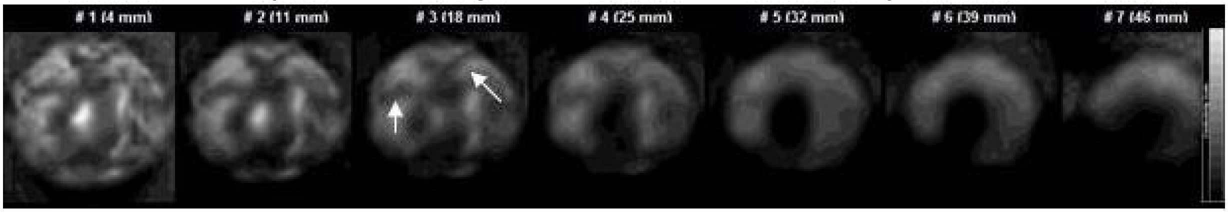



**Fig. 5-2.** EIM. Seven scan planes. The first and second scans show the connective tissue septa, radiating from the areola.

The septa forming the connective tissue frame are imaged as hyperimpedance zones radiating from the center with the conductivity equal to 0.3-0.4 cu. Low conductivity values of the septa are conditioned by the dielectric properties of non-polar collagen, which is a constituent of the septa, acting as an insulator. The adipose capsule as the consequence of hyperimpedance areas possessing electrical conductivity index less than 0.2 cu is clearly visible on the periphery of the mamma.

*Parenchyma*

The anatomic structure of the mammary gland permits to distinguish the parenchyma (parenchyma gl. mammariae), consisting of tubuloacinar glands and the connective tissue stroma. Tubuloacinar glands, consisting of ductal and secretory epithelia, are gathered in small lobules which serve to make up bigger lobes.

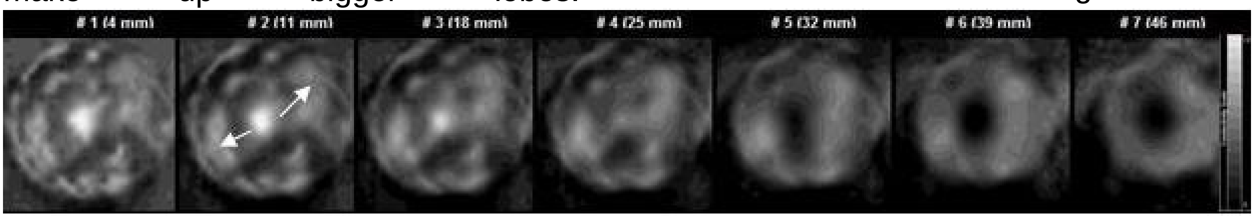



**Fig. 5-3.** EIM. Seven scan planes. Parenchyma is visualized as isoimpedance areas located between the connective tissue septa.

The connective tissue stroma is represented by a small amount of cells, delicate fibers and ground intercellular substance. The figure 5-3 shows the electrical impedance tomogram: the parenchyma is represented as isoimpedance areas with electrical conductivity index from 0.4 to 0.7 cu, locating between the septa. Large spread of electrical conductivity values is conditioned by different combinations of tissues possessing high impedance, such as membranes of epithelial cells, and tissues having low impedance, such as ground intercellular substance with hyaluronic acid, which carries a large number of negative charges.

*The Reservoir for Secreta Accumulation*

A lobe of the mammary gland contains a multitude of lobules which are made up of repeatedly branching lactiferous ducts and are separated by the connective tissue. Every lobe has one main excretory duct which opens on the outside surface of the nipple. Before reaching the nipple milk ducts gain in breadth and create a lactiferous sinus (sinus lactiferi) which accumulates secreta as well as the milk produced in the alveoli, both being characterized by low electric impedance. There are about 15-25 sini in the retromammilary area.

The figure 5-4 shows an electric impedance tomogram of a mamma. The lactiferous sinus zone is imaged as a vast centre-based hypo-impedance area, the electric conductivity exceeding 0.7 cu.

*Nipple and areola*

The nipple of the mammary gland, as well as the mammary areola,

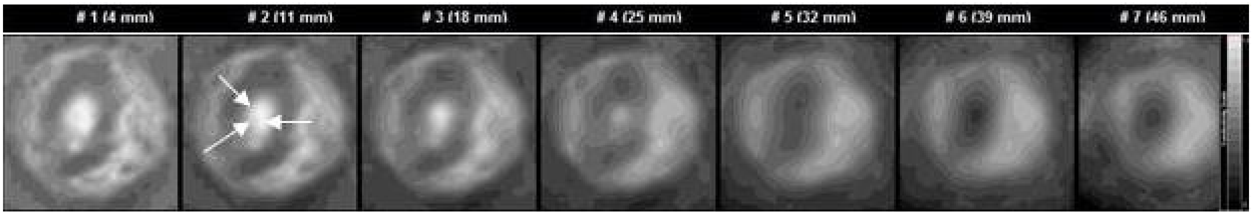



**Fig. 5-4.** EIM. Seven scan planes. There is a hypoimpedance area in the center of the mammogram, which corresponds to the location of the lactiferous sinus zone.

is the area of hairless pigmented epidermis. The nipple consists of the lactiferous sinus, a large number of sebaceous glands as well as of the extension which is the opening of the excretory ducts of the breast lobules, surrounded by fibrous tissue. High electrical impedance of the nipple is determined by the absence of the excretory ducts of perspiratory glands in it. In the electrical impedance tomogram the nipple is visualized as a centre-based linear hyperimpedance formation at 1st and 2nd scans, located closely to the lactiferous sinus zone (Fig. 5-5).

large number of pigment cells. High electrical impedance of the areola, as well as that of the nipple, is determined by the absence of the excretory ducts of perspiratory glands in it. In the electrical impedance tomogram the areola is visualized as a circular hyperimpedance formation surrounding the lactiferous sinus zone (Fig. 5-6).

Thus, when probing the breast with an alternating current with 50 kHz frequency the dispersion of electrical conductivity is observed due to the different impedance of breast tissues (Fig. 5-7). Tissue dispersion conditions the “mosaic” mode of the electrical

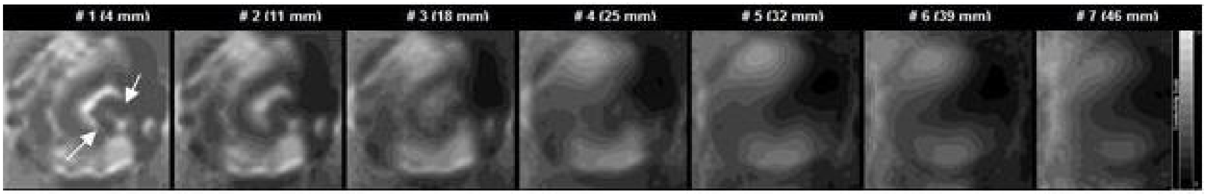



**Fig. 5-5.** EIM. Seven scan planes. Outer segment. A centre-based linear hyperimpedance formation is visualized at 1st and 2nd scan planes which is typical for the nipple.

In the dermis of the areola there are circular smooth muscle fibers which cause the nipple erection when contracting. In the interior of the areola there are numerous sebaceous and apocrine glands. Large sebaceous glands located on the periphery of the areola cause the formation of protrusions, Montgomery's tubercles. The dermis of the nipple also contains a

impedance images of mammary gland.

Given anatomical peculiarities of mammary gland structure manifested to less extent can be observed in the electrical impedance tomograms of the women of different age during various physiological periods. The "mosaic” electrical impedance image with smooth transition from hyperimpedance areas (areas of high electrical impedance) to hypoimpedance areas (areas of low

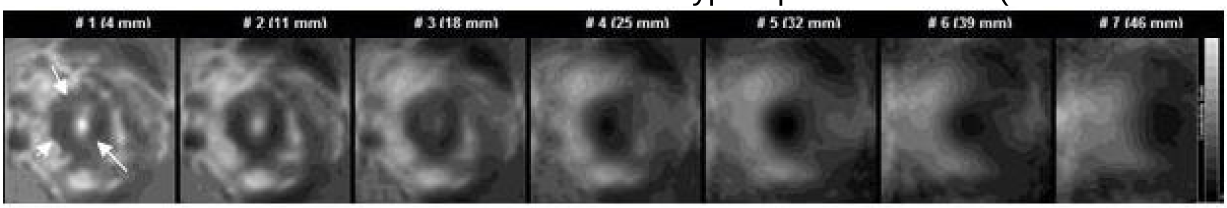



**Fig. 5-6.** EIM. Seven scan planes. The hyperimpedance area in the center of the mammogram corresponds to the location of the areola.

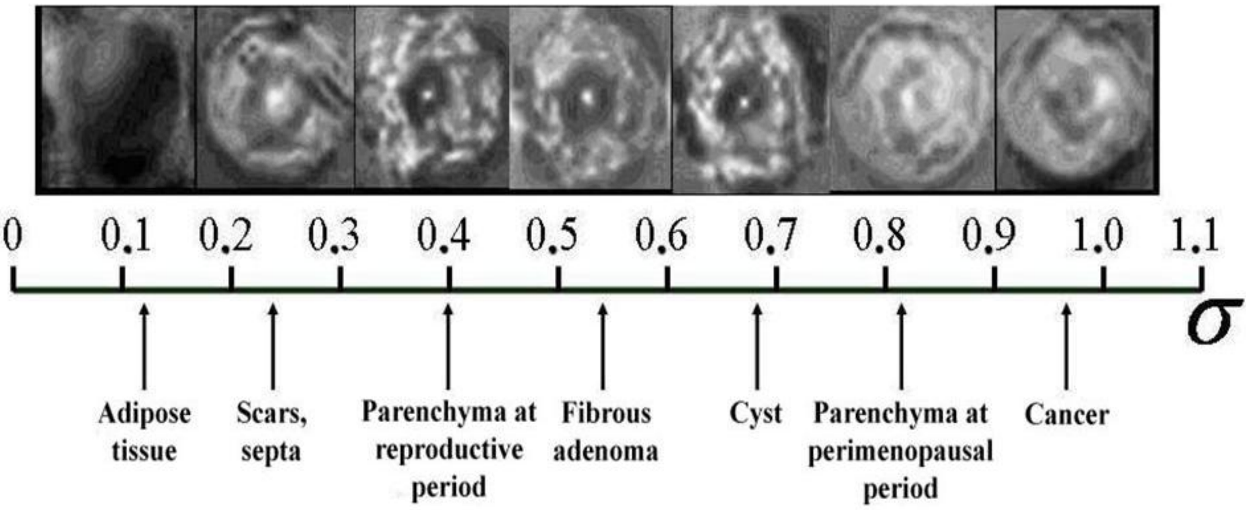



**Fig. 5-7.** Electrical conductivity dispersion in tissues.

electrical impedance) is typical for the mammogram of a normal breast. Electrical impedance distribution imaged on the tomograms of healthy women is unimodal and symmetric and belongs to the distribution types described by the law of normal distribution.

## Age-specific aspect

Since there is no way to determine the electrical conductivity of breast tissues in vivo, one should assay to analyze the changes of electrical conductivity on the basis of electrical impedance images of the breast in different age periods.

*Women under 20 years of age*

This group of women is characterized by the prevalent amount of ductal epithelium with the rudiment of the alveolar glandular epithelium in the mammary gland structure. Ductal epithelium is a single-layered cuboidal epithelium with the basic membrane. The electrical impedance image of the mammary gland, typical for this age group, is dark, electrical conductivity is usually low (Fig. 5-8).

This phenomenon can be explained by the presence in the mamma of a large number of ductal epithelium membrane cells which do not perform secretory functions. It is known that cell membranes possess capacitance and act as a strong barrier for alternating electrical current. Thus, the parenchyma, in the form of ducts, prevails over the stroma. Therefore, a large amount of lactiferous ducts in the mamma (implying the presence of a

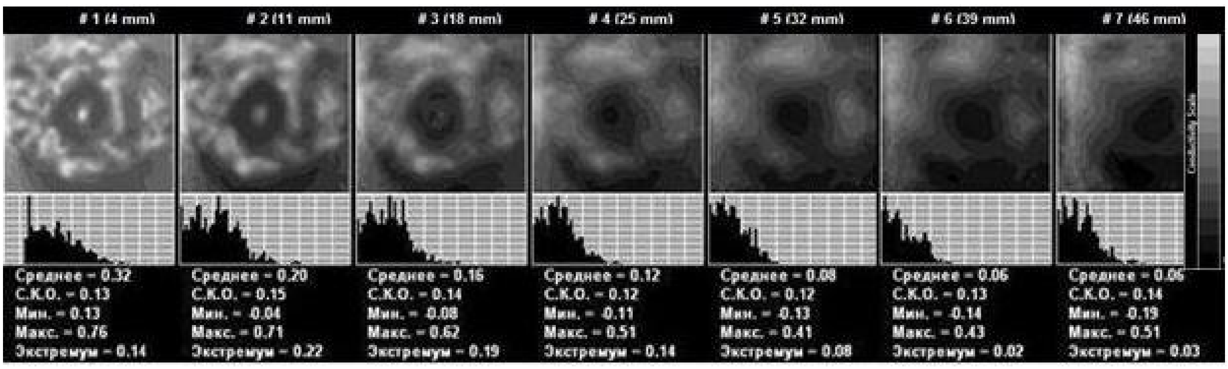



**Fig. 5-8.** EIM. Seven scan planes. 20-year-old patient. Quantitative information: mean electrical conductivity index, СКО – standard deviation, Min. – minimum index of the electrical conductivity, Max. – maximum index of electrical conductivity, extremum - the most frequently occurring values of mean electrical conductivity index.

large number of cell membranes) conditions low electrical conductivity. The average index of electrical conductivity ($50^{th}$ percentile) for this age group is 0.18 cu, varying from 0.07 to 0.27 cu. ($5^{th}$ and $95^{th}$ percentile, respectively). It should be observed that the electrical impedance tomograms of this age group clearly visualize anatomical structures such as areola, lactiferous sinus zone, septa, parenchyma and adipose capsule.

*Women 20 to 30 years of age (parous)*

The processes which result in electrical conductivity increase are the following: during pregnancy and lactation the alveolar glandular epithelium is developing. It is located on the periphery of the gland and possesses higher conductivity than the ductal epithelium, because of the presence of secretory component.

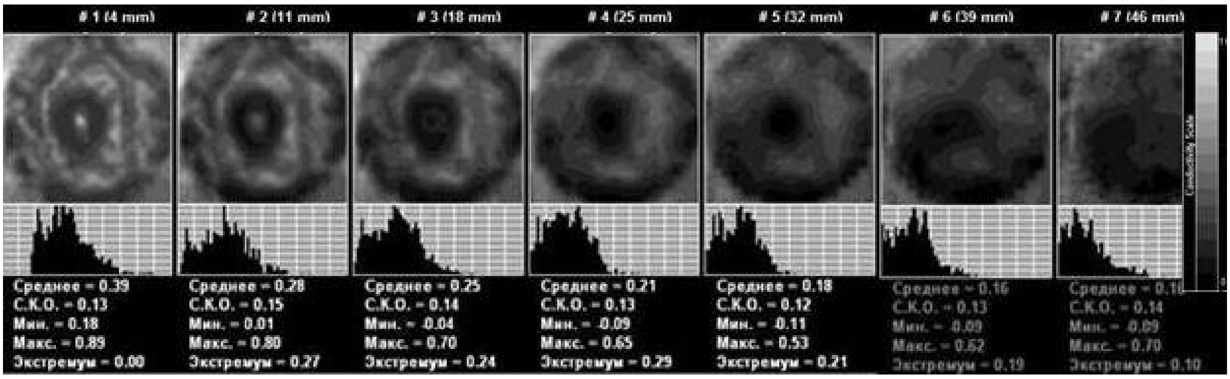



**Fig. 5-9.** EIM. Seven scan planes. 28-year-old patient. Quantitative information: mean electrical conductivity index, CKO – standard deviation, Min. – minimum index of the electrical conductivity, Max. – maximum index of electrical conductivity, extremum - the most frequently occurring values of mean electrical conductivity index.

During lactation part of alveoli undergoes involution, which leads to loss of their cell membranes and the development of fibrous loose connective tissue with ground substance predominance. The processes which result in electrical conductivity decrease are the following: the developing of interlobular and interlobar connective tissue with fibrous component (collagen) predominance. The average index of electrical conductivity ($50^{th}$ percentile) for this age group is 0.21 cu, varying from 0.08 to 0.33 cu ($5^{th}$ and $95^{th}$ percentile, respectively). The electrical impedance tomograms of this age group also clearly visualize the anatomical structures such as areola, lactiferous sinus zone, septa, parenchyma and adipose capsule (Fig. 5-9).

*Women 30 to 40 years of age (parous)*

The processes which result in electrical conductivity increase are the following: during pregnancy and lactation the alveolar glandular epithelium is developing. It is located on the periphery of the gland. During lactation a significant part of alveoli undergoes involution with the development of fibrous loose connective tissue with ground substance predominance. The processes which result in electrical conductivity decrease are the following: interlobular and interlobar connective tissue with fibrous component predominance development; connective tissue in the form of adipocytes surrounding the excretory ducts area; formation of separate fat lobules composed of adipocytes possessing the cell membrane and a single large drop of neutral fat having high impedance.

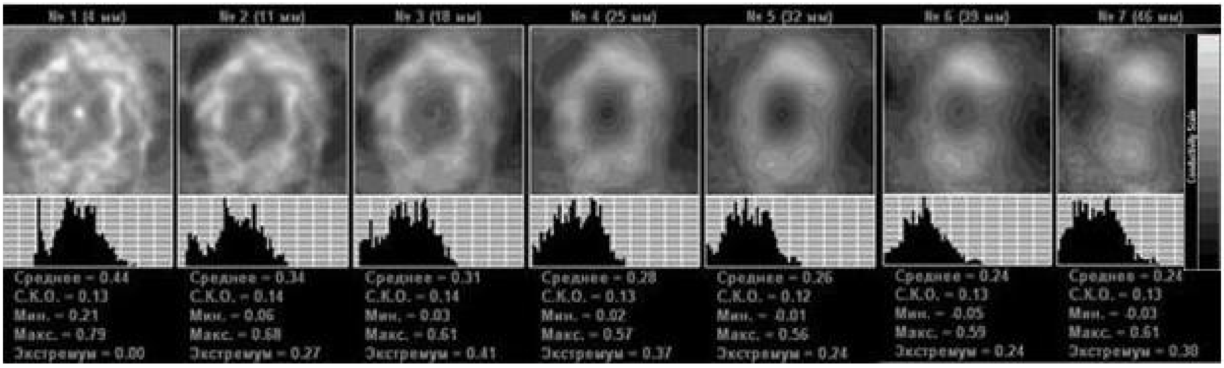



**Fig. 5-10.** EIM. Seven scan planes. 36-year-old patient. Quantitative information: mean electrical conductivity index, CKO – standard deviation, Min. – minimum index of the electrical conductivity, Max. – maximum index of electrical conductivity, extremum - the most frequently occurring values of mean electrical conductivity index.

The average index of electrical conductivity (50th percentile) for this age group is 0.25 cu, varying from 0.12 to 0.41 cu (5th and 95th percentile, respectively). Electrical impedance tomograms become lighter. The following anatomical structures are visualized: areola, lactiferous sinus zone, adipose capsule. The parenchyma of the mamma becomes "poorer" and more homogeneous (Fig. 5-10).

*Women 40 to 50 years of age (parous)*

The processes which result in electrical conductivity increase are the following: continuing loss of alveolar epithelium and substitution of alveoli with fibrous loose connective tissue with ground substance predominance. The processes which result in electrical conductivity decrease are the following: interlobular and interlobar connective tissue with a predominance of fibrous component; hyperplasia of fat lobules. The average index of electrical conductivity (50th percentile) for this age group is 0.33 cu, varying from 0.20 to 0.46 cu (5th and 95th percentile, respectively). In the electrical impedance tomograms the anatomical structures of the mamma blur: areola grows lighter, lactiferous sinus zone decreases, parenchyma structures cannot be differentiated (Fig. 5-11).

*Women 50 to 60 years of age (parous)*

The processes which result in electrical conductivity increase are the following: development of fibrous loose connective tissue with ground substance predominance; obliteration of lactiferous ducts. The processes which result in electrical conductivity decrease are the following: interlobular and interlobar

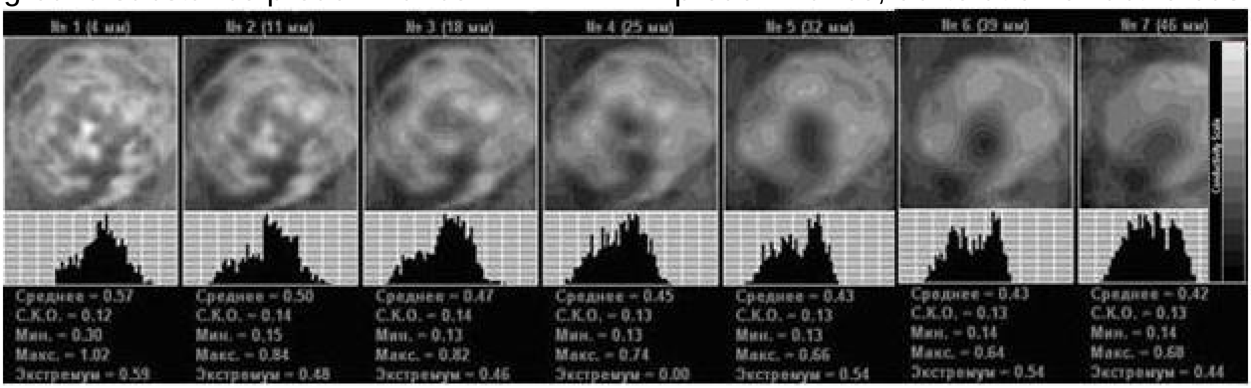



**Fig. 5-11.** EIM. Seven scan planes. 43-year-old patient. Quantitative information: mean electrical conductivity index, CKO – standard deviation, Min. – minimum index of the electrical conductivity, Max. – maximum index of electrical conductivity, extremum - the most frequently occurring values of mean electrical conductivity index.

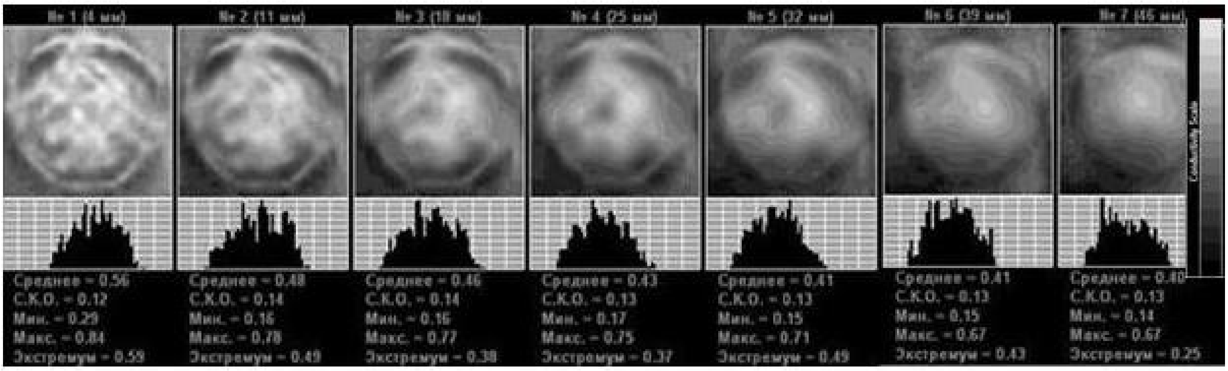



**Fig. 5-12.** EIM. Seven scan planes. 59-year-old patient. Quantitative information: mean electrical conductivity index, CKO – standard deviation, Min. – minimum index of the electrical conductivity, Max. – Maximum index of electrical conductivity, extremum - the most frequently occurring values of mean electrical conductivity index.

connective tissue with fibrous component predominance; fat lobules.

The average index of electrical conductivity ($50^{th}$ percentile) for this age group is 0.41 cu, varying from 0.30 to 0.52 cu (5th and 95th percentile, respectively). Anatomical structures in the electrical impedance tomograms undergo significant changes: lactiferous sinus zone disappears, the structure of the parenchyma is not differentiated (Fig. 5-12). Thus, the average electrical conductivity index increases with age. This phenomenon is conditioned by the remodeling of breast tissues and, especially, by the process of replacement of duct components with connective tissue structures.

The so-called percentile method as an approach to brief description of distributions is wide-spread in medical and biological research. This method does not require the data on distribution structure, i.e. is non-parametric. The figure 5-13 shows the percentile curves of the age-related electrical conductivity, where each age group corresponds to a certain range of electrical conductivity. According to the suggested estimation, the values, falling into the first range (less than $5^{th}$ percentile) shall be considered as pronouncedly low, into the second range (5-25 percentiles) - as low, into the third and fourth ranges (25-75 percentiles) - as medium, into the fifth (75-95 percentiles) - as heightened, Into the sixth (above 95 percentile) – as pronouncedly heightened.

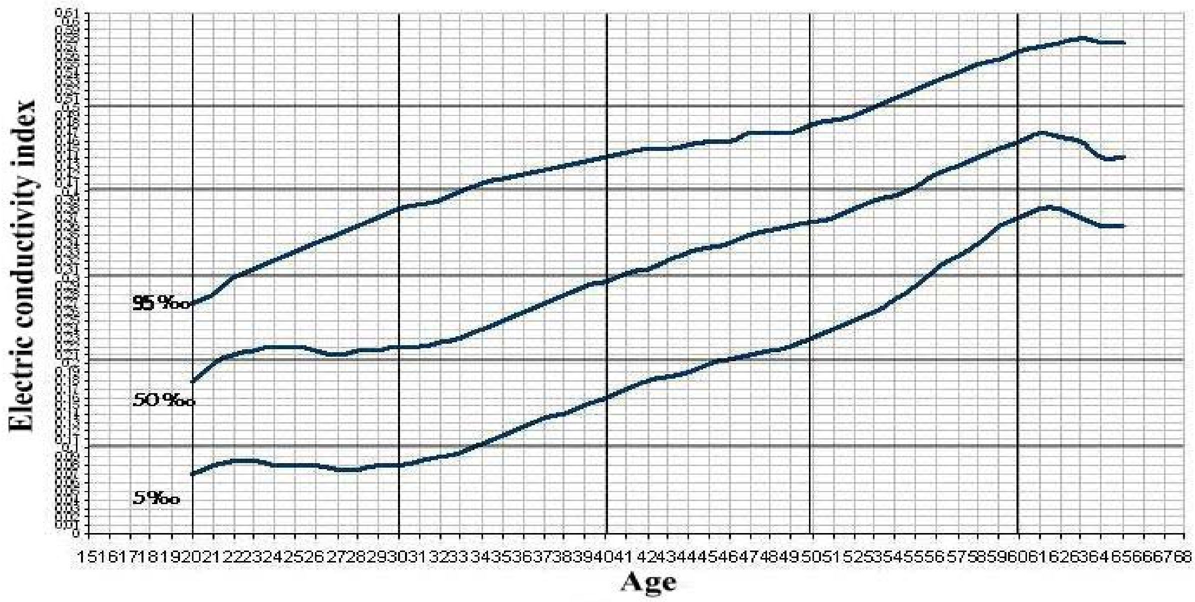



**Fig. 5-13.** Percentile curves of age-related electrical conductivity of the mammary gland.

# Evaluation of Electrical Impedance Images of the Mammary Gland

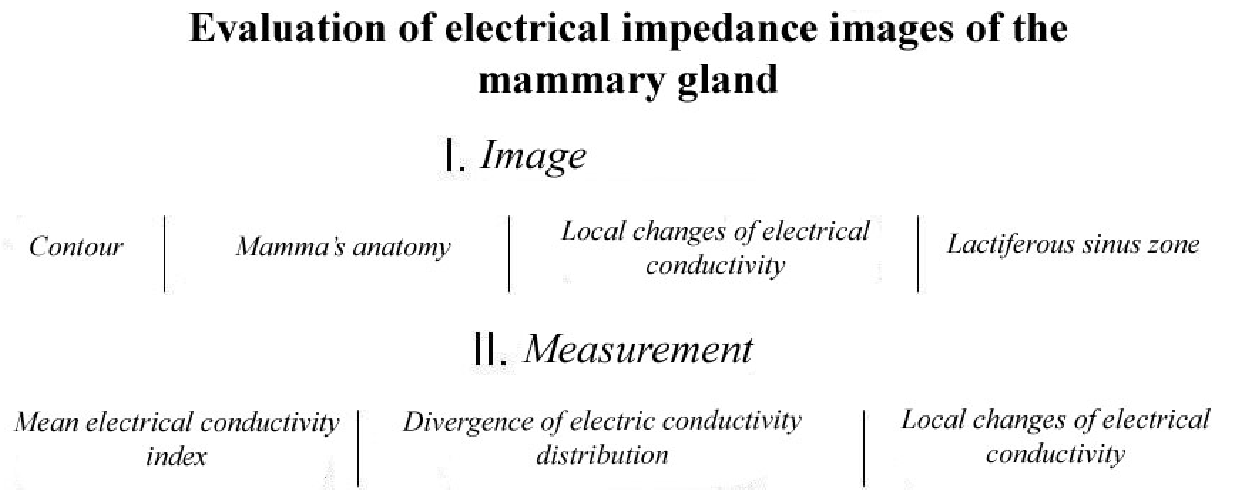
# 6

The method for assessment and evaluation of electrical impedance images is a key part of the diagnostic process. Modern diagnostic techniques concerned with imaging (MRI, CT, X-ray, US) urge specialists to employ visual image evaluation. Visual assessment is based on knowledge of the anatomical peculiarities of the organ under examination. Method of electric impedance mammography has been implemented in clinic for several years. There are several methods for mamma examination. However, universal criteria of mammary gland image evaluation have not been worked out so far. Practical application of the method for the assessment of the electrical impedance images of the breast would minimize the percentage of omitted pathologies of the mammary gland.

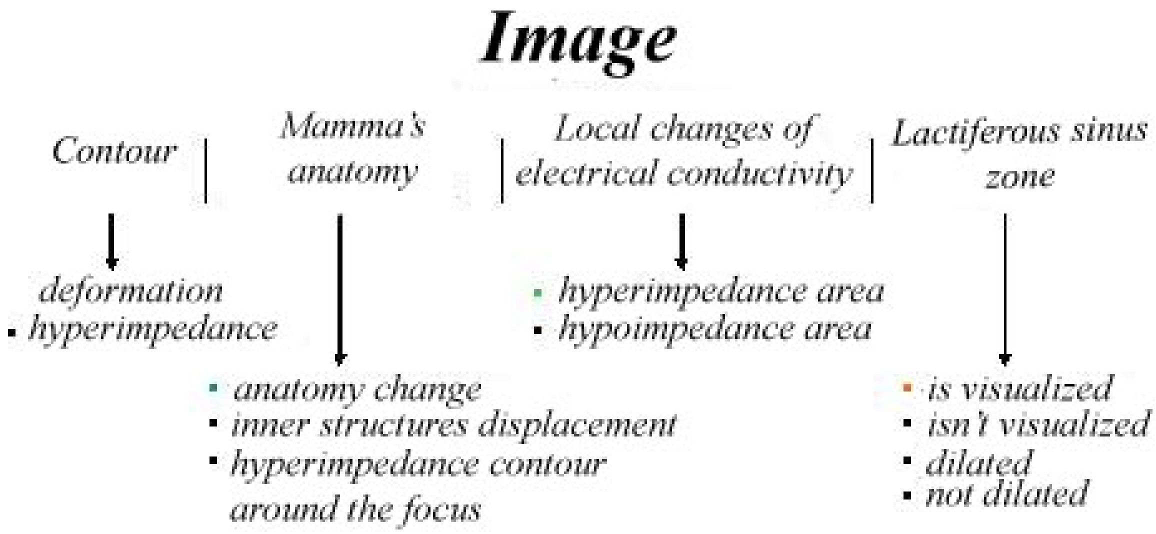
Studies have shown that in certain cases visual evaluation of the images is enough, other diseases require quantitative analysis, often the situation requires a combination of assessment methods. Therefore, method for the assessment of the electrical impedance images is to consist of both visual and quantitative analyses (Figure 6-1).

**Visual evaluation of electrical impedance images**

Visual evaluation of electric impedance images involves the analysis of the following aspects: breast contour, anatomy of the breast, local changes of electrical conductivity, lactiferous sinus zone (Figure 6-2).




**Scheme 6-1.** Evaluation of electrical impedance images of the mammary gland




**Scheme 6-2.** Visual evaluation of electrical impedance images of the breast.

## Analysis of the breast contour

Visual evaluation of the mamma's electric impedance image should start with the analysis of its contour. Normally the contour of the mammary gland has an isoimpedance structure; it is regular, without distortions. In case of certain breast diseases the contour may be distorted. Moreover hyperimpedance of the contour may be present too (Fig. 6-1).

. *Deformation of the contour*

Deformation of the breast contour is an important diagnostic criterion in case of some breast diseases. Often deformation is conditioned by the expansive processes in the mammary gland, such as cancer or mastitis. Inflammatory and cancerous infiltration of the tissues may lead to local deformation of the contour, its retraction or extrusion.

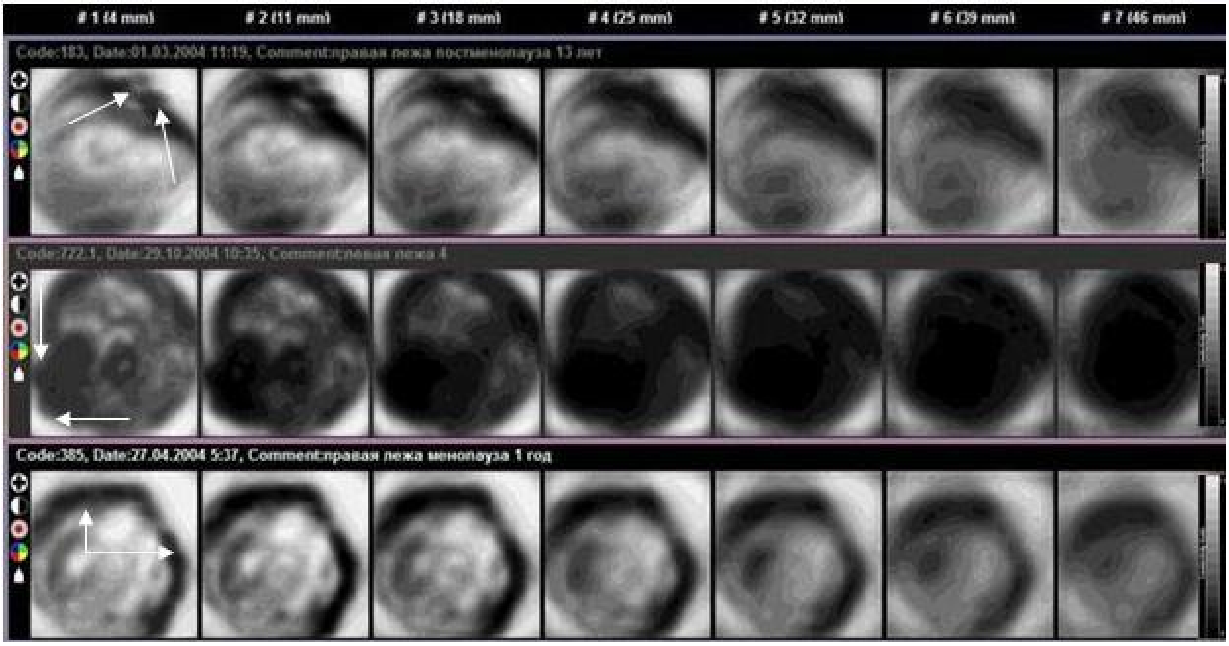



**Fig. 6-1.** EIM. Seven scan planes. The deformation of the breast contour (retraction) in case of cancer is represented in the first line. The deformation of the breast contour (extrusion) in case of mastitis is shown in the second line. The hyperimpedance contour, which is shown in the third line, manifests itself by considerable thickening in comparison with a healthy gland.

In the upper row of Figure 6-2 there is a tomogram of a healthy mammary gland. The fourth row shows a tomogram of the mammary gland in case of cancer with a local deformation of the contour of the breast in the form of extrusion. In the upper row of Figure 6-3 there is a tomogram of a healthy mammary gland. The fourth row shows a tomogram of the mammary gland in case of cancer with a local deformation of the contour of the breast in the form of retraction.

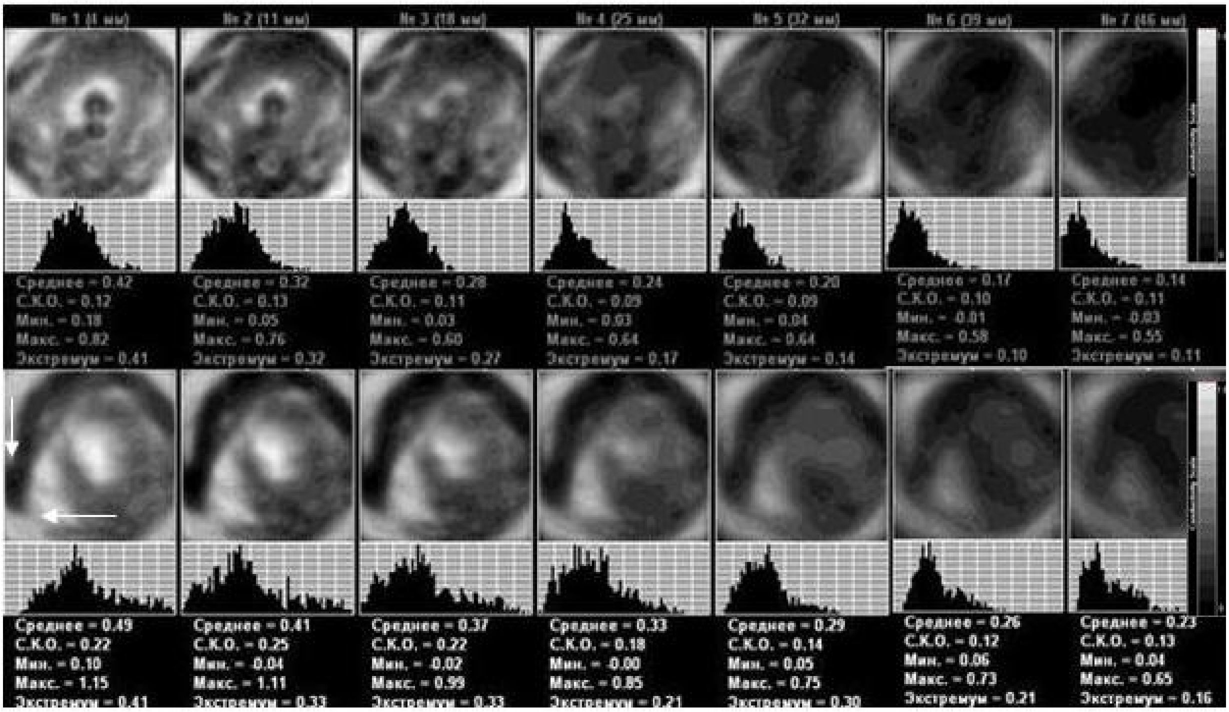


**Fig. 6-2.** EIM. Seven scan planes. A 39 years-old patient. A tomogram of a healthy mammary gland is shown n the first line. The deformation of the breast contour (extrusion) in case of cancer is represented in the fourth line (at 7 o'clock position).

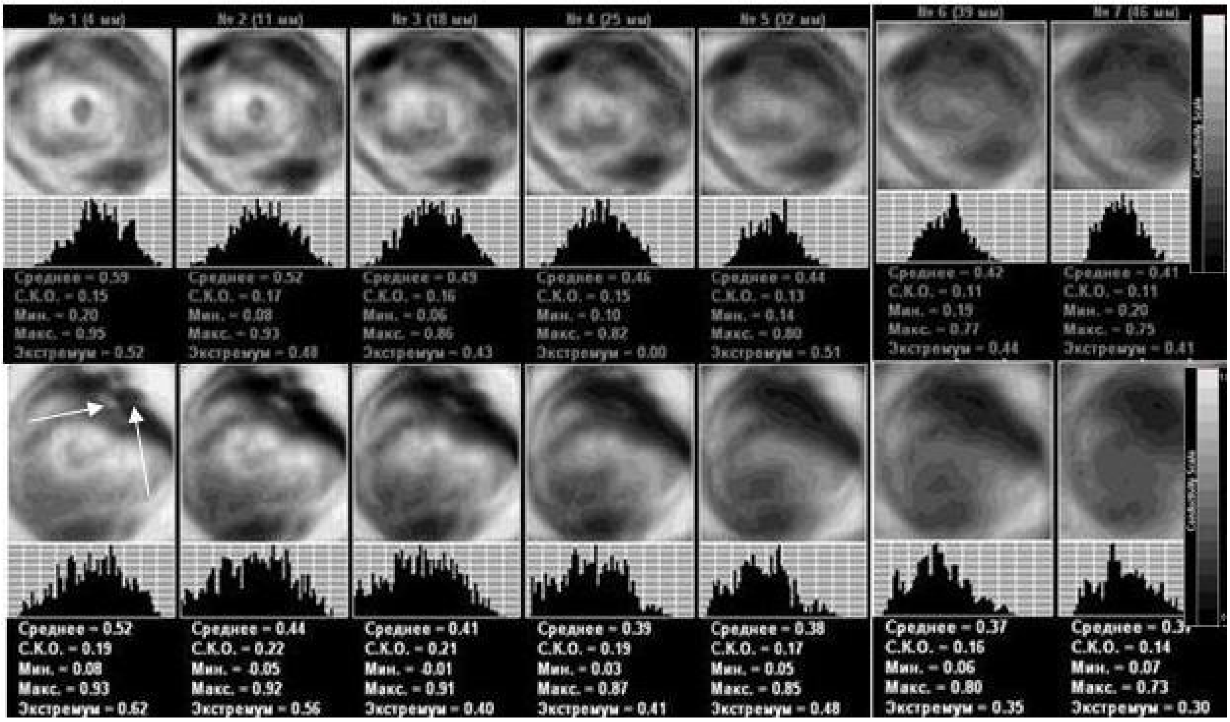


**Fig. 6-3.** EIM. Seven scan planes. A 65 years-old patient. A tomogram of a healthy mammary gland is shown n the first line. The deformation of the breast contour (retraction) in case of cancer is represented in the fourth line (at 1 o'clock position).

<u>*Hyperimpedance contour*</u>

Under hyperimpedance contour should be understood a significant increase of electrical impedance at the periphery of the breast. This phenomenon should be regarded as the reaction of the breast tissues on the exclusively malignant processes. In electrical impedance images hyperimpedance contour manifests itself by thickening and intense black colour.

In the upper row of Figure 6-4 there is a tomogram of a healthy mammary gland. The fourth row shows a tomogram of the mammary gland with the hyperimpedance contour conditioned by complicated cancer.

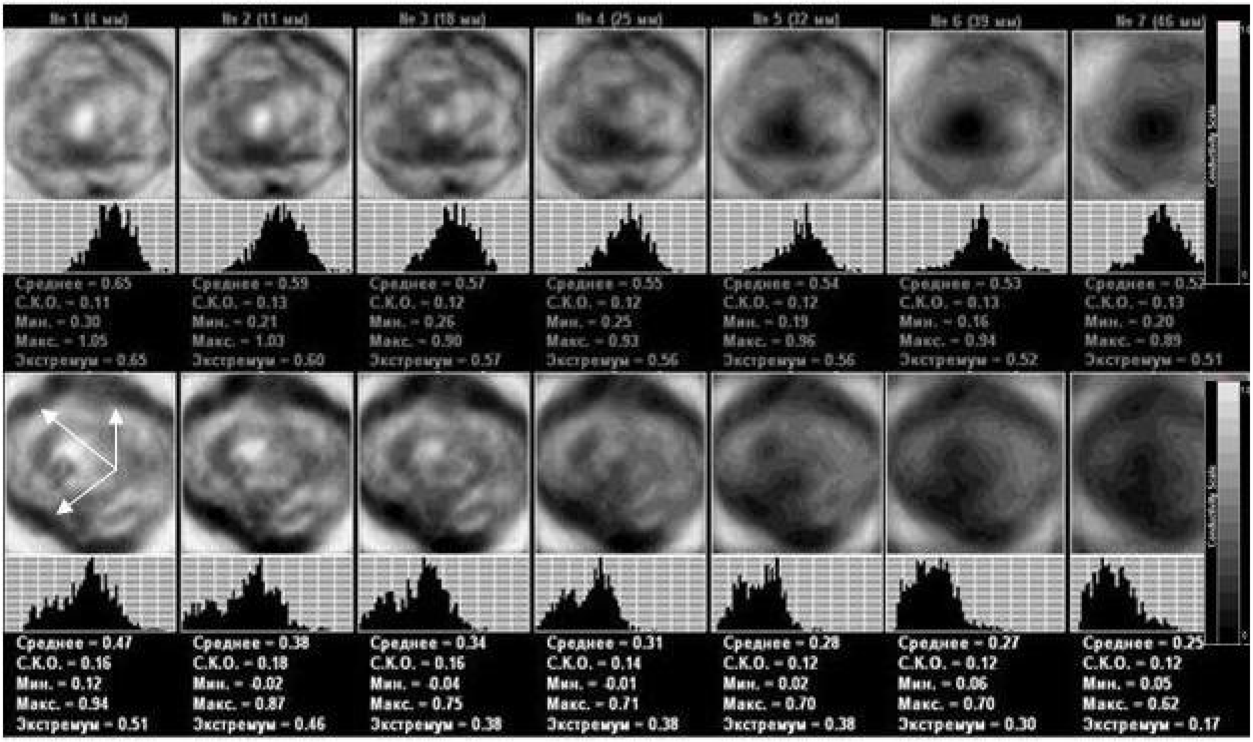


**Fig. 6-4.** EIM. Seven scan planes. A 75 years-old patient. A tomogram of a healthy mammary gland is shown n the first line. The hyperimpedance breast contour in case of cancer is represented in the fourth line.

The hyperimpedance contour manifests itself by change of its colour and considerable thickening in comparison with a healthy gland.

**Analysis of the mammary glands anatomy**

The next step of visual evaluation is the analysis of the mammary glands anatomy. Normally, the image of the gland must reflect all anatomic structures with respect to the patient's age. No displacements of them should be observed. (Fig. 6-5).

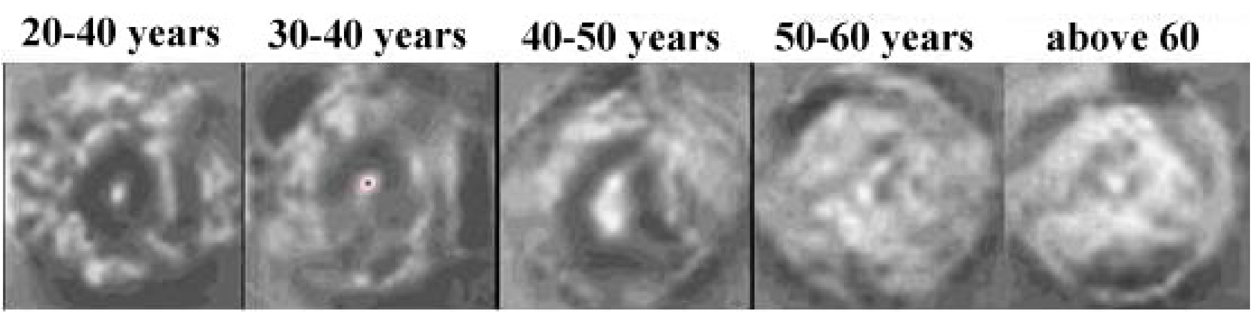



**Fig. 6-5.** Electrical impedance mammograms, typical for different age groups.

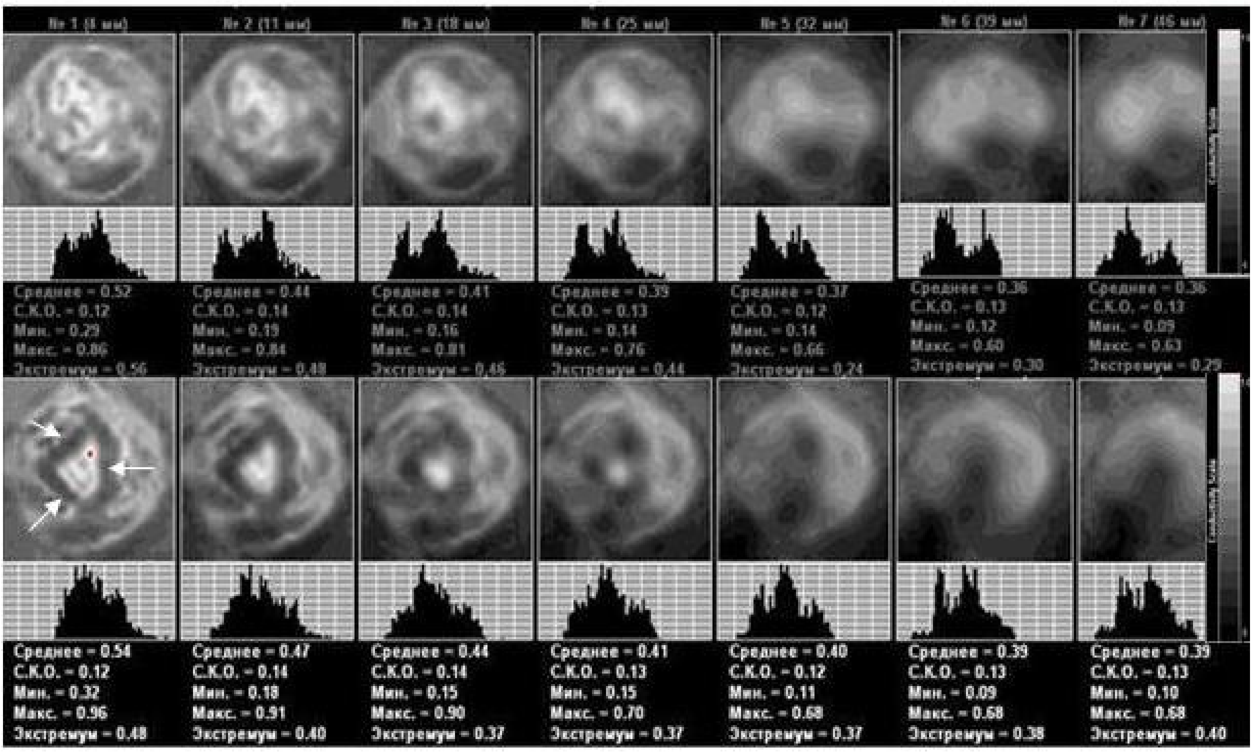



**Fig. 6-6.** EIM. Seven scan planes. A 70 years-old patient. A tomogram of a healthy mammary gland is shown n the first line. The change of the breast anatomy in case of cancer is represented in the tomogram in the fourth line.

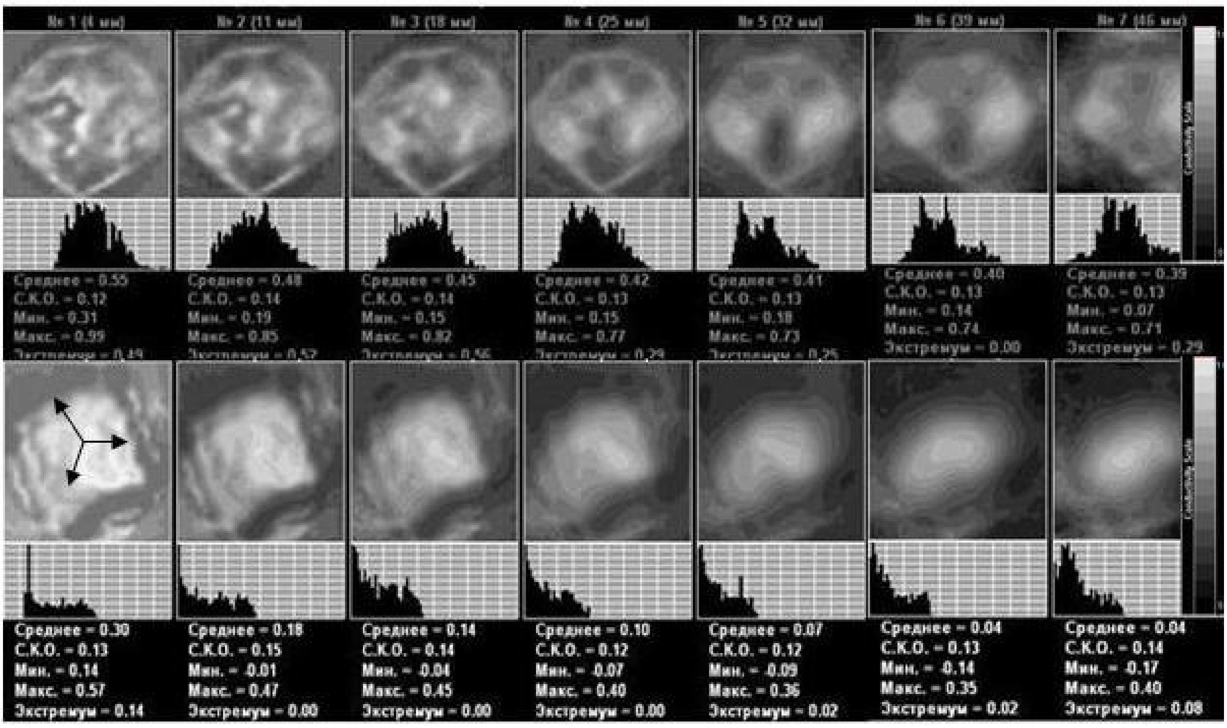



**Fig. 6-7.** EIM. Seven scan planes. A 70 years-old patient. A tomogram of a healthy mammary gland is shown n the first line. The total change of the breast anatomy in case of inflammatory cancer is represented in the tomogram in the fourth line.

A pathology arising, the anatomy is changed. The fourth rows of Figures 6-6 and 6-7 show the images of the mammary gland in case of different cancer types. Change of the mammary glands anatomic structure typical of cancer (fourth row) is evident as compared to the anatomy of the healthy gland (first row).

When the mamma undergoes cicatricial changes, its inner structures are displaced too. Figures 6-8 and 6-9 represent the images of the breast with cicatricial changes. The peculiarities of electrical impedance images of the mammary gland with scars are conditioned by the fact that the lesion location is delimited from the rest of the tissue by collagen fibers, and its focus is represented by the amorphous substance of connective tissue, the main component of which is hyaluronic acid. Therefore, the recovery zone is represented by the areas of high impedance (which is the characteristic of collagen) as well as by the areas of low impedance (which is the characteristic of amorphous substance of connective tissue).

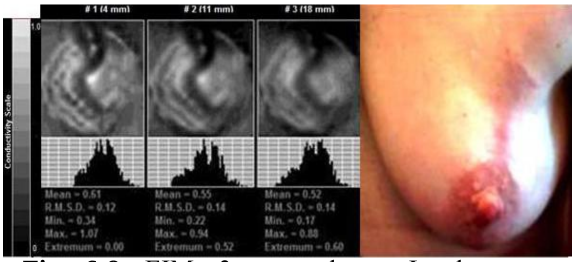


**Fig. 6-8.** EIM. 3 scan planes. In the upper segment there can be visualized a hyperimpedance stripe corresponding to the location and shape of the scar.

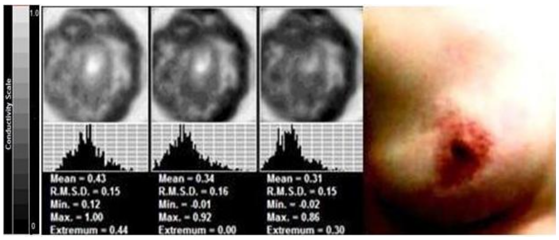



**Fig. 6-9.** EIM. 3 scan planes. In the upper segment there can be visualized a hyperimpedance area corresponding to the location and shape of the scar.

## Local electrical conductivity changes

One of the most important aspects of visual evaluation is the analysis of local conductivity changes outside the lactiferous sinus zone, which should not occur normally. When the gland is affected by a disease, its images can display both hyperimpedance areas (where impedance is high) and hypoimpedance areas (where impedance is low).

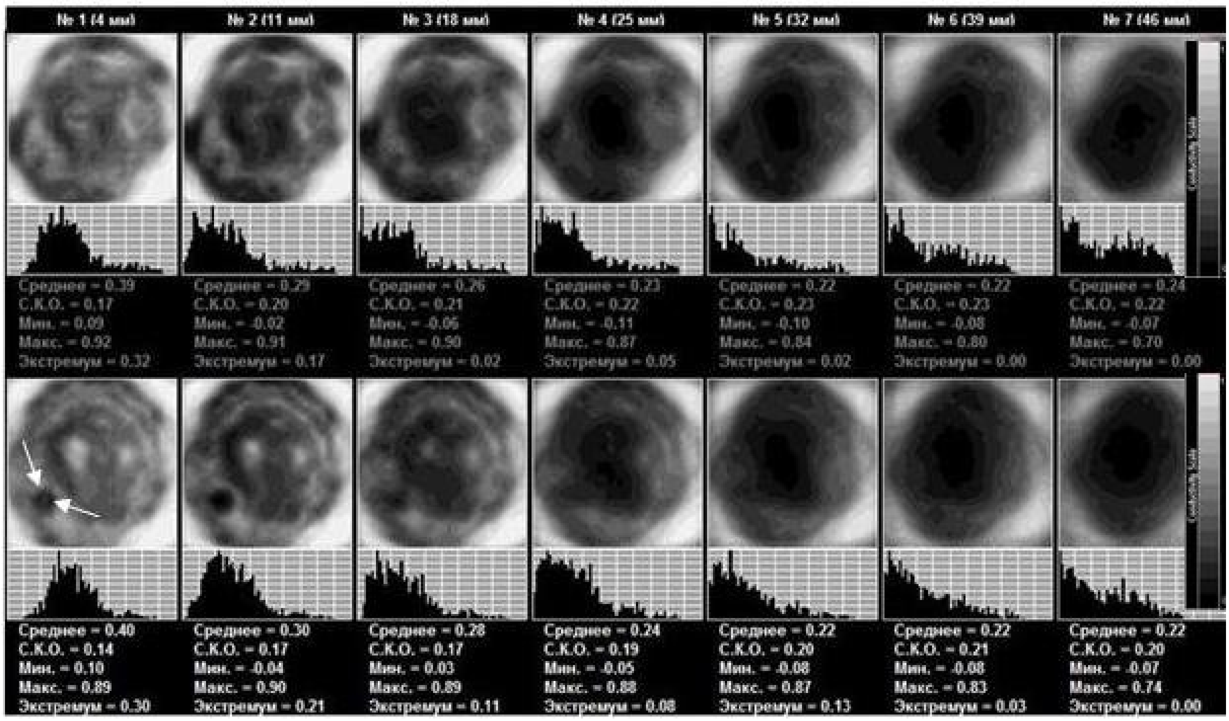



**Fig. 6-10.** EIM. Seven scan planes. A 26 years-old patient. A tomogram of a healthy mammary gland is shown n the first line. A local hyperimpedance focus (at 7 o'clock position) in case of mastitis in the stage of infiltration is represented in the tomogram in the fourth line.

*Local hyperimpedance areas*

The figure 6-10 in the fourth row represents the image of the breast affected by mastitis in stage of infiltration. Local conductivity changes are represented as a hyperimpedance well-contoured homogeneous area of rounded shape which can be visualized at 7 o'clock position; it is typical of infiltrative mastitis.

at 1 o'clock position, the electrical conductivity index of which is greater than 0.95. The hyperimpedance contour surrounding it is typical of cancer.

*Total hyperimpedance*

One of the options of electrical conductivity change is a total impedance increase. It is observed in case of infiltrative-edematous form of breast

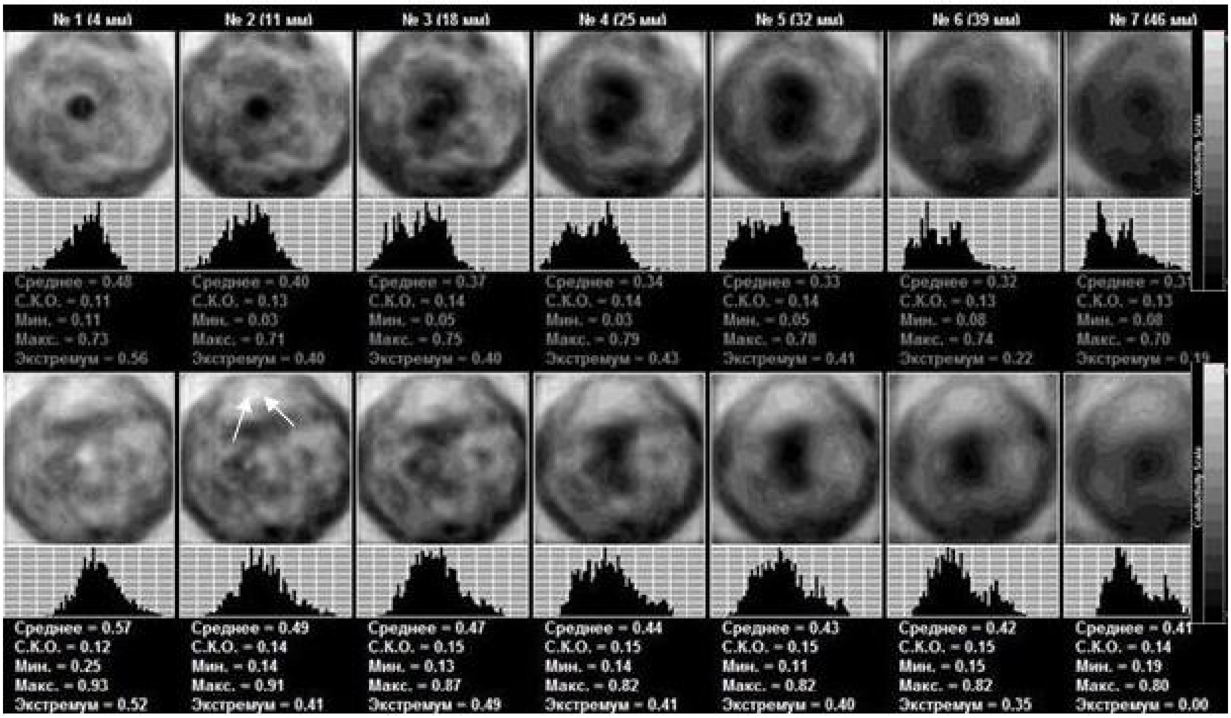



**Fig. 6-11.** EIM. Seven scan planes. A 54 years-old patient. A tomogram of a healthy mammary gland is shown n the first line. A local hypoimpedance focus (at 12 o'clock position) in case of incomplicated cancer is represented in the tomogram in the fourth line.

*Local hypoimpedance areas*

The figure 6-11in the fourth row represents the image of the breast with local conductivity changes which are represented as a hypoimpedance area with blurred contours visualized at 7 o'clock position, its electrical conductivity index is greater than 0.95, which is characteristic of cancer.

Moreover, in cases of breast cancer, a hyperimpedance contour as well as an infiltration zone may visualize themselves around the damaged area. The figure 6-12 in the fourth row the fourth row represents the image of the breast affected by complicated cancer.

Local conductivity changes are represented as a hypoimpedance area

cancer. The figure 6-13 in the fourth row represents the image of the breast with total hyperimpedance typical of cancer.

**Lactiferous sinus zone**

The last aspect of visual evaluation is the lactiferous sinus zone. The peculiarities of lactiferous sinus zone visualization depend on the menstrual cycle phase and the physiological period. The figure 6-14 in the first row represents the image of the breast typical of the first phase of the menstrual cycle. The lactiferous sinus zone is visualized in the center of the image as a hyperimpedance area of rounded shape. The fourth row represents the image of the breast typical of the second phase of the

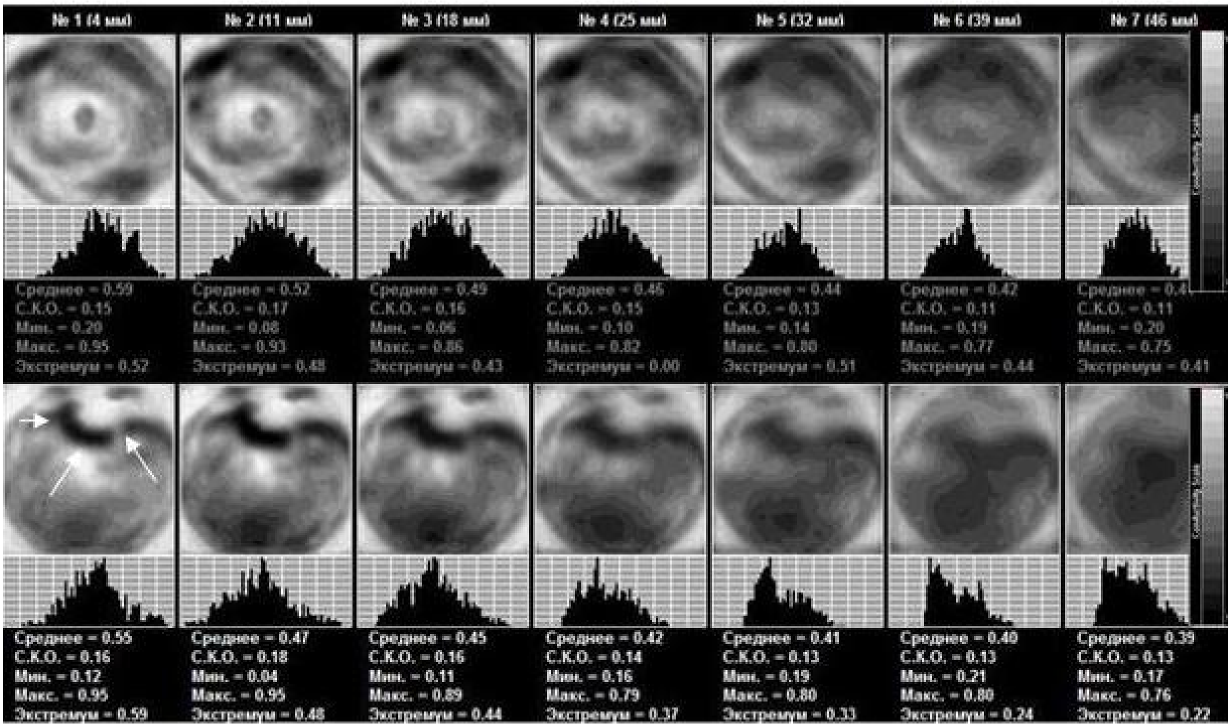



**Fig. 6-12.** EIM. Seven scan planes. A 67 years-old patient. A tomogram of a healthy mammary gland is shown n the first line. A local animpedance focus (at 1 o'clock position) surrounded by a hyperimpedance contour in case of complicated cancer is represented in the tomogram in the fourth line.

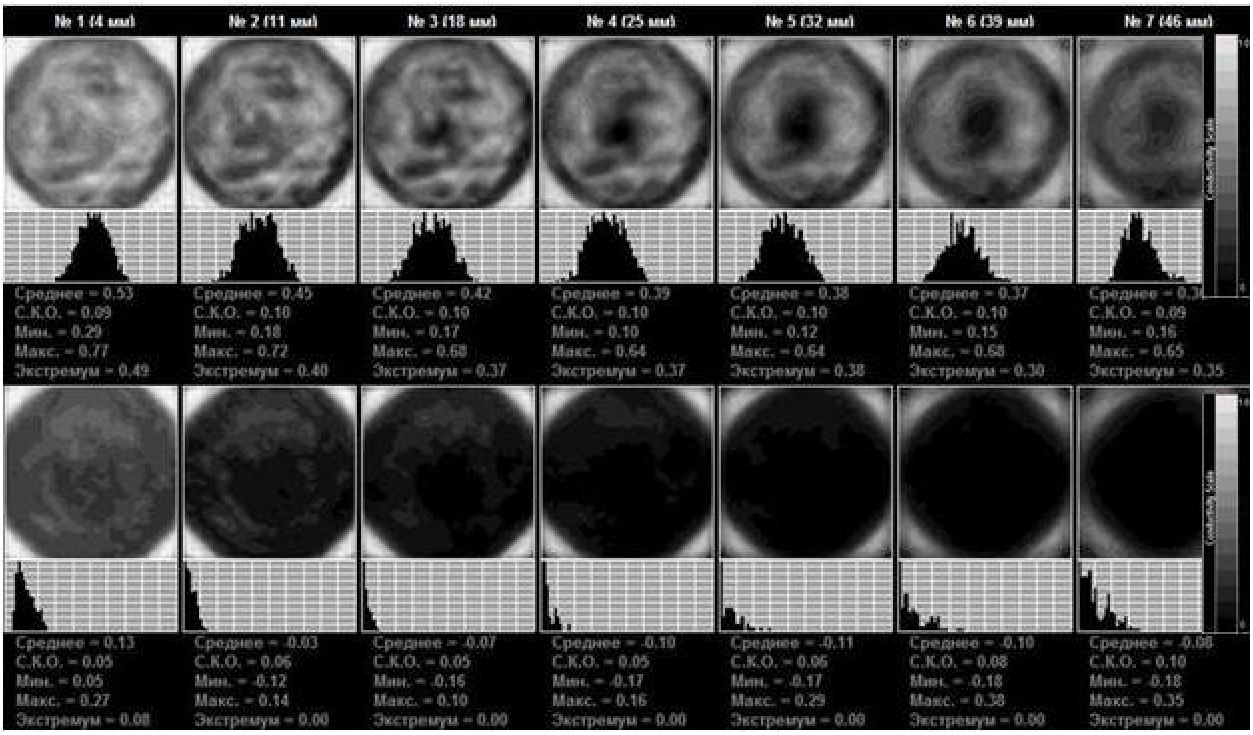



**Fig. 6-13.** EIM. Seven scan planes. A 59 years-old patient. A tomogram of a healthy mammary gland is shown n the first line. The tomogram in the fourth line represents the total hyperimpedance increase in case of infiltrative-edematous form of breast cancer.

menstrual cycle. The lactiferous sinus zone is visualized in the center of the image as a hyperimpedance area of rounded shape. The peculiarities of the physiological period (pubertal, pregnancy, lactation, etc.) affect electrical impedance images of the mammary gland. Figure 6-14 in the seventh and tenth row represents the image of the breast during lactation (before and after feeding), where, before the feeding the lactiferous sinus zone is

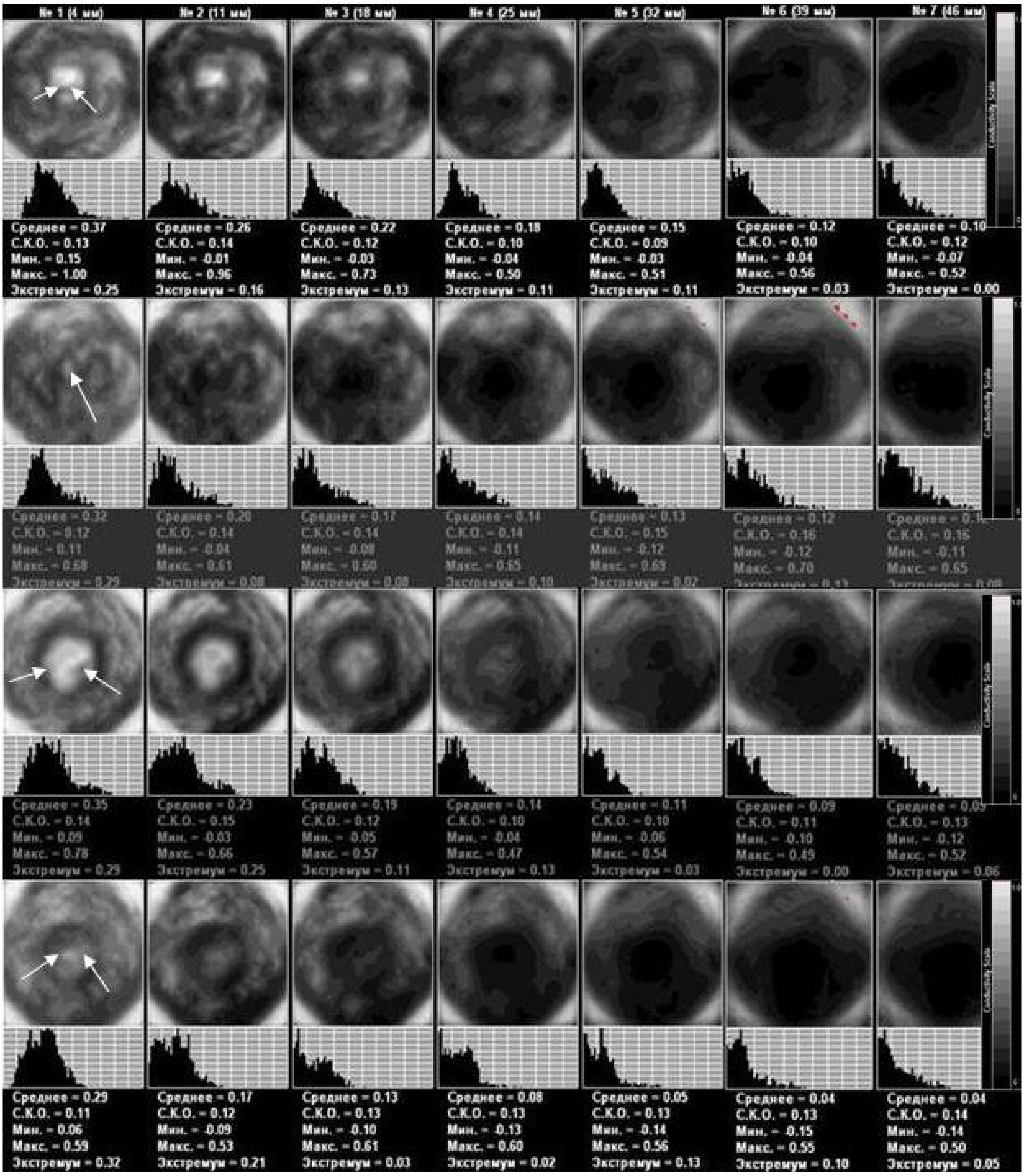


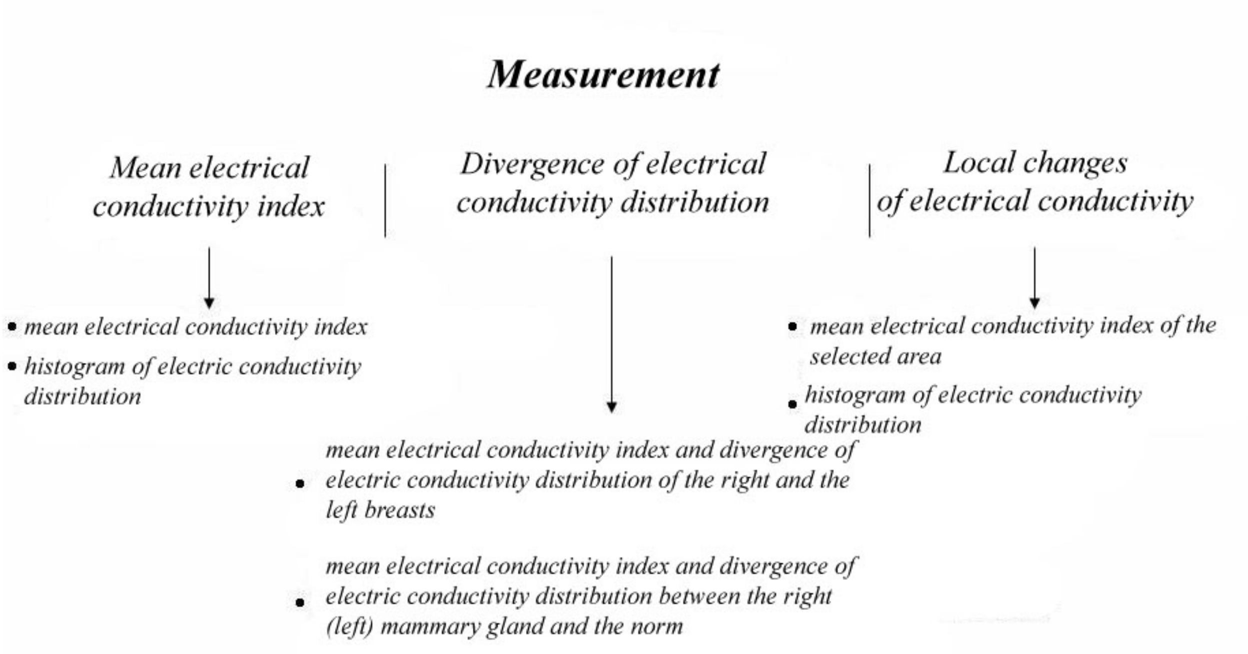

**Fig. 6-14.** EIM. Seven scan planes. The first line shows the tomogram during the first phase of the menstrual cycle. The fourth line represents the tomogram during the second phase of the menstrual cycle. The seventh line shows the tomogram during lactation period before feeding. The tenth line shows the tomogram during lactation period after feeding.

visualized in the central segment as an extensive hypoimpedance area.

## Quantitative assessment of electrical impedance images

Electrical impedance method as opposed to other imaging techniques allows conducting quantitative analysis of the image.The quantitative analysis of electric impedance images involves calculation of the following parameters: mean electrical conductivity index, the histogram of electric conductivity distribution, the results of comparative analysis with the reference data (with the norm) (Scheme 6-3).

The basic quantitative characteristics employed for image evaluation include the mean electric conductivity index and the histogram of conductivity distribution.




**Scheme 6-3.** Quantitative analysis of electrical impedance images of the breast.

Figure 6-15, below the image, provides the histogram of conductivity distribution and quantitative information: mean electric conductivity index, standard deviation, minimum and maximum conductivity values, and the most frequent value of electrical conductivity (extremum).

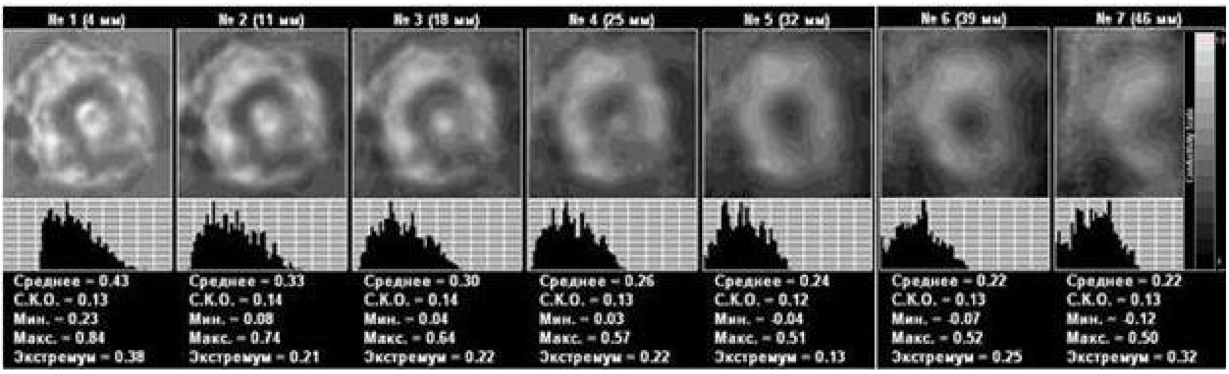



**Fig. 6-15.** EIM. Seven scan planes. The first line represents tomograms. The second line shows the histograms of electric conductivity distribution: The third line: mean electrical conductivity index, CKO – standard deviation, Min. – minimum conductivity index, Max. - maximum conductivity index, Extremum - the most frequent value of electrical conductivity.

. The next step in the process of image quantitative evaluation is the comparison of electric conductivity distribution of the right and the left breasts. Normally, the histograms of electric conductivity distribution are nearly identical for both mammary glands (Fig. 6-16).

When the gland is involved in a pathologic process, a shift of the affected gland's histogram is observed. Figure 6-17 shows the images of the left and the right breast of a patient suffering from infiltrative-edematous form of cancer (the first line contains images of the affected gland, the lower row displays the images of the healthy gland). The second line presents histograms of electric conductivity distribution: that of the affected mamma - in yellow, that of the one - in blue. A significant divergence between the

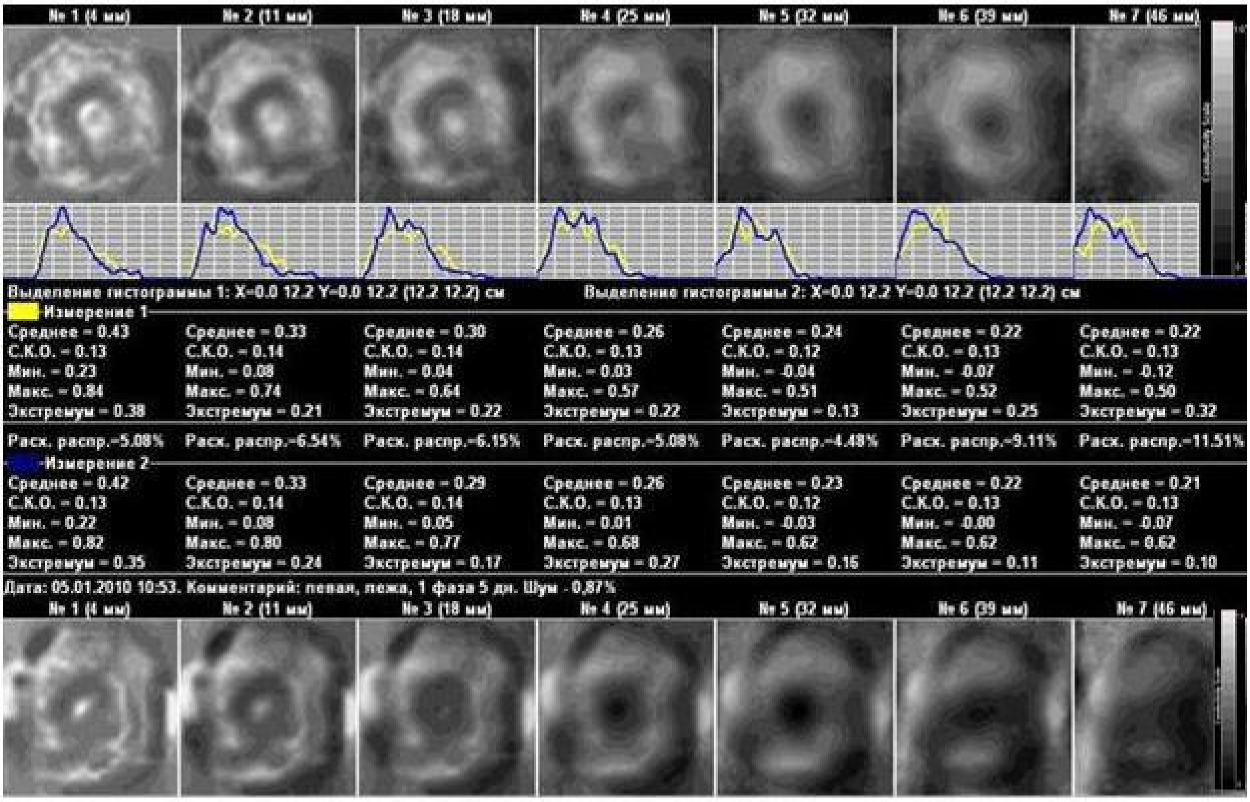



**Fig. 6-16.** EIM. Seven scan planes. The first line represents tomograms. The second line shows the comparison of electric conductivity distribution histograms tho images. The third and fourth lines: quantitative information. The fifth line shows tomograms.

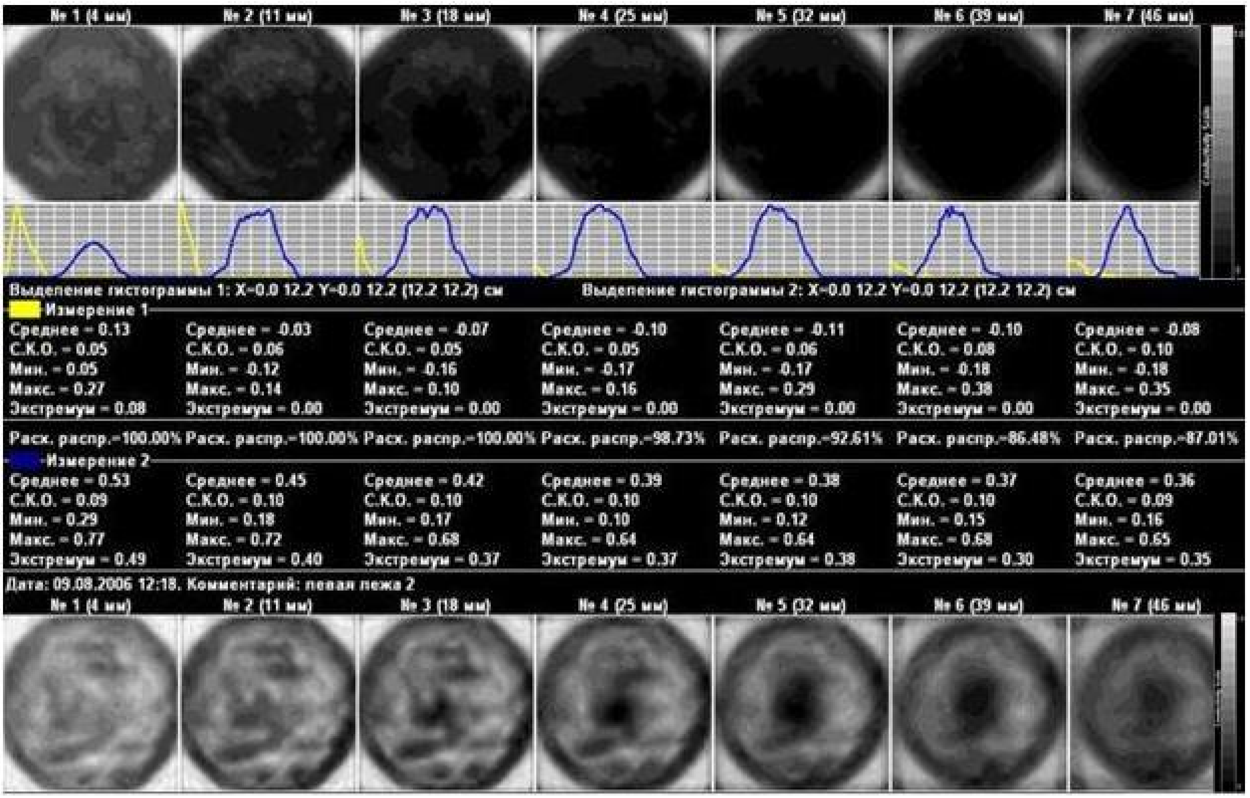



**Fig. 6-17.** EIM. Seven scan planes. The first line represents the tomograms of the affected mamma. The second line shows the comparison of electric conductivity distribution histograms of two images. The third and fourth lines: quantitative information. The first line represents the tomograms of the healthy mamma.

histograms of electric conductivity distribution of the affected mamma and the healthy one is observed (almost 100%).

The final aspect of the quantitative analysis is the comparison of the mamma's average electric conductivity with the norm. The norm values are represented as a complex histogram of electric conductivity distribution, which takes into account current season, age, parity, physiological period and the peculiarities of the examination. When the mamma is not involved in any pathologic process, the histogram of the electric conductivity distribution practically coincides with that of the norm (the divergence is less than 40%). When the mamma is affected by a disease, a shift of the affected gland's histogram is observed. The divergence between it and a complex histogram is more than 40% (Fig. 6-18).

Visual and quantitative evaluation criteria of mammary gland electric impedance images determine a universal approach to diagnostics of pathologies and render assistance in their better understanding by the doctors.

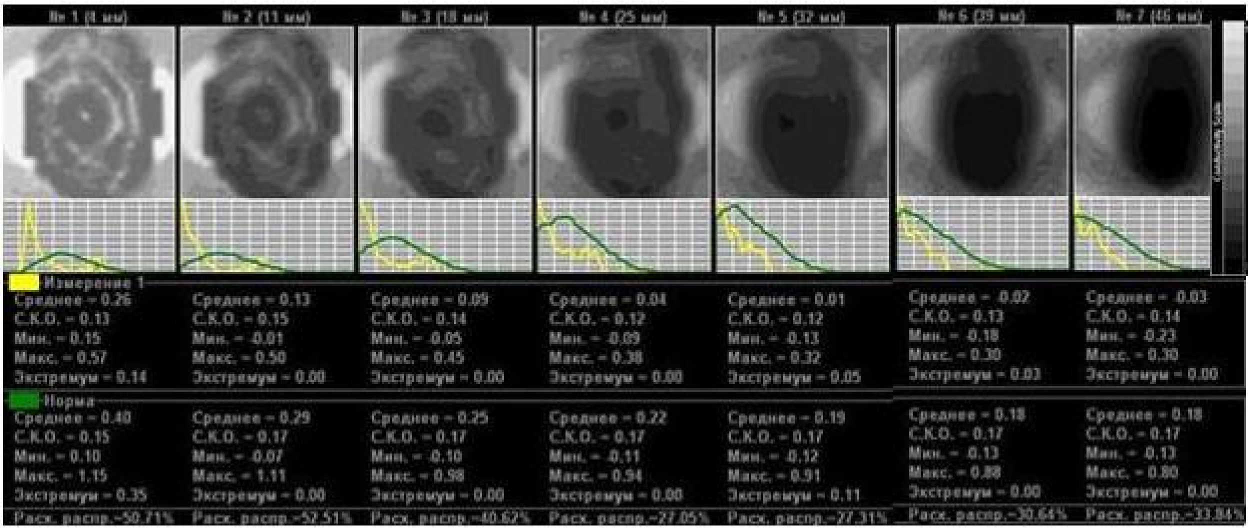
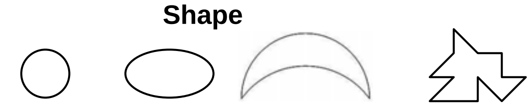



**Fig. 6-18**. The comparison of electrical conductivity index of the mamma with norm (the first line shows the tomograms, the second - the histograms of electrical conductivity distribution compared to the norm, the third and fourth lines - quantitative information).

## Supplement

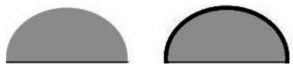
### Diagnostic Criteria for Electrical Impedance Mammography

**Shape**



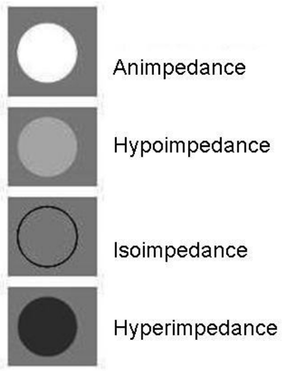
Round Oval Crescent Irregular

**Contour (hyperimpedance fringe)**



Absent Present

**Inner electrical structure**




**Surrounding tissues**

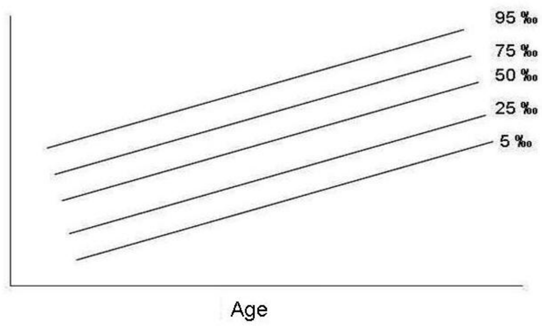
- Structure alteration
- Structure displacement
- Skin thickening
- Skin extrusion or retractionОтек
- Oedema
- Duct alteration

**Mean electrical conductivity/potential**

- Less than 5% - ductal type of mammary gland structure
- 5-25 % – mixed type of mammary gland structure with duct component predominance
- 25-75 % – mixed type of mammary gland structure
- 75-95 % – mixed type of mammary gland structure with amorphous component predominance
- Above 95% – amorphous type of mammary gland structure

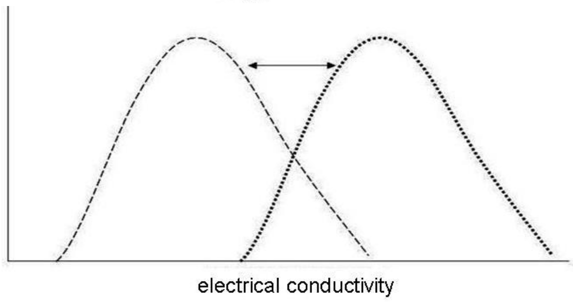
**Age-related electrical conductivity /potential**

- less than 25th percentile

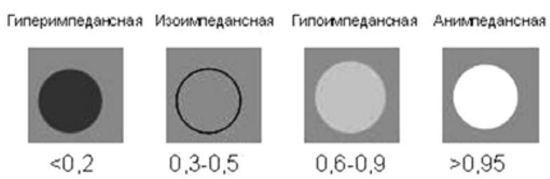



**Comparative electrical conductivity /potential**

- divergence between the histograms > 40%




**Local electrical conductivity /potential**



# Factors Affecting Electrical Impedance Image

# 7

All the factors having their influence on the electrical impedance image of biological objects, such as physical, mathematical, instrumental, procedural and biological, can be divided into internal and external ones.

| Internal factors | External factors |
|---|---|
| 1) Change of tissue composition (e.g., with age)<br>2) Histological structure of tissues<br>a. cell mass<br>b. ion concentration<br>c. amorphous substance<br>d. fibers<br>3) Physiological processes<br>4) Temperature<br>5) Diffusion<br>6) Volumetric fluxes<br>7) Infiltration<br>8) Skin conditions | 1. Electric field intensity<br>2. Electric current frequency<br>3. Electric field homogeneity<br>4. Parameters of the hardware and software<br>a. impulse shape and frequency<br>b. matrix format<br>c. electrodes quantity<br>d. pixel size<br>e. artifact reduction<br>5. Mathematical model chosen<br>6. Reconstruction Algorithm |

Each group is characterized by its distinctive features. Firstly, one should consider the biological factors affecting the electrical impedance image.

### Biological factors

In general, electrical impedance images depend on the chemical composition of the structures that make up the mamma and metabolic processes occurring in it (Fig. 7-1). All these phenomena can be explained by a single feature, notably by their susceptibility to electric field: either enhanced conductivity, or high permittivity, or their combination.

These factors determine different behaviour of structures and phenomena in electric field and, finally, the way they

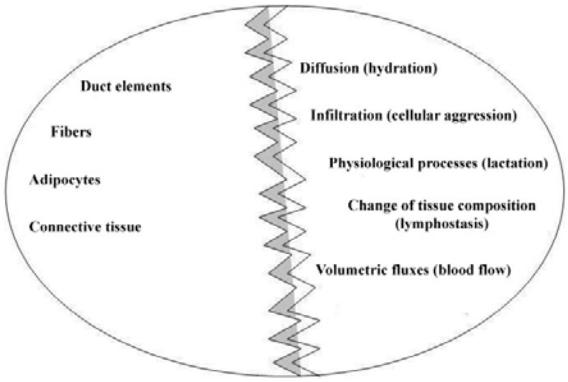



**Fig. 7-1.** The structures and phenomena affecting an electrical impedance image.

affect electrical impedance images. Getting the real values of electrical conductivity or permittivity of breast tissues in vivo presents insurmountable difficulties. Therefore, when describing the physical and chemical properties of mamma's structures, which have their influence on electrical conductivity, we rely on empirical data taken from monographs on physics, chemistry, biochemistry, biophysics, physiology and pathophysiology.

It is noteworthy that these data are reflected in the electrical impedance images and moreover, are confirmed by the comparative ultrasound examination.

### Structure of tissues

Physical-chemical properties of the breast are determined by the number and / or the ratio of the major tissue elements: ductal and alveolar epithelium cells, collagen and elastic fibers, adipocytes and ground (amorphous) substance of connective tissue (Fig. 7-2).

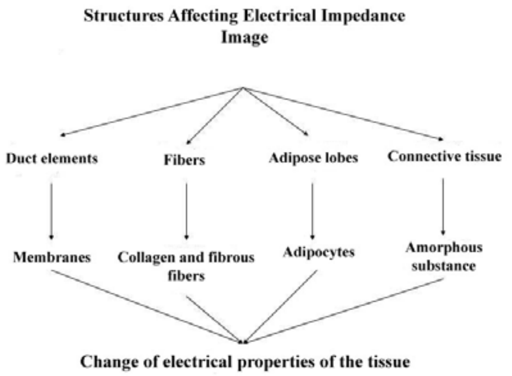



**Fig. 7-2.** The structures affecting an electrical impedance image.

*Duct elements*

The predominance of ductal component in the structure of mamma's parenchyma, which is more typical for women of early reproductive period, gives to the electrical impedance image the following specific features: predominance of dark colours of the gray scale, absence of anatomical landmarks, mean electrical conductivity index is lower than age norm. The peculiarities of electrical conductivity are conditioned by the presence of a large number of epithelial cells membranes that behave as electrical capacitors. High density of ductal component is a significant obstacle to electric current. This gave grounds to define this kind of mammary gland structure as a membrane type (Fig. 7-3, 7-4).

*Collagen fibers*

Collagen fibers are the fibers of the extracellular substance of connective tissue, consisting mainly of collagen. Collagen molecules consist of three polypeptide chains twisted into helices.

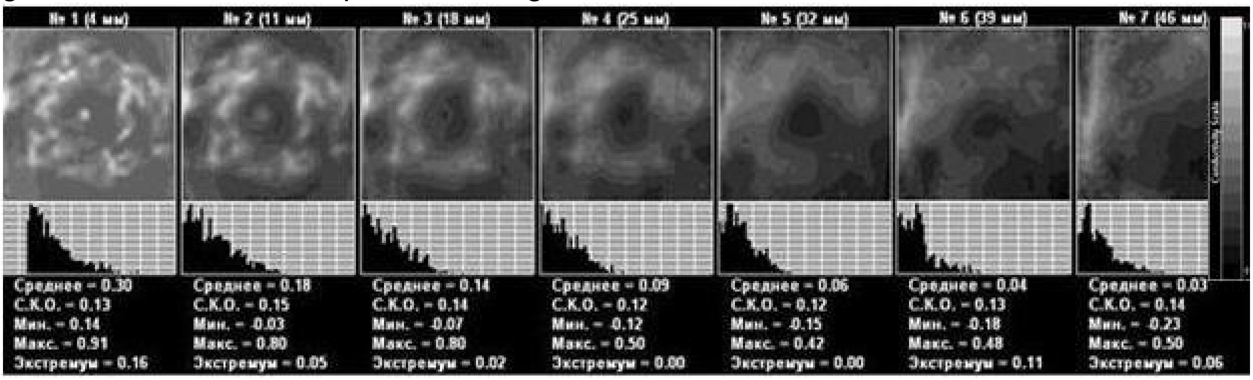



**Fig. 7-3.** EIM. Seven scan planes. A 38 years-old patient. The image of mamma has well-defined anatomical landmarks.

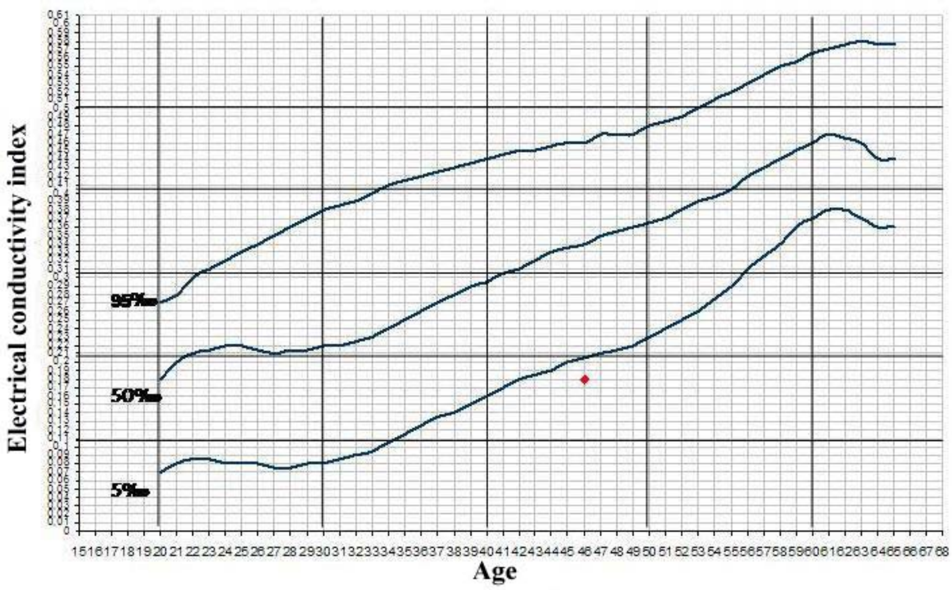



**Fig. 7-4.** Percentile curves of age-related electrical conductivity of the mammary gland. Ductal type of mammary gland structure. Mean electrical conductivity index (red marking) is lower than age norm (<5‰).

The primary structure of collagen molecules is characterized by frequent repetition of the sequence glycine - proline - oxyproline.The collagen in mature fibers is non-polar and insoluble in water; this determines its electrical properties - the properties of a non-polar dielectric. In case of fibrous component prevalence in the parenchyma structure of the mamma, which sometimes occurs during women's reproductive and peri-menopausal periods, the electrical impedance image is characterized by the following: predominance of dark colours of the gray scale, absence of anatomical landmarks, mean electrical conductivity index is low. In this case we can speak of a fibrous type of the mammary gland structure (Fig. 7-5, 7-6).

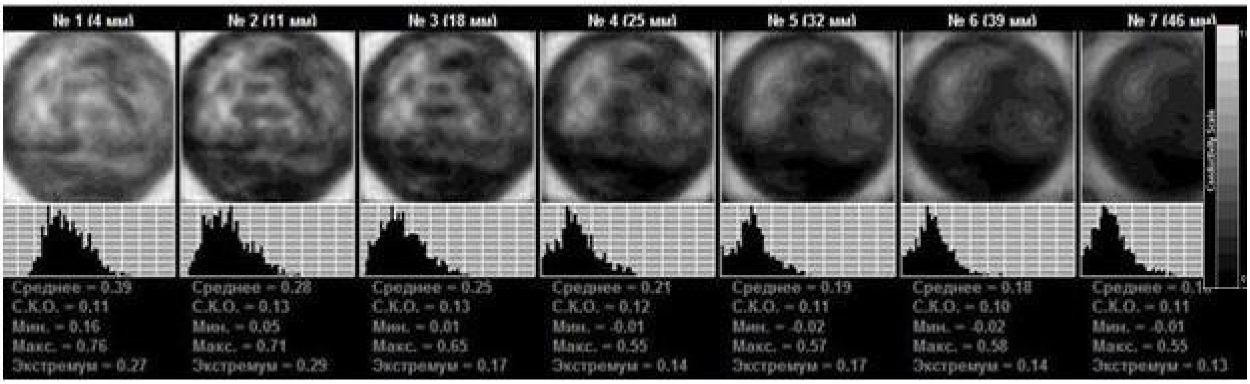



**Fig. 7-5.** EIM. Seven scan planes. A 63 years-old patient. The image of mamma has no anatomical landmarks.

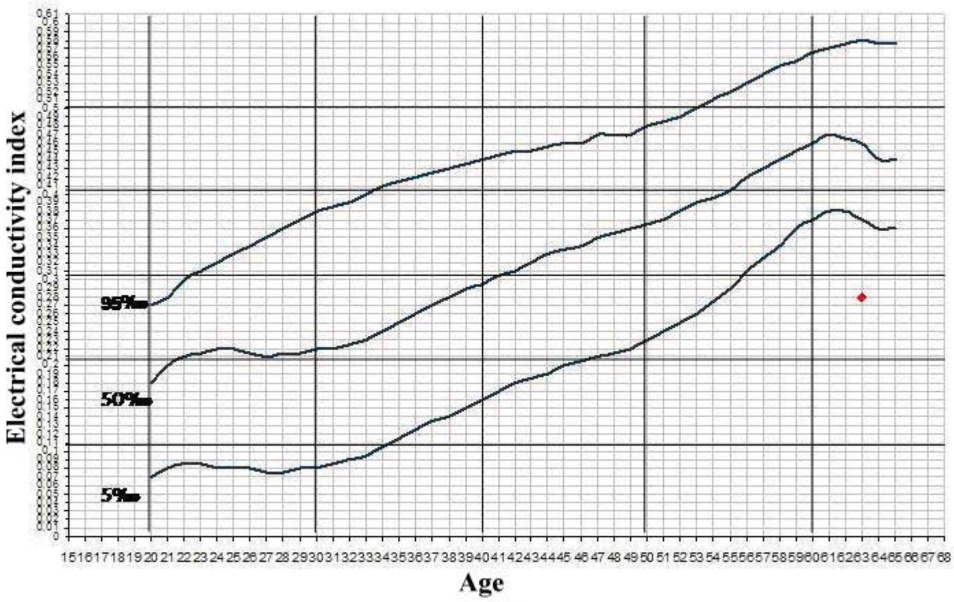



**Fig. 7-6.** Percentile curves of age-related electrical conductivity of the mammary gland. Fibrous type of mammary gland structure. Mean electrical conductivity index (red marking) of the mammary gland is lower than age norm (<5‰).

*Amorphous substance of connective tissue*

Apart fibers, intercellular substance includes the ground substance, which contains a large amount of mucopolysaccharides. Loose connective tissue, filling the space between bodies, blood vessels, nerves, muscles and other structures of the body, creates the internal environment, through which the delivery of nutrients to cells and the removal of the waste products of their metabolism are carried out. The major mucopolysaccharide of the ground substance of connective tissue is hyaluronic acid, which carries a large number of negative charges. Its ability to bind and retain water dipoles determines the electrical properties of amorphous substance of connective tissue, making it a good conductor. The predominance of amorphous substance in the structure of the parenchyma is mainly observed during perimenopausal period. This fact imparts to electrical impedance images structures that determine the conductivity and permittivity of tissues, creates a mixed heterogeneous electrical impedance image; however the values of mean electrical conductivity index al-

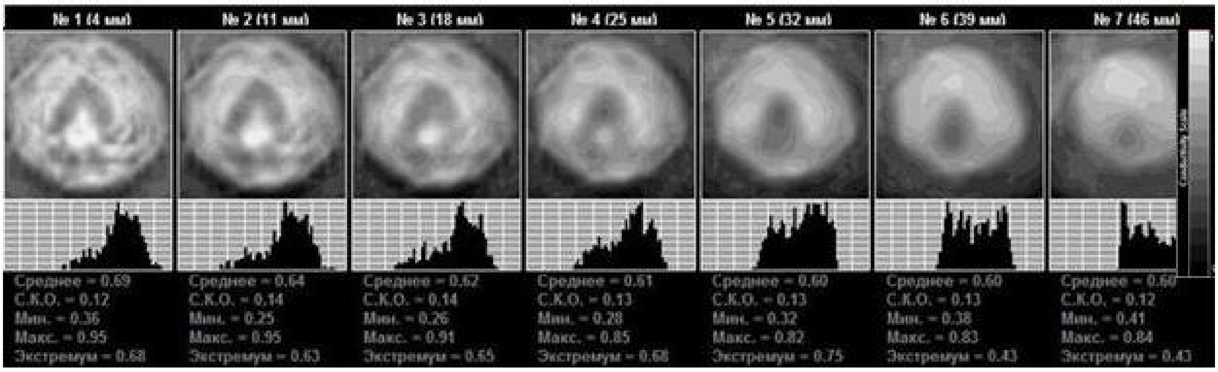



**Fig. 7-7.** EIM. Seven scan planes. A 46 years-old patient. The image of mamma has no anatomical landmarks.

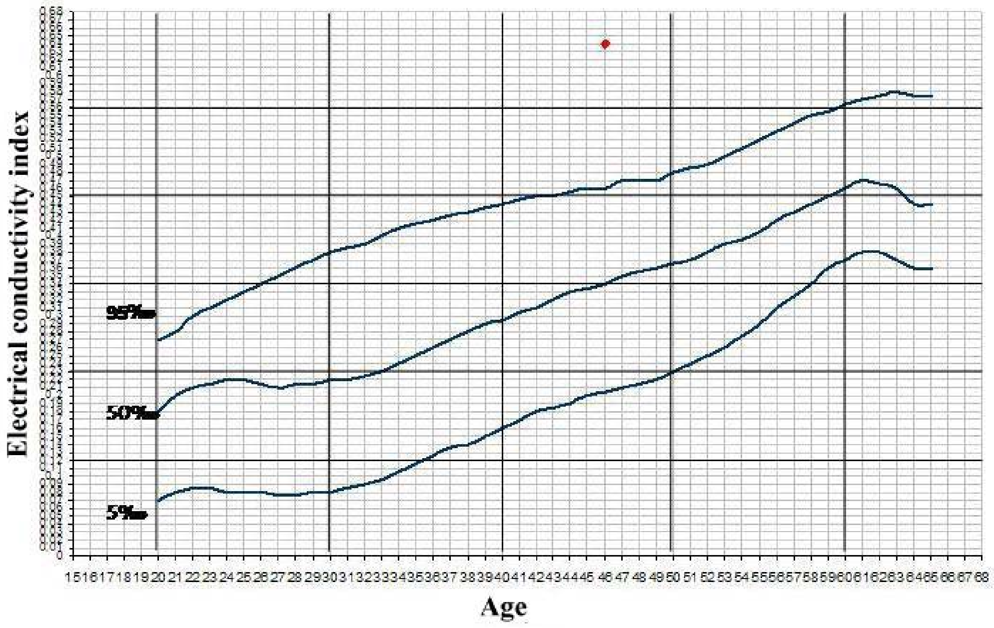



**Fig. 7-8.** Percentile curves of age-related electrical conductivity of the mammary gland. Amorphous type of mammary gland structure. Mean electrical conductivity index of the mammary gland is higher than age norm (>5‰).

the following characteristics: predominance of light colours of the gray scale, the absence of anatomical landmarks, mean electrical conductivity index is above the age norm. This description is typical of the amorphous type of the mammary gland structure (Fig. 7-7, 7-8).

*Cells of adipose tissue in combination with the above mentioned structures*

The combination of the above-listed structures with adipocytes is observed during the reproductive period of women. Different combination of the ways correspond to the age norm. This is the most common kind of mammary gland structure – the so-called mixed type (Fig. 7-9, 7-10).

**Metabolic processes**

Local metabolic processes may include tissue hydration, lymph drainage disorder, cellular 'aggression', lactation, etc. These dynamic actions occur gradually and the characteristic changes of the electrical properties of participating tissues are well predictable.

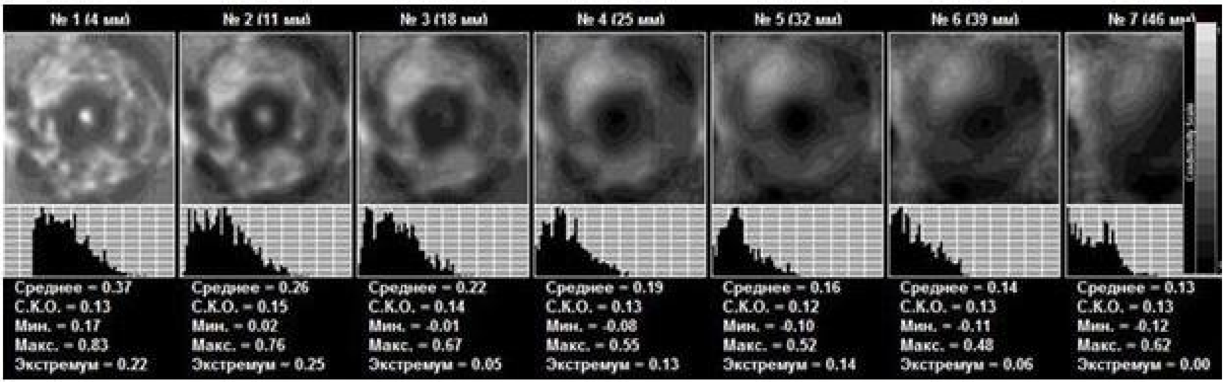



**Fig. 7-9.** EIM. Seven scan planes. A 20 years-old patient. Heterogeneous electrical impedance image.


**Fig. 7-10.** Percentile curves of age-related electrical conductivity of the mammary gland. Mixed type of mammary gland structure. Mean electrical conductivity index of the mammary gland is within age norm (5-95‰).

Change in electrical conductivity is usually associated with the local effect of "accumulation". Electrically active compounds possessing various behaviours in the electric field are accumulated in a single place, causing local changes of electrical conductivity and permittivity. Such chemical compounds as ions and dipoles are considered responsible for the electrical conductivity change of the metabolic system, while the tissue structures, such as cells, are responsible for permittivity.

*Tissue Hydration*

Tissue hydration is observed during many pathophysiological processes. In case of mammary gland deceases this process often develops in the nidus of inflammation. During the active (arterial) hyperemia stage linear and volume blood velocity increase. Arteriotony in the capillaries and veins increases because blood flow prevails over blood outflow. High blood pressure leads to the structural alteration of endothelial capillary walls. The structure of endothelial walls is unstable, movable. Pores and fissures are generated in it under the influence of high blood pressure. High osmotic and oncotic pressure in the nidus of inflammation create diffusion and osmotic flow of fluid into the tissue inflamed. Thus, an extracellular oedema arises in the nidus of in-

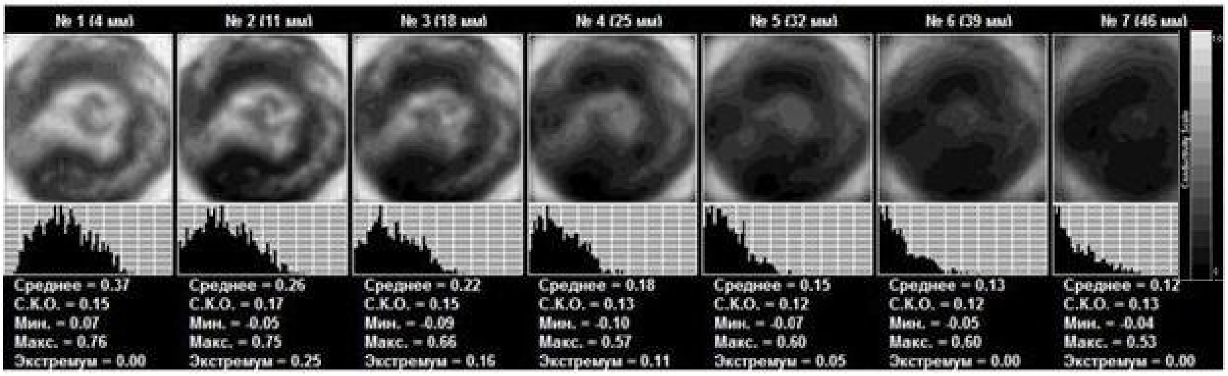



**Fig. 7-11.** EIM. Seven scan planes. Lactation. Mastitis. Active (arterial) hyperemia stage. The hypoimpedance area with high conductivity index corresponds to the location of the oedema area.

flammation. Exudation in the arterial hyperemia stage leads to alteration of the electrical situation in the damage area. Hydropic fluid which contains positive ions suppresses negatively charged hydroxyl and carboxyl groups of hyaluronic acid. Neutralization of local electronegativity of connective tissue and formation of free and bound water occur. These processes result in decrease of active component of impedance and in increase of conductivity in the inflammation area.

During the stage of vascular changes, hyperemia area and oedema can be observed clinically. Increase of blood flow and formation of extracellular oedema leads to electrical conductivity increase. In the electric impedance

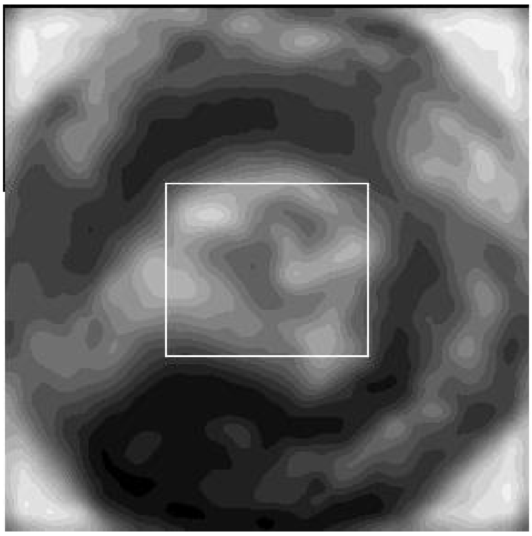


**Fig. 7-12.** Electrical impedance mammogram. On the periphery of the oedema area there is a hyperimpedance infiltration contour.

mammograms hypoimpedance areas can be visualized, they possess high conductivity index and their location corresponds with the oedema area (Fig. 7-11), Leukocytic infiltrate emerges on the periphery of this area to delimit the nidus of inflammation. 7-12).

*Lymph Drainage Disorder*

Lymph drainage disorder becomes very apparent in case of oncologic deceases of mamma. Apparent lymph outflow disorder is observed in case of infiltrative-edematous form of breast cancer. Intracellular and lymphatic oedema leads to sharp increase of total impedance: intracellular oedema decreases the volume of intercellular space, while lymphatic oedema increases cell mass in the damage area, first of all, at the expense of lymphocytes. Both processes result in increase of reactive component of impedance and in significant decrease of electrical conductivity. Fig. 7-13 represents the electrical impedance image of the patient aged 72, diagnosed diffuse infiltrative cancer of the right mammary gland. The anatomy of the affected mammary gland (lower row of images) is extremely changed and anhistous (structureless). Mean electrical conductivity index of the affected mammary gland is more than fourfold less than mean electrical conductivity index of a normal (upper row of images) mammary gland and also is lower than age norm.

*Cellular Aggression*

Cellular aggression manifests itself most apparently during the venous

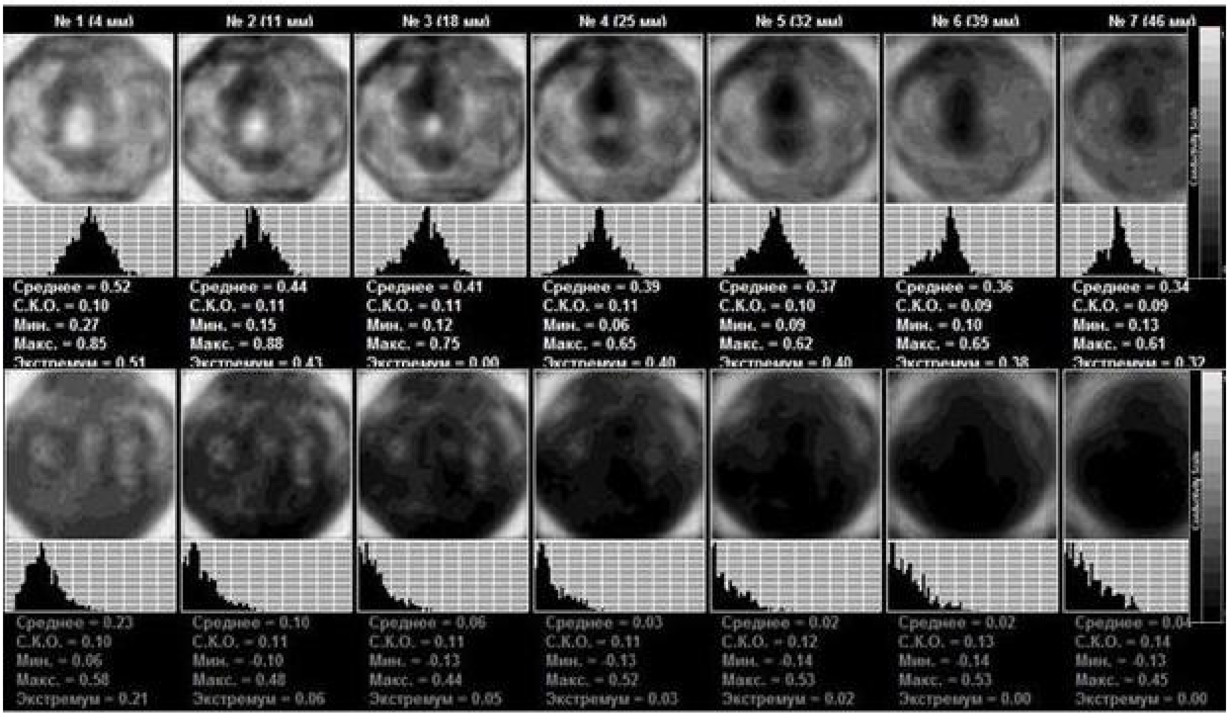



**Fig. 7-13.** EIM. Lymph drainage disorder. Infiltrative edematous form of breast cancer (the first line represents the tomograms of the healthy mamma, the fourth one - of the affected gland).

hyperemia stage of mastitis as a leukocytic infiltration. Shortness of blood and lymph outflow from the nidus of the inflamed tissue as the result of growing extracellular oedema plays a big part in qualitative alteration of the inflammatory oedema. Already during the active hyperemia stage the leukocyte exit into the inflamed tissue begins, however it reaches the maximum in the passive hyperemia stage. The slowdown of the blood flow up to its arrest contributes to this process. When the inflammation develops the leucocytes infiltrate tissues,

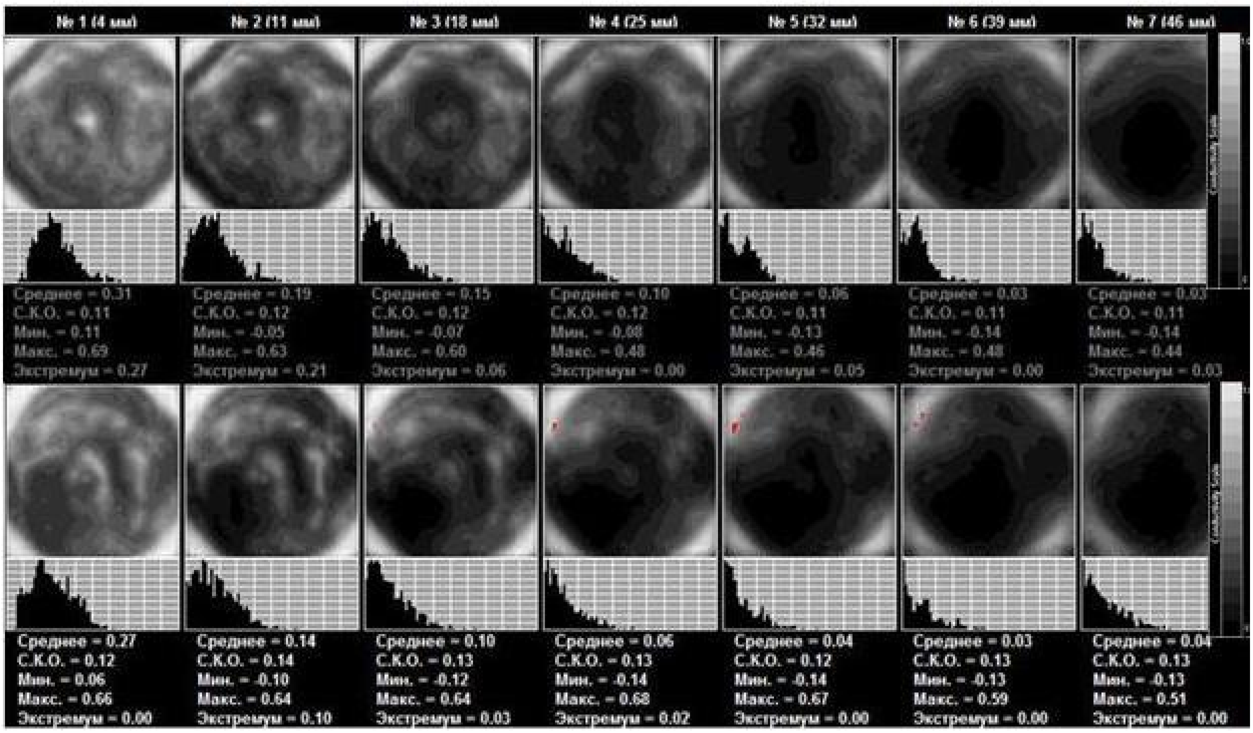



**Fig. 7-14.** EIM. Mastitis. Passive (venous) hyperemia stage. The hyperimpedance area with low conductivity index at 7 o'clock position corresponds to the location of the infiltration area.

locating in large amounts around blood vessels and between the cells of inflamed tissue. During migration the leucocytes lose their negative charge. Such

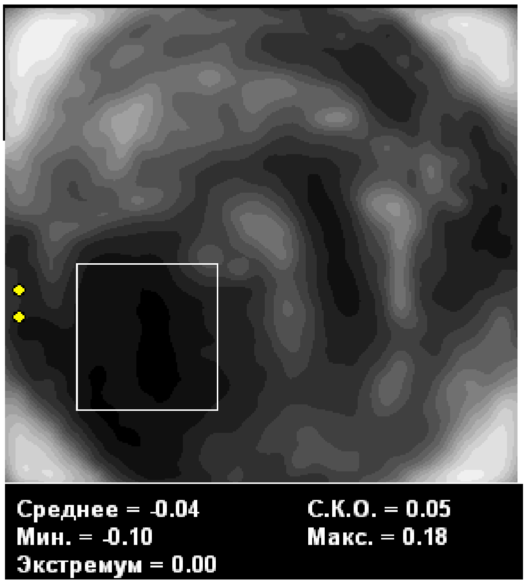



**Fig. 7-15.** Electrical impedance mammogram. Mastitis. A hyperimpedance formation at 7 o'clock.

factors as connective tissues negative charge neutralization, leukocytes' loss of negative charge and "free" water quantity increase simplify leukocytes' movement in the inflammation area. Leukocytes' movement leads to the formation of leukocytic infiltrate with abundance of cell-substratum which contains different types of leukocytes. Thereby the area of cell membranes grows significantly and this fact results in increase of reactive component of impedance and in decrease of conductivity in the inflammation area. In the electrical impedance mammograms (Fig. 7-14) infiltrate can be visualized in the outer segment (at 7 o'clock position) as a homogeneous well-defined hyperimpedance area with low electrical conductivity index (Fig. 7-15).

*Lactation*

After childbirth the blood concentration of progesterone and estrogens drops abruptly, making the glands secrete prolactin. Prolactin takes part in the processes of the mammary glands' secretory activity, immediately before the outlet the lactiferous ducts form lactiferous sinuses which serve as reservoirs during the process of lactation. They accumulate secretion and milk, which is generated by lactocytes in alveoli. Caloric value of breast milk is 65-70 kcal/100 g, pH = 6.9-7.5, density - about 1.030-1.032 g/cm3. Chemical

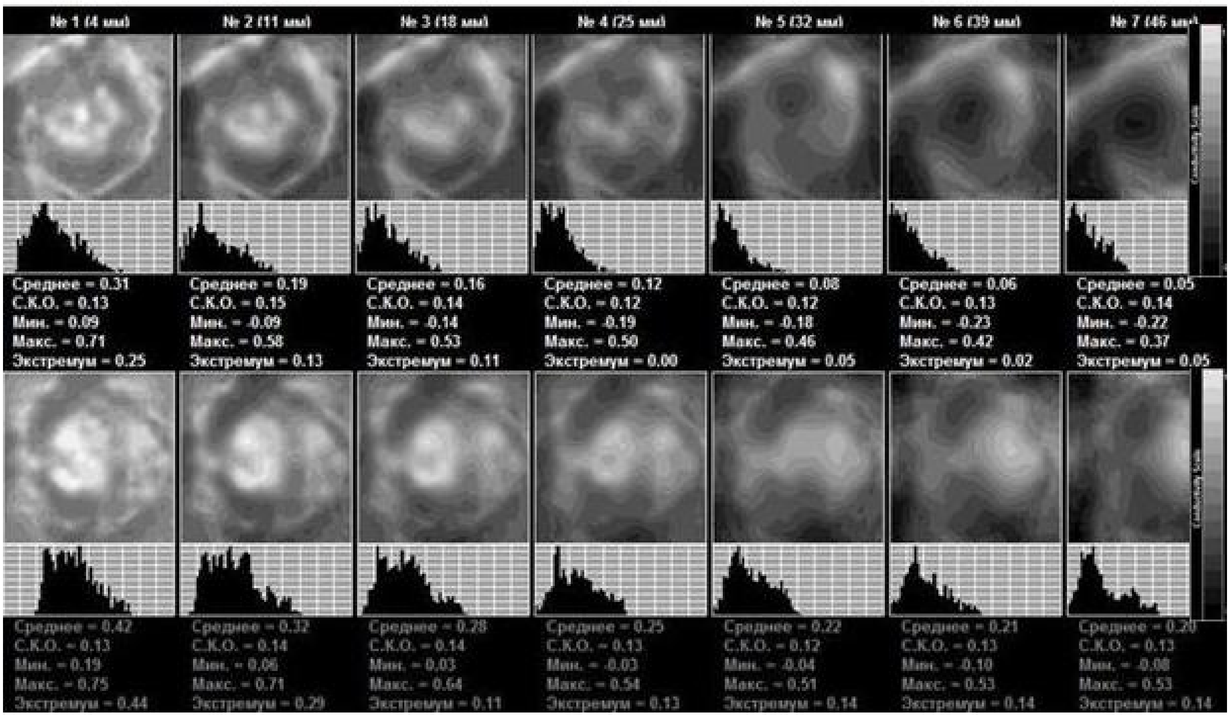


**Fig. 7-16.** EIM. Seven scan planes. Lactation. The image of the mamma after breastfeeding (upper line) and before feeding (fourth line).

composition of breast milk: water 87.4%, casein 0.91%, albumen and globulin 1.23%, fat 3.76%, lactose 6.29%, alkali 0.31%; it also contains a certain value of mineral salts as well as A, B, C and D vitamins.

The composition of milk, containing almost 90% of water, defines the high electrical conductivity value of filled lactiferous sinus zone. In the electric impedance mammogram (Fig. 7-16, fourth row) the lactiferous sinus zone filled up with milk can be visualized as a vast well-defined hypoimpedance area (of high mean electrical conductivity index) located in the center of the mammogram. After the expression of breast milk the lactiferous sinus area empties. And in the electric impedance mammogram (Fig. 7-16, first row) the empty lactiferous sinus zone is visualized as an iso/hyperimpedance area with slightly blurred contours, located in the centre of the mammogram.

Thus, the anatomical structures of the mamma, as well as the metabolic processes, which occur in it, influence the electrical properties of tissues and define the peculiar features of the mammary gland electric impedance image. That is why electric impedance mammography method can be defined as a method of **histofunctional scanning**.

# Electric Impedance Visualization Concerning Cutis Affections

# 8

Electric impedance scanning of the mammary gland is a complex process, studying of which still continues. Tissues of opposing electrical properties can occur on the way of electric charges. But the main obstacle is presented by cutaneous covering consisting of the cell mass. It is a kind of dead wall for the charges. However this obstacle contains a lot of excretory ducts of perspiratory eccrine glands (200 ducts per sq.cm). Inside these glands there is electroconductive secretion, which, theoretically, makes the process of electrical current penetration through epidermis and derma easier (Fig. 8-1).

Moreover, we should not forget that the area under examination should be moistened. Homogeneity and integrity of the cutaneous covering does not affect the image of the mammary gland. But there occur such skin affections (either normal or pathological) which possess different conductivity and thus can distort the image of the mammary gland. This type of affections include: nevus, wart (papilloma) and others.

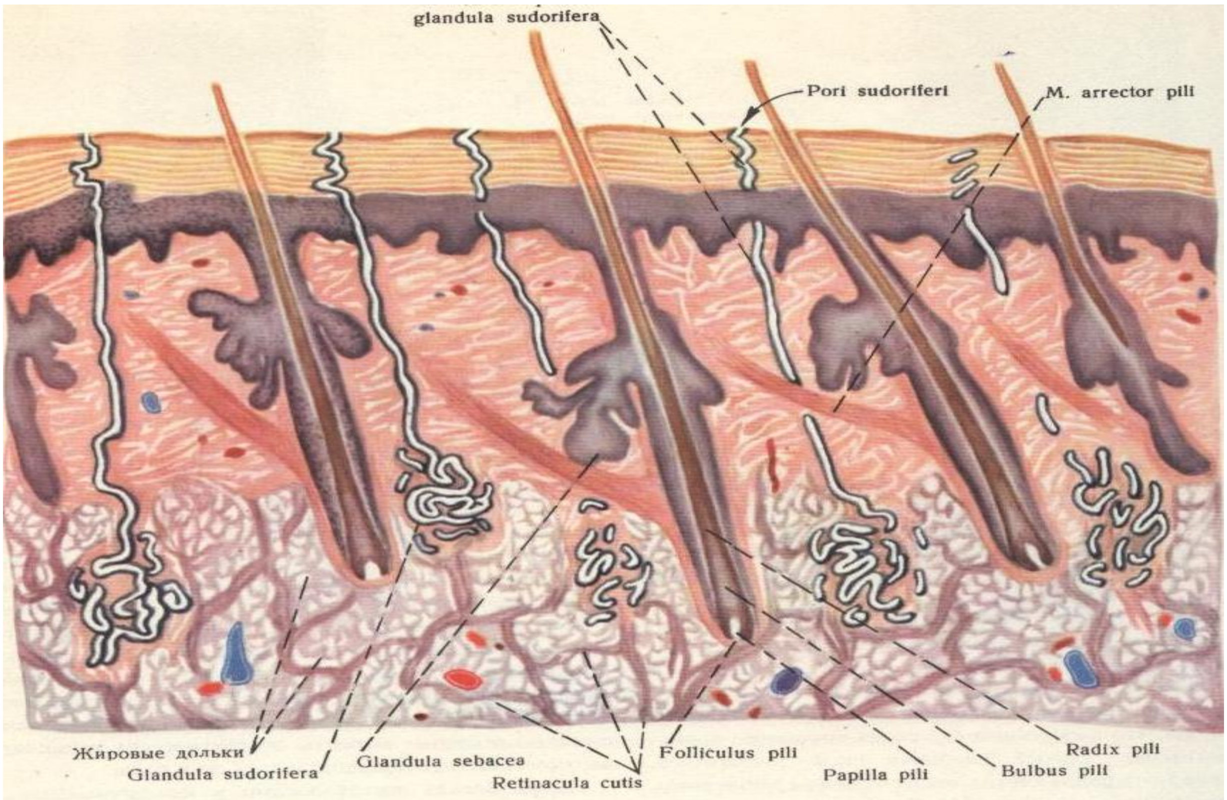



**Fig. 8-1.** Epidermis and derma.

*Electric impedance imaging of the mammary gland and nevus*

Intradermal Nevus (also known as birthmark) is the most common skin affection. It is a spot on the skin of the brownish colour, appx. 1 cm in diameter with distinct rounded borders (Fig. 8-2).

**Fig. 8-2.** The mammary gland with a nevus in upper segment.

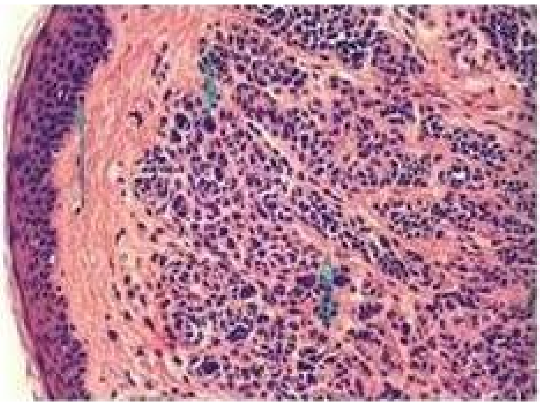


**Fig. 8-3.** Histological structure of a nevus («Atlas of Human Morphology» DiamedInfo, 1997).

Histologically, it is presented by bonds and locules of nevus cells containing melanin in the center of the derma. Between the cell groups the fibrous interlayers can be observed (Fig. 8-3).

The peculiarities of the electrical impedance image of the mammary gland with simple nevus are specified by the absence of the changes in the epidermis and derma structure and by the absence of the ducts' elements of perspiratory glands inside the nevus. In the electrical impedance image simple nevus is observed as a round hyper-impedance area (electrical conductivity index, IC =0.15-0.20) with distinct contour, appx. 7 mm in diameter (Fig. 8-4). The depth of its distribution (up to 18 mm) can be explained by the properties of the research – compression of the mammary gland.

**Рис. 8-5.** Histological structure of a wart («Atlas of Human Morphology» DiamedInfo, 1997).

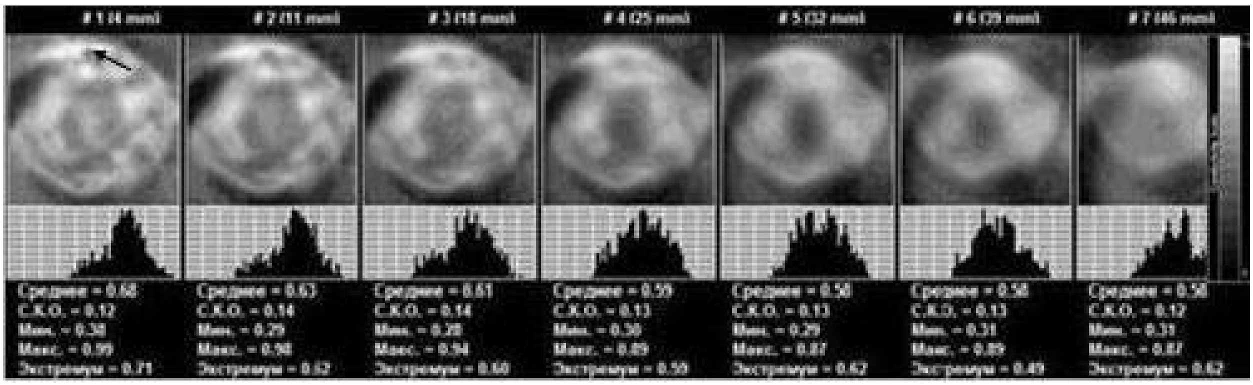


**Fig. 8-4.** EIM. In the upper segment (at 12 o'clock position) there can be visualized a round hyper-impedance area with distinct contour corresponding to the location of the nevus.

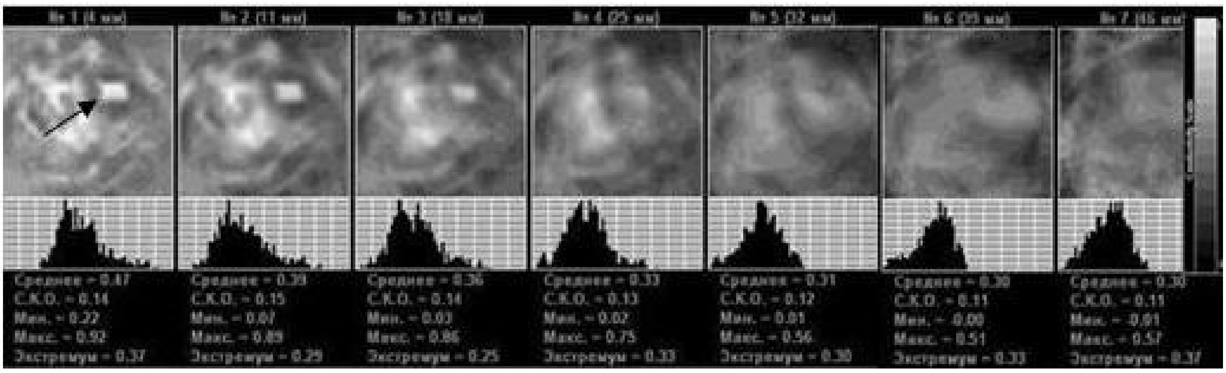


**Fig. 8-6.** EIM. In the electrical impedance image the location of a wart is observed as a round iso-impedance area with distinct hyper-impedance contour on the periphery.

*Electric impedance imaging of the mammary gland and wart (papilloma)*

Warts (or papillomas) are benign tumours of the skin in the form of distinctly contoured dense brown semispherical papules 5-20 mm in diameter. The surface of the papule is covered with sebum. Histologically, it is a focal epidermal hyperplasia with acanthosis, hyperkeratosis and papillomamatosis. The skin in this area is of the papillary architecture.

The perculiarities of the electrical impedance image of the mammary gland with seborrheic papilloma are specified by the changes in the structure of the epidermis and derma layers as well as by the large amount of the sebum-impregnated friable horny mass (fig. 8-5) In the electrical impedance image papilloma is observed as a round iso-impedance (IC=0.7-0.8) area with distinct hyper-impedance contour (IC=0.2) on the periphery, 30 to 20 cm in size (Fig. 8-6).

*Electric impedance imaging of the mammary gland with scars*

Scarring is the last stage of the inflammation process. The infiltrate regression is accompanied by its substitution by connective tissues and by the restoration of the electrical properties of the affected tissue. If there takes place a significant damage of the tissue, two variants of healing are possible. During the healing by the primary intention there is formed a scar (fig. 8-7) which consists of unstriated epithelium and derma (which in its turn consists completely of collagen fibers and posses no appendages of skin (hair, perspiratory and sebaceous glands).

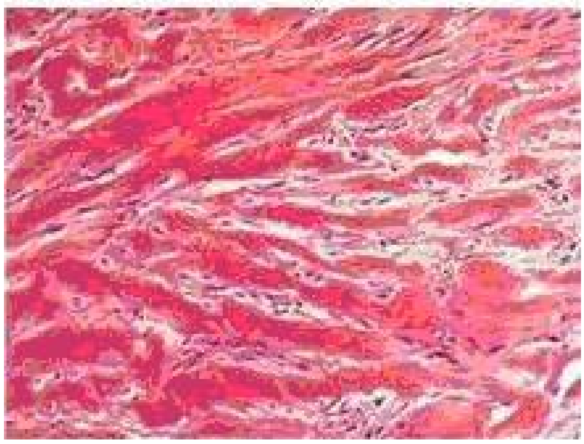


**Fig. 8-7.** histological structure of a scar («Atlas of Human Morphology» DiamedInfo, 1997).

During the healing by the secondary intention the affected area is separated from the rest of the tissue by collagen fibers, the focus itself consists

**Fig. 8-8.** The mammary gland with a postoperative scar in the outer segment (healing by the primary intention).

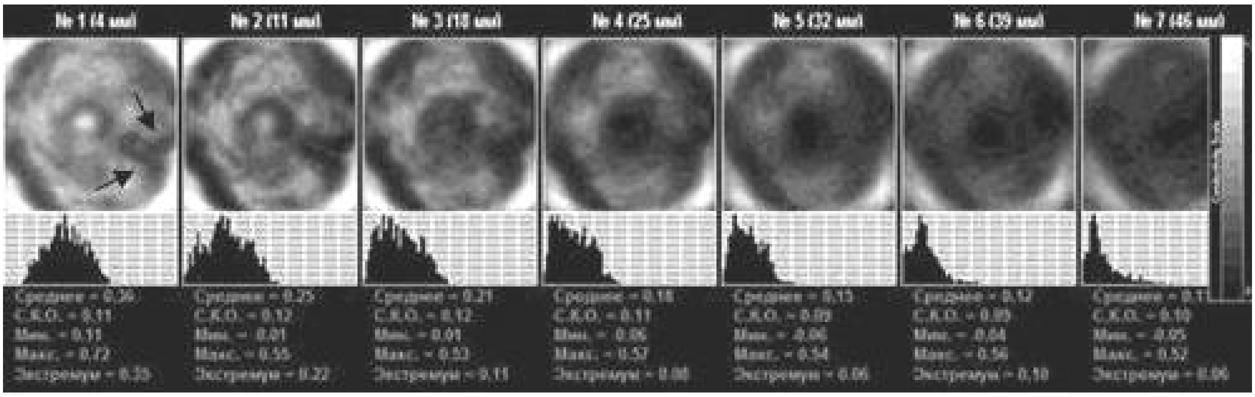


**Рис. 8-9.** EIM. In the outer segment of the electrical impedance image at 3 o'clock position there is observed a hyper-impedance linear area which corresponds with the scar on the skin in its size and form.

of the amorphous substance of the connective tissue. The peculiarities of the electric impedance image of the mammary gland with scar of the first variant (fig 8-8) are specified by the presence of numerous collagen fibers, which are dielectrics. In the electrical impedance image the scar is observed as a hyper-impedance linear area (IC=0.1-0.2) which corresponds with the scar on the skin in its size and form (Fig. 8-9). The peculiarities of the electrical impedance image of the mammary gland with scar of the second variant are specified by the fact that the affected area is separated from the rest of the tissue by collagen fibers, the focus itself consists of the amorphous substance of the connective tissue, the main component of which is hyaluronic acid (Fig. 8-10). That is why in the healing zone one can observe the areas of high impedance (which is the characteristic of collagen) as well as these with low impedance (which is the characteristic of the amorhous substance of the connective tissue). In this case the scar is observed (Fig. 8-11) as hyper-impedance lines (IC=0.1-0.2) with iso-impedance area between them (IC=0.3-0.4).

**Рис. 8-10.** The mammary gland with a scar in the outer segment (healing by the secondary intention).

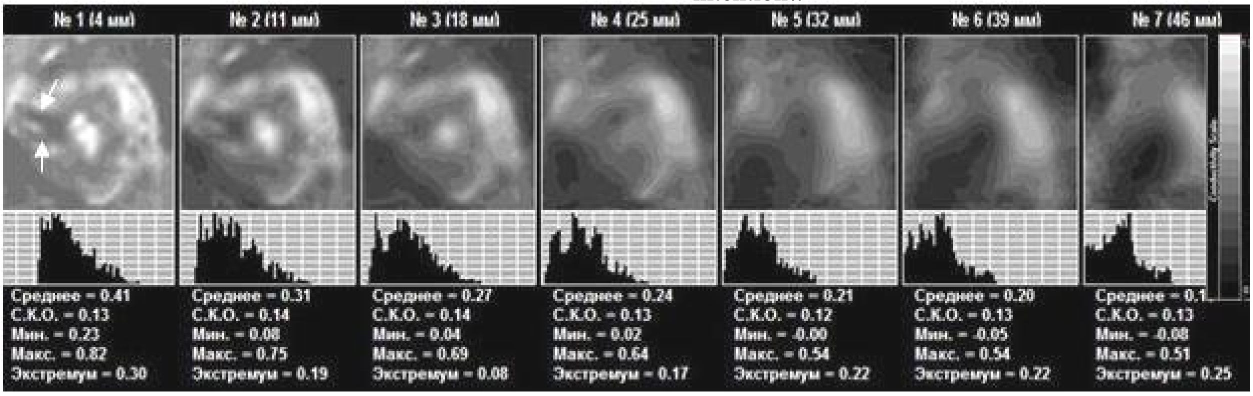



**Рис. 8-11.** EIM. In the outer segment of the electrical impedance image at 9 o'clock position there is observed a hyper-impedance linear area with an iso-impedance line in the middle which corresponds with the scar on the skin in its size and form.

*Electric impedance imaging of the mammary gland and suntan*

The ultraviolet radiation affects the skin like aseptic inflammation (fig. 8-12). So that firstly in the radiation zone the phase of the arterial hyperemia takes place, which increases the permeability of the vascular walls, is accompanied by oedema. Clinically it shows itself in the form of erythema. The next phase changes to the passive [venous] hyperemia with migration of leukocytes, clinically shown by infiltration. In the process of the migration of leukocytes to the focus of inflammation, infiltrate appears. Large amounts of cellular substance causes the sharp decrease of electrical conductivity. In the electric impedance mammograms the infiltrate is observed as a homogeneous hyper-impedance area (IC<0.1) with a distinct contour (Fig. 8-13).

**Рис. 8-12.** The image of the mammary gland with a solar burn in the upper-inner segment.

*Electric impedance imaging of the mammary gland and acne consequences*

Acne is caused by staphylococcus and reveals in the inflammatory bright-pink tubercle up to 5 mm in diameter. The process results in the formation of the light spot with distinct contour in the place of affection. Hystologically, the inflammatory focus is substituted by the connective tissue, mainly, by the amorphous substance of the connective tissue. These processes cause the decrease of the electrical

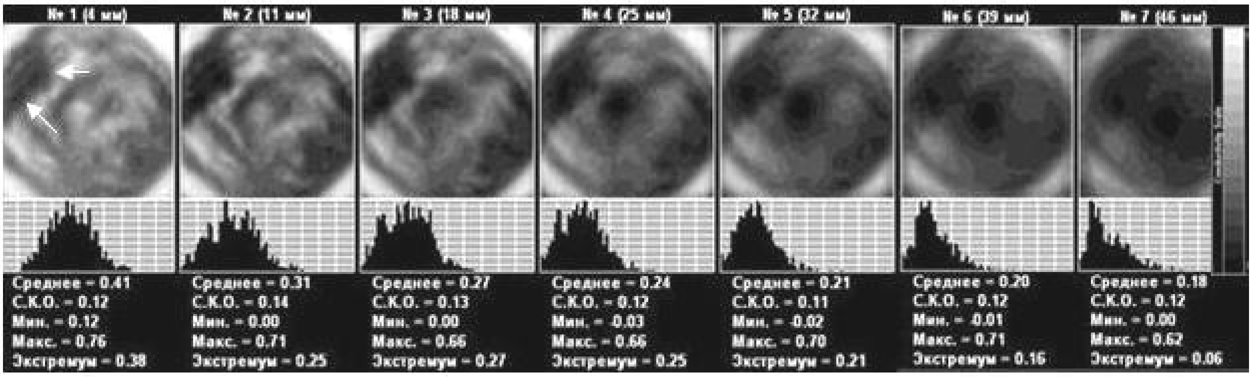



**Рис. 8-13.** EIM. In the upper-inner segment there is observed a wide hyper-impedance area corresponding with the location of the solar burn on the skin.

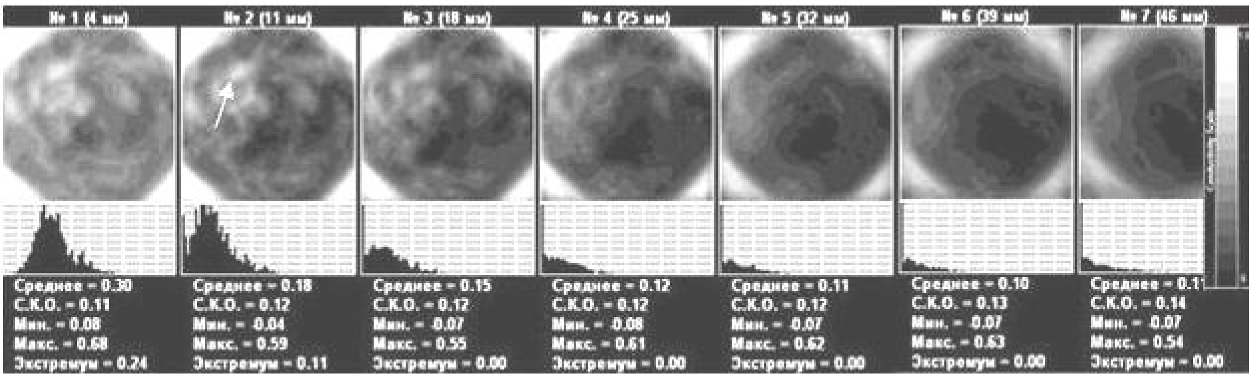



**Рис. 8-14.** EIM. In the upper segment at 11 o’clock position there can be visualized an iso-impedance formation of rounded shape with clear contours..

impedance of the affected area. In the electrical impedance image it is observed as a homogeneous iso-impedance area (IC=0.6-0.7) with sufficiently distinct contours (Fig. 8-14).

Thus the given research proves that the method of the electrical impedance mammography allows diagnosing various skin affections. The state of the cutaneous covering can affect the electrical impedance image, but, mainly, this influence has local nature, the fact that should be taken into consideration when analyzing the electrical impedance image. The detected peculiarities of the local changes of electrical conductivity in the case of various skin affections depend on the histological tissue architecture.

Collagen fibers and epithelium with hyperkeratosis cause the increase of the electrical impedance. And on the contrary, amorphous substance of the connective tissue and the large amount of the sebaceous humour cause the decrease of the electrical impedance. Further research in this sphere can help to describe in detail the peculiarities of the electrical impedance image in the cases of benign or malign tumors, inflammations or skin affections. So that it will be possible to use the electrical impedance method not only for diagnostics of mammary gland deceases, but also to detect and dynamically control the treatment of the skin affections.

# Electrical Impedance Scanning during Menstrual Cycle

# 9

Mammary gland is a functionally important female sexual character. Development and functions of mammary glands are closely connected with reproductive processes which are characterized by the specific rhythmicity. Mammary gland gradually reaches its full growth under the influence of hormones. Hormonal regulation of the mammary gland function represents more difficult phenomenon than the mechanisms, which control the sexual function. Synchronic participation of several endocrine mechanisms is necessary for normal development and functioning of mammary glands. Hypothalamic-hypophyseal system, ovaries, placenta, adrenal glands and thyroid gland participate in this synchronization of functions.

## Physiology

The production of estrogens, progestins and prolactin in the organism of an adult woman undergoes cyclic changes (Fig. 9-1). During the menstrual cycle the mammary glands are affected by sex hormones. The cells are differentiated under the influence of estrogens but do not produce any secreta until they are repeatedly stimulated by progesterone.

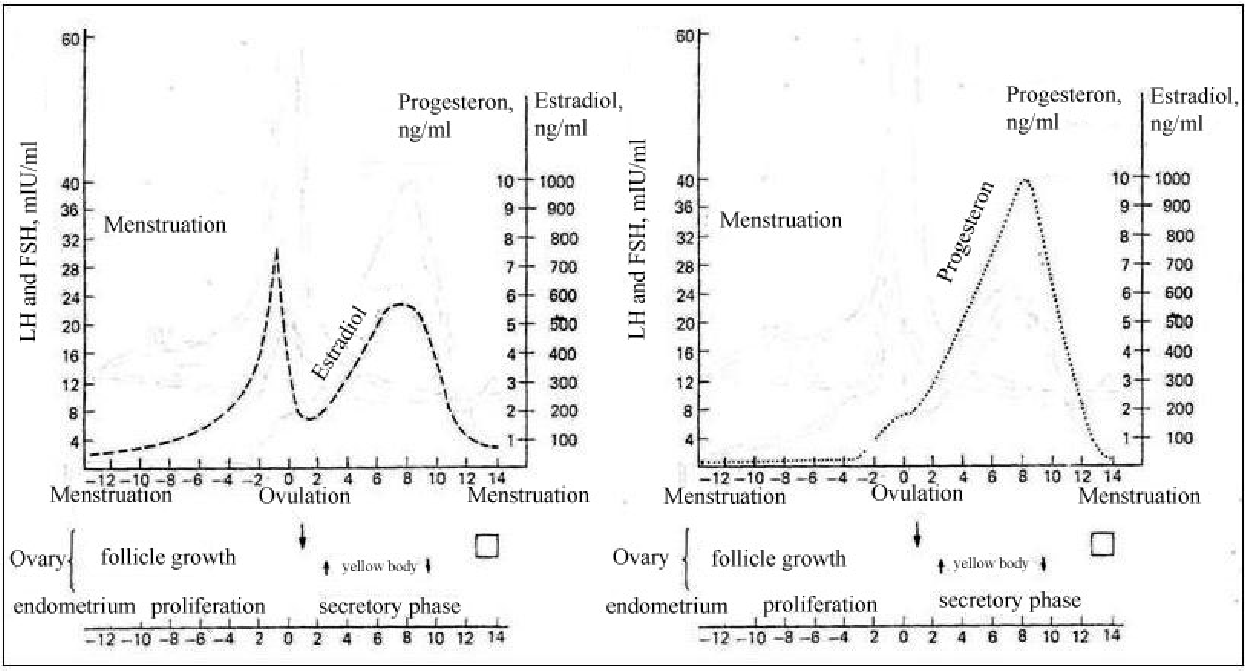



**Fig. 9-1.** The concentration of hormones in the blood during the structural and functional changes in the ovaries and endometrium during the menstrual cycle in humans {Speroff L., Van de Wiele R.L. (1971) Am. J. Obstet. Gynecol. 109, 234}, amended).

## Histology

The development of gland tissue structures is ensured by the equilibrium of proliferation, differentiation and apoptosis. At childbearing age the mammary gland epithelium exposes itself to cyclic cell proliferation and apoptosis both being secondary to the cyclic function of the ovaries. Encouraged by estrogens, the proliferation processes in the duct epithelium are observed throughout the menstrual cycle. The indications of the glandular epithelium secretion maintained by progesterone appear on the 20th day of the menstrual cycle.

## Quantitative assessment of electrical impedance images

Electric impedance imaging of the mammary gland has specific age-related peculiarities, which are connected with age-related anatomic and histological changes.

Two determining factors can be marked out in visual evaluation procedure of the electrical impedance image of a healthy breast:

- anatomical structure of the mamma shall correspond to the age period;
- absence of focal symptoms beyond the lactiferous sinus zone in all scan planes.

Fig. 9-2 shows electrical impedance images of mamma of women of different age. Anatomical structures, which are typical for younger women, gradually disappear when a woman grows older. Pathologic focal symptoms are absent in all the electrical impedance images.

## Electrical Impedance Measurement

*Phase electrical conductivity*

The analysis of mammas electric conductivity in different phases of the menstrual cycle showed that there is no significant difference in phase

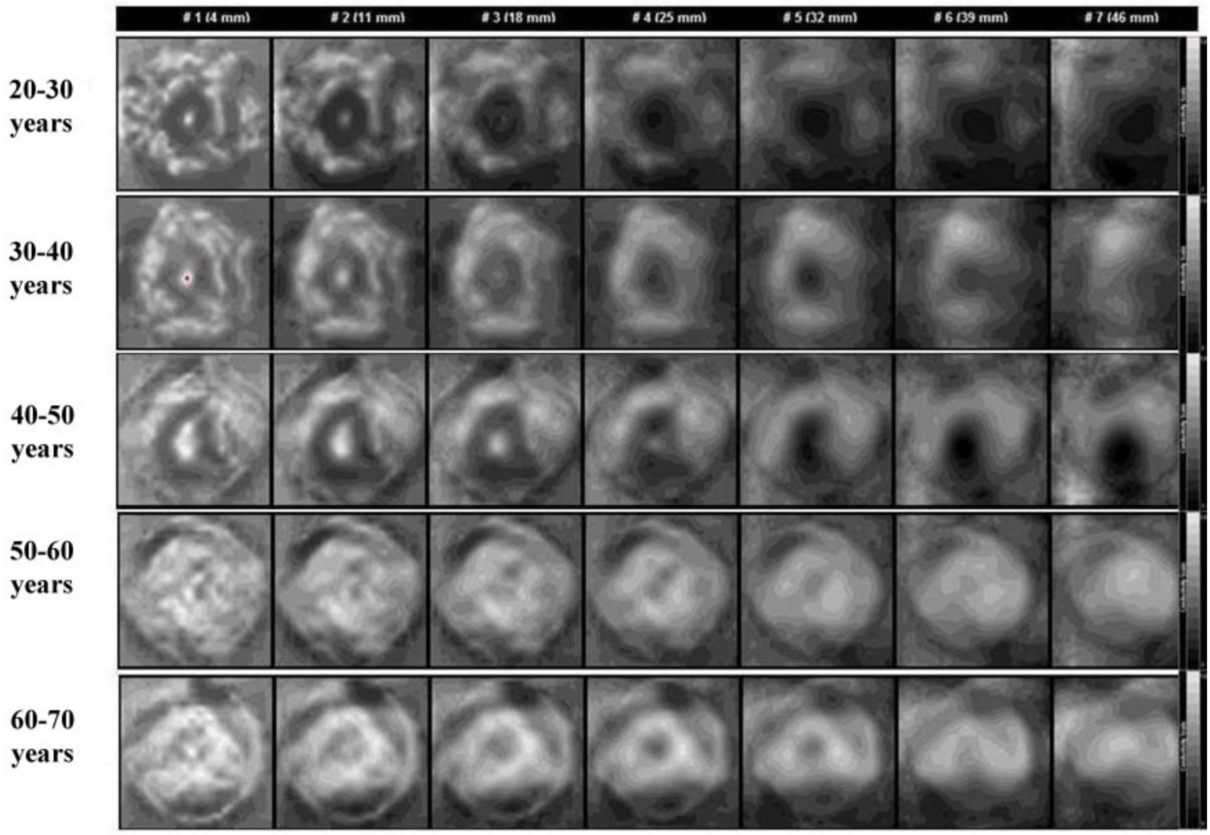



**Fig. 9-2.** EIM. Age-related peculiarities of electrical impedance images

electrical conductivity.

Phase electrical conductivity values vary within a level, slightly increasing either during first of during second phase of menstrual cycle (0±2SD) (Fig. 9-3).

shape with distinct contour. The second row represents the image of the breast typical of the second phase of the menstrual cycle. The lactiferous sinus zone is visualized in the center of the

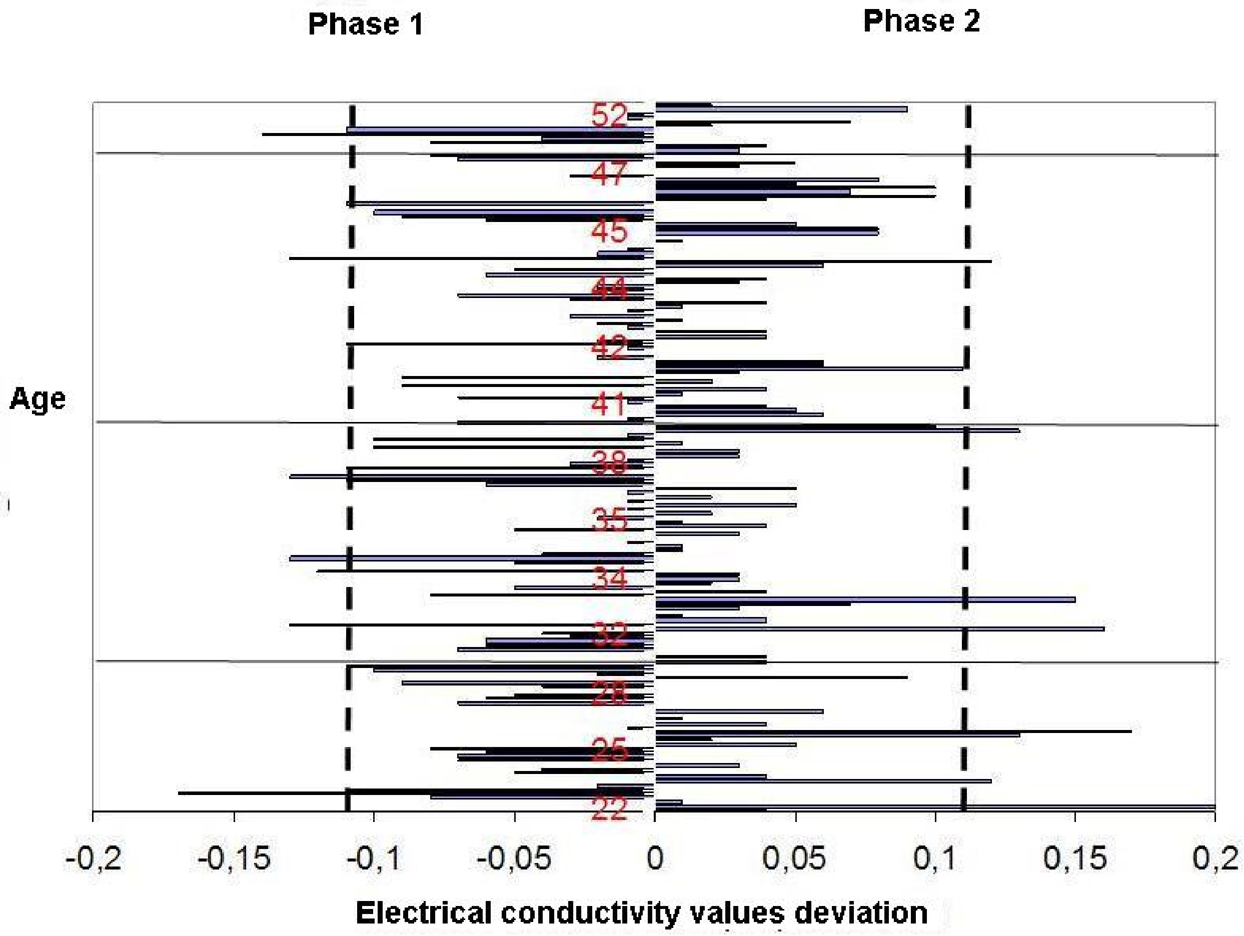



**Fig. 9-3.** Age-related variability of average electrical conductivity index during 1st and 2nd phases of menstrual cycle (dotted line correspond to two standard deviations).

This phenomenon indicates that the processes, which lead to significant local or total changes of electrical conductivity, do not occur in a healthy mammary gland during menstrual cycle.

The lactiferous sinus zone is the exception to this rule, as it can accumulate electrically active compounds of secreta or milk, which lead to the local "storage" effect. Most often the lactiferous sini can be visualized during first phase of the cycle and during lactation (Fig. 9-4). The image of the breast in the first row is typical of the first phase of the menstrual cycle. The lactiferous sinus zone is visualized in the center of the image as a hyperimpedance area of rounded image as a hyperimpedance area with blurred contour. The third row represents the image of the breast during lactation. The lactiferous sinus zone is visualized in the center of the image as a vast hypo-impedance area.

*Comparative electrical conductivity*

The comparison of electrical conductivity values of left and right mammary gland showed that during the first phase of cycle the difference in electrical conductivity values of them is insignificant.

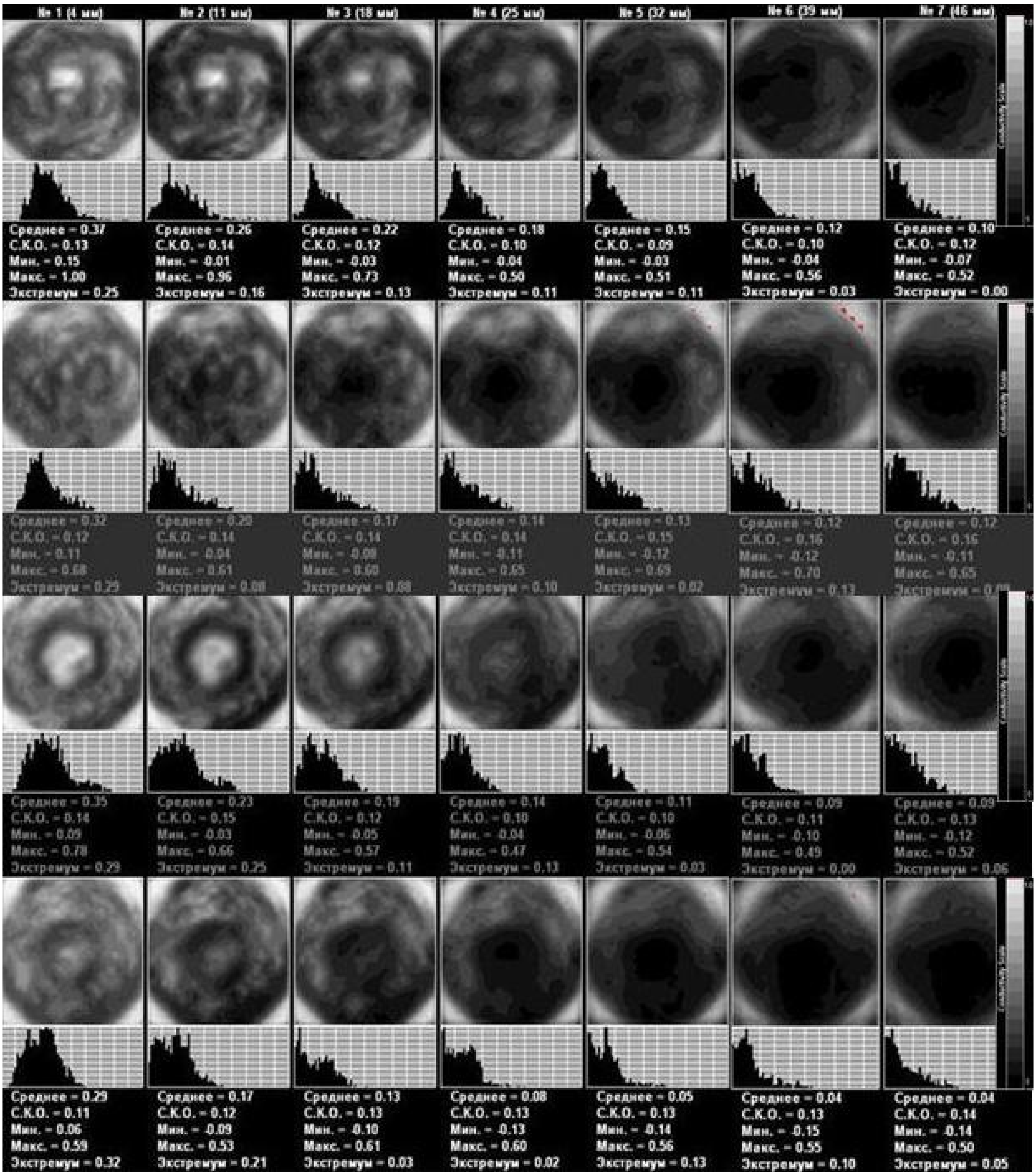



**Fig. 9-4.** EIM. Seven scan planes. The first line shows the tomogram during the first phase of the menstrual cycle. The fourth line represents the tomogram during the second phase of the menstrual cycle. The seventh line shows the tomogram during lactation period before feeding. The tenth line shows the tomogram during lactation period after feeding.

There is no electrical conductivity predominance of any gland. The difference in electrical conductivity values varies within a certain range (0±2SD) (Fig. 9-5).

The comparison of electrical conductivity values of left and right mammary gland during the second phase of menstrual cycle showed that a certain predominance of electrical conductivity values of the right mammary gland takes place, as can be seen from the figure (Fig. 9-6).

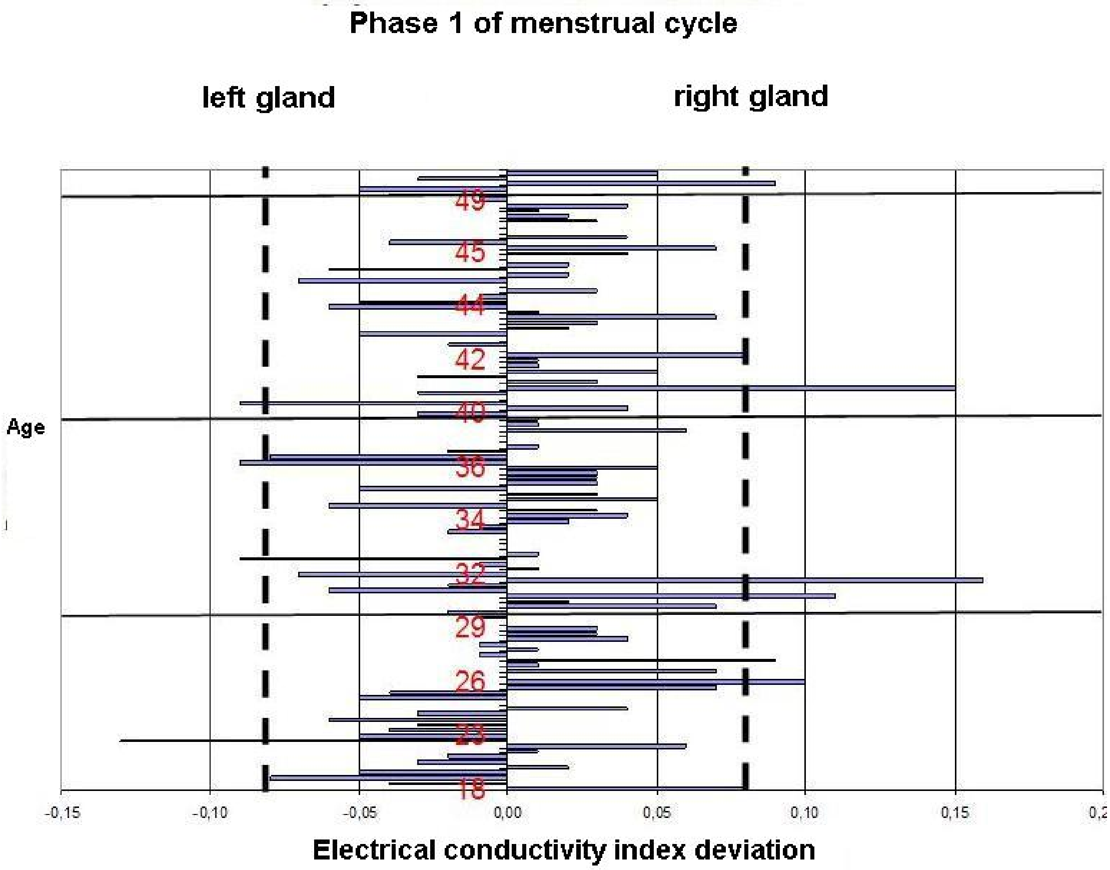



**Fig. 9-5.** Age-related variability of average electrical conductivity index of left and right mammary gland during 1st phase of menstrual cycle (dotted line correspond to two standard deviations).

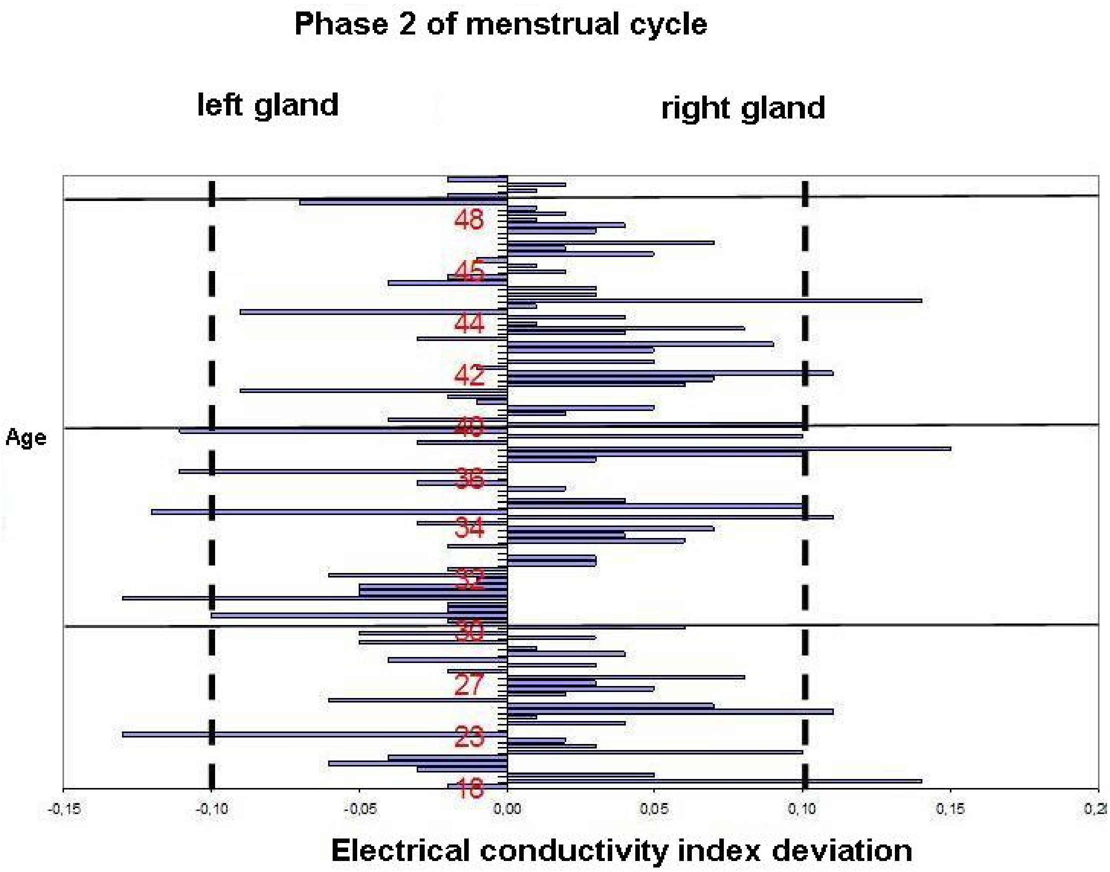



**Fig. 9-6.** Age-related variability of average electrical conductivity index of left and right mammary gland during 2nd phase of menstrual cycle (dotted line correspond to two standard deviations).

*Age-related electrical conductivity*

The analysis of age-related electrical conductivity of mammas showed that the average electrical conductivity index increases with age.

This phenomenon is conditioned by the remodeling of breast tissues and, especially, by the process of replacement of duct components with connective tissue structures. Fig. 9-7 shows the percentile curves of age-related electrical conductivity of the mammary gland. Each age group corresponds to a certain range of electrical conductivity.

Also it was observed that the variability of electrical conductivity index of left and right mammas reduces with age (Fig. 9-8).

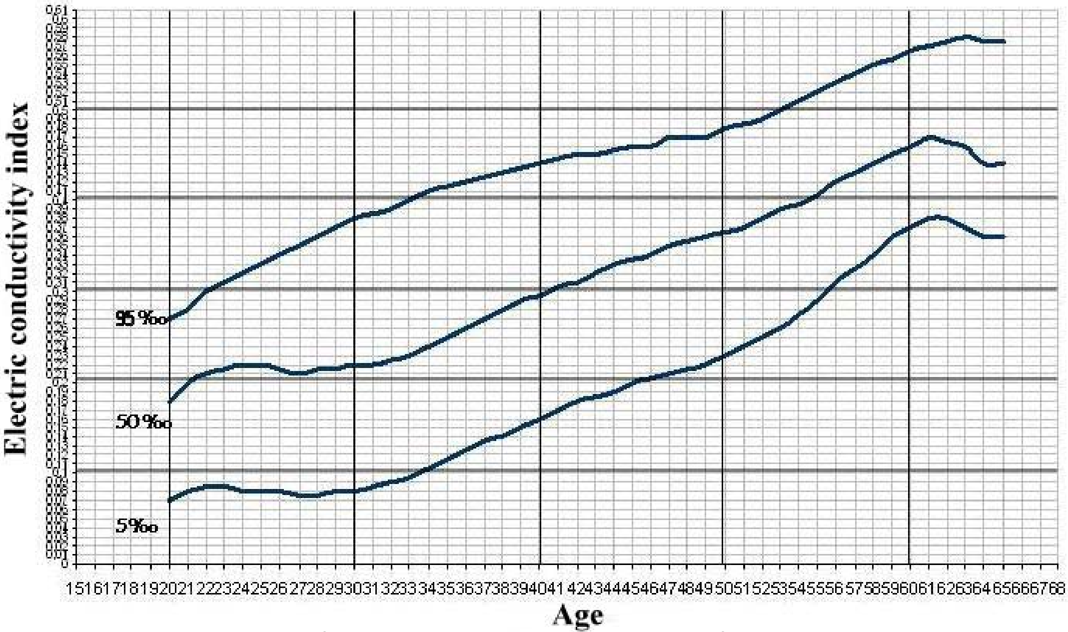



**Fig. 9-7.** Percentile curves of age-related electrical conductivity of the mammary gland.

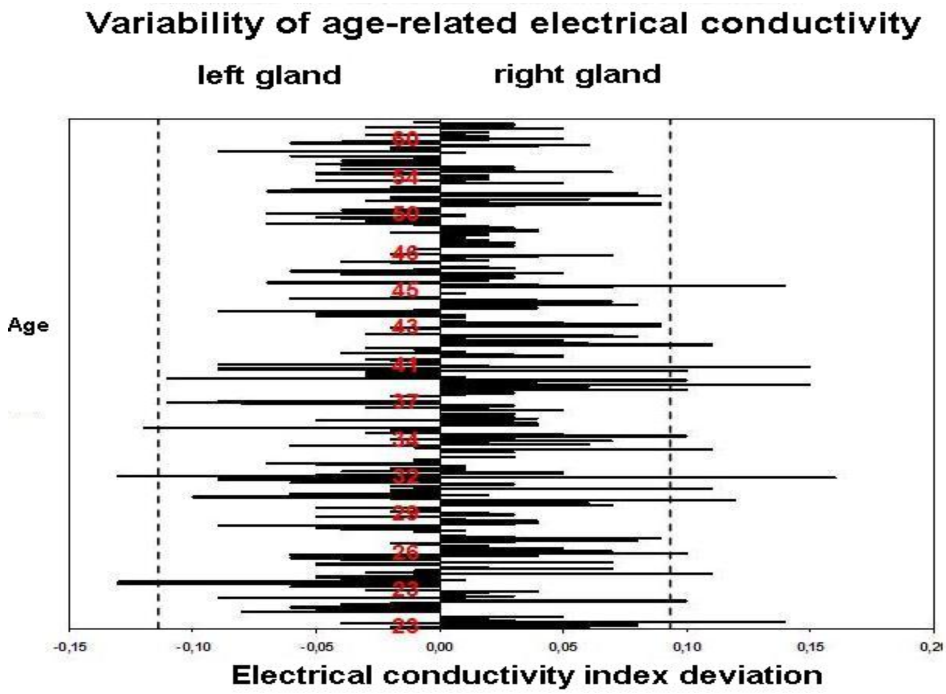



**Fig. 9-8.** Age-related variability of average electrical conductivity index of left and right mammary gland (dotted line correspond to two standard deviations).

This is conditioned by the fact that the activity of ovaries gradually changes during childbearing age, these changes are mainly represented by sex hormones synthesis alteration and reduction.

Age-related involutive processes are observed in the mammary gland against the background of estrogens and gestagens production reduction (Fig. 9-9).

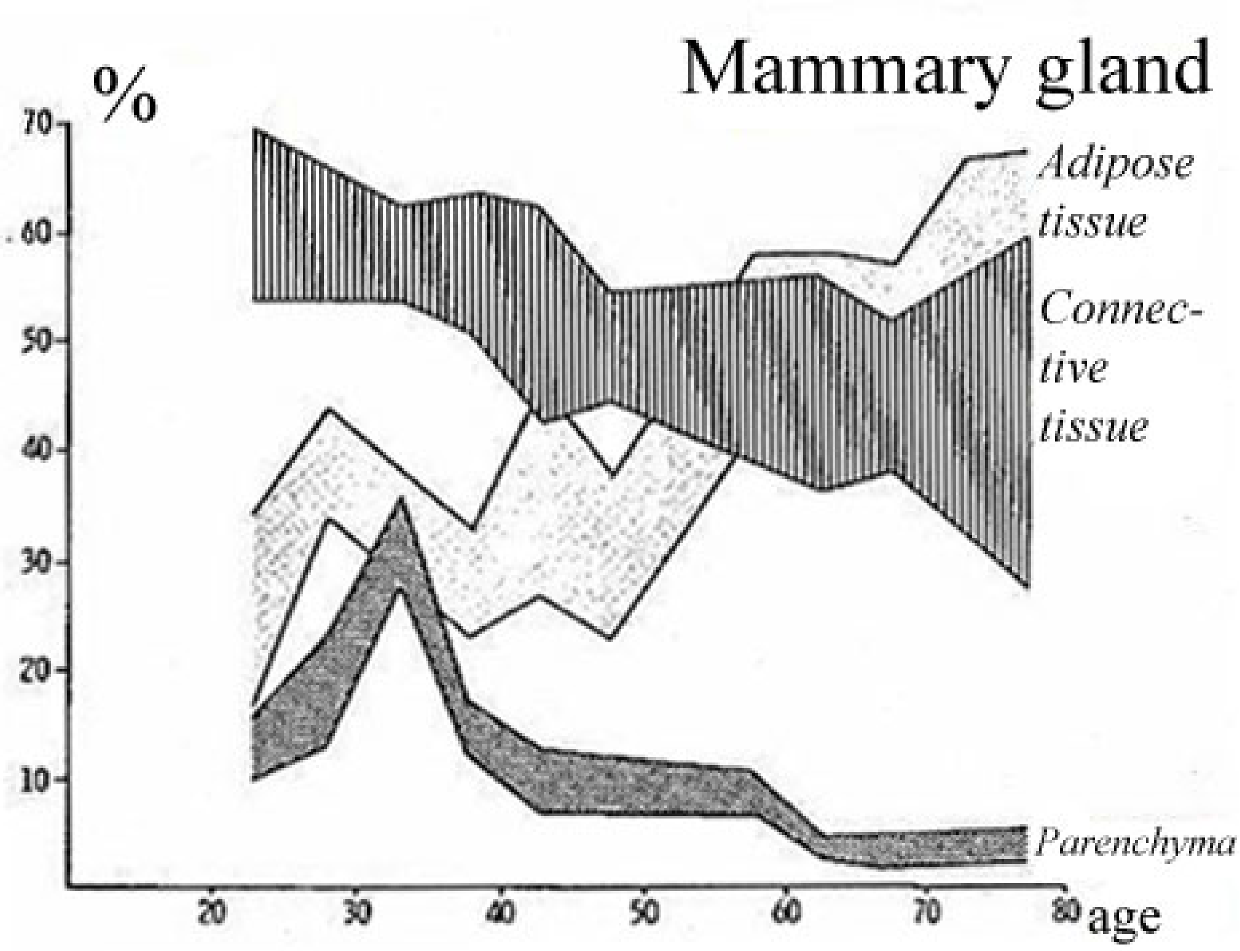


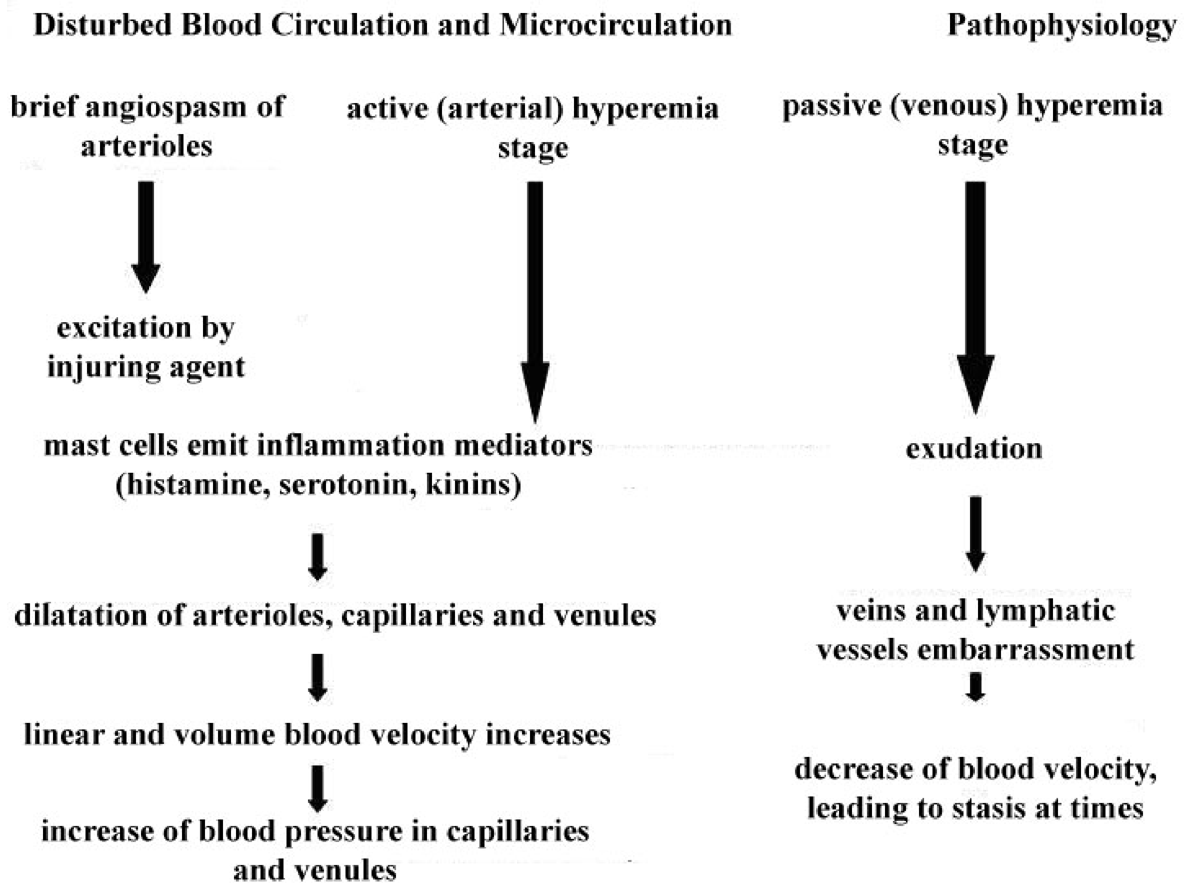

**Fig. 9-9.** Age involution of the parenchyma, connective and fatty tissues of the mammary gland (Page D.L., Anderson T.J. Stages of breast development. In: Diagnostic histopathology of the breast. Churchill Livingstone, New York 1987, 11-29).

# Electrical Impedance Measurement in Case of Mastitis

# 10

Inflammation (Lat. inflammatio – ignite, set on fire) - pathological process characterized by the development of local alterative, vascular and proliferative reactions of an organism to ill effects. Inflammation is one of fundamental pathologic processes, which compose the pathophysiological basis of many human's deceases (for instance: encephalitis, myocarditis, pneumonia, stomatitis, influenza, diphtheria etc.). The mechanisms of the inflammatory process are universal. The laws of its development are common irrespective of the structural and functional peculiarities of the tissue. Every inflammatory process passes several stages in its development, though any phase division should be considered relative. One distinguishes the following stages in the development of the inflammatory process: alteration, disorder in vascular supply and microcirculation, proliferation.

As far as the mammary gland is concerned, the inflammatory processes develop in the loose connective tissue and are accompanied by a complex of vascular changes with the exudation of




**Scheme 10-1.** Pathophysiology of inflammation. Disturbed Circulation and Microcirculation Stage.

plasma liquid elements, the emigration of blood cells and the proliferation of stroma cells.

### Alteration

Alteration (L. alterare – change) is a lesion in the structure of cells, tissues and organs. Initial alteration arises from a direct disease-producing impact on the cell structures of the organ. This phase is very short-term and quickly passes into the second stage – the stage of disorder in vascular supply and microcirculation (Scheme 10-1).

### Disorder in Vascular Supply and Microcirculation

In response to the excitation by an injuring agent of vasoconstrictive nerves in the smooth muscle cells of arterioles there emerges a brief angiospasm, which, however, quickly subsides as the mediator of the sympathic innervation – noradrenalin – is destroyed by monoamine oxidase, the amount of which grows rapidly in the inflammatory tissue.

### I. Active (Arterial) Hyperemia Stage

*Pathophysiology*

Mast cells emit inflammation mediators (histamine, serotonin, kinins, heparin, etc.), which results in the dilatation of arterioles, capillaries and venules (capillary veins). Linear and volume blood velocity increases. Blood pressure rises in the capillaries and veins, arterial flow dominating over venous drainage.

*Histology*

Rise of the blood pressure brings about the structural change of the endothelial capillary wall. The structure of endothelial walls is unstable, movable. Pores and fissures are generated in it under the influence of

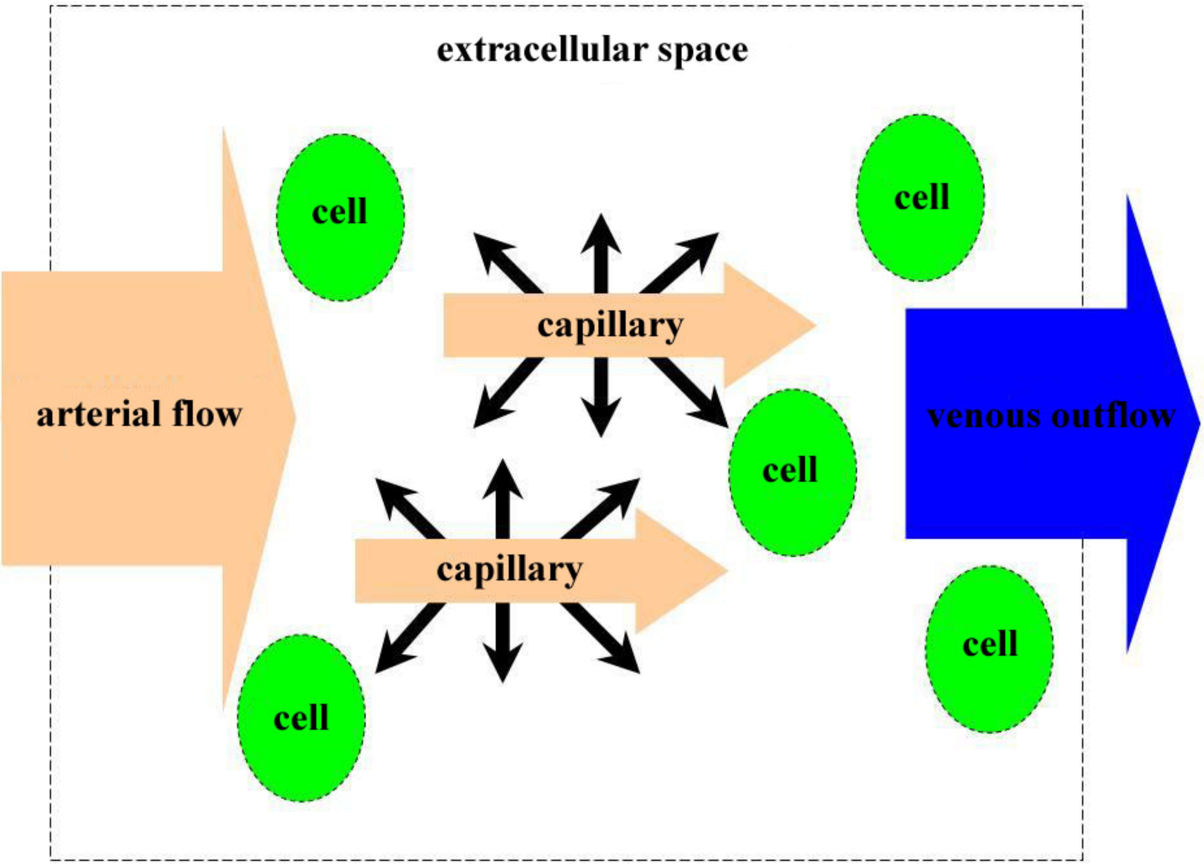



**Fig. 10-1.** Pathophysiology of inflammation. Disturbed Circulation and Microcirculation Stage. Active (Arterial) Hyperemia Stage (A.Kink, M.Min et all. Bioimpedance Based Analysis of Tissue Oedema. Proceedings of ICEBI XII – EIT V, 2004, amended).

high blood pressure. High osmotic and oncotic pressure in the inflammatory tissue creates diffusion and osmotic liquid flows hereto (Fig. 10-1). It is in the tiniest ducts (pores) where ions, water and blood plasma proteins dissolved in it are filtered. This process is maintained by such mediators as histamine, bradykinin and others. As inflammation develops, they induce the compression of actomyosin fibers of endothelial cells. The compression of the cells results in the widening of the interendothelial fissures, the formation of fenestras and pores as well as causes an edema under the endothelium, whereas the edema itself stimulates the formation of fissures and pores. All this encourages an activation of exudative processes. Thus the inflammatory tissue experiences the development of extra-cellular edema.

*Electrical Impedance Dynamics*

The amorphous substance of the connective tissue is a semiliquid heavy-bodied gel which consists of macromolecules, polysaccharides mostly, and a large amount of tissue fluid. The base component of the substance is glycosaminoglycan, i.e. hyaluronic acid (Fig. 10-2). The presence of hydroxyl and carboxyl functional groups in the acid provides for a big number of negative charges born by it. This determines the pronounced electronegativity of the connective tissue. By the instrumentality of the charges do glycosaminoglycans bind intercellular water as well as control the osmotic pressure and the ion content of the connective tissue base substance. At the stage of arterial hyperemia the exudation process leads to a change of electrical impedance figures in the zone of lesion. The hydropic fluid containing positively charged ions suppresses the negatively charged hydroxyl and carboxyl groups of the hyaluronic acid. Thus, the local electronegativity of the connective tissue is neutralized, free and associated water being formed. This brings about a decrease in the resistive component of impedance and raises the electrical conductivity in the zone of inflammation.

*Electrical Impedance Visualization*

In the alteration stage that is characterized as short-term, no significant change in the electrical properties of the affected tissue is observed. Besides, it often remains undiagnosed as patients as a rule fail to seek medical advice at this point.

During the stage of vascular changes, hyperemia area and oedema can be observed clinically (Fig. 10-3). The increase of blood flow and the appearance of intra-cellular edema lead to a rise in the electrical conductivity. During this stage electrical impedance mammograms image hypo-impedance regions with high electrical conductivity index which correspond to the zones of oedema. On the periphery it is

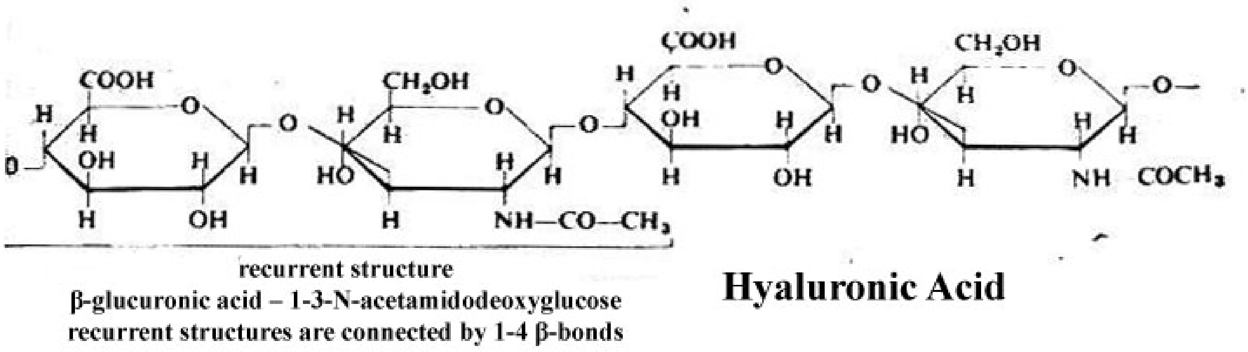



**Fig. 10-2.** Hyaluronic acid is the base component of the connective tissue. Molecular weight exceeds 10 million Its recurrent structure - β-glucuronic acid – N-acetamidodeoxyglucose (Biochemistry, D. Metzler, 1980).

**Fig. 10-3.** Image of the mammary gland during the vascular changes stage.

contoured by the leukocytic infiltrate delimiting the nidus of inflammation. This finds its reflection in the electrical impedance image in the form of a hyper-impedance contour passing along the periphery of the inflammatory tissue and having high electrical conductivity index (Fig. 10-4).

**II. Passive (Venous) Hyperemia Stage**

*Pathophisiology*

With the augmentation of the inflammatory edema the venous drainage becomes hampered, which causes the transition of arterial

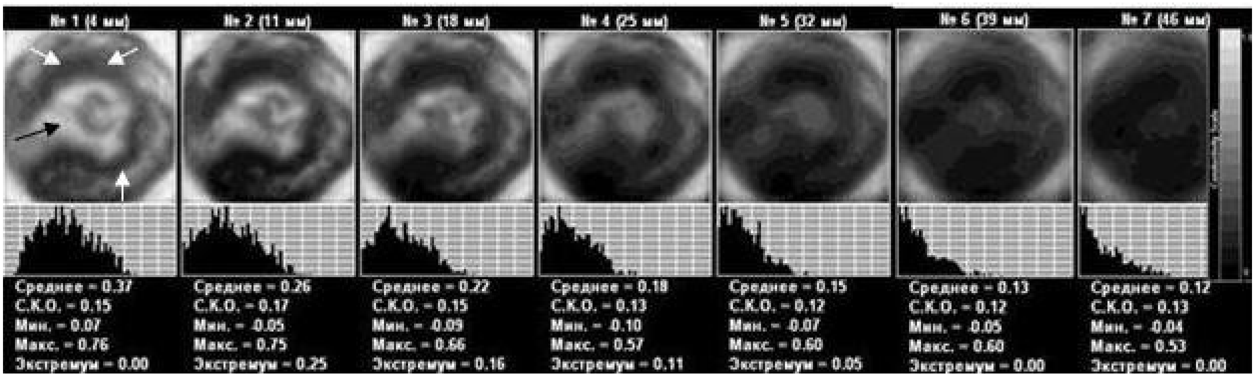



**Fig. 10-4.** EIM. Disturbed Circulation and Microcirculation Stage. Active (Arterial) Hyperemia Stage. A significant hypoimpedance mass with a hyperimpedance contour is situated in the center of the mammogram.

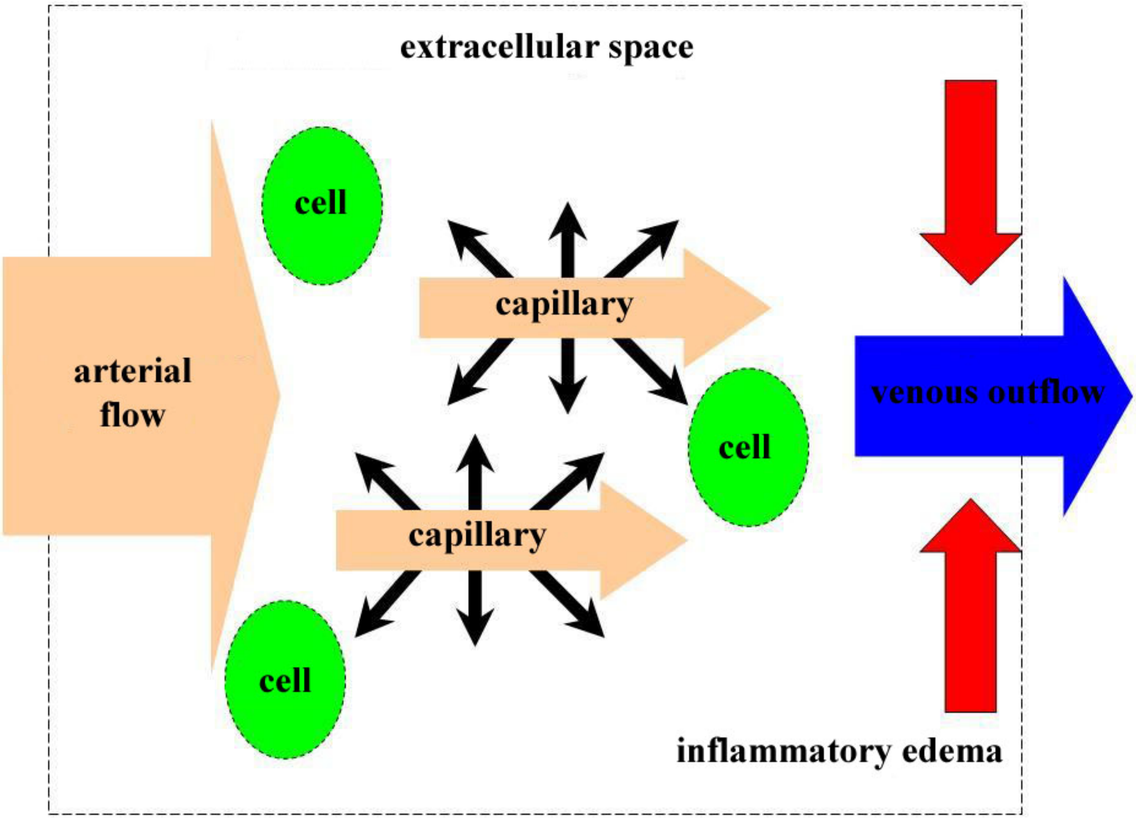
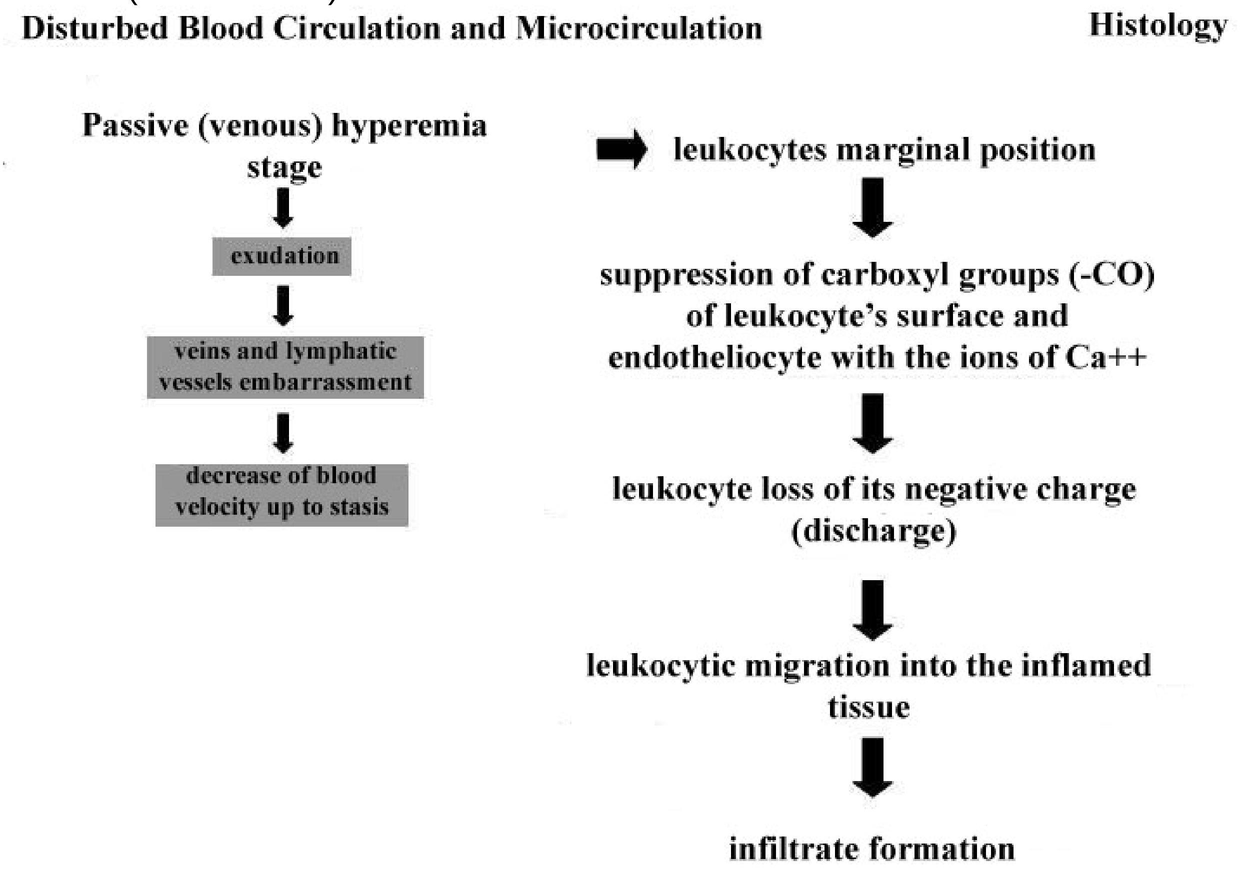



**Fig. 10-5.** Pathophysiology of inflammation. Disturbed Circulation and Microcirculation Stage. Passive (Venous) Hyperemia Stage (A.Kink, M.Min et all. Bioimpedance Based Analysis of Tissue Oedema. Proceedings of ICEBI XII – EIT V, 2004, amended).

hyperemia into venous (Fig. 10-5). This process is determined by the rise of blood pressure (hydrostatic uplift) in the venous part of the inflammatory tissue capillaries as well as the decrease of linear and volume blood velocity, leading to stasis at times.

*Histology*

Caused by an increasing extra-cellular oedema, the blood and lymph drainage of the inflammatory zone becomes difficult, which stimulates a quality change of the inflammatory oedema (Scheme 10-2).




**Scheme 10-2.** Pathophysiology of inflammation. Disturbed Circulation and Microcirculation Stage. Passive (venous) hyperemia stage.

negotiation of the capillary basal membrane and the transfer to the inflammatory zone. The intense flow of the exudate significantly facilitates the passage of the leukocytes through the capillary wall. A leukocytic infiltrate emerges in just 6 hours after the inflammation starts. Neutrophilic leukocytes display high phagocytal activity mainly eating up microorganisms. Some of the neutrophils decompose emitting large amounts of lysosomal hydrolysts, which leads to pyogenesis.

The emigration of leukocytes to the inflammatory tissue starts in the stage of arterial hyperemia reaching its peak in the stage of venous hyperemia. This is assisted by feebleness of blood flow or its complete stop at times. The migration of leukocytes comes through several phases: marginal position, the

*Electrical Impedance Dynamics*

When the inflammation develops the leucocytes infiltrate tissues, locating in large amounts around blood vessels and between the cells of inflamed tissue. During migration leukocytes lose their negative charge as the carboxyl groups of their membranes enter into combination with the ions of Ca++ thus forming the so called “calcium bridges”. The neutralization of negatively charged connective tissue, the loss of the negative charge by leukocytes as well as

**Table 10-1.** Content of substances (in percentage terms) in liquor puris and blood plasma (A.Ado et all. «Physiopathology» Moscow, 1973).

| Composition | liquor puris | blood plasma |
|---|---|---|
| Water | 90-91 | 90-93 |
| Solid substances | 9-10 | 7-10 |
| Proteins | 6.3-7.7 | 6.1-7.8 |
| Fats and lipoids with cholesterol | 1-2 | 1-2 |
| Inorganic salts | 0.7 | 0.8 |

the increase in the amount of free water helps the leukocytes to easily move in the inflammatory zone. The migration of leukocytes results in the formation of an infiltrate which contains a generous amount of cell substrate with leukocytes of various types. The surface area of the cell membranes increases substantially leading to a rise in the inductive component of impedance and a reduction of the electrical conductivity in the zone of inflammation.

The inflammatory process is accompanied by the destruction of leukocytes. Granular leukocytes contain a lot of hydrolytic enzymes (proteases, cathepsin, chymotripsin, etc.) which with the destruction of the leukocytes emerge in the surrounding tissue. The enzymes melt the tissue down providing for pyogenesis. The pus contains a residue consisting of cell elements and a liquid part, i.e. liquor puris (Table 10-1). The latter does not differ to any considerable extent from blood plasma. These processes result in decrease of reactive component of impedance and in increase of conductivity in the abscess formation area.

*Electrical Impedance Visualization*

When leukocytes migrate to the zone of inflammation an infiltrate is formed. The cumulation of cell substrate causes a plunge of electrical conductivity. In the electrical impedance

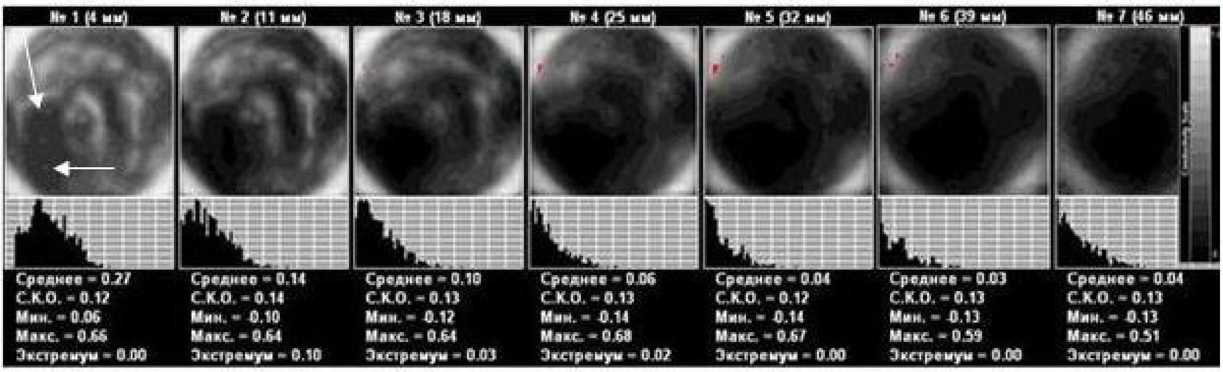



**Fig. 10-6.** EIM. Disturbed Circulation and Microcirculation Stage. Infiltration. A homogeneous hyperechoic mass can be visualized over an area from 7 to 9 on the clock dial.

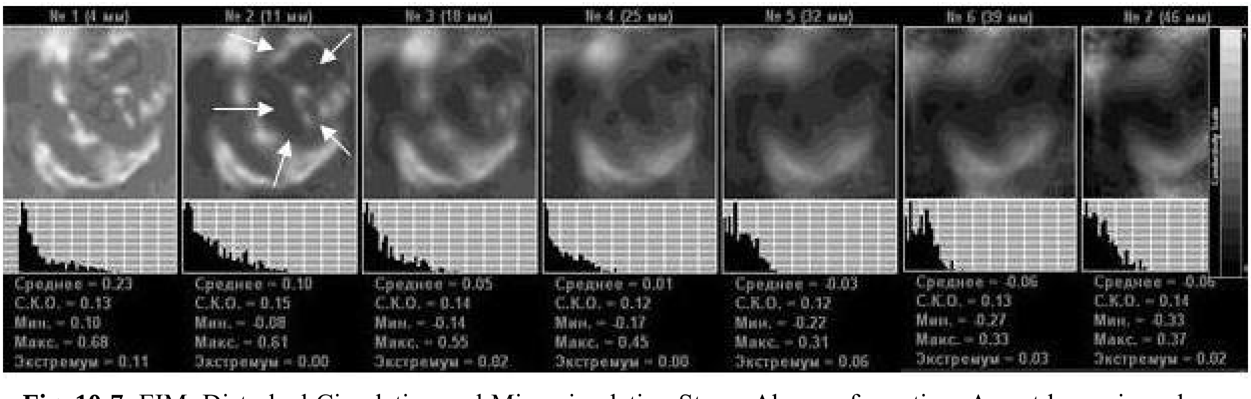



**Fig. 10-7.** EIM. Disturbed Circulation and Microcirculation Stage. Abscess formation. A vast hyper-impedance formation with isoimpedance inclusions can be visualized over an area from 12 to 3 on the clock dial.

mammograms (Fig. 10-6) the infiltrate can be visualized as a homogeneous well-defined hyper-impedance area with low conductivity index. Abscess formation displays itself by mollities of the inflammatory zone. Since pus is little different to blood plasma in its content, the leukocytic infiltrate loses its hyper-impedance homogeneity. The zones of pus accumulation are distinguished by high electrical conductivity.

The pyogenic infiltrate melt is shown on the electrical impedance mammograms as a process supported by a loss of homogeneity and appearance of hypo-impedance areas with high electrical conductivity index, which correspond to the zones of pus accumulation (Fig. 10-7).

## Proliferation

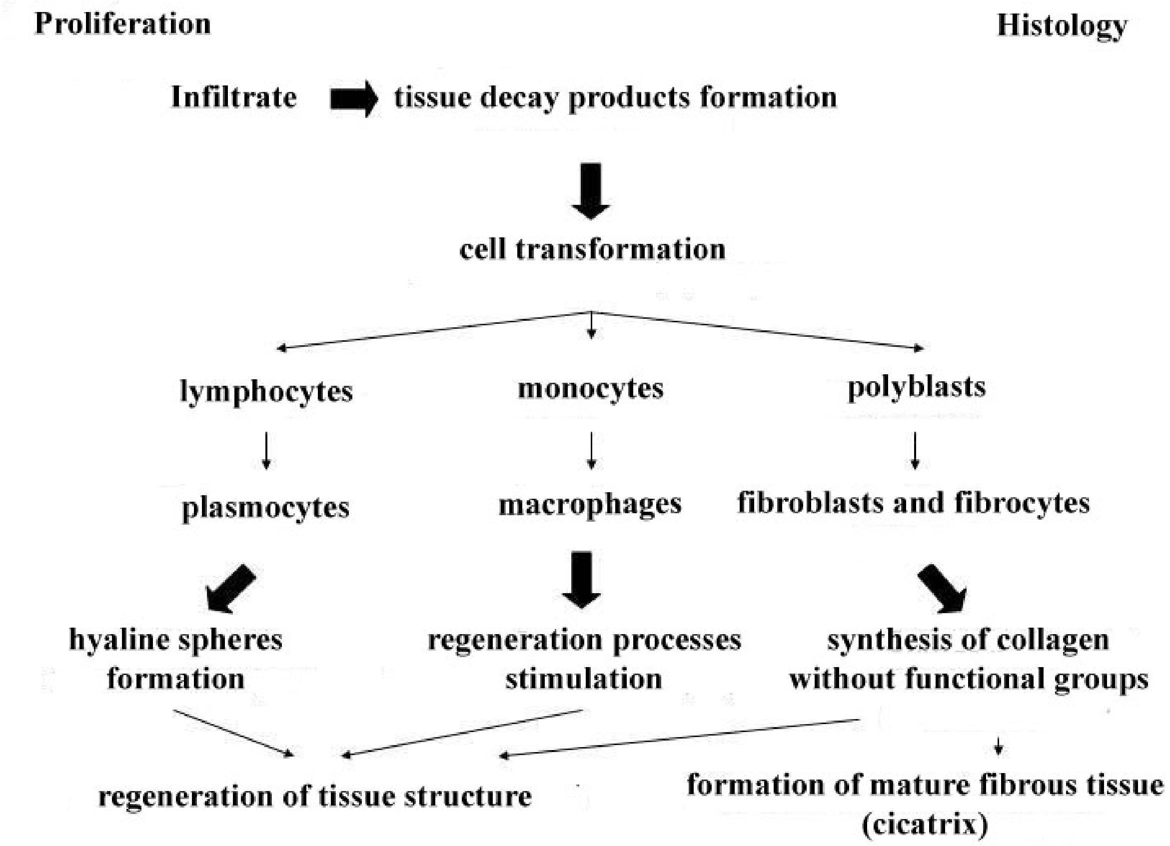
*Pathophisiology*

During inflammation the tissue always dissolves to a greater or lesser extent. Subsidence of a lesion at the stage of infiltration enables the affected tissue structure to recover completely and saves from any functional disorders. The tissue suffers to the utmost when undergoing purulent (suppurative) inflammation that normally leaves a cavity. Due to the proliferation of local connective tissue cells, i.e. fibroblasts, the tissue defect is gradually remedied, but neither the tissue structure nor its function is restored.

*Histology*

Macrophages actively phagocytize tissue decay products simultaneously differentiating into fibroblasts and fibrocytes.

They produce substances stimulating regeneration processes in the inflammatory zone. Cells of the fibroblastic family intensively proliferate. Fibroblasts make good the gross defect of the tissue. They produce the inter-cellular substance intensively, thus providing for the formation of collagen fibers. The fibers bound the




**Scheme 10-3.** Pathophysiology of inflammation. Proliferation Stage

inflammatory zone from the unaffected tissue. The development of fibroblasts gradually leads to the substitution of the former for the connective tissue. The tissue defect being substantial, a cicatrix appears in its place. When defect healing by primary intention, the cicatrix is formed which fully consists of collagen fibers. The defect healing by secondary intention, the cicatrix is formed of collagen fibers and the base substance of the connective tissue (Scheme 10-3).

*Electrical Impedance Dynamics*

The regression of the infiltrate is accompanied by its substitution for the connective tissue and the restoration of the electrical properties of the affected tissue (Fig. 10-8).

In case of significant tissue defect there are two possible variants of healing, which differ by the electrical properties of cicatrices being formed. When defect healing by primary

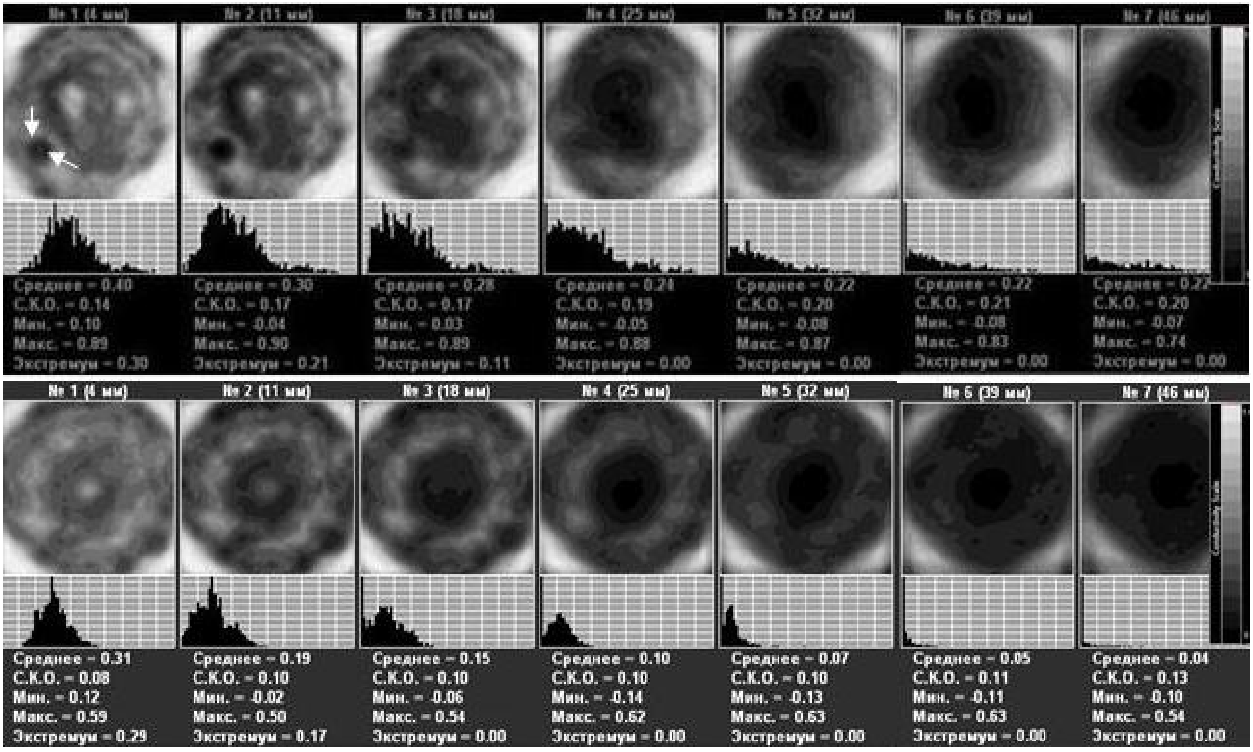



**Fig. 10-8.** EIM. First row – infiltration stage. A hyperechoic well-contoured mass can be visualized at 7 on the clock dial. Fourth row - structure recovery after the treatment.

intention, the cicatrix is formed of collagen fibers which have no polar functional groups and act as dielectrics. When healing by the second intention, the defect is articulated from the rest of the tissue by collagen fibers, and the nidus itself consists of amorphous substance of the connective tissue, the main component of which is hyaluronic acid. Therefore, the recovery zone is represented by the areas of high impedance (which is the characteristic of collagen) as well as by the areas of low impedance (which is the characteristic of amorphous substance of connective tissue).

*Electrical Impedance Visualization*

The stage of proliferation is characterized by the formation of a cicatrix. When defect healing by primary intention, the cicatrix turns out to have low electrical conductivity due to the presence of collagen fibers. In the electric impedance mammograms a cicatrix can be visualized as a hyper-impedance often irregular-shaped strip, which possesses low conductivity index (Fig. 10-9).

The defect healing by secondary intention, it has a heterogeneous structure with the inclusion of the connective tissue. In this case the cicatrix is represented as hyper-

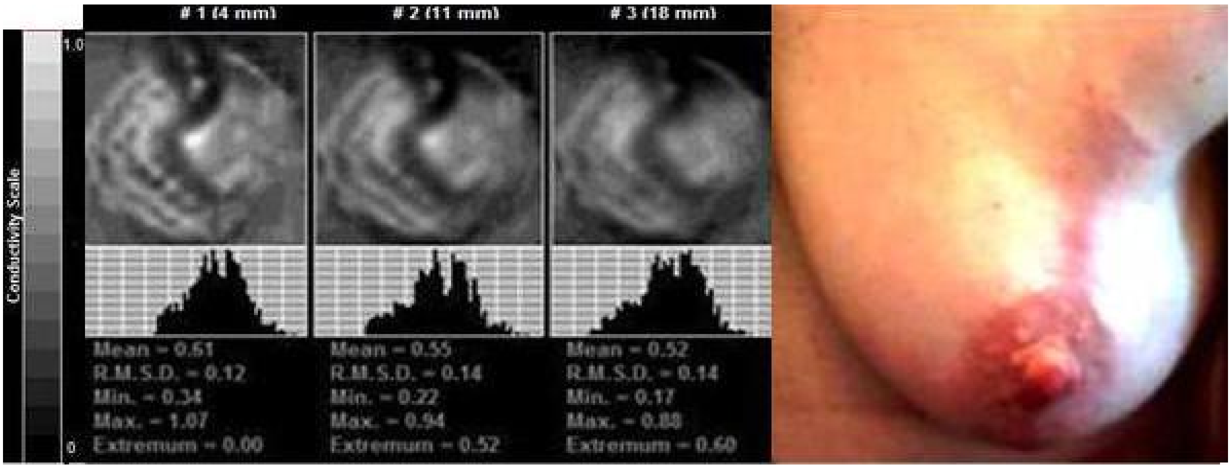



**Fig. 10-9.** 3 scan planes. In the upper segment there can be visualized a hyperimpedance strip corresponding to the location and shape of the scar.

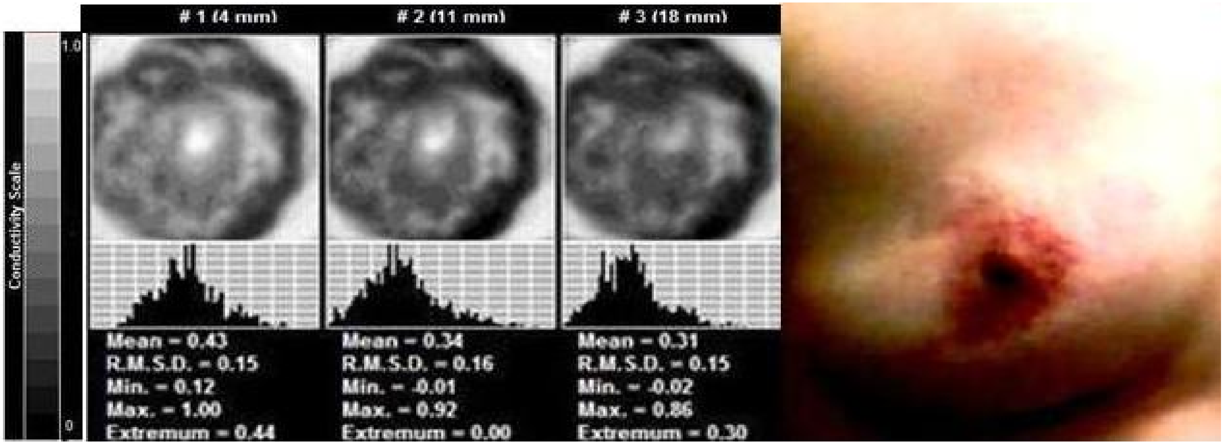



**Fig. 10-10.** EIM. 3 scan planes. In the upper segment there can be visualized a hyperimpedance area corresponding to the location and shape of the scar.

impedance stripes with a low index of electrical conductivity and an isoimpedance zone with a mean value of electrical conductivity located between them (Fig. 10-10).

Thus, pathophysiological stages of the inflammation process are accompanied by the alteration of the electrical properties of damaged tissues of the mammary gland.

Stage-dependent alterations of the electrical properties of mammary gland tissues define the peculiar features of the mammary gland electric impedance image. The imaging of different inflammation process stages by means of electrical impedance tomograms allows using this method to diagnose mastitis, choice of treatment and its monitoring.

# Electrical Impedance Measurement in Case of Benign Tumours

# 11

## Cyst

One of the causes why women consult a doctor is a formation in the mammary gland. Most often these formations are diagnosed as cysts. These benign tumours can be found during various age periods of woman.

*Pathophsiology*

Several factors contribute into the development of cysts. Firstly, the alveolar-ductal type of mammary gland structure presumes the possibility of cyst formation during any stage of secreta emerging and transporting via the complex system of ducts, starting from the generation of secreta (secretion proper), its transportation via the ducts and, finally, its suction (Fig. 11-1).

The fact that there are progesterone and estrogens receptors in the tissue of a mamma, makes the latter dependent on the hormonal function of the ovaries. Ovaries dysfunction leads to changes of quantity and physical and chemical properties of ductal secreta, which result in duct blocking, so that a cyst can emerge (Fig.11-2).

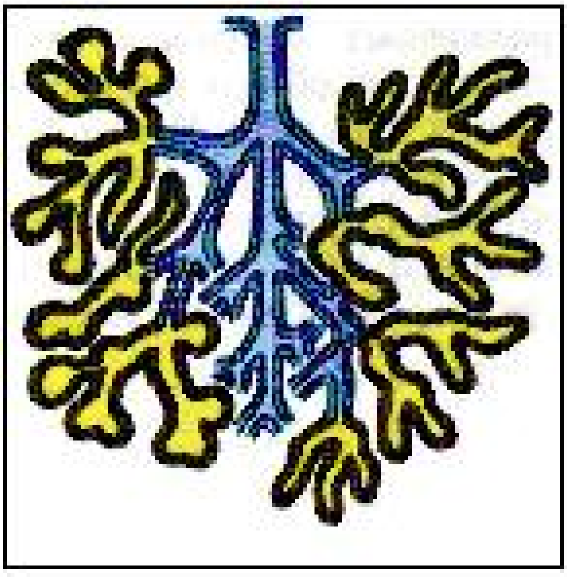


**Fig. 11-1.** Compound alveolar-tubular gland with branched acini.

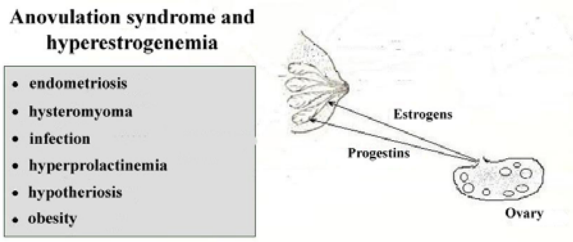



**Fig. 11-2.** Anovulation syndrome and hyperestrogenemia of various genesis can result in change of volume and physical and chemical properties of ductal secreta.

Moreover, one should bear in mind that mammas originate from perspiratory glands. The structure and function of mamma's glandular epithelium of non-pregnant women is very similar to the activity of the glandular epithelium of apocrine perspiratory glands: *location* – clusters in certain places of the cutaneous covering, for instance, apocrine perspiratory glands are located in axillary creases, forehead cutis, large lips of pudendum, anus area); *development time* – pubertal period; *structure* – tubular glands; *histology* – there are vacuoles in the epithelium cells which emerge and disappear depending on the phases of the menstrual cycle; *physiology* – these glands do not participate in perspiration; *function* – their function is closely connected with that of sex glands, it increases in premenstrual period, during this period the epithelium cells change their volumes; *secretion type* – apocrine.

Unsurprisingly, the mamma possesses an excretory function. It is known that many eatables and medicines can be excreted either with human milk or with mamma's secreta (Table 11-1). Unfortunately, there's no comprehensive information on the excretion of medicines. Almost all of them can be found in mamma's secreta. First of all, they are represented by the unionized substances, such as ethanol and urea. The table below represents the most commonly used medicines which can be found in human milk and mamma's secreta.

**Table 11-1.** Some medicines being excreted with milk and secreta (Pharmacology and Pharmacotherapeutics. RS.Satoskar, S.D.Bhandarkar 1986).

| | |
|---|---|
| **Antibacterial agents** | **Tranquilizers** |
| Streptomycin | Phenothiazines |
| Sulfanilamides | Diazepam |
| Nitrofurans | |
| Chloramphenicol | **Cytostatics** |
| Tetracyclines | |
| Nalidixic acid | **Miscellaneous** |
| | Ergot alkaloids |
| **Analgetics** | Oral anticoagulants |
| Morphine | Metronidazole |
| Methadone | Butamide |
| | Quinidine |
| **Sedatives and soporifics** | Some laxatives |
| | Lithium preparations |
| Barbiturates | Oral contraceptives |
| Chloral hydrate | Phenytoin |
| | |
| Scopolamine | |

The change of physical and chemical properties of the secreta under the influence of above mentioned medicines can lead to the formation of a cyst. The outer-ductal factors, such as post-operative scars, can result in mechanical compression of ducts and disturb secreta transport, which can further conduce to the formation of a cyst.

And, finally, the disorder of mammary gland tissue differentiation during pubertal period can result in the formation of large cysts (Fig. 11-3).

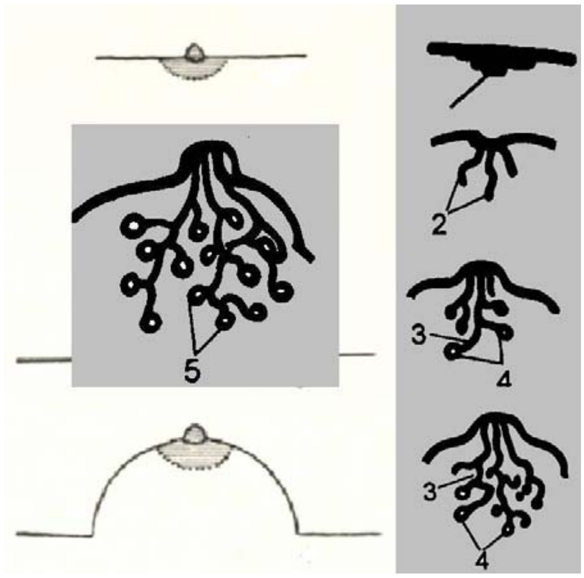



**Fig. 11-3.** Mamma's morphogenesis (top-down – embryogenesis, neonatal period, pubertal period, non-lactating gland. In the center – lactating gland

In connection with physiological peculiarities of each age period there are various mechanisms of these benign tumours formation.

*Histology*

In its structure a cyst cannot be considered as a proper tumour, as the proliferation element is missing. A cyst is a stretched epithelial "bag" filled with secreta of different viscosity. It's in case of the so-called retention cyst. In other cases various parietal spreads of cells emerge in the cavity of the cyst. These phenomena are typical of a proliferative cyst (Fig. 11-4).

*Electrical Impedance Dynamics*

Local accumulation of ductal secreta results in local changes of electrical conductivity. As a rule electrical conductivity in this area differs from that of surrounding tissues and the increase of electrical conductivity is due to chemical composition of secreta. Ductal secreta contains water, N-acetyllactoseamine, fat drops, a certain value of mineral salts and cast-off epi-

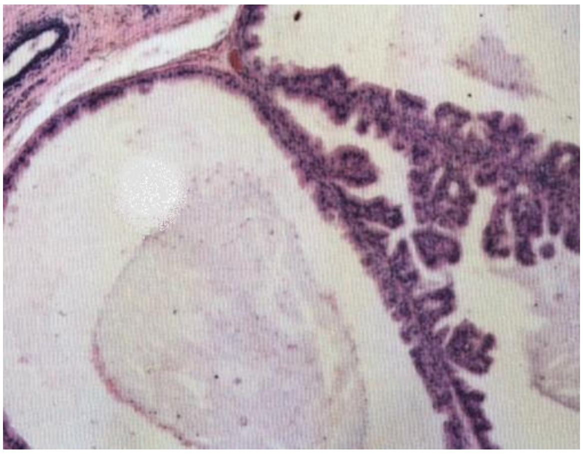


**Fig. 11-4.** There can be observed the cysts, lined with the epithelium of apocrine type containing papillary spreads (M. Paltsev et al. «Pathologic Anatomy Atlas», Moscow, 2003).

thelium. The combination of these elements brings about a decrease in the resistive component of impedance and raises the electrical conductivity.

*Electrical Impedance Visualization*

In the electric impedance mammograms cysts are observed as the well-defined areas of heightened electrical conductivity in several scan planes (Fig. 11-5).

The size of diagnosed cysts varies from 3 up to 40 mm, the index of electrical conductivity in these areas - from 0.5 up to 0.8 depending on secreta viscosity. The typical changes in electrical impedance images are observed during the whole menstrual cycle, but cysts are better visualized in the second phase of the cycle (Fig. 11-6).

This is explained by the fact that the secretory activity of the epithelial cells goes up in the second phase of the cycle, which increases the amount of cystic secreta and reduces their viscosity. All these factors affect the cyst's electric properties: the electric conductivity grows. This process is observed most distinctly when the cyst is imaged interactively: its imaging gets better from one mammographic examination to another.

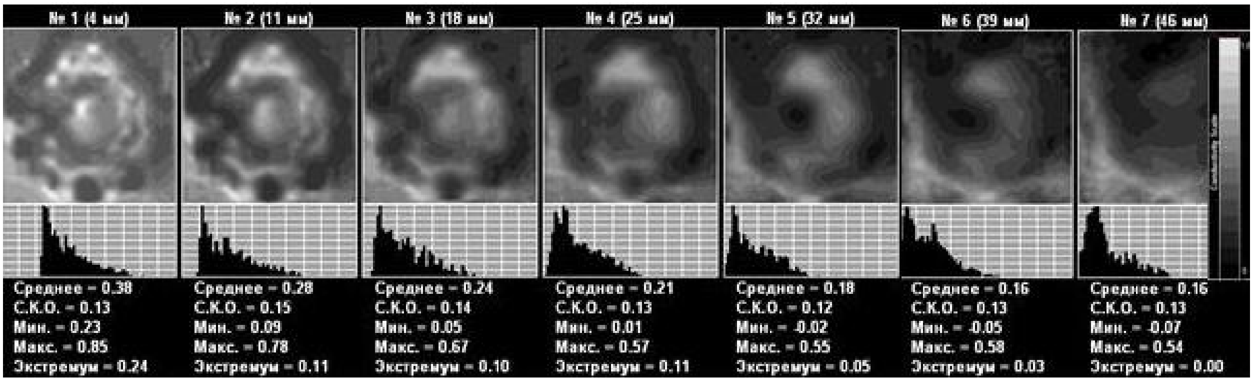



**Fig. 11-5.** EIM. In the upper segment there can be visualized three isoimpedance formations of rounded shape with clear contours measuring about 4 mm each.

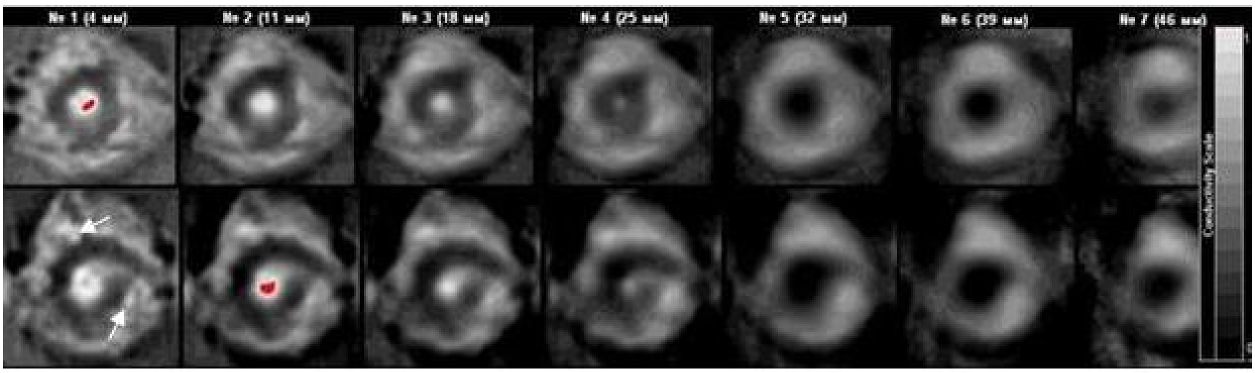



**Fig. 11-6.** EIM. Upper row – the image in the 5th day of menstrual cycle Bottom row - the image in the 25th day of menstrual cycle. In the second phase there can be visualized two isoimpedance formations of rounded shape with clear contours at 11 and 4 on the clock dial.

## Fibrous Adenoma

*Histology*

Fibrous adenoma is a mixed benign tumour, consisting of proliferating epithelial elements and connective tissue. Depending on the rate of stromal and epithelial component fibrous adenomas are divided into intracanalicular and pericanalicular (Fig.11-7, 11-8).

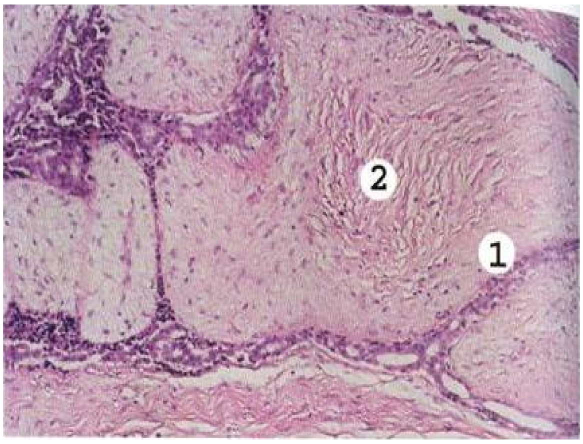



**Fig. 11-7.** Intracanalicular fibrous adenoma of mamma. The parenchyma of the tumour is represented by the complexes of various shape and size (1), and its stroma – by the spreads of intralobular connective tissue (2), ingrowing into the duct wall (M. Paltsev et al. «Pathologic Anatomy Atlas», Moscow, 2003).

The stromal component can be represented by mucopolysaccharides,

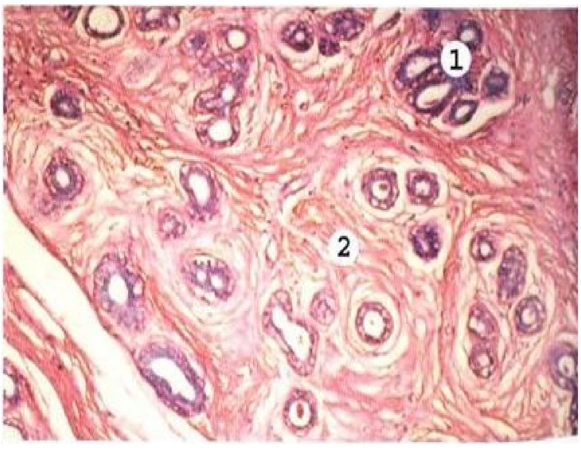



**Fig. 11-8.** Pericanalicular fibrous adenoma of mamma. The parenchyma of the tumour is represented by the glandular complexes of various shape and size (1), and its stroma - by the spreads of intralobular connective tissue (2), prevailing over the glandular tissue (M. Paltsev et al. «Pathologic Anatomy Atlas», Moscow, 2003).

fibres or their combination. The epithelial component comprises of ductal or secretory epithelium, multicellular in some cases.

*Electrical Impedance Dynamics*

Local hyperplasia of tissue elements is accompanied by the local electrical conductivity changes. The intensity of these changes is conditioned by the peculiarities of fibrous adenomas histological structure. For instance, in case of oedematous stroma high with mucopolysaccharides the increase of local electrical conductivity is connected with the dielectric permittivity change. In case of fibrous component prevalence the reduced local electrical conductivity is conditioned by the increase of the resistive component of impedance. The introduction of the vascular component, which is the indication of high proliferative activity of the fibrous adenoma, is accompanied by the sharp increase of electrical conductivity due to the ionic conductivity.

*Electrical Impedance Visualization*

The visualization of fibrous adenomas depends both on its histological structure and its size. In the electric impedance mammograms fibrous adenomas sized less than 1 cm are observed as well-defined hypo-impedance areas possessing electrical conductivity index 0.5-0.6 in several scan planes (Fig. 11-9).

It is impossible to distinguish between a cyst and a fibrous adenoma which is smaller than 1 cm in the electrical impedance mammograms.

Larger fibrous adenomas, as a rule, are characterized by lobulation and a capsule. In the electric impedance mammograms they are observed as iso-impedance areas possessing electrical conductivity index 0.4-0.5, with heterogeneous structure, well-contoured periphery, the anatomy of the mamma remains unchanged (Fig. 11-10).

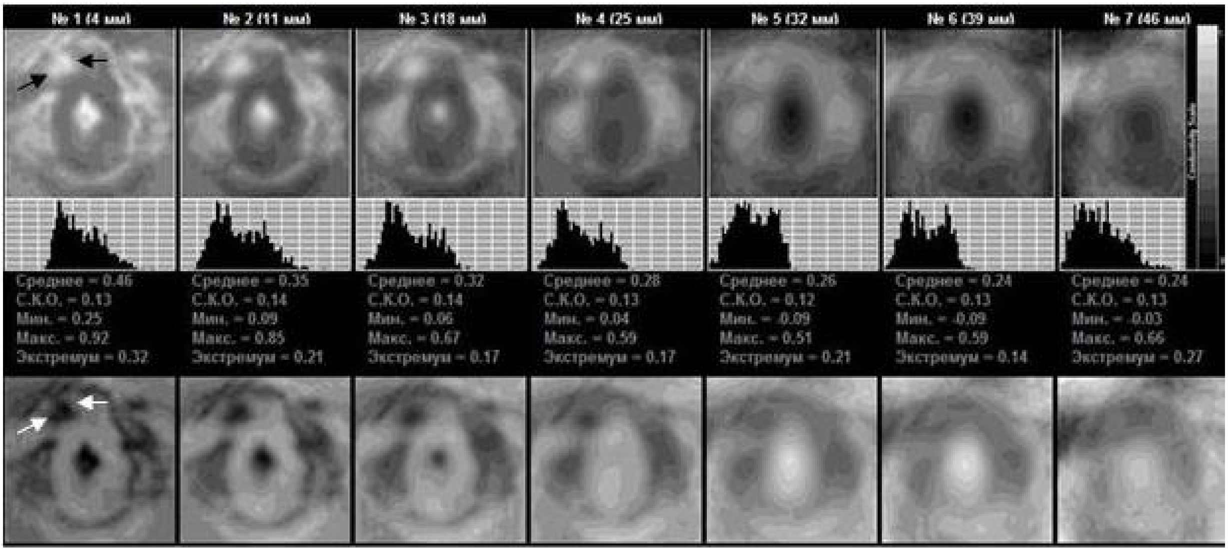



**Fig. 11-9.** EIM. Top row – in the upper segment, at 11 on the clock dial, there can be observed three hypo-impedance formations, 7 mm in size, adjoining each other. Bottom row - inversion of EIM: at 11 on the clock dial, there can be clearly observed three hypo-impedance formations, 7 mm in size.

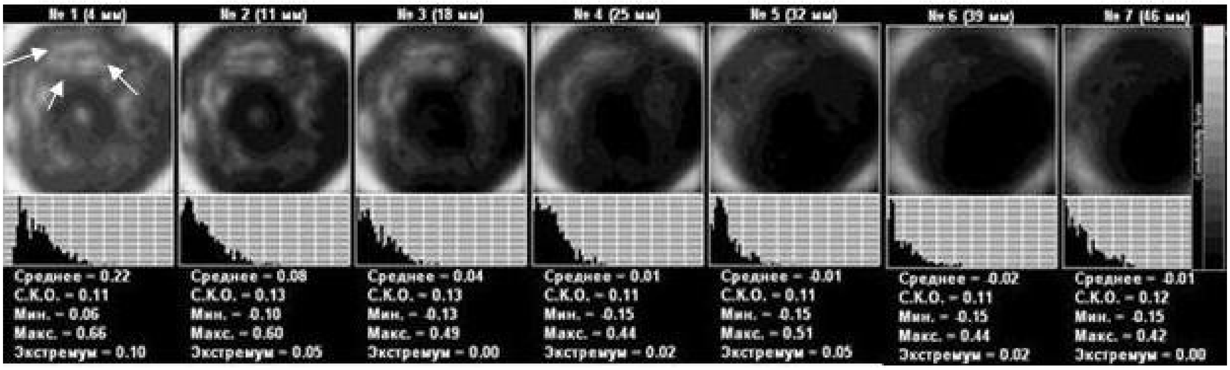



**Fig. 11-10.** EIM. In the upper segment there is a well-contoured isoimpedance formation measuring 41x27 mm with a hyper-impedance contour. **Ultrasound**: in the upper segment there is an iso-echoic structure in the capsule with septa (sized 36x29 mm).

# Electrical Impedance Measurement in Case of Malignant Tumours

# 12

*Pathophisiology*

For convenience the course of oncologic process can be divided into 2 stages: intraductal (taking place without crippling (breakup) of basal membrane and extraductal, ensuing after the basal membrane is destroyed.

Intraductal stage (Fig. 12-1) can be characterized by the loss of the specific functions of parent tissue, the so-called "dedifferentiation" process. The return to dedifferentiated state is closely connected to the change-over of bioenergetic mechanisms from breathing to glycolysis. The transition of the oxidizing process to glycolysis does not need synthesis of new glycolytic enzymes; glycolysis goes on automatically in case of respiratory disorder (Scheme 12-1).

The transition of the oxidizing process to glycolysis does not need

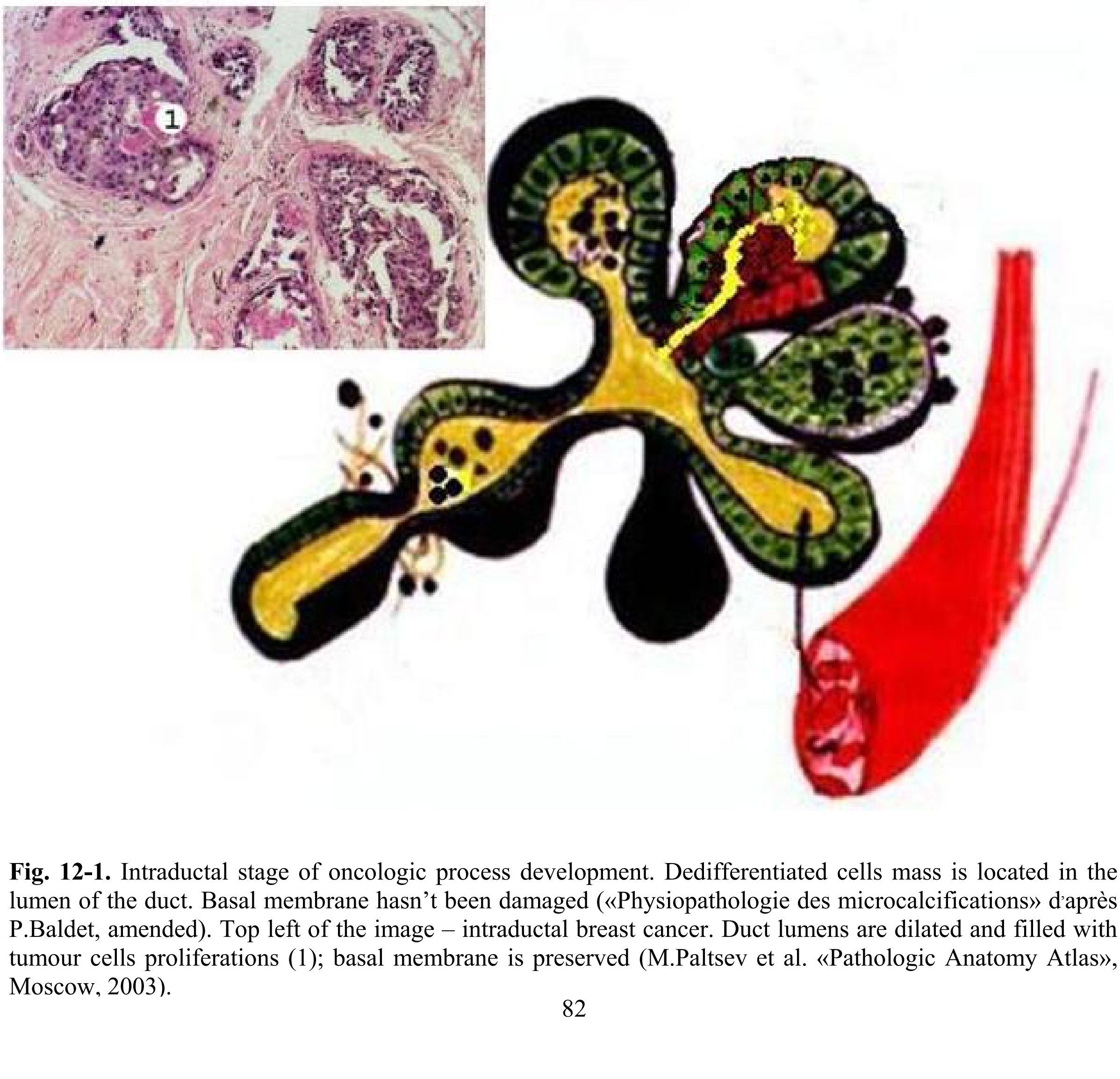
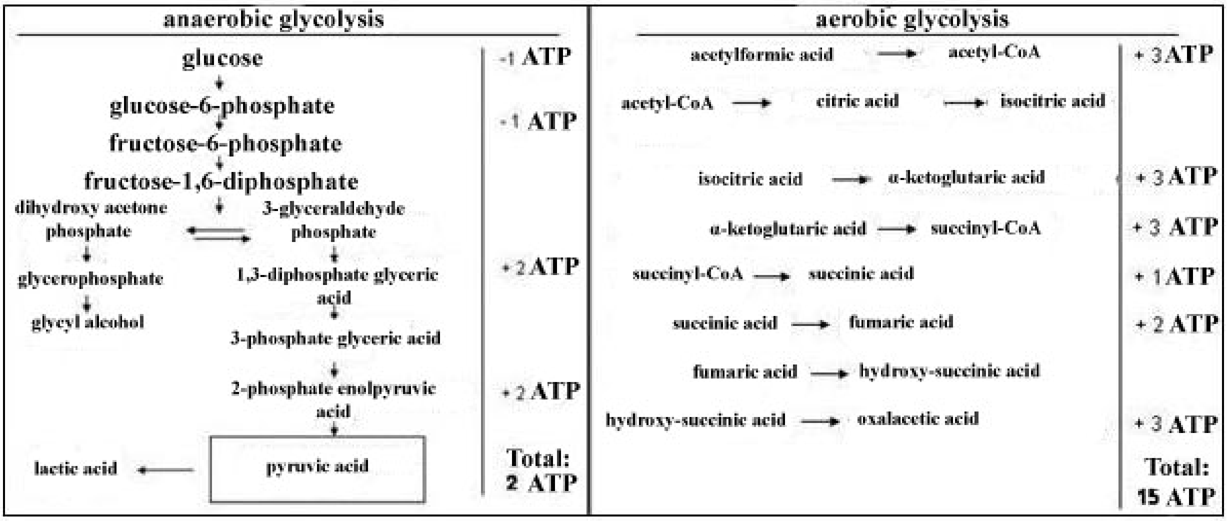



**Fig. 12-1.** Intraductal stage of oncologic process development. Dedifferentiated cells mass is located in the lumen of the duct. Basal membrane hasn't been damaged («Physiopathologie des microcalcifications» d·après P.Baldet, amended). Top left of the image – intraductal breast cancer. Duct lumens are dilated and filled with tumour cells proliferations (1); basal membrane is preserved (M.Paltsev et al. «Pathologic Anatomy Atlas», Moscow, 2003).




**Scheme 12-1.** Aerobic and anaerobic glycolysis energy balance (J.Kruh «Biochimie», Paris, 1979).

synthesis of new glycolytic enzymes; glycolysis goes on automatically in case of respiratory disorder (Scheme 12-1). Then a whole series of cytocinesis is necessary, before the irreversible malignant growth will continue according to Mendel's law. However, because of the fact that the energy intraductal potential is limited to a certain extent, as the cell mass increases, energy crisis occurs and some part of cells can necrotize. On this stage the forced destruction of dedifferentiated cells mass is quite possible.

**Fig. 12-2.** Extraductal stage of oncologic process development. Basal membrane damage («Physiopathologie des microcalcifications» d'apres P.Baldet, amended).

When basal membrane of epithelium is destroyed atypical cells get into the medium with totally different energy conditions (Fig. 12-2). There are several causes of basal membrane breakup. *High density of duct component* is potentially dangerous as it can be accompanied by insufficient trophic function of the ground substance of the connective tissue which leads to dystrophic processes in basal membrane. *Not natural untimely termination of lactation* is accompanied by uncontrolled death of numerous alveoli with subsequent development of connective tissue on their place, which causes the alteration of ductal tree topography. *Inflammation, wound healing after surgery, mechanical effect* – trauma, for instance, are accompanied by the cell death and basal membrane damage. The trophic function of connective tissue (and its ground substance in particular) is generally known. The amorphous component of the intercellular substance is a jelly-like matter surrounding the cellular and fibrous structures of the connective tissue, nervous and vascular elements. The constituents of ground substance are the following: plasma protein, water, inorganic ions, collagen and elastin precursors, proteoglycans, glycoproteins etc. Thus, uncontrolled dedifferentiated cell growth receives energy "recharge". During this phase the speed of tumour growth increases sharply. New vessels are formed. Tumour cells stimulate division of endothelium cells and cause capillary proliferation – “pathological angiogenesis”.

*Histology*

It seems that membrane permeability increase is necessary in both directions to support vital activity of dedifferentiated cells during the intraductal stage of oncologic process. During the extraductal stage the decease develops in multicomponent connective tissue where these or that structures prevail. The correlation between parenchyma and stroma is variable (Fig. 12-3, 12-4).

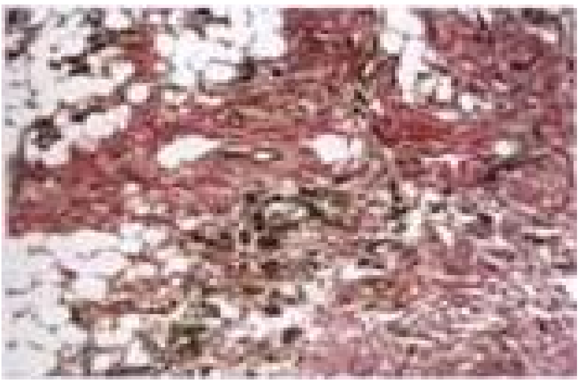


**Fig. 12-3.** Lobular infiltrative scirrhous carcinoma of the breast. Colour according to Van Gison (G. Bondar et al. «Primary-inoperable breast cancer». St. Petersburg, 2006).

**Fig. 12-4.** Moderately differentiated infiltrating carcinoma. Hematoxylin and eosin stain. (G. Bondar et al. «Primary-inoperable breast cancer». St. Petersburg, 2006).

Stroma is represented by various fascicles of connective tissue of different size, thickness and direction. They are formed of collagen fiber fibrils. Parenchyma cells are characterized by the heightened level of proliferative activity. Vascularization increase is accompanied by heightened permeability of microvessels, mural vascular and lymphatic invasion and tumour embolus formation. Numerous necrosis areas of different size appear. Dead tumour tissue is replaced by fibrous connective tissue. In addition such phenomena as edema or loosening of fibrous connective tissue can be observed as well as suppurative inflammation, sliming, hyalinosis and calcification. In the structure of cellular infiltrate (both in tumour tissue itself and around it) lymphocytes prevail. Their content reaches 90% (Table 12-1). Lymphocytic infiltration may reach significant size.

**Table 12-1.** Structure of cellular infiltrate.

| The cellular structure of infiltrate, % | |
|---|---|
| lymphocytes | 91,11±6,13 |
| plasmocytes | 1.86±0,09 |
| eosinophils | 0,03±0,01 |
| neutrophils | 3,83±0,12 |
| macrophages | 2,94±0,13 |
| tissue basocytes | 0,23±0,01 |

Thus, as the tumour grows various transitional histological variants can be observed: scirrhous (fibrous) carcinoma, in case of which tumour cells are located between fascicles of collagen fibers; solid carcinoma with typical alveolar-tubular structure; solid-glandular carcinoma etc.

*Electrical Impedance Dynamics*

The membrane permeability of cancer cells during intraductal and early extraductal stage increases both for chemical compounds and electric charges. This phenomenon causes electrical conductivity increase at the expense of tumour cells permittivity decrease. As the decease connected with the breakup of epithelium basal membrane progresses, various phenomena can occur in tumour and surrounding tissues. These processes are always accompanied by the alteration of electrical properties of tumour mass. Increased vascularization leads to electrical conductivity increase due to ionic conduction. Replacement of dead tumor cells by collagen fibers leads to electrical conductivity decrease. The emergence of purulent inflammation areas is accompanied by permittivity decrease as a result of cell membranes death. Lymphocytic infiltration causes tumour and surrounding tissues impedance increase, because of significant local concentration of cell membranes. Thus, tumour growth is regularly accompanied by the alteration of the electrical properties both of the tumour itself and of surrounding tissues.

*Electrical Impedance Visualization*

Breast cancer staging is accompanied by alterations of electrical conductivity in case of various forms\types of this pathology.

## Nodular Type of Cancer

It is essentially important for electrical impedance diagnostics to distinguish non-complicated types of decease (which can be observed during the stage of intraductal growth and in the initial stages of extraductal growth) and complicated types of cancer (which are the characteristics solely for the extraductal stage of tumour development).

In case of non-complicated forms of breast cancer, the lesions of small size are usually observed - less than 1 cm in diameter (Fig. 12-5). Diagnostic criteria are the following: no distortion of the mamma's contour, absence of hyper-impedance contour, unchanged anatomy of the mammary gland, visualization of focal electric conductivity changes in the form of hypo-impedance areas on several scan planes. The electric conductivity index of the healthy and the affected gland do not differ to any reliable extent.

If the method of diagnostics under examination permits to acquire a numerical result, the so-called "breaking point" (the value exceeding of which is considered as a sufficient cause for qualitative assessment) should be determined. In this case the estimation of diagnostic technique efficiency may be limited to sensitivity and specificity assessment. Sensitivity of diagnostic sample can be increased by reducing its specificity. Thus the accurate determination of the breaking point is extremely important. If sensitivity of a test is insufficient, it can be modified by means of sensitivity increase due to the change of the breaking point. Electrical conductivity index ≥ 0.95 is considered as the breaking point between healthy mammary gland tissue and a non-complicated tumor. Left shift causes sensitivity to increase and specificity to decrease, right shift leads to sensitivity decrease and specificity increase. With the breaking point of electrical conductivity index exceeding or equal to 0.95, sensitivity is 84-93%, specificity – 87-99% (according to the data given by different authors).

Figure 12-5 represents EIM without hyper-impedance contour and the anatomy of the mammary gland remained unchanged, but in the second scan plane a focal change can be visualized, as an animpedance area, highlighted in red, with electrical conductivity index >0.95. These are the criteria of the non-complicated form of breast cancer. Roentgenogram and US image of the same mammary gland are represented below (12-5a, 12-5b).

Figure 12-6 represents EIM without hyper-impedance contour and the anatomy of the mammary gland remains unchanged, but a focal change can be visualized, as an animpedance area, highlighted in red, with electrical conductivity index >0.95 in several scan planes. Roentgenogram and US image of the same mammary gland are represented below (12-6a, 12-6b).

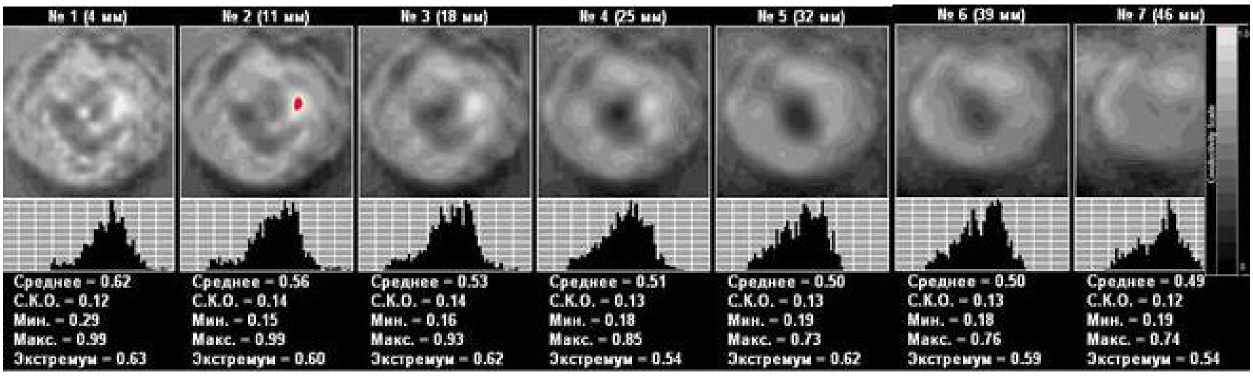



**Рис. 12-5.** EIM. Amorphous type of mammary gland structure. In the outer segment of the left mammary gland, at 3 o'clock position there is observed an an-impedance area, which is highlighted with red in the second scan plane, less than 10 mm in size.

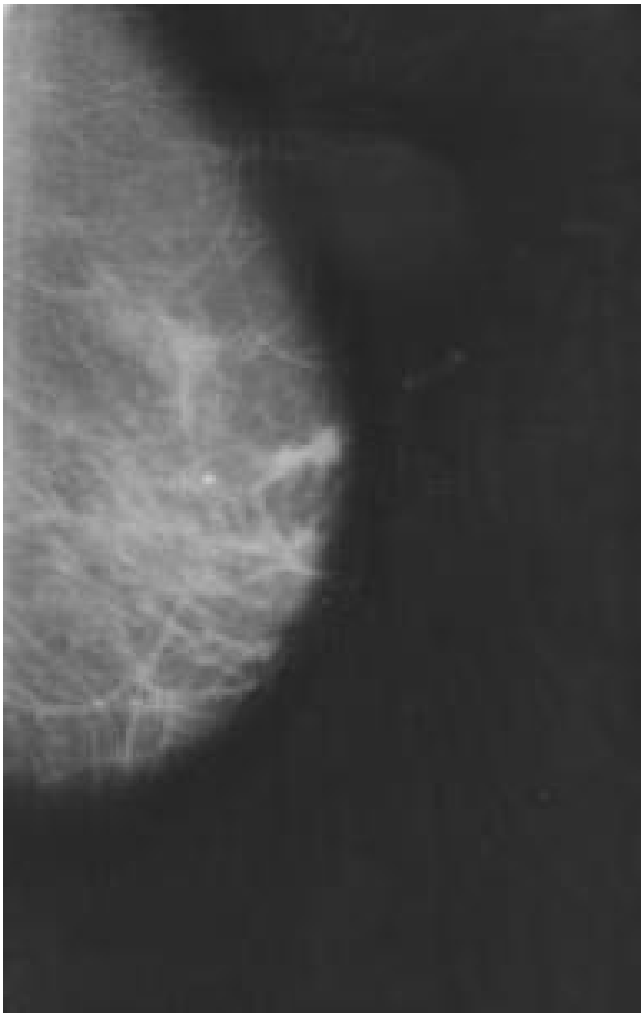



**Рис. 12-5а.** ULTRASOUND: The structure of parenchyma with adipose lobules and connective tissue layers. An inhomogeneous lesion of irregular shape is located at 28 mm distance from the nipple and at 12 mm depth, its size is 9x9 mm without vascularization. Axillary lymph nodes are not visualized.

**Рис.12-5б.** Roentgenogram: fibro-fatty involution. In upper-outer segment there is observed a lesion up to 1 cm in size with a radiant contour, the skin is slightly drawn-in. Microcalcification clusters are not observed.

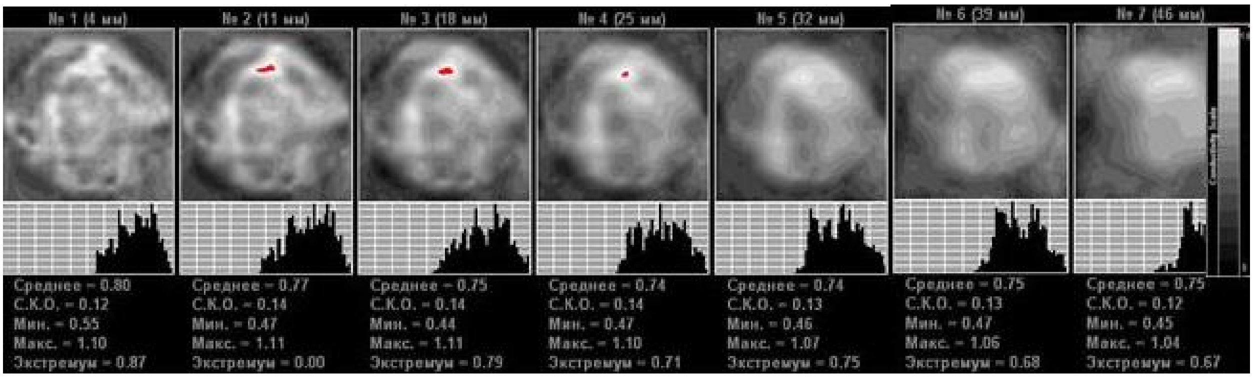
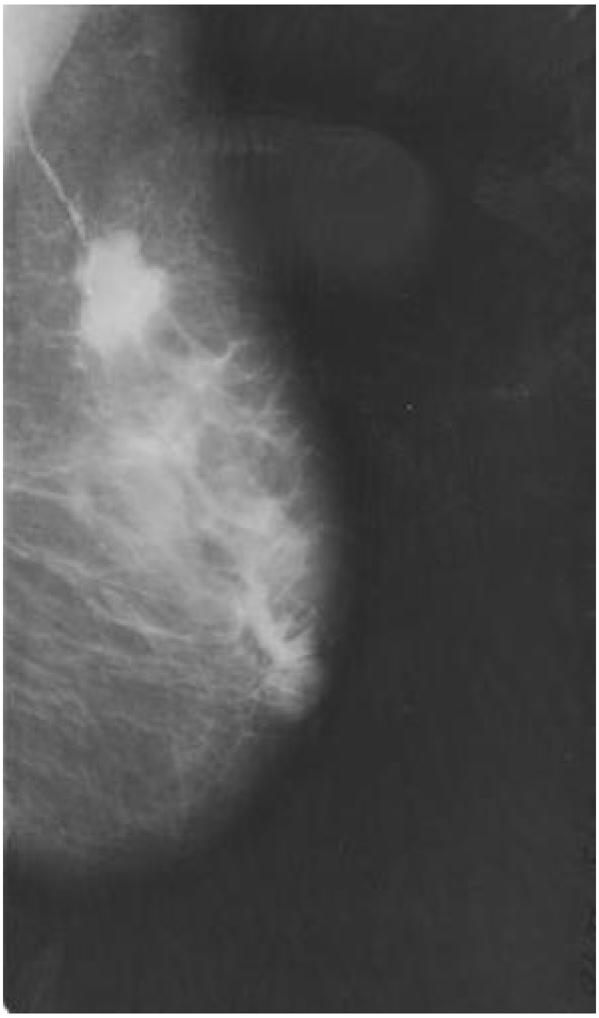



**Рис. 12-6.** EIM. Upper-outer segment. Amorphous type of mammary gland structure. At 12 o'clock position there is observed an an-impedance area, which is highlighted with red in three scan planes, 18x10 mm in size.



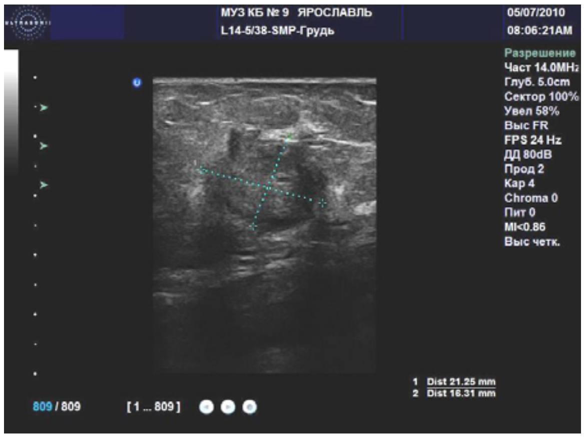



**Рис. 12-6а.** ULTRASOUND: The structure of parenchyma with adipose lobules and connective tissue layers prevailing. The left gland – at 1 o'clock position there is located an inhomogeneous lesion of irregular shape, 6 mm away from the nipple with vascularization. 21x16 mm. Periphery lymph nodes are not visualized.

**Рис. 12-6б.** Roentgenogram: fibro-fatty involution. In the upper-outer segment of the left gland there is a nodule with distinct irregular contours of high density and with rays going to the periphery, up to 25x25 mm in size.

Then we would like to provide various electrical impedance images and the data of different diagnostic techniques in case of the non-complicated form of breast cancer.

A 54 years-old patient with an induration in the upper-outer segment of the left gland. Postmenopause duration: 8 years. Anamnesis: somatic - gastric ulcer; gynecological – hysteromyoma; obstetrical - labours 2, abortion 2; lactation – more than a year. Diseases of the breast – no (Fig. 12-7). Histology - invasive ductal carcinoma.

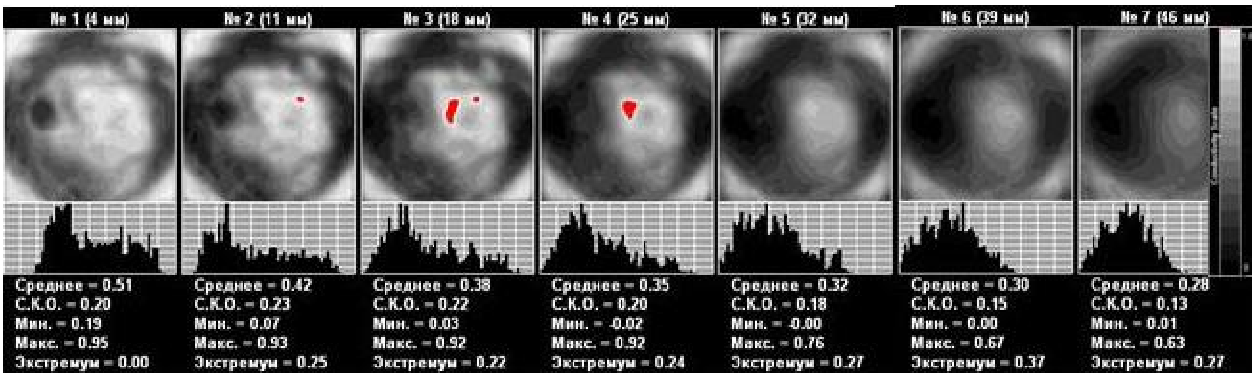



**Рис. 12-7.** EIM. Outer segment. Mixed type of mammary gland structure. In the outer segment of the left gland there is observed an an-impedance area, which is highlighted with red in three scan planes, 7x14 mm in size. **ULTRASOUND:** A 0.7x1.0 cm lesion of low echogenicity is located in the upper-outer segment of the left mammary gland. Axillary lymph nodes are enlarged.

A 59 years-old patient. Complaints concerning pain and serous discharge from the left mammary gland. Postmenopause duration: 7 years. Anamnesis: somatic – no; gynecological – no; obstetrical - labours 1, abortion 5; lactation – more than a year. Diseases of the breast – no (Fig. 12-8).

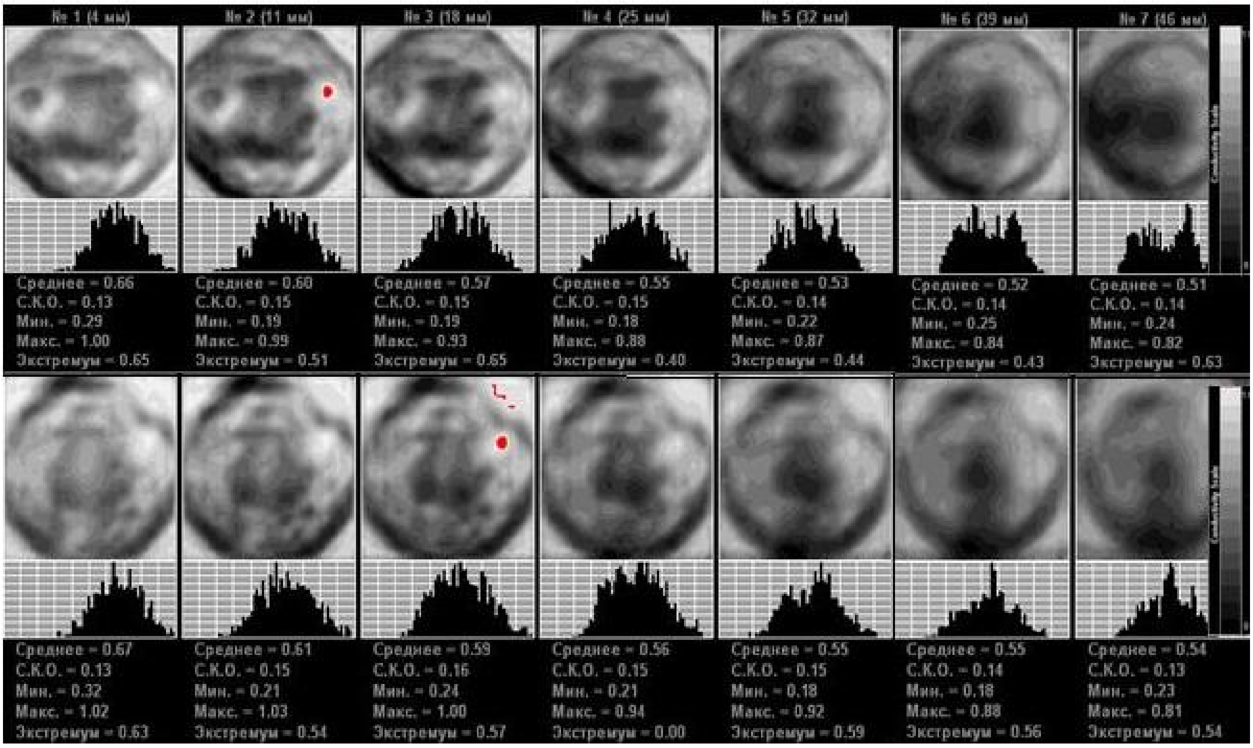



**Рис. 12-8.** EIM. Outer segment. Amorphous type of mammary gland structure. In the outer segment of the left mammary gland (upper row), at 3 o'clock position there is observed an an-impedance area, which is highlighted with red in the second scan plane, 10 mm in size. The same area is visualized in the upper segment of the gland (second row) in the third scan plane, corresponding to the location of the lesion. **ULTRASOUND:** In the outer segment of the left gland there is an inhomogeneous lesion with blurred contour and with a hyper-echoic inclusion in the center with active blood circulation, its size is 1.7x0.9 cm. In the left axillary area there is a "set" of lymph nodes with hyper-echoic inclusions in the center.

A 50 years-old patient. Complaints concerning a nodularity in the outer segment of the right gland. Perimenopause. Anamnesis: somatic - no; gynecological – no; obstetrical - labours 2, abortion 2; lactation – up to a year. Diseases of the breast – no (Fig. 12-9).

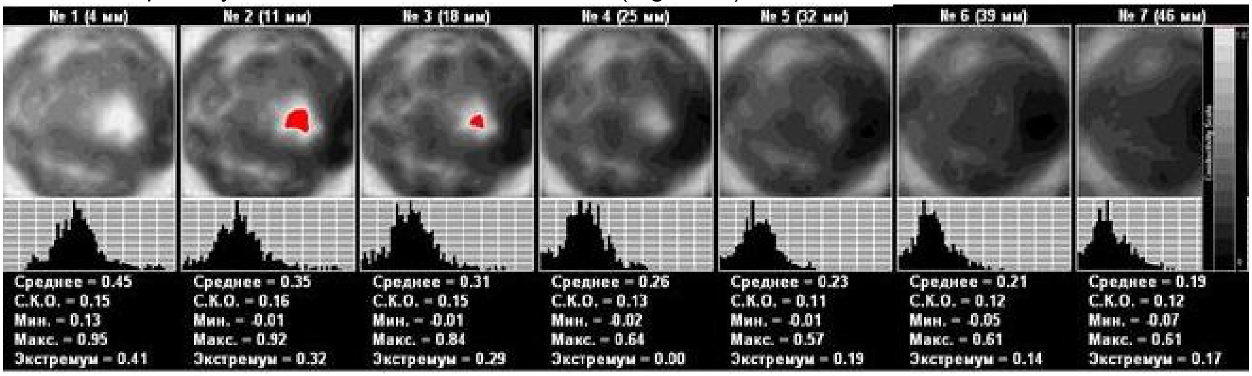



**Рис. 12-9.** EIM. Outer segment. Fibrous type of mammary gland structure. In the outer segment of the right gland there is observed an an-impedance area, which is highlighted with red in two scan planes, 24x24 mm in size. **ULTRASOUND:** In the outer segment of the right gland there is an an-echoic lesion of irregular shape, 2.6x1.7 cm in size, with parietal inclusions. Axillary lymph nodes are not visualized.

A 61 years-old patient. Complaints concerning a nodularity in the right gland. Postmenopause duration: 11 years. Anamnesis: somatic - no; gynecological – no; obstetrical - labours 2, abortion 4; lactation – more than a year. Diseases of the breast – no (Fig. 12-10). Histology - invasive ductal carcinoma.

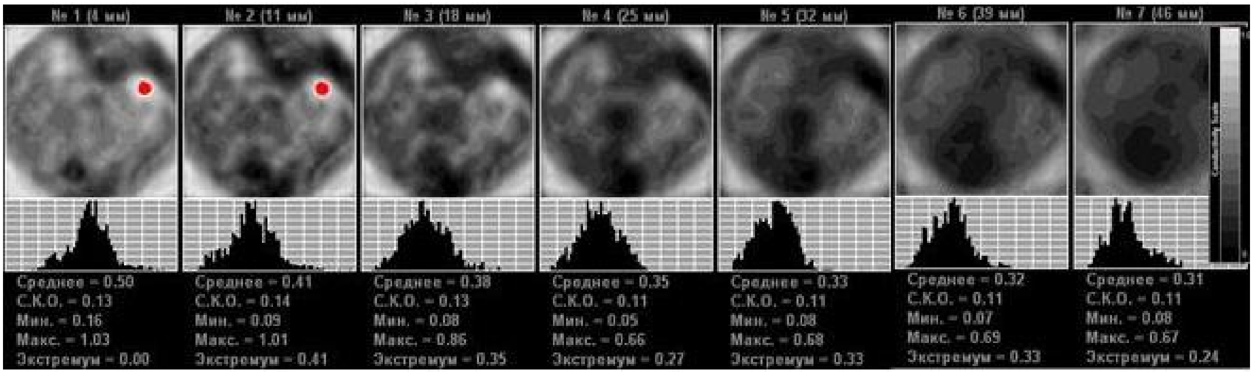



**Рис. 12-10.** EIM. Upper segment. Mixed type of mammary gland structure. In the upper-outer segment of the right gland there is observed an an-impedance area, which is highlighted with red in two scan planes, 20x20 mm in size. **ULTRASOUND:** In the inner segment of the right gland at 1 o'clock position, there is an irregular shaped lesion with blurred contours and vascularization, approximately 2.0 cm in size. Roentgenogram: A 3 cm lesion with a radiating contour and calcification is located in the right gland.

A 54 years-old patient. No complaints. Postmenopause duration: 10 years. Anamnesis: somatic - no; gynecological – no; obstetrical - labours 2, abortions 3; lactation – up to a month. Diseases of the breast – no (Fig. 12-11).

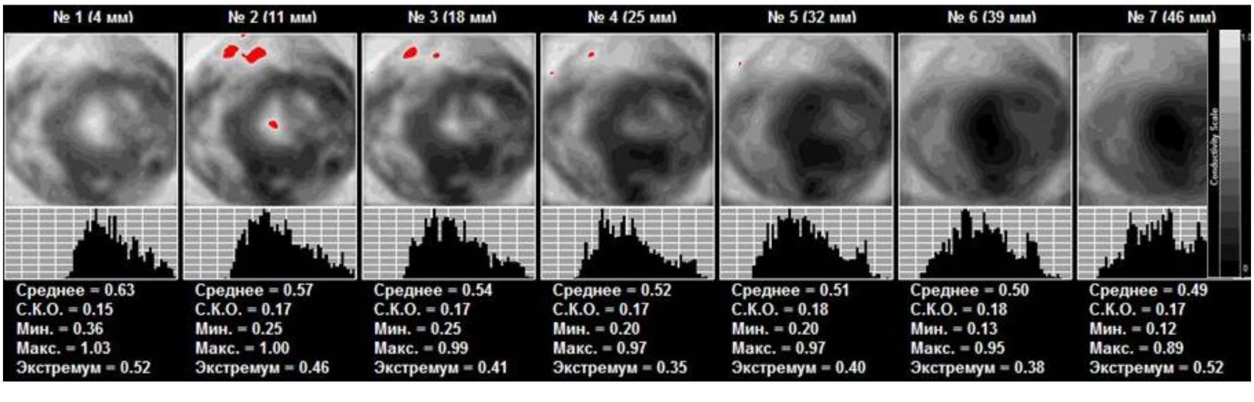



**Рис. 12-11.** EIM. Mixed type of mammary gland structure. In the upper-outer segment of the left gland there is observed an an-impedance area, which is highlighted with red in two scan planes, 7x20 mm in size. **ULTRASOUND:** In the upper-outer segment of the right gland, there is a lesion with blurred contours and vascularization, 1.1x0.7 cm in size.

A 49 years-old patient. Complaints concerning a nodularity in the left gland. 28th day of menstrual cycle. Anamnesis: somatic – thyroid decease; gynecological – no; obstetrical - labours 1, abortions 0; lactation – up to a year. Diseases of the breast – trauma (Fig. 12-12).

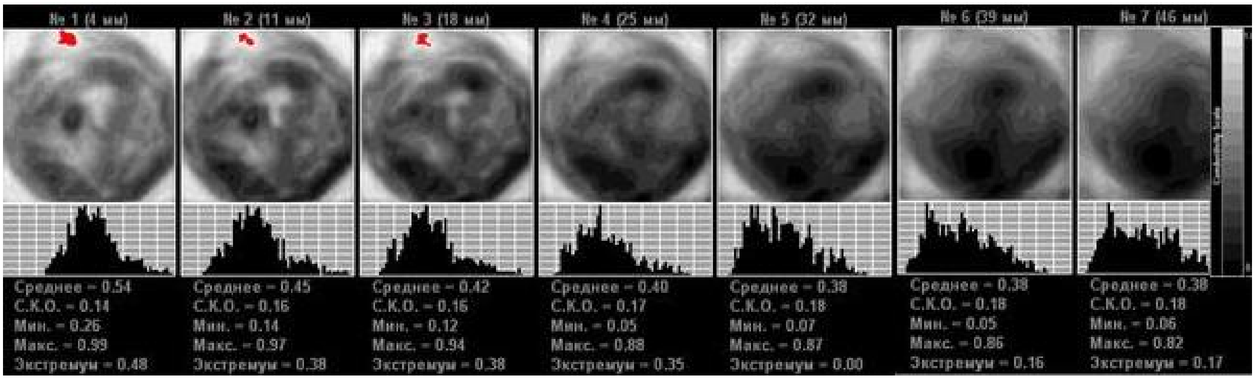



**Рис. 12-12.** EIM. Mixed type of mammary gland structure. In the upper segment of the left gland there is observed an an-impedance area, which is highlighted with red in three scan planes, 17x10 mm in size. **ULTRASOUND:** In the upper segment of the left gland there is observed an irregular-shaped inhomogeneous area with quite distinct contours, 24x16 mm in size, with abundant vascularization. There are two lymph nodes * 15 mm of inhomogeneous structure in the left axillary crease area.

A 48 years-old patient. Complaints concerning a painful nodularity in the inner segment of the left gland. 12th day of menstrual cycle. Anamnesis: somatic - no; gynecological – myoma; obstetrical - labours 1, abortions 2; lactation – more than a year. Diseases of the breast – no (Fig. 12-13).

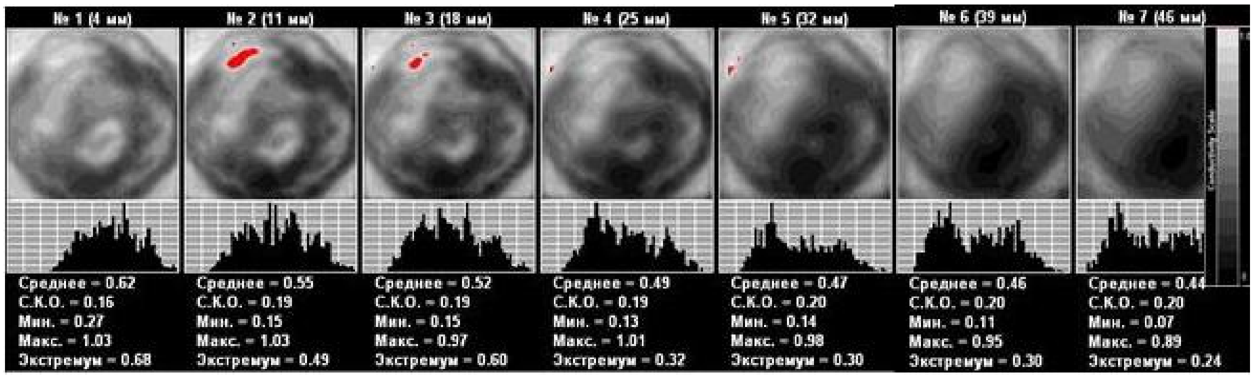



**Рис. 12-13.** EIM. Mixed type of mammary gland structure. In the upper-inner segment of the left gland there is observed an an-impedance area, which is highlighted with red in two scan planes, 14x28 mm in size. **US:** In the upper-inner segment of the left gland there is observed a well-contoured thick-walled an-echoic area at 11 o'clock position, 30 mm in size, with hyper-echoic parietal inclusions. Lymph nodes are not visualized.

During extraductal stage in tumour and surrounding tissues the processes of inflammation, necrosis, vascularization disturbance, infiltration etc take place. This is a complicated form of breast cancer (Fig. 12-14). As a rule, tumours bigger than 1 cm in diameter can be observed in case of a complicated cancer form. The criteria of a different kind than above-listed are to be used for complicated cancer diagnostics. The ability to analyze electrical impedance images comes in the forefront.

The main indications of the complicated form of breast cancer are the following: common - deformation of the breast contour, hyper-impedance of the contour, the change of mamma's anatomy and the displacement of internal structures (Fig . 12-16) and local – visualization of focal changes in form of iso / hypo-impedance areas, the presence of hyper-impedance contour on the border of the tumor and surrounding tissue (Fig.12-15).

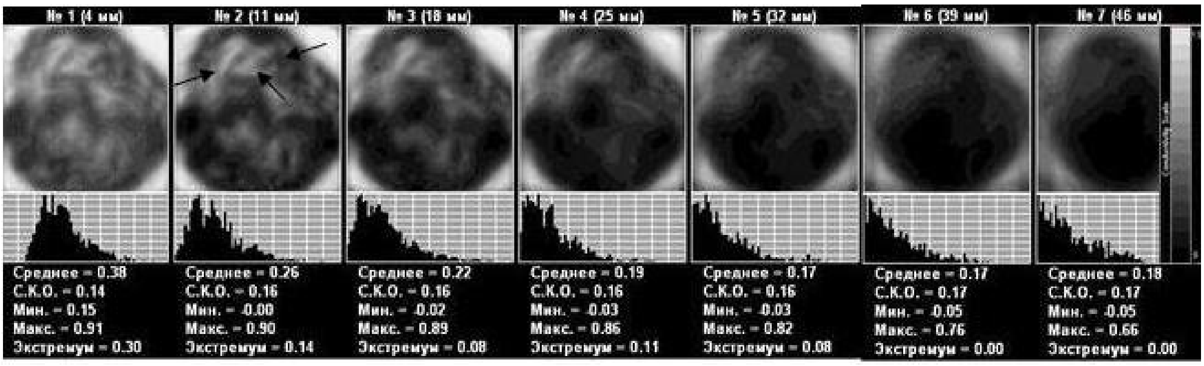



**Рис. 12-14.** EIM. Fibrous type of mammary gland structure. The anatomy of the gland has been changed. In the upper segment there is an irregular-shaped inhomogeneous iso-impedance formation measuring 51x27 mm with a hyper-impedance contour.

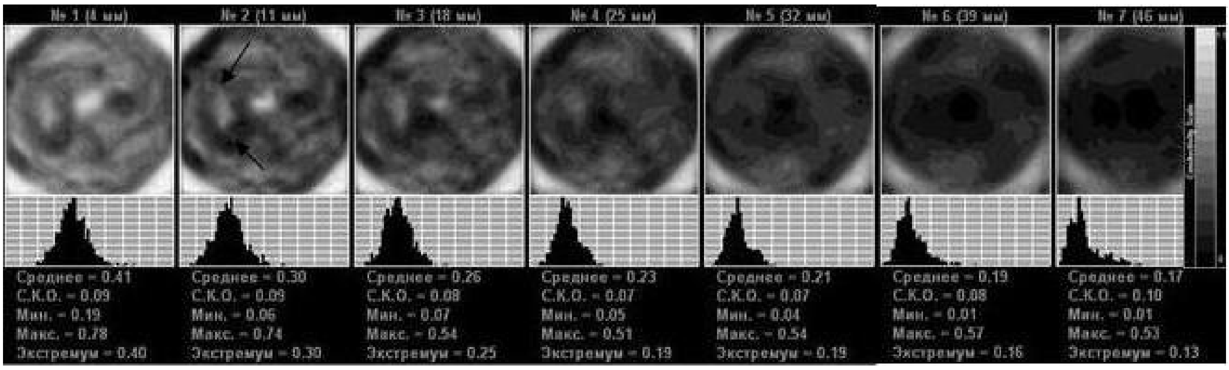



**Рис. 12-15.** EIM. Fibrous type of mammary gland structure. The iso-impedance area with the hyper-impedance contour and hyper-impedance reaction at the periphery of the gland on the affected side can be visualized at 9 on the clock dial close to the areola.

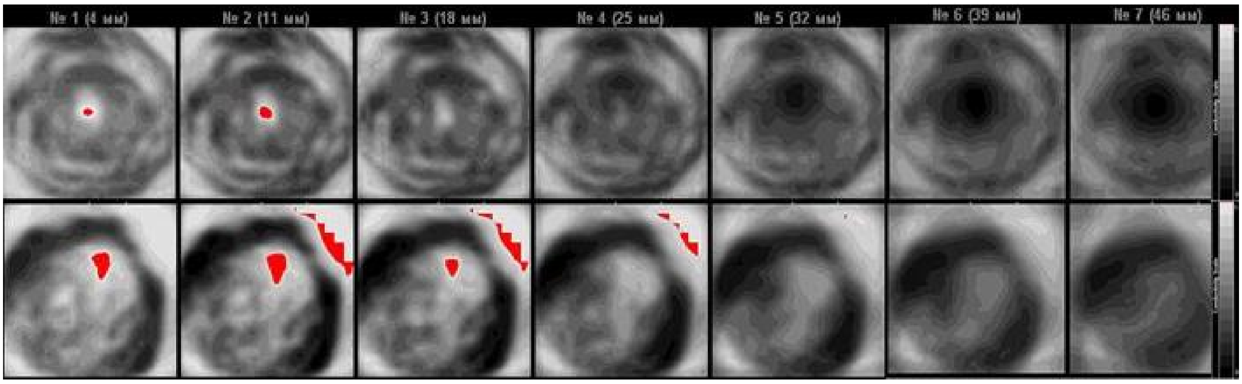



**Рис. 12-16.** EIM. Top row – healthy left gland. Lower row – affected right gland. Well-defined hyper-impedance contour. The anatomy of the gland has been changed. In the upper segment at 1 o'clock position there is observed an an-impedance area, which is highlighted with red in three scan planes, 24x17x14 mm in size. **US:** In the upper-inner segment of the right gland there is observed an area of inhomogeneous echostructure with irregular contours, 2.5x3.0 mm in size. There are two altered lymph nodes measured 1.3 and 1.2 cm in the axillary crease area. Histology – moderately differentiated adenocarcinoma (glandular cancer).

The electrical conductivity index is definitely higher for the healthy gland than for the affected one. Indispensable condition is the comparison of electrical impedance mammograms of healthy and affected mammary gland (Fig. 12-16).

Then we would like to provide various electrical impedance images and the data of different diagnostic techniques in case of the complicated form of breast cancer.

A 49 years-old patient. Complaints concerning a nodularity in the left gland. Perimenopause. Anamnesis: somatic - no; gynecological – no; obstetrical - labours 2, abortions 4; lactation – up to a year. Diseases of the breast – trauma (Fig. 12-17, 12-17a).

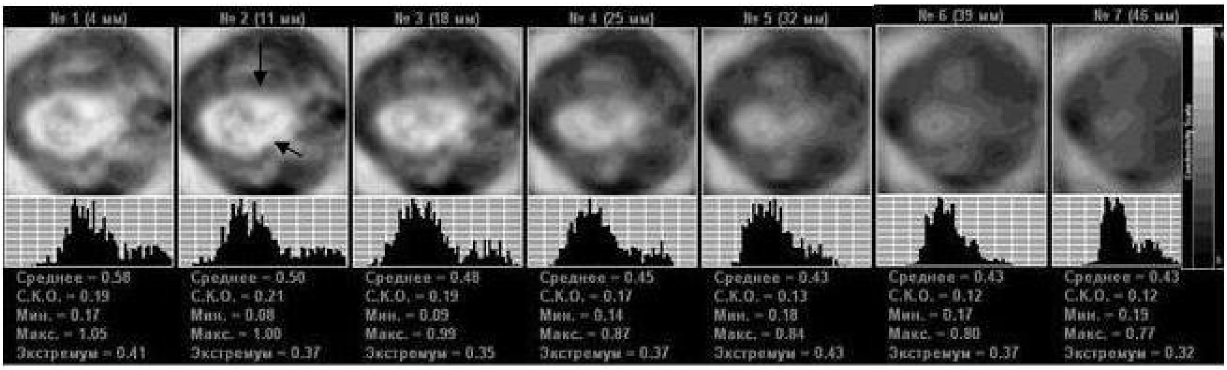



**Рис. 12-17.** EIM. Mixed type of mammary gland structure. The inner segment of the left gland. In the center of the image is an inhomogeneous hypo-impedance oval formation measuring 20x18 mm.

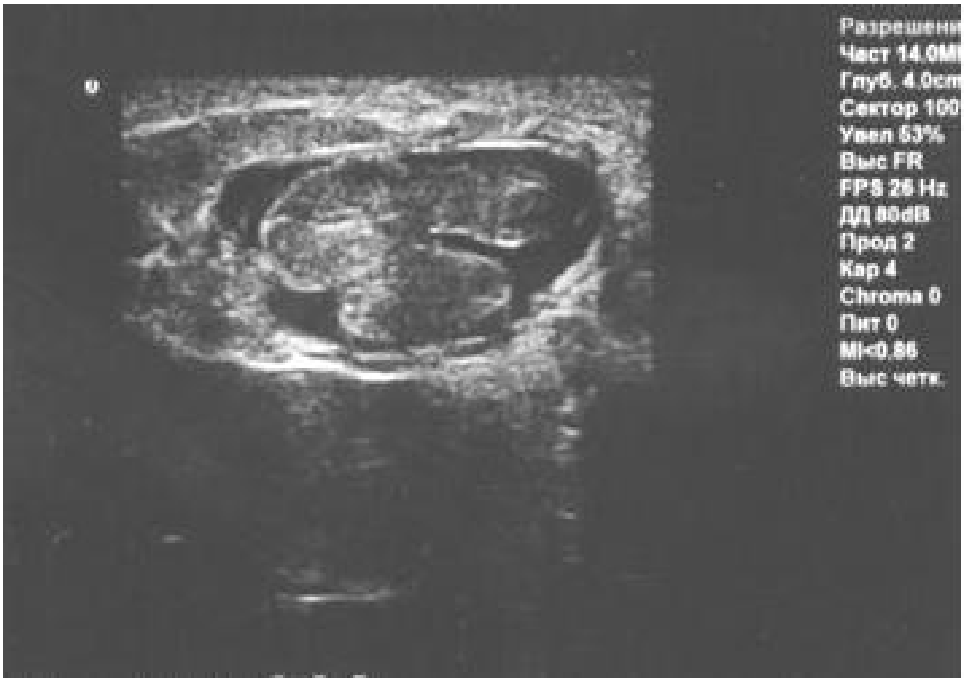



**Рис. 12-17a.** ULTRASOUND: In the boundary of the inner segments of the left gland there is observed an inhomogeneous area with distinct contours, 28x18 mm in size, with the an-echoic component and vascularization.

A 70 years-old patient. No complaints. Postmenopause duration: 22 years. Anamnesis: somatic - diabetes, gynecological - no, obstetrical - labours 1, abortions 1, lactation - up to a year. Diseases of the breast – no. Histology - infiltrating ductal carcinoma, cancer of solid-trabecular structure (Fig. 12-18, 12-18a, 12-18b).

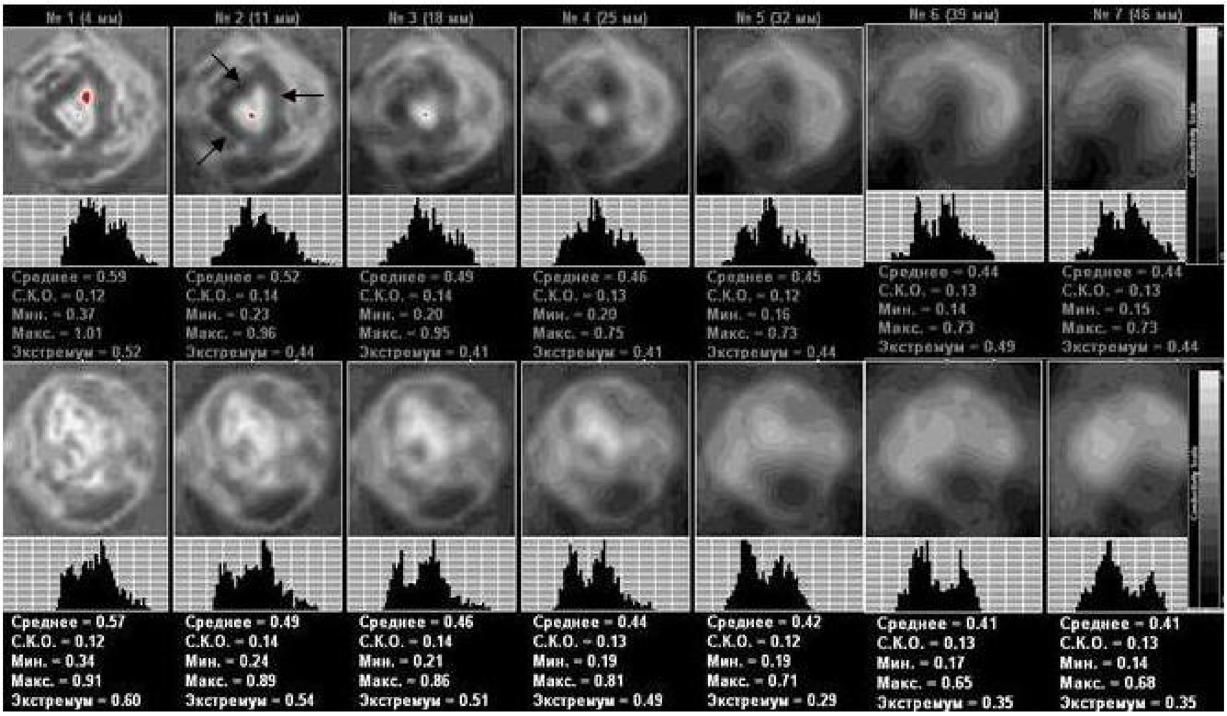



**Рис. 12-18.** EIM. Mixed type of mammary gland structure. Top row – left gland. In the central segment hypo-impedance formation of irregular shape measuring 27x41 mm with a hyperimpedance contour and animpedance areas highlighted in red. Lower row – right gland. Age norm.

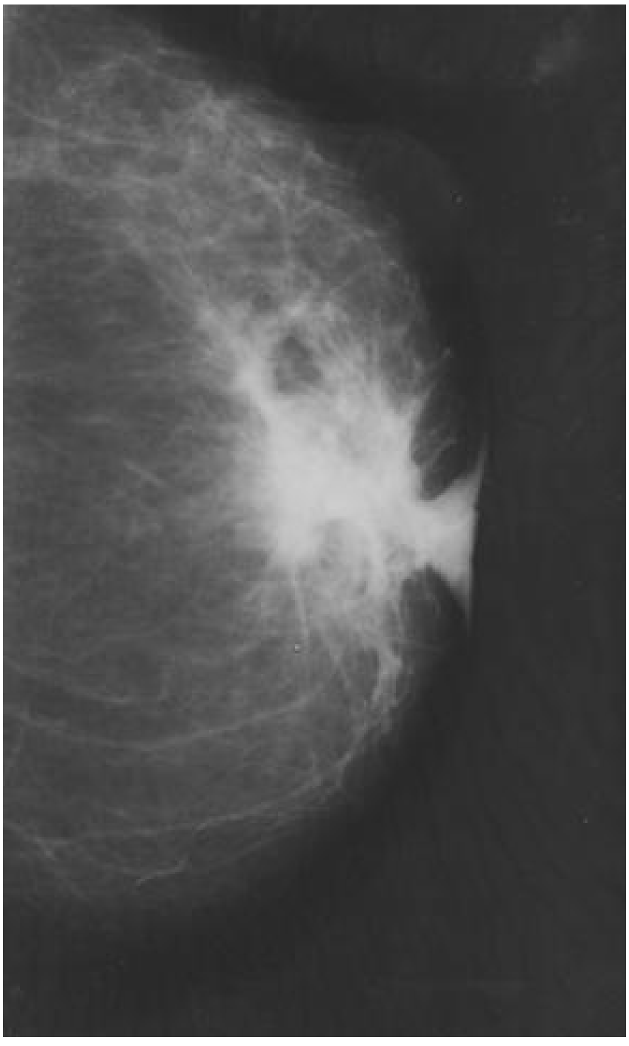



**Рис. 12-18а.** ULTRASOUND: In the left gland there is observed a subareolar inhomogeneous area without distinct contours, with low-grade vascularization and intensive shadow. There are three lymph nodes * 7 mm in the left axillary crease area.

**Рис. 12-18б.** Roentgenogram: Against the background of fibro-fatty involution in the left gland in subareolar area there is observed an irregular-shaped area measured 35x45 mm with blurred irregular contours, connected to areola. Nipple retraction and skin thickening in the areolar area is observed.

A 57-year-old patient. Complaints concerning a nodularity in the right gland. Post-menopause duration: 2 years. Anamnesis: somatic - hypertensive disease, gynecological - no, obstetrical - labours 1, abortions 2, lactation - up to a month. Diseases of the breast – no. Histology – invasive ductal carcinoma (Fig. 12-19, 12-19a, 12-19b).

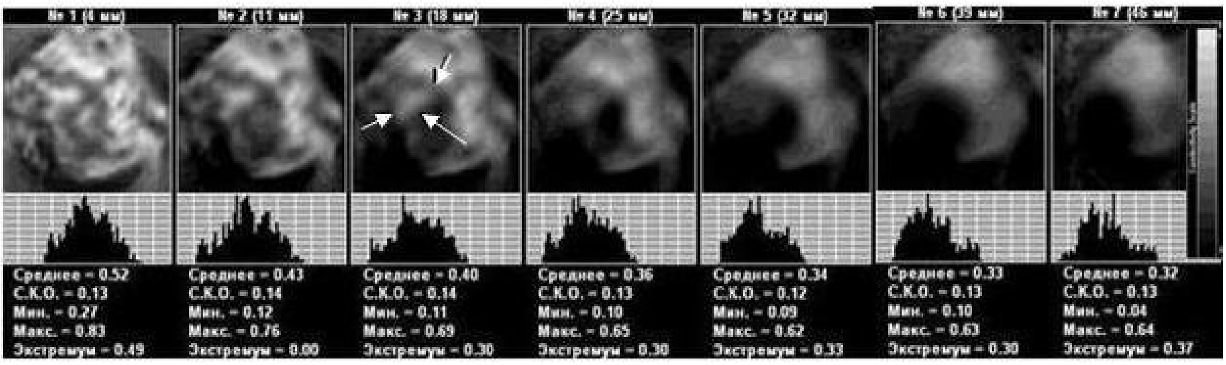



**Рис. 12-19.** EIM. Upper segment. Mixed type of mammary gland structure. At 10 o'clock position, there is observed a hypo-impedance formation of irregular shape measuring 30x17 mm with a hyperimpedance contour. It is more distinct in 2nd and 3rd scan planes. Histology – solid carcinoma.

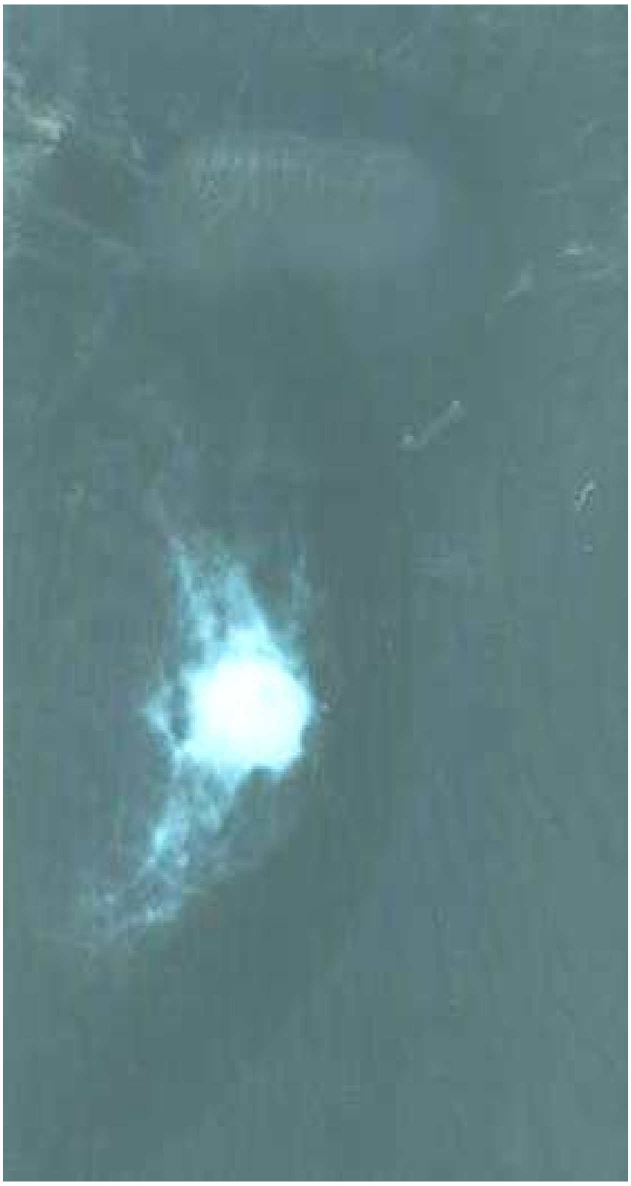


**Рис. 12-19a.** ULTRASOUND: In the upper segment of the right gland there is observed an area of an-echoic structure, having thick, irregular-shaped capsule filled with inhomogeneous suspension, with vascularization on the perimeter

**Рис. 12-19б.** Roentgenogram: In the upper-outer segment of the right mammary gland there is observed a oval homogeneous area of high intensity, measuring 20x30 mm, possessing distinct irregular-shaped contours.

A 57-year-old patient. Complaints concerning a nodularity in the right gland. Postmenopause duration: 2 years. Anamnesis: somatic - hypertensive disease, gynecological - no, obstetrical - labours 1, abortions 2, lactation - up to a month. Diseases of the breast – no. Histology – invasive ductal carcinoma (Fig. 12-20, 12-20a, 12-20b).

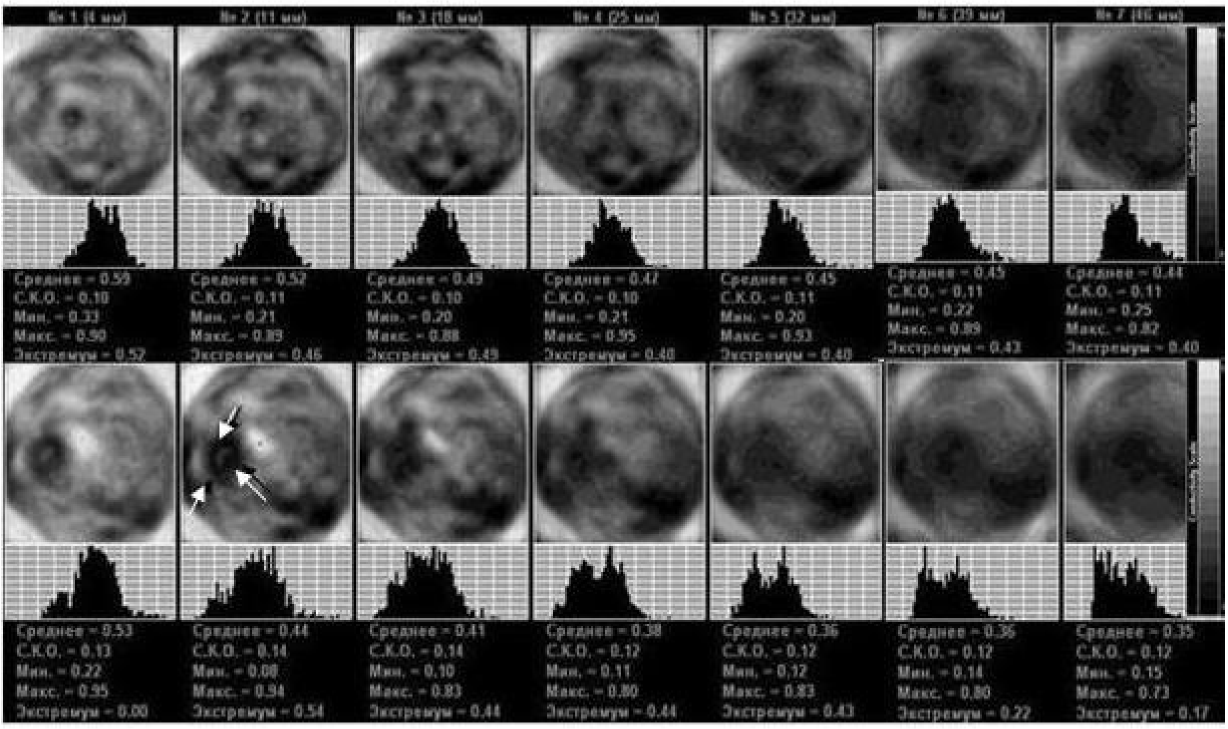
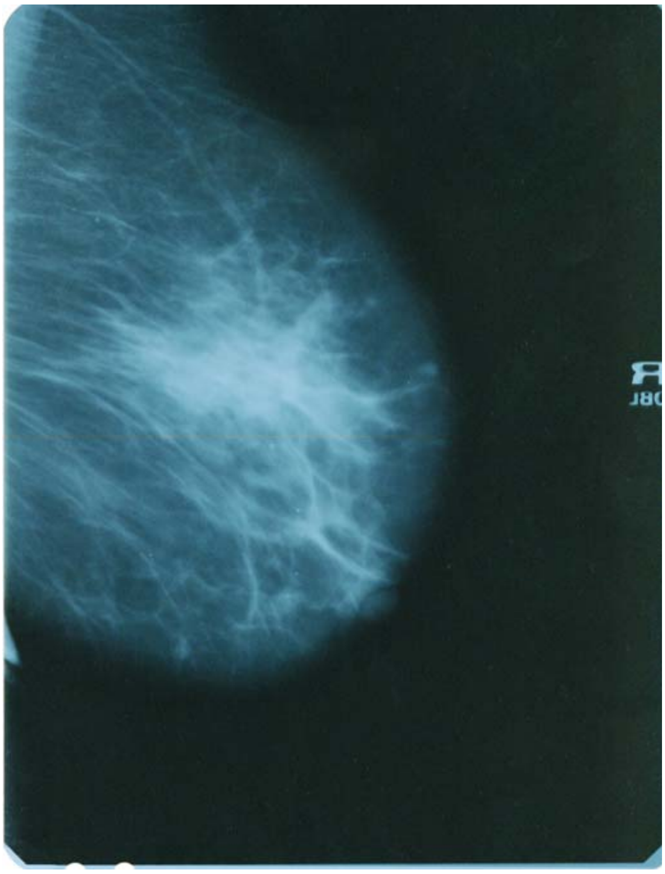



**Рис. 12-20.** EIM. Mixed type of mammary gland structure. Top row – left gland. Age norm. Lower row – right gland. In the outer segment there is an isoimpedance formation measuring 30x20 mm with a hyperimpedance contour.



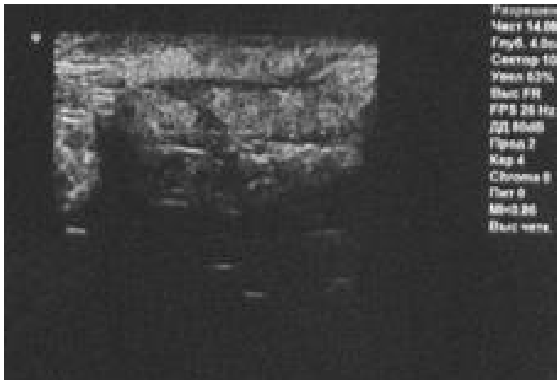


**Рис. 12-20а.** ULTRASOUND: In the outer segment of the right gland there is observed an inhomogeneous area with an-echoic inclusions, measured 28x12 mm, with vascularization.

**Рис. 12-20б.** Roentgenogram: Local induration of mamma's structure.

A 69 years-old patient. Complaints concerning a nodularity in the left gland. Postmenopause duration: 16 years. Anamnesis: somatic - hepatic cyst; gynecological – no; obstetrical - labours 1, abortions 1; lactation – more than a year. Diseases of the breast – no (Fig. 12-21, 12-21a, 12-21b).

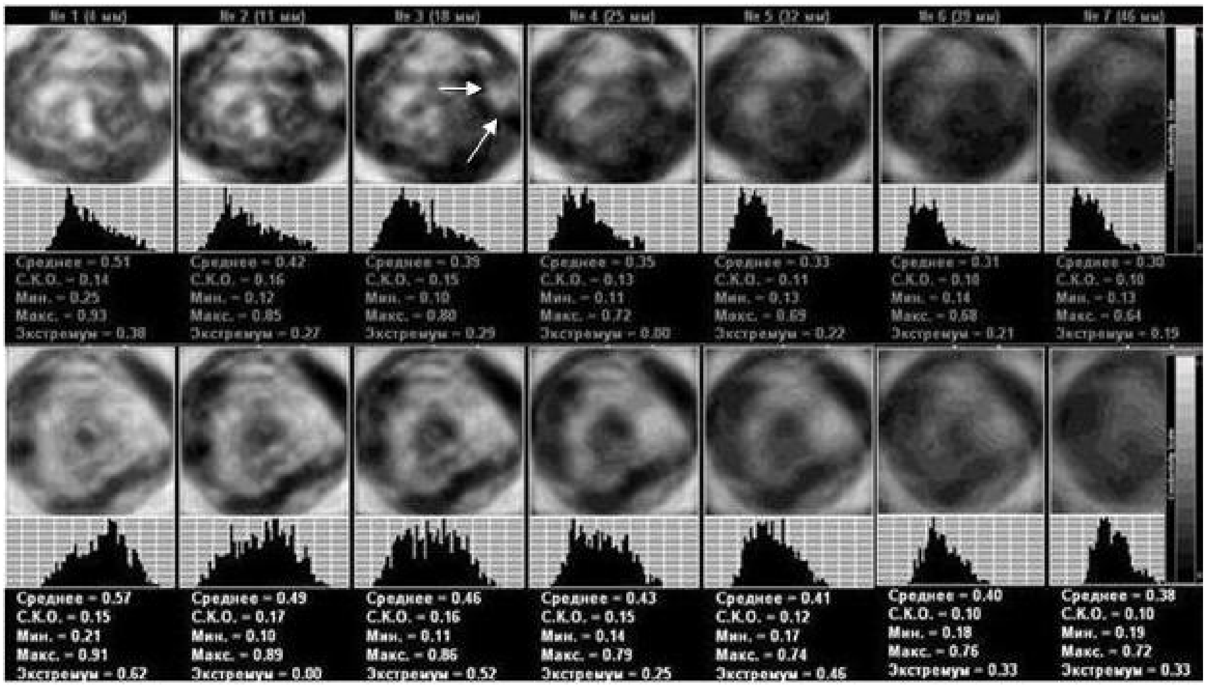
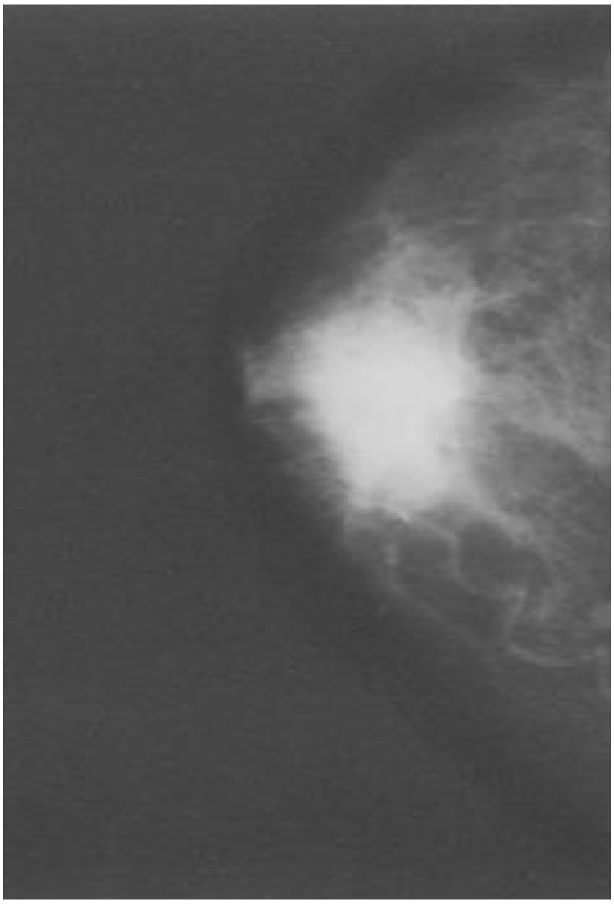



**Рис. 12-21.** EIM. Mixed type of mammary gland structure. Top row – left gland. In the outer segment there is an hypo-impedance formation measuring 30x20 mm with a hyper-impedance contour. The anatomy of the gland has been changed, hyper-impedance inclusions are present. Above the formation at 1 o'clock position there can be visualized an iso–impedance formation – it is a wart. Lower row – right gland. Age norm.



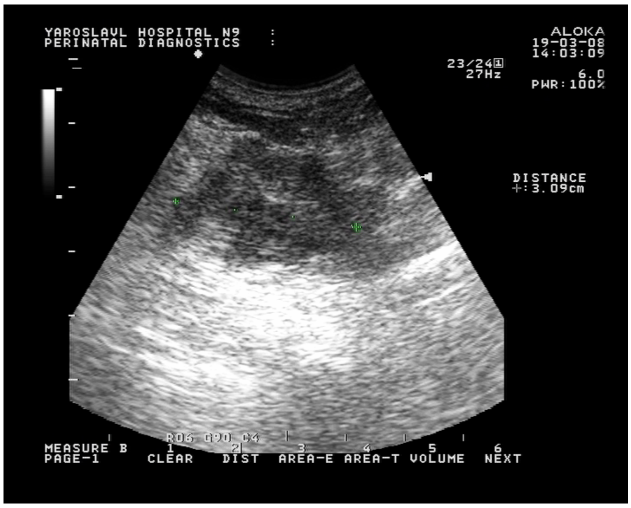



**Рис. 12-21a.** ULTRASOUND: In the outer segment of the left gland there is observed an inhomogeneous area of hypo-echoic structure with irregular-shaped contours, 3 mm in size, with moderate vascularization.

**Рис. 12-21б.** Roentgenogram: In the left there is the retracted nipple, in the center an area measured 3x4.5 cm with blurred contour can be observed.

A 76 years-old patient. Complaints concerning a nodularity in the left gland. Postmenopause duration: 28 years. Anamnesis: somatic - hepatic cyst; gynecological – no; obstetrical - labours 1, abortions 1; lactation – more than a year. Diseases of the breast – cancer of the right mammary gland. Mastectomy was conducted 7 years ago (Fig. 12-22, 12-22a, 12-22b).

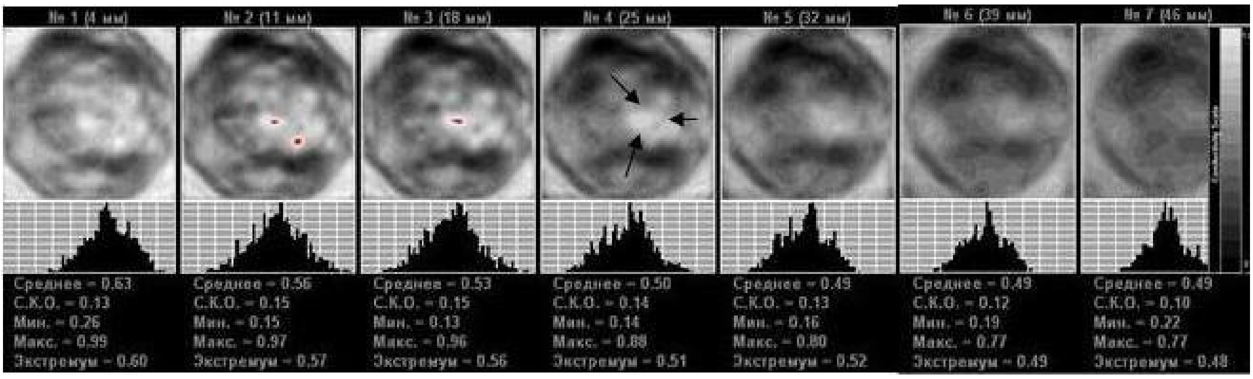
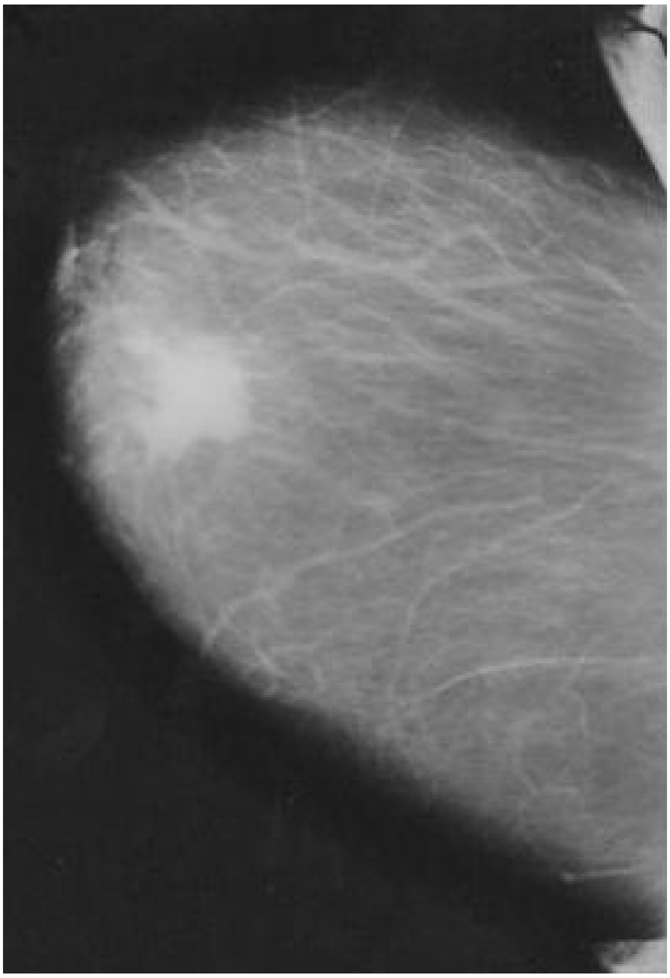



**Рис. 12-22.** EIM. Mixed type of mammary gland structure. In the boundary of the outer segments of the left gland there is observed a hypo-impedance area without distinct contours, 37x34 mm in size. The anatomy of the gland has been changed, hyper-impedance inclusions are present. **US:** In the boundary of the outer segments of the left gland there is observed a formation without distinct contours, approximately 28x16 mm in size, with intensive shadow. The structure of parenchyma with adipose lobules and connective tissue layers is observed.



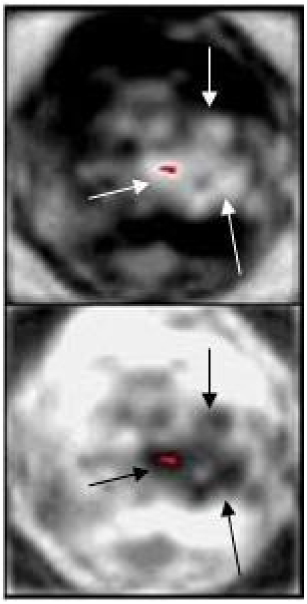


**Рис. 12-22a.** The image after contrasting and inversion.

**Рис. 12-22б.** Roentgenogram: In the boundary of the outer segments of the left gland there is observed a formation with a radiant contour.

A 53 years-old patient. Complaints concerning a nodularity in the left gland. 4th day of menstrual cycle. Anamnesis: somatic - hypertensive disease, gynecological - no, obstetrical - labours 3, abortions 1, lactation – more than a year. Diseases of the breast – mastitis. Histology – moderately differentiated adenocarcinoma (glandular cancer) (Fig. 12-23).

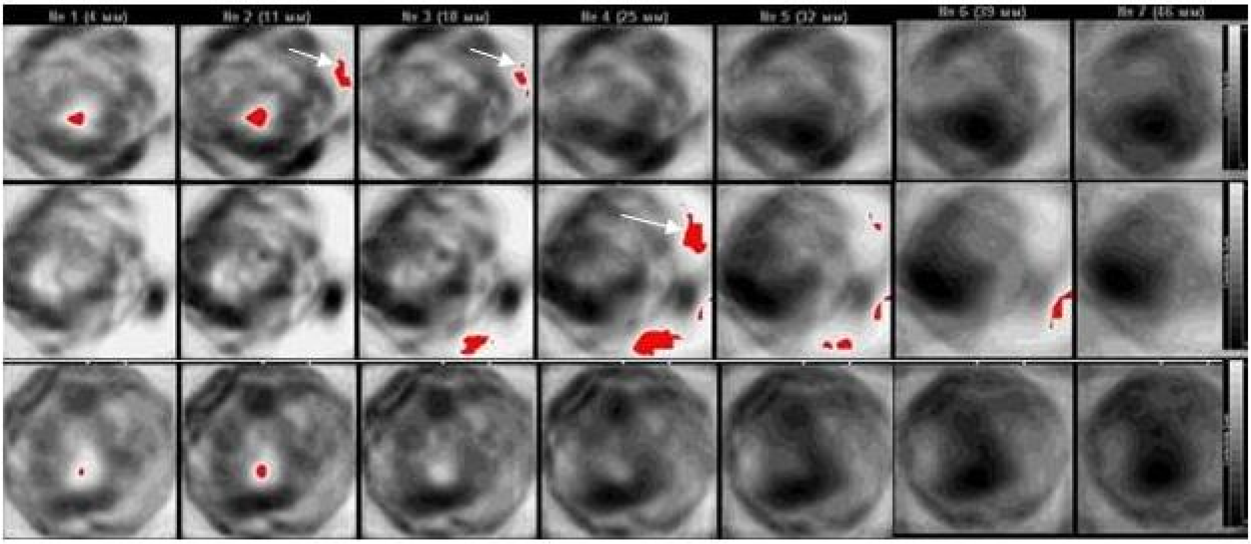


**Рис. 12-23.** EIM. Top row – left gland. The anatomy of the gland has been changed, hyper-impedance inclusions are present. At 3 o'clock position there is observed an an-impedance area, which is highlighted with red in two scan planes, 31x17 mm in size. The middle row represents the outer segment of the left gland. At 3 o'clock position there is observed an an-impedance area, which is highlighted with red. Lower row – right gland. Age norm. **US:** In the boundary of the outer segments of the left gland there is observed a hypo-echoic stellate formation measured 3.0x2.5x2.0 cm. The axillary lymph nodes are enlarged up to 2.2 cm.

A 77 years-old patient. Complaints concerning a nodularity in the right gland. Postmenopause duration: 35 years. Anamnesis: somatic - no; gynecological – no; obstetrical - labours 1, abortions 5; lactation – more than a year. Diseases of the breast – no (Fig. 12-24).

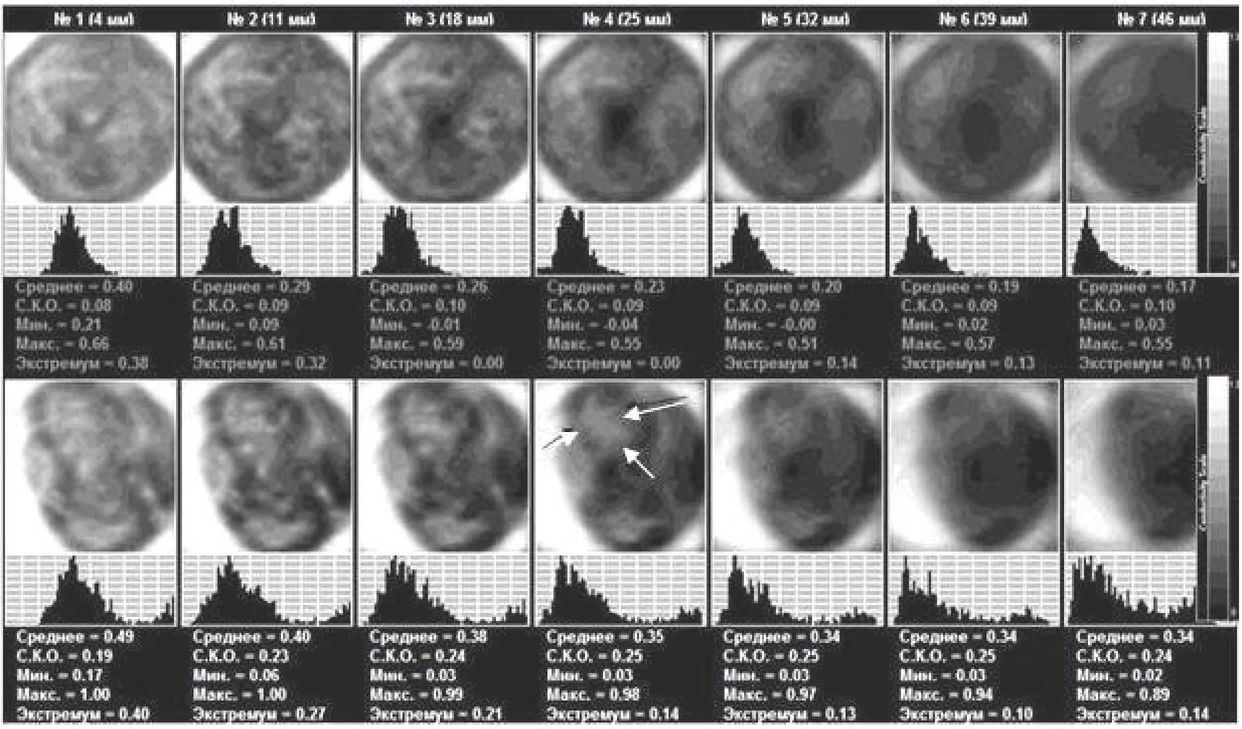



**Рис. 12-24.** EIM. EIM. Top row – left gland. Fibrous type of mammary gland structure. Lower row – right gland. Fibrous type of mammary gland structure. Outer segment. At 12 o'clock position there is an irregular-shaped inhomogeneous iso-impedance formation measuring 37x24 mm with a hyper-impedance contour. **ULTRASOUND:** In the upper-outer segment of the right gland, there is a formation with blurred contours and vascularization, 15x20 mm in size. An enlarged lymph node can be visualized in the axillary area.

A 50 years-old patient. Complaints concerning pain in the left mammary gland. Postmenopause duration: 5 years. Anamnesis: somatic - hypertensive disease, gynecological - no, obstetrical - labours 1, abortions 2, lactation – up to a year. Diseases of the breast – no (Fig. 12-25).

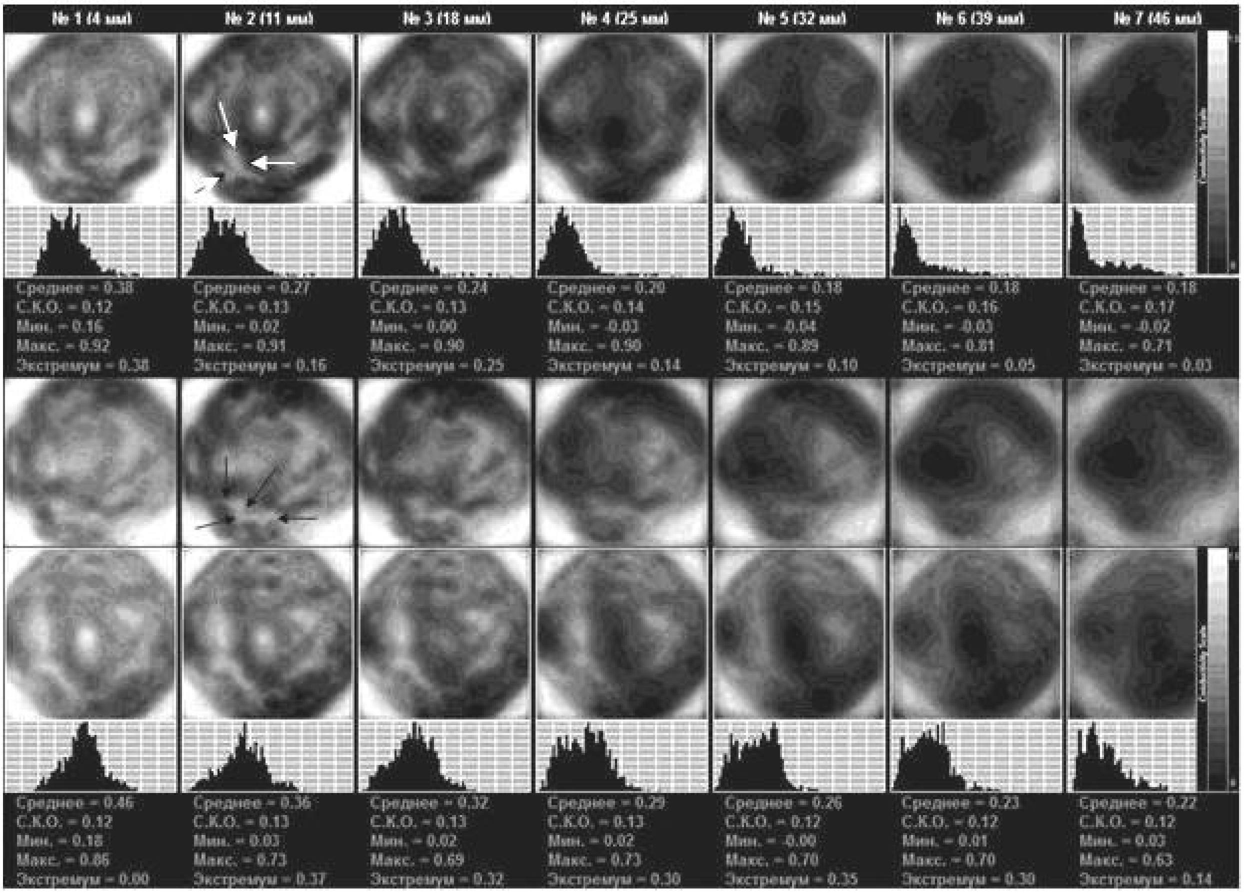



**Рис. 12-25.** EIM. Top row – left gland. Fibrous type of mammary gland structure. The hyper-impedance contour can be observed around the gland. In the lower segment there is an irregular-shaped iso-impedance formation measuring 27x17 mm with a hyperimpedance contour. The middle row represents the outer segment of the left gland. Lower row – right gland. Fibrous type of mammary gland structure. **ULTRASOUND:** In the lower segment of the left gland there is observed an inhomogeneous area with irregular blurred contours, measured 23x25x18 mm, with vascularization. There are two lymph nodes 15x8 and 13x8 mm in the axillary crease area..

A 67 years-old patient. Complaints concerning a nodularity in the right gland. Postmenopause duration: 13 years. Anamnesis: somatic - hypertensive disease, gynecological - no, obstetrical - labours 1, abortions 4, lactation – up to a year. Diseases of the breast – no (Fig. 12-26).

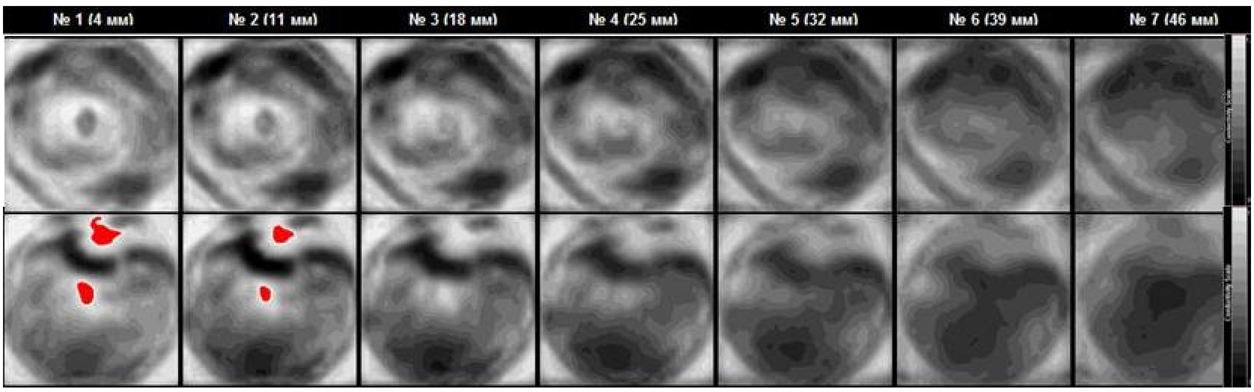



**Рис. 12-26.** EIM. Top row – left gland. Age norm. Lower row – right gland. In the upper segment there is observed an an-impedance area, which is highlighted with red in two scan planes, with hyper-impedance contour, measured 27x27 mm. **ULTRASOUND:** In the upper-inner segment of the right gland there is observed an area *4 cm in size with moderate blood flow.

A 75 years-old patient. Complaints concerning a nodularity in the left gland. Postmenopause duration: 22 years. Anamnesis: somatic - hypertensive disease, gynecological - no, obstetrical - labours 2, abortions 4, lactation – up to a year. Diseases of the breast – trauma (Fig. 12-27). Histology - infiltrate ductal carcinoma.

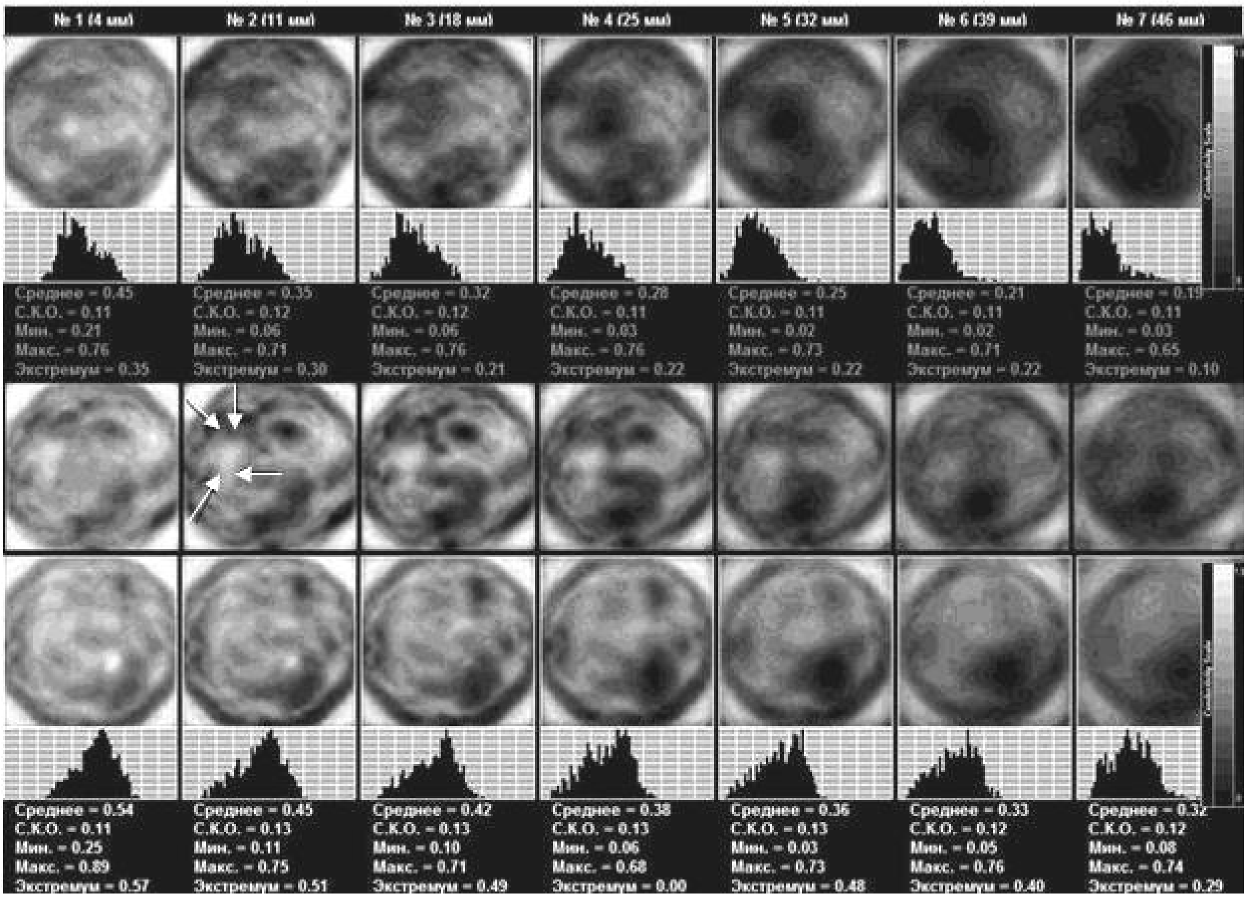



**Рис. 12-27.** EIM. Top row – left gland. Fibrous type of mammary gland structure. Hyper-impedance contour and background. The middle row represents the upper-outer segment of the left gland. At 9 o'clock position there is an irregular-shaped iso-impedance formation measuring 34x27 mm with a hyper-impedance contour. Lower row – right gland. Mixed type of mammary gland structure. **ULTRASOUND:** A 23x44x33 mm formation with blurred irregular-shaped contours is located in the boundary of upper-outer and lower segments of the left mammary gland.

A 56 years-old patient. Complaints concerning pain in the left mammary gland. Postmenopause duration: 8 years. Anamnesis: somatic - hypertensive disease; gynecological – hysteromyoma; obstetrical - labours 1, abortions 4; lactation – up to a year. Diseases of the breast – trauma. Histology – infiltrative ductal moderately differentiated cancer (Fig. 12-28).

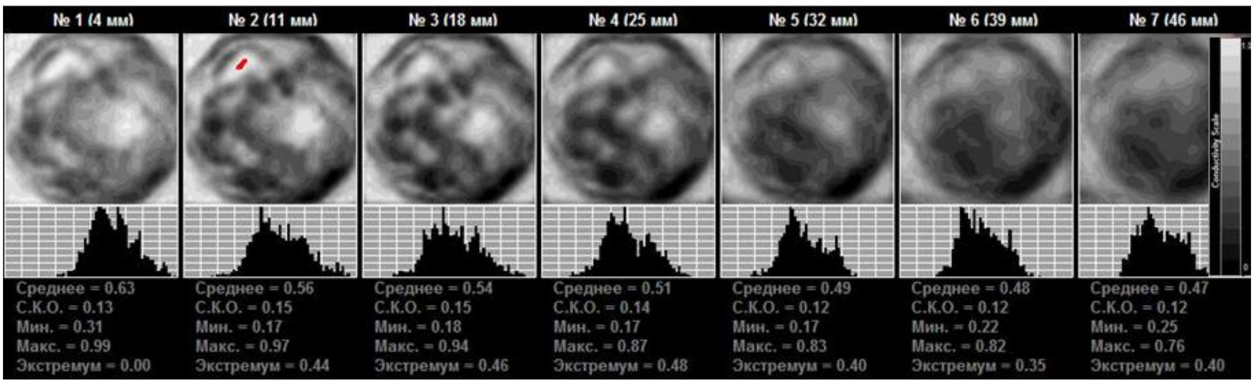



**Рис. 12-28.** EIM. The upper-inner segment of the left gland. Mixed type of mammary gland structure. At 11 o'clock position there is observed a hypo-impedance formation with the hyper-impedance contour and an an-mpedance area, highlighted with red, in the 2nd scan plane, measured 20x14 mm. **ULTRASOUND:** In the upper-inner segment of the left gland there is observed a hypo-echoic formation without distinct contours but with microcalcifications present, measured 16x10x11 mm.

A 55 years-old patient. Complaints concerning a nodularity in the left gland. Postmenopause duration: 14 years. Anamnesis: somatic - hypertensive disease; gynecological – hysteromyoma; obstetrical - labours 2, abortions 2; lactation – up to a year. Diseases of the breast – no. Histology – infiltrative ductal cancer of high malignancy with scirrhous nodes formation (Fig. 12-29).

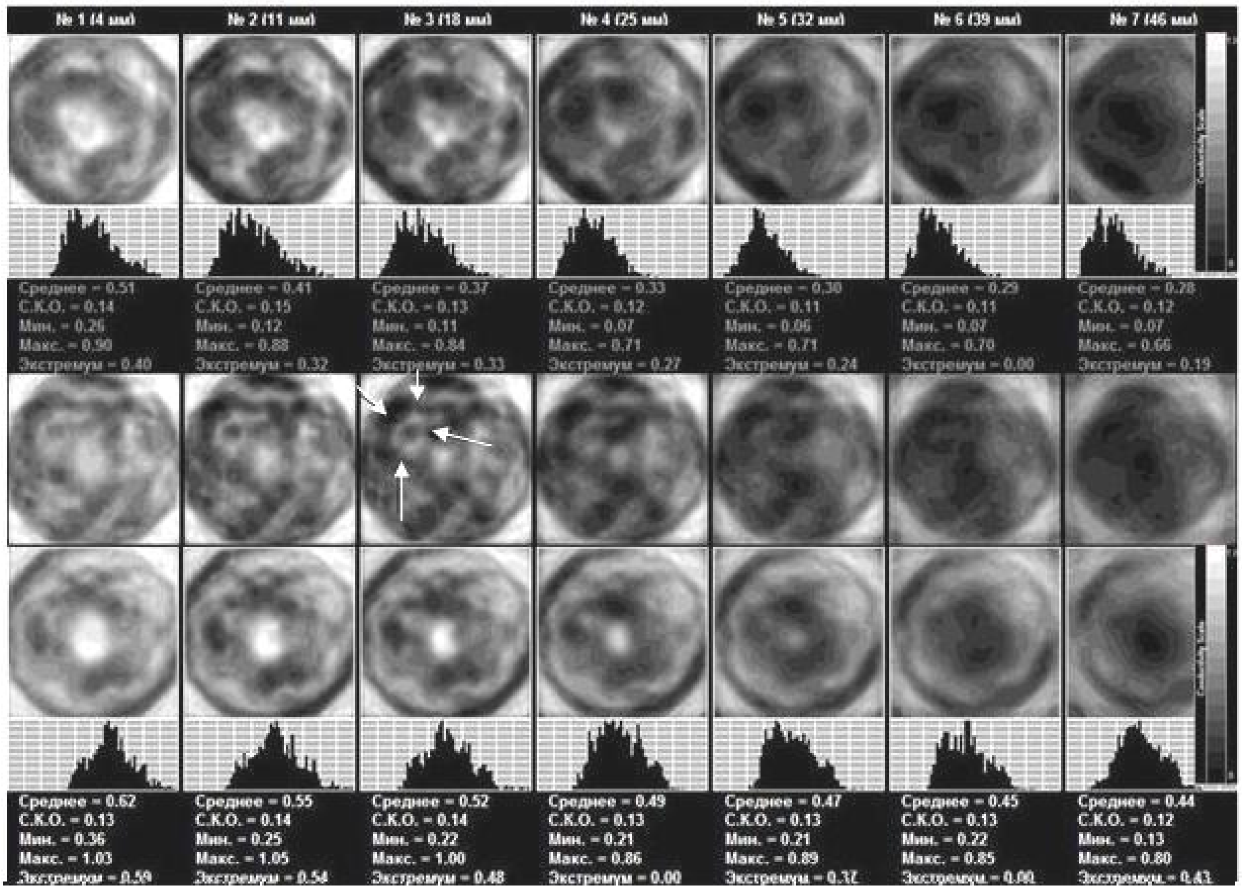



**Рис. 12-29.** EIM. Top row – left gland. Mixed type of mammary gland structure. Hyper-impedance contour and background. The middle row represents the upper-outer segment of the left gland. At 10 o'clock position there is an irregular-shaped iso-impedance formation measuring 37x27 mm with a hyper-impedance contour. Lower row – right gland. Mixed type of mammary gland structure. **ULTRASOUND:** In the upper-outer segment of the left gland there is a steady formation without distinct contours 35x37 mm in size (oedema, infiltration)..

A 56 years-old patient. Complaints concerning a nodularity in the left gland. Postmenopause duration: 4 years. Anamnesis: somatic - hypertensive disease, gynecological - no, obstetrical - labours 1, abortions 8, lactation – up to a year. Diseases of the breast – fibrocystic decease. Histology - low differentiated cancer (Fig. 12-30).

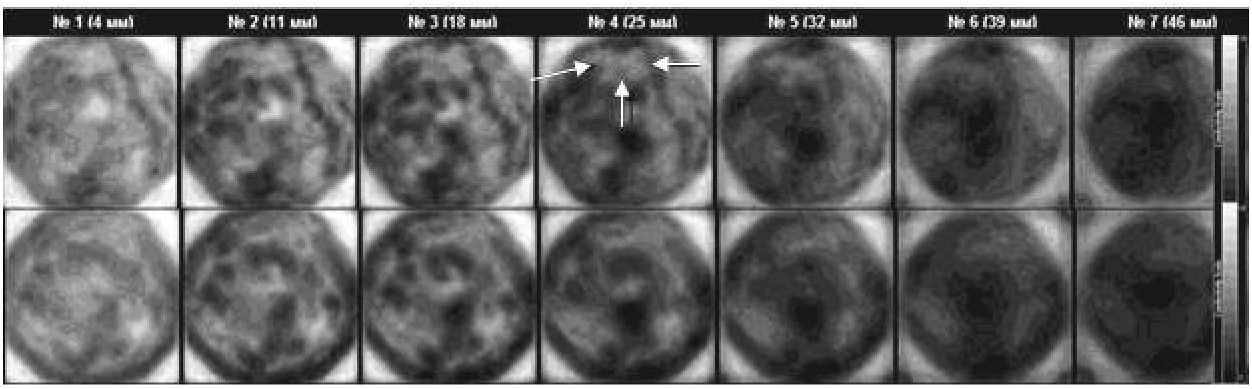



**Рис. 12-30.** EIM. Top row – left gland. In the upper segment there is an irregular-shaped iso-impedance formation measuring 30x17 mm with a hyper-impedance contour. Lower row – right gland. Fibrous type of mammary gland structure. **ULTRASOUND:** In the border of upper segments of the left gland there is observed a hypoechoic formation with distinct contours and microcalcifications present, measured 22x11x12 mm.

A 74 years-old patient. Complaints concerning pain in the left mammary gland. Postmenopause duration: 30 years. Anamnesis: somatic - hypertensive disease, gynecological - no, obstetrical - labours 2, abortions 2, lactation – more than a year. Diseases of the breast – no. Histology - infiltrate ductal carcinoma with necrosis areas (Fig. 12-31).

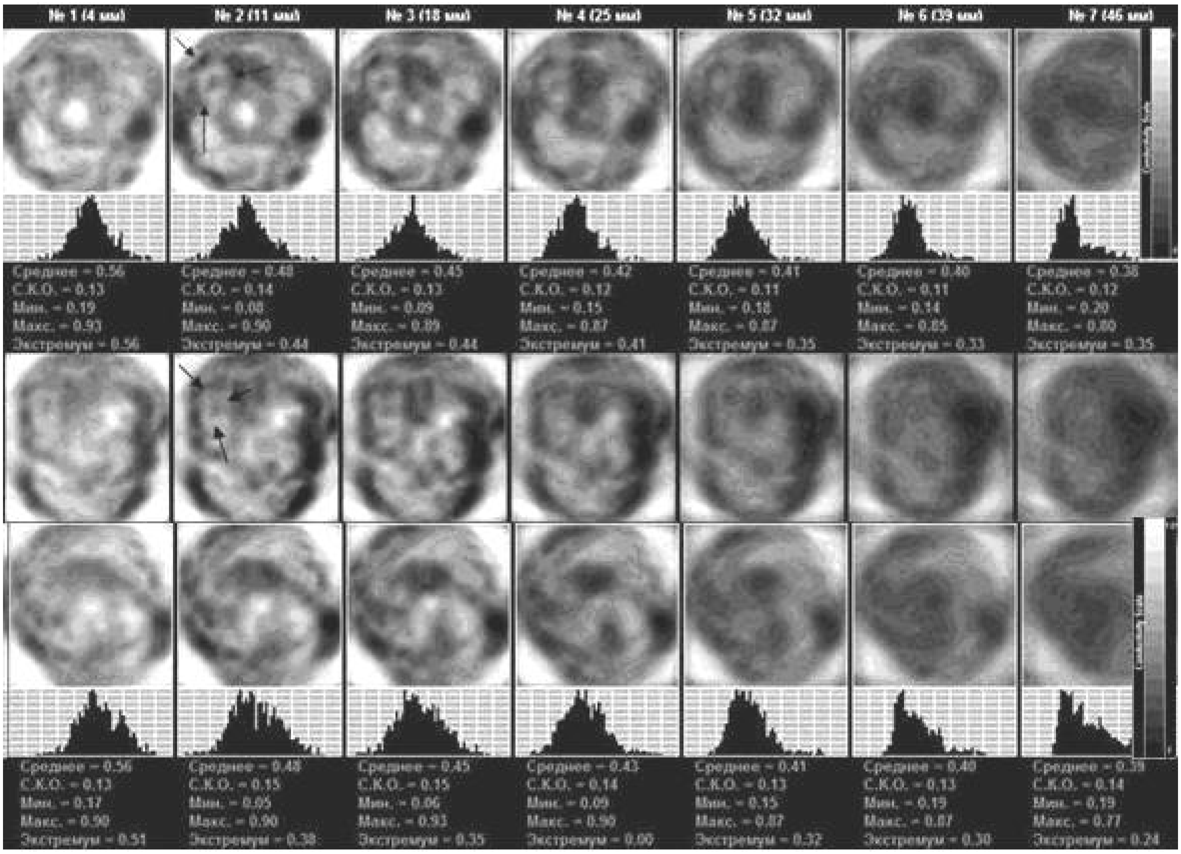


**Рис. 12-31.** EIM. Top row – left gland. Mixed type of mammary gland structure. At 10 o'clock position there is an iso-impedance formation measuring 27x22 mm with a hyper-impedance contour. The middle row represents the upper segment. At 10 o'clock position there is an iso-impedance formation with hyper-impedance intensification. Lower row – right gland. Mixed type of mammary gland structure. **US:** In the boundary of the inner segments of the left gland close to areola, there is observed an inhomogeneous area with irregular-shaped indistinct contour and side shadow effect, 13x14x15 mm in size, nearby there is an an-echoic formation, measured 11x6x7 mm with parietal component.очным компонентом.

A 74 years-old patient. Complaints concerning a nodularity in the right gland. Postmenopause duration: 24 years. Anamnesis: somatic - hypertensive disease, gynecological - no, obstetrical - labours 2, abortions 4, lactation – more than a year. Diseases of the breast – no. Histology - infiltrative ductal highly differentiated lobular cancer (Fig. 12-32).

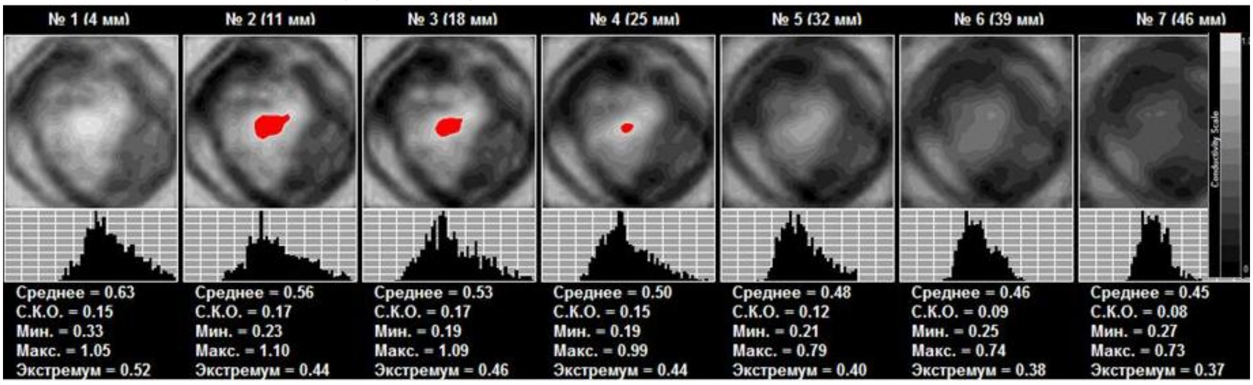



**Рис. 12-32.** EIM. The right gland. Outer segment. Hyper-impedance background. In the center - an an-impedance area, which is highlighted with red in three scan planes, 20x14x18 mm in size. **US:** In the outer segment of the right gland there is observed an echo-positive area, measured 28x19x31 mm, most likely - fibrolipoma.

## Diffuse Type of Cancer

The peculiarity of the pathophysiological mechanism of this kind of decease is the total lymphatic edema which causes the increase of general electrical impedance. Diagnostic criteria are the following: pronouncedly high impedance of the affected mammary gland, changed anatomy of the gland, absence of an-impedance area with the conductivity index >0.95. The electrical conductivity index is definitely lower for the affected gland than for both the healthy gland and the age-specific norm.

Then we would like to provide various electrical impedance images and the data of different diagnostic techniques in case of the diffuse type of breast cancer.

### *Infiltrative-Edematous Form of Breast Cancer*

A 70 years-old patient. Complaints concerning redness and infiltration in the right gland. Postmenopause duration: 20 years. Anamnesis: somatic - hypertensive disease, gynecological - no, obstetrical - labours 2, abortions 8, lactation – up to a year. Diseases of the breast – trauma. Histology - infiltrating ductal carcinoma with scirrhous structures prevailing (Fig. 12-33).

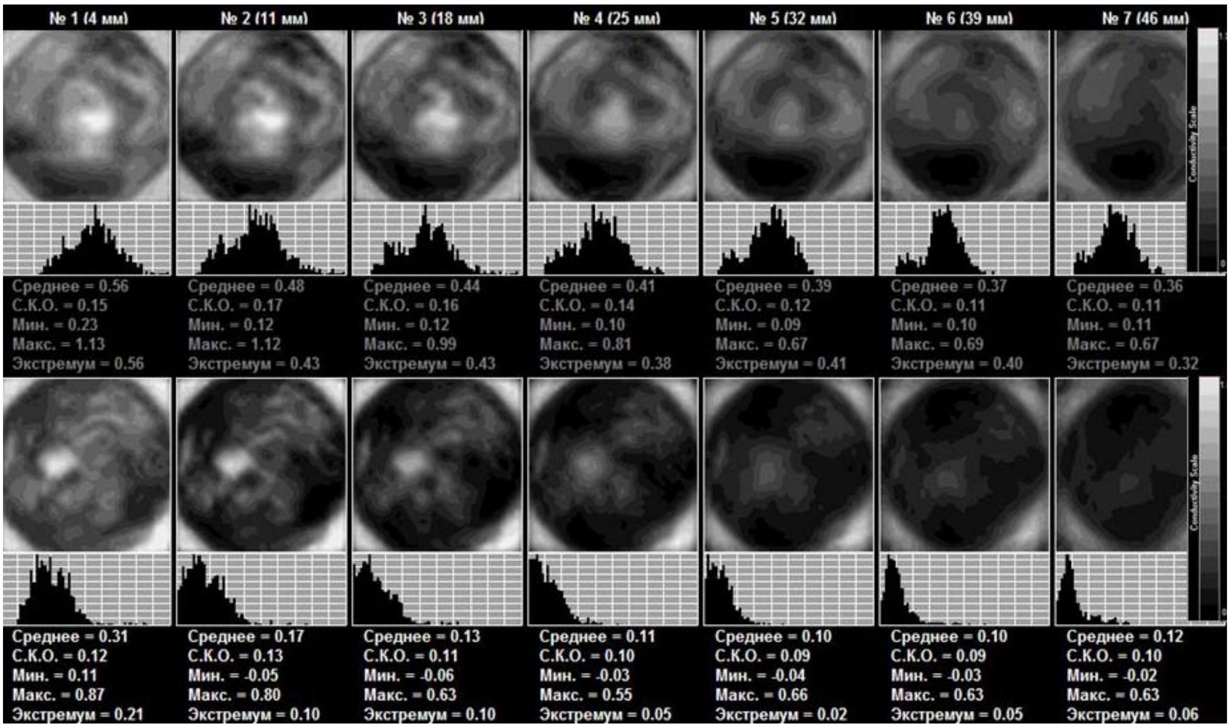



**Рис. 12-33.** EIM. Top row – left gland. Mixed type of mammary gland structure. Lower row – right gland. Well-defined hyper-impedance background. The anatomy is altered. Electrical conductivity index is three-fold less than normal. **ULTRASOUND:** Diffuse Type of Cancer

A 59 years-old patient. Complaints concerning redness and infiltration in the right gland. Post-menopause duration: 15 years. Anamnesis: somatic - no; gynecological – no; obstetrical - labours 1, abortions 5; lactation – up to a year. Diseases of the breast – no. (Fig.12-34).

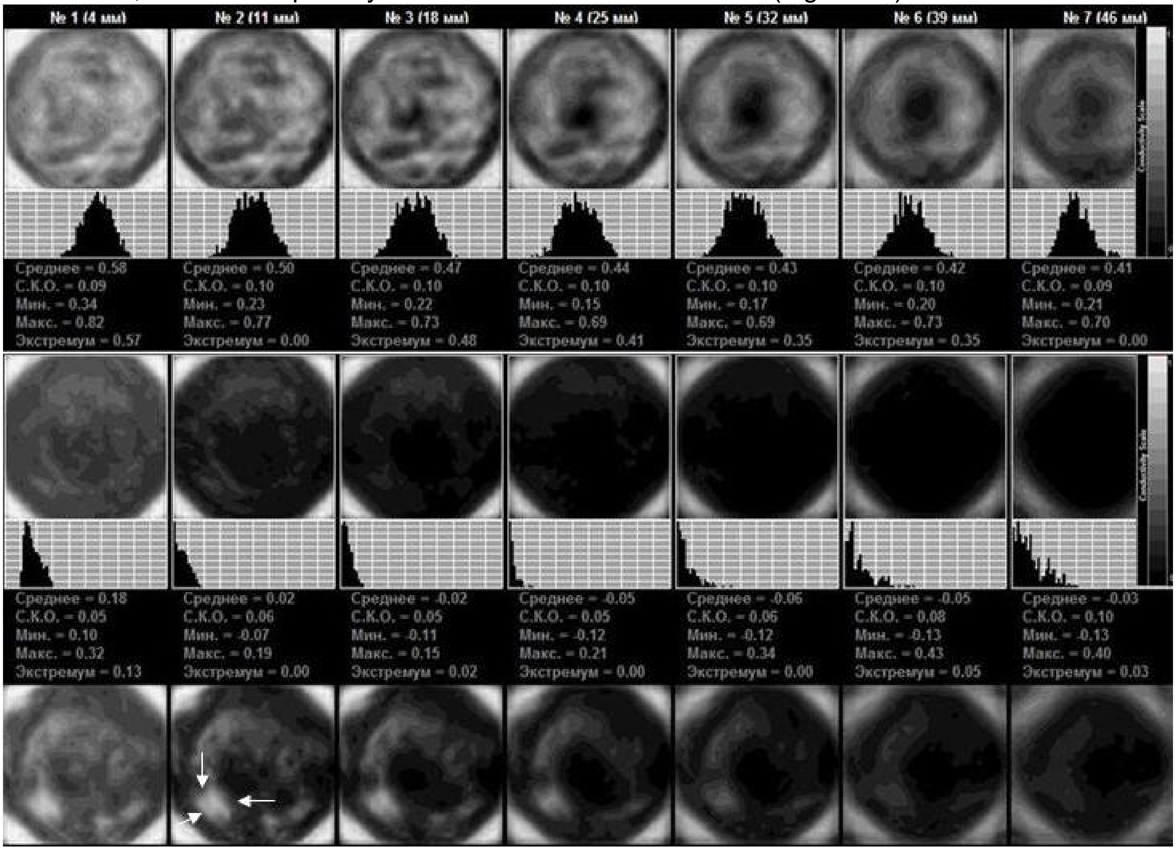
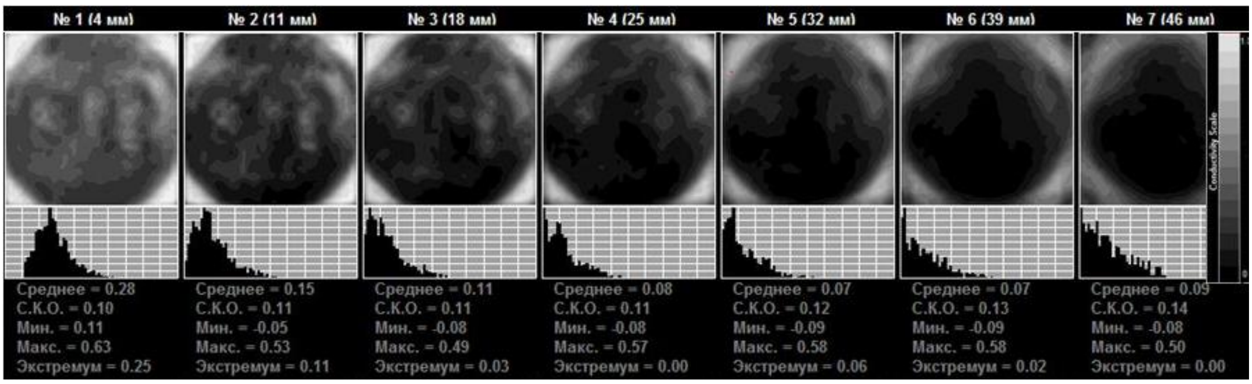
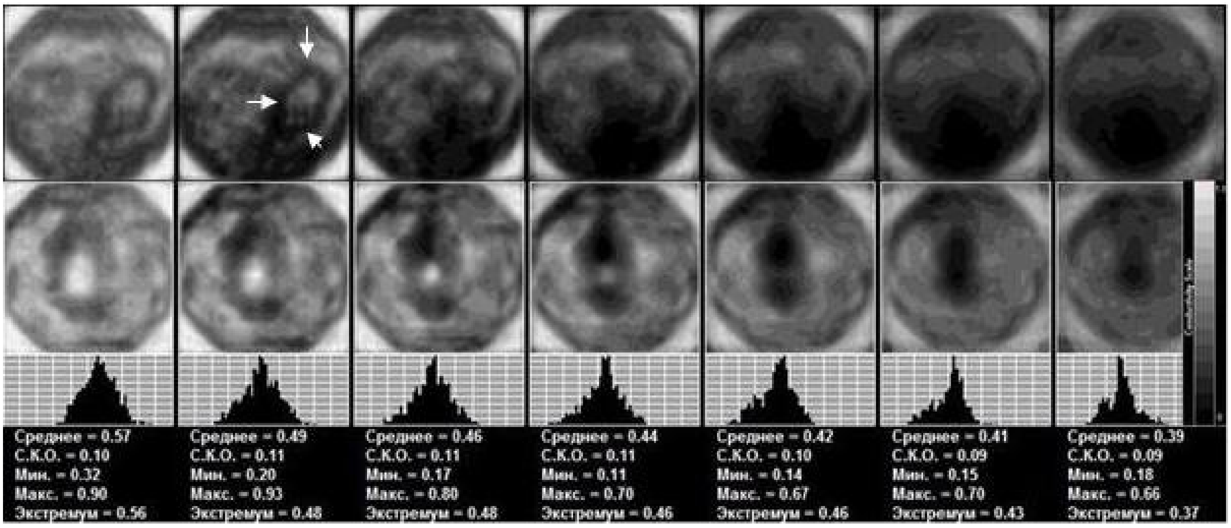



**Рис. 12-34.** EIM. Top row – left gland. Mixed type of mammary gland structure. Middle row – right gland. Well-defined hyper-impedance background. The anatomy is altered. Electrical conductivity index is significantly reduced. The lower row represents the upper segment. At 7 o'clock position there is an iso-impedance formation measuring 20x27 mm. **ULTRASOUND:** In upper-outer segment close and above the nipple there is an inhomogeneous vascular formation without indistinct contours, 30x19 mm.

A 72 years-old patient. Complaints concerning oedematous left hand. Postmenopause duration: 22 years. Anamnesis: somatic - hypertensive disease, gynecological - ovarian carcinoma, obstetrical - labours 1, abortions 1, lactation – up to a year. Diseases of the breast – trauma (Fig. 12-35).

**Рис. 12-35.** EIM. Top row – left gland. Well-defined hyper-impedance background. The anatomy is altered. Electrical conductivity index is three-fold less than normal, left gland. The middle row represents the upper segment. At 4 o'clock position there is an iso-impedance formation measuring 24x34 mm with a hyper-impedance contour. Lower row – right gland. Mixed type of mammary gland structure. **ULTRASOUND:** In upper-outer segment at the areola level there is an avascular formation, measured 9x4x8 mm. In the boundary of the outer segments there is observed a formation, 6x5x8 mm in size, with calcification area in the centre.






A 58 years-old patient. Complaints concerning oedema and hyperemia of the right mammary gland and bloody discharge from the nipple. Postmenopause duration: 10 years. Anamnesis: somatic - hypertensive disease, gynecological - no, obstetrical - labours 2, abortions 3, lactation – up to a year. Diseases of the breast - no (Fig. 12-36).

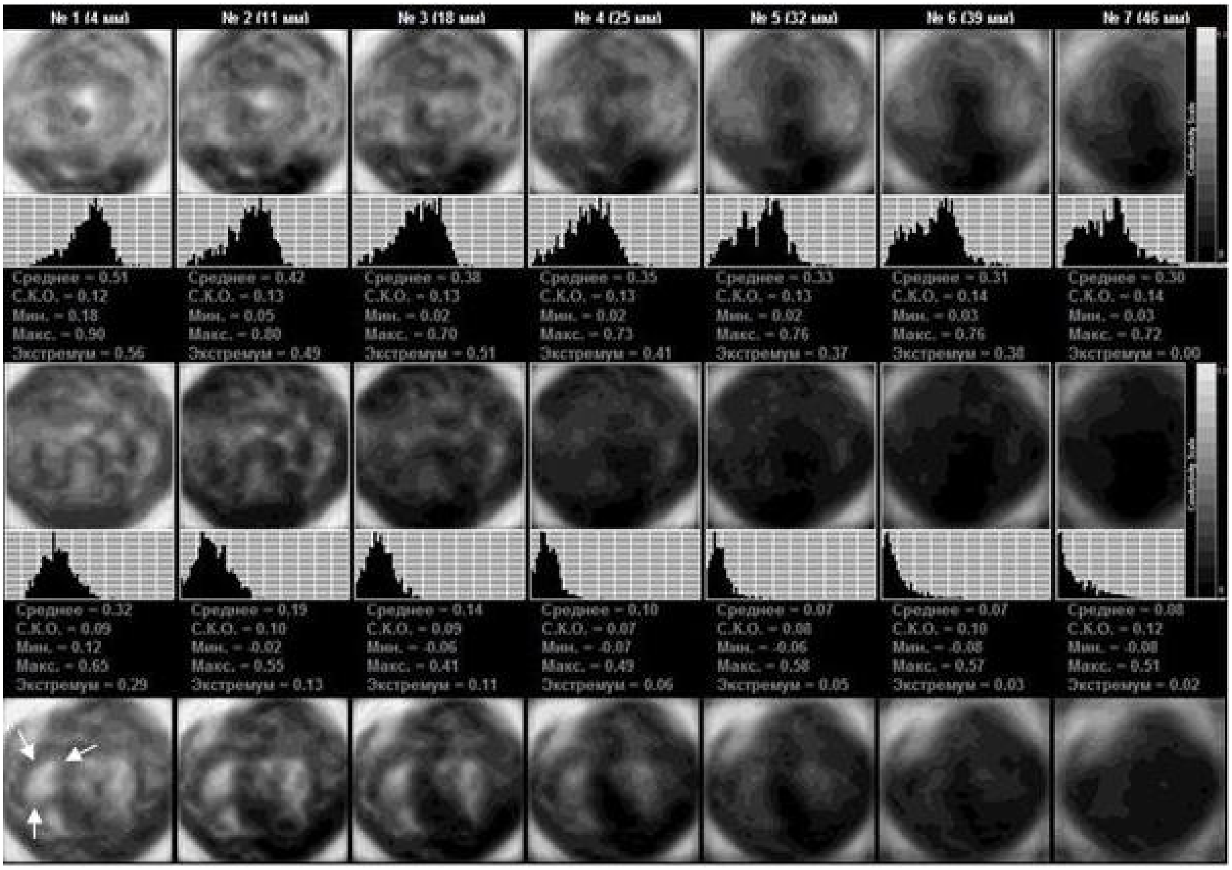



**Рис. 12-36.** EIM. Top row – left gland. Mixed type of mammary gland structure. Middle row – right gland. Well-defined hyper-impedance background. The anatomy is altered. Electrical conductivity index is significantly reduced. The lower row represents the upper segment. At 9 o'clock position there is an iso-impedance formation measuring 17x24 mm. **ULTRASOUND:** In the boundary of the outer segments of the right gland there is observed an inhomogeneous avascular formation without distinct contours, 18x12 mm in size.

## *Carcinomatous Mastitis*

A 56 years-old patient. Complaints concerning an oedema and a nodularity in the left gland. Postmenopause duration: 12 years. Anamnesis: somatic - hypertensive disease, gynecological - no, obstetrical - labours 1, abortions 1, lactation – up to a year. Diseases of the breast – trauma (Fig. 12-37).

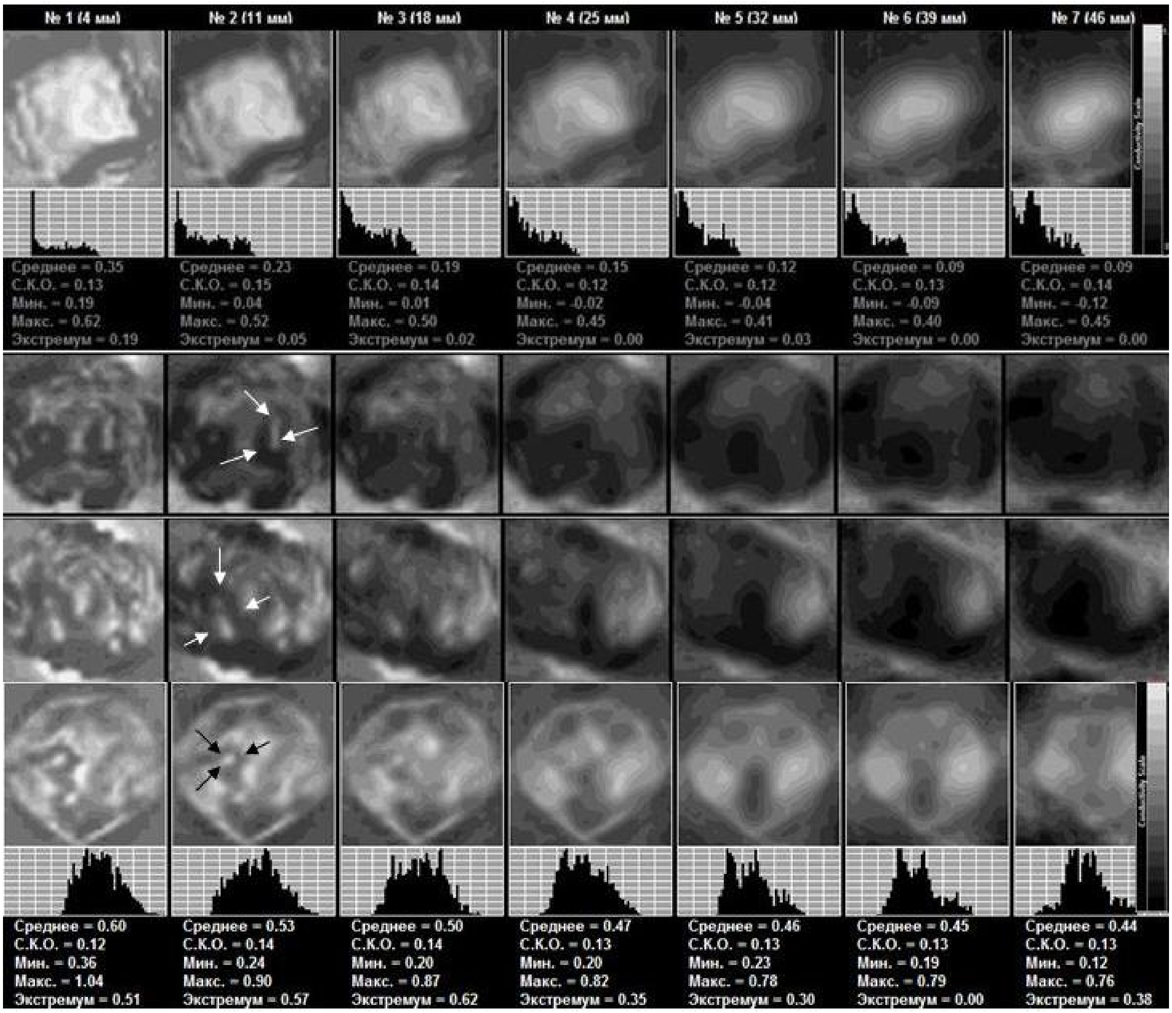



**Рис. 12-37.** EIM. First row – left gland. The anatomy is altered. Well-defined hyper-impedance contour. Local changes are not present. The second row represents the upper segment. In the upper-outer segment there is an iso-impedance formation with a hyper-impedance contour, measuring 27x10 mm. The third row represents the outer segment. At 7 o'clock position there is an iso-impedance formation with a hyper-impedance contour. Fourth row – right gland. Mixed type of mammary gland structure. The anatomy is altered. In the outer segment there is an iso-impedance formation with a hyper-impedance contour, measuring 14x10x14 mm.
**ULTRASOUND:** In the lower-outer segment of the left gland there is observed an inhomogeneous irregular-shaped area with hyper-echoic inclusions, measured 26x20 mm, with vascularization on the periphery. Total infiltration hampers visualization. The structure of the mamma is characterized by the prevalence of adipose lobules and connective tissue layers. In the upper-outer segment of the right gland there is observed a homogeneous area with distinct contours, intensive shadow and peripheral vascularization, measured 20x15 mm. The structure of the mamma is characterized by the prevalence of adipose lobules and connective tissue layers. A set of enlarged lymph nodes can be visualized in the left axillary crease area.
**Roentgenogram:** fibro-fatty involution. The left gland is distorted, tightened, the nipple is retracted. There is an area measured up to 7 cm with blurred contour in the centre. In upper-outer segment of the right gland there is observed a lesion up to 25 cm in size with a radiant contour, microcalcifications cluster is present. Carcinoma of both mammary glands.

Table 12-2 provides generalized data for visual and quantitative evaluation of electrical impedance mammograms of the patients with various cancer forms.

Thus, the revealed peculiarities of the electrical impedance image typical for different forms of infiltrative breast cancer growth correspond to pathophysiological phases of tumour development. It is essentially important for electrical impedance diagnostics to distinguish non-complicated and compli cated forms of the decease. The basic features of non-complicated forms of breast cancer reflected in the images include a high local electrical conductivity index of the tumor and zero reaction of the surrounding tissue. To diagnose infiltrating cancers complicated by oedema, inflammation or vascularization disturbance one is to employ other criteria, such as the change of the mamma's contour, the displacement of the inner structures of the gland, perifocal infiltration, etc.

**Table 12-2.** Data for visual and quantitative evaluation of electrical impedance mammograms of the patients with various cancer forms.

| **Indication** | | **Norm** | **Non-complicated form** | **Complicated form** | **Infiltrative-edematous form** |
|---|---|---|---|---|---|
| **Contour** | Deformation | - | 0% | 50% | 0% |
| | Hyper-impedance | - | 11% | 61% | 100% |
| **Anatomy** | Preserved | 100% | 100% | 22% | 0% |
| | Changed | - | - | 78% | 100% |
| **Animpedance area (electrical conductivity index >0,95)** | Observed | - | 100% | 22% | - |
| | Absent | 100% | - | 78% | - |
| **Hyper-impedance infiltration** | Observed | - | 11% | 94% | 100% |
| | Absent | - | - | 6% | - |
| **Electrical conductivity index of the mammary gland** | Affected gland | - | 0,51±0,09 | 0,39±0,09 | 0,12±0,08 |
| | Healthy gland | 0,53±0,069 | 0,50±0,10 | 0,46±0,10 | 0,48±0,03 |
| | Focus (area) | - | 0,97±0,03 | 0,61±0,23 | |

## Paget's (nipple) cancer

Paget's cancer is a rare, hard-to-diagnose decease, which is histologically characterized by the emergency of numerous adenocarcinoma nidi in epidermis, which is distributing via hair follicles and perspiratory glands.

Histological peculiarity of this decease consist in the fact that tumour area comprises not only parenchyma (as in case of ordinary cancer), but also a nipple area and junctions of many ducts. Paget's cells are the result of a peculiar transformation of the Malpighian layer. Firstly epidermis is still not much disorganized (that is similar to the ordinary cancer development in the early stage), but then epitheliomatous stage begins, when epithelium thickens and forms a plaque. Epithelioma develops and makes for infiltrate appearance. In junctions of large ducts the same alterations take place with moderate disorganization.

Electrical impedance manifestations of the decease are not specific. However it is possible to distinguish the following diagnostic criteria: pronounced hyperimpedance area in the nipple zone, mamma’s anatomy change compared to a healthy one (Fig . 12-38).

Then we would like to provide various electrical impedance images and the data of different diagnostic techniques in case of Paget's (nipple) cancer.

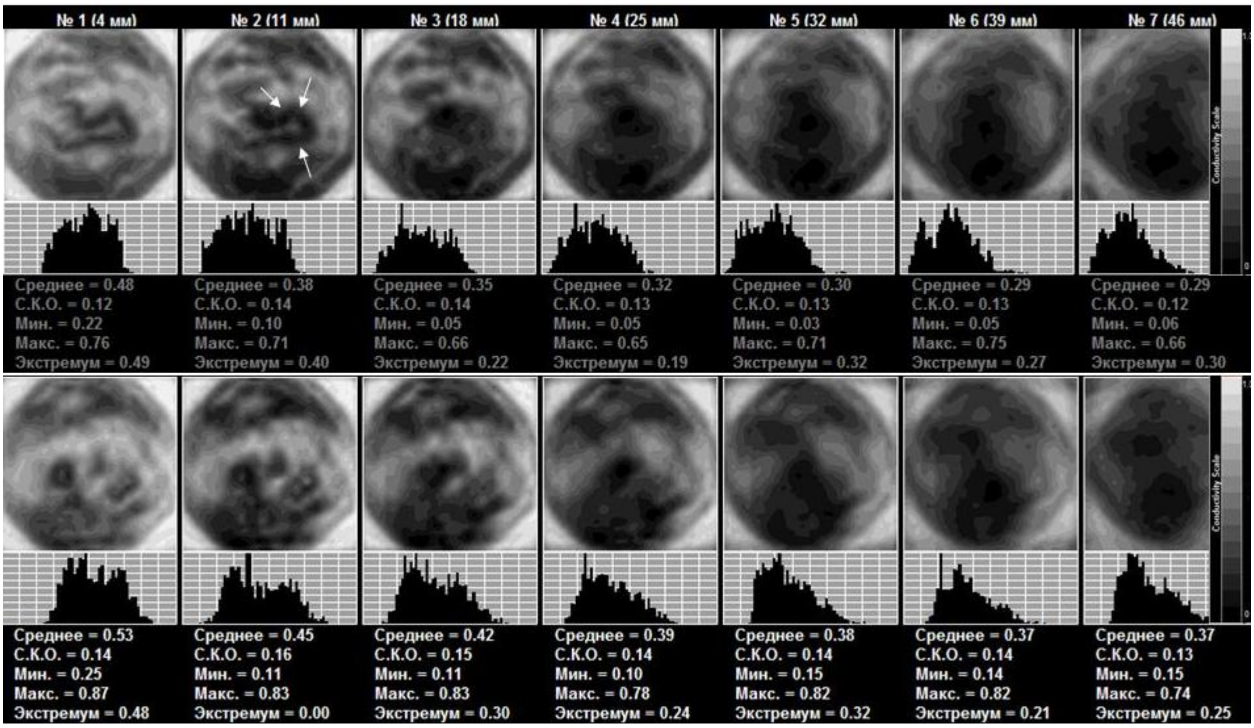



**Рис. 12-38.** EIM. Top row – left gland. Hyper-impedance background. The thickened nipple with blurred hyper-impedance contours is visualized in the central segment. Lower row – right gland. Mixed type of mammary gland structure.

A 39 years-old patient. Complaints concerning redness of the areola skin of the right breast, emergency of crusts in this area. 4th day of menstrual cycle. Anamnesis: somatic - no; gynecological – no; obstetrical - labours 1, abortions 2; lactation – more than a year. Diseases of the breast – no. Histology (scraping) – Paget's cancer (Fig. 12-39).

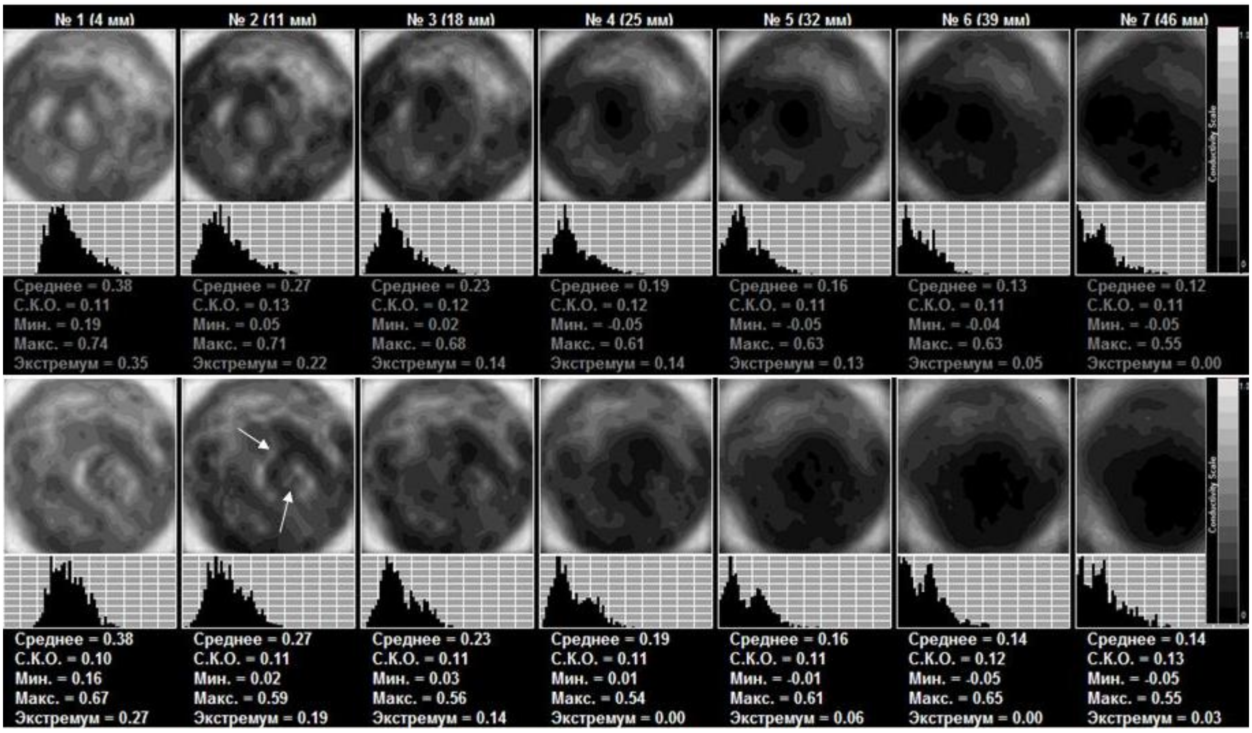



**Fig. 12-39.** EIM. Top row – left gland. Ductal type of mammary gland structure. Lower row – right gland. Ductal type of mammary gland structure. The anatomy of the areolar area is altered. Hyper-impedance contour. **ULTRASOUND**: Areolar oedema characters in the right. **Roentgenogram:** In areolar and nipple area on the right, there is an area with irregular blurred contours, emerging above the surface.

A 77 years-old patient. Complaints concerning a nodularity in the nipple area of the left gland. Postmenopause duration: 28 years. Anamnesis: somatic - no; gynecological – no; obstetrical - labours 2, abortions 2; lactation – more than a year. Diseases of the breast - fibrocystic decease. Histology (scraping) – Paget's cancer (Fig. 12-40).

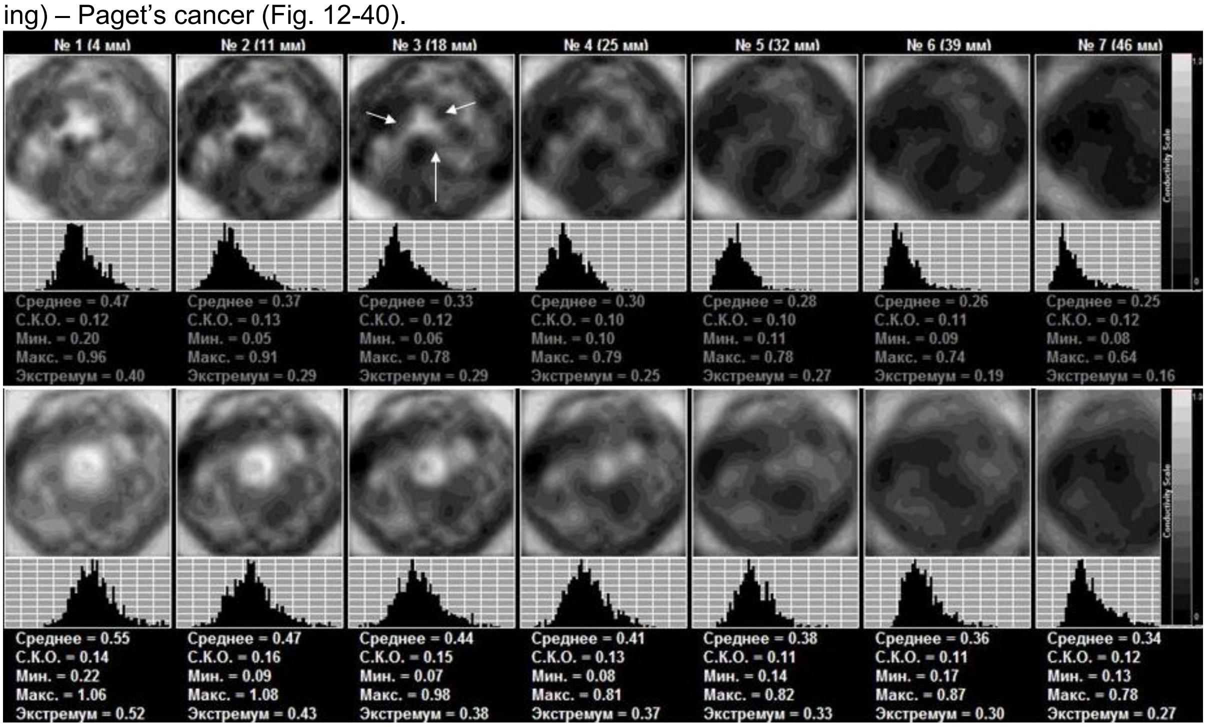



**Fig. 12-40.** EIM. Top row - left gland. Hyper-impedance background. The areolar area is irregular-shaped with a hyper-impedance contour. Lower row – right gland. Mixed type of mammary gland structure.

# Breast Cancer Screening

# Addendum

World Health Organization defines screening as the presumptive identification of unrecognized disease or defects by means of tests, examinations, or other procedures that can be applied rapidly and for the large population groups.

It is reasonable to develop such tests, which do not require high-skilled experts, though use widely computer aids and application software. Nowadays pre-clinical diagnostic criteria, which are acquired after statistical processing of great diagnostic information arrays and which enable to determine high-risk cancer groups of patients, become more and more important.

A high-risk cancer group should be defined as the group of people in the community with symptoms of the so-called "pre-existing disease" which can be detected due to various reasons. The "pre-existing disease" concept is of special importance in connection with the given opportunity to actively conduct cancer prevention measures already on such an early stage.

Screening is a dynamic process. And in this connection, the usage of safe screening methods makes sense, because it enables to conduct multiple repeated examinations. Electrical impedance mammography is just the sort of method which can be repeatedly used to examine a patient. Examination frequency, particularly for the patients belonging to the high-risk cancer group, shall be selected individually, depending on the pathology revealed.

*Early Diagnostics of Breast Cancer*

In majority of medical research statistical diversion validation criteria are calculated to validate the diagnostic significance of a test. However, these criteria are not enough. If the method of diagnostics under examination permits to acquire a numerical result, the so-called "breaking point" (the value exceeding of which is considered as a sufficient cause for qualitative assessment) should be determined. In this case the estimation of diagnostic technique efficiency may be limited to sensitivity and specificity assessment.

The diagnostic criterion, employed in electrical impedance mammography method when screening for early stages of breast cancer, is the detection of the high electrical conductivity areas (above 0.95 cu) – the so-called animpedance areas, which differ markedly from electrical conductivity of healthy mamma's areas - in the electrical impedance mammogram outside the lactiferous sinus zone.

With such a breaking point the sensitivity and specificity of electrical impedance mammography are quite high: sensitivity is 84-93%, specificity –

87-99% (according to the data given by different authors).

The following is the example of electrical impedance diagnostic. Figure 1 represents the electrical impedance mammogram of a patient. There can be distinguished a focal lesion, in the form of animpedance area, highlighted with red, with electrical conductivity index over 0.95 conditional units.

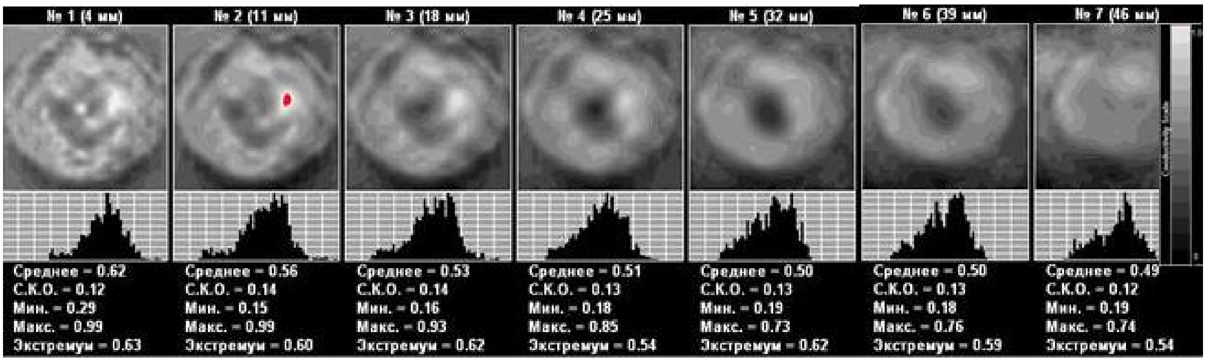



**Fig. 1.** EIM. Amorphous type of mammary gland structure. In the outer segment of the left mammary gland, at 3 o'clock position there is observed an an-impedance area, which is highlighted with red in the second scan plane, less than 10 mm in size.

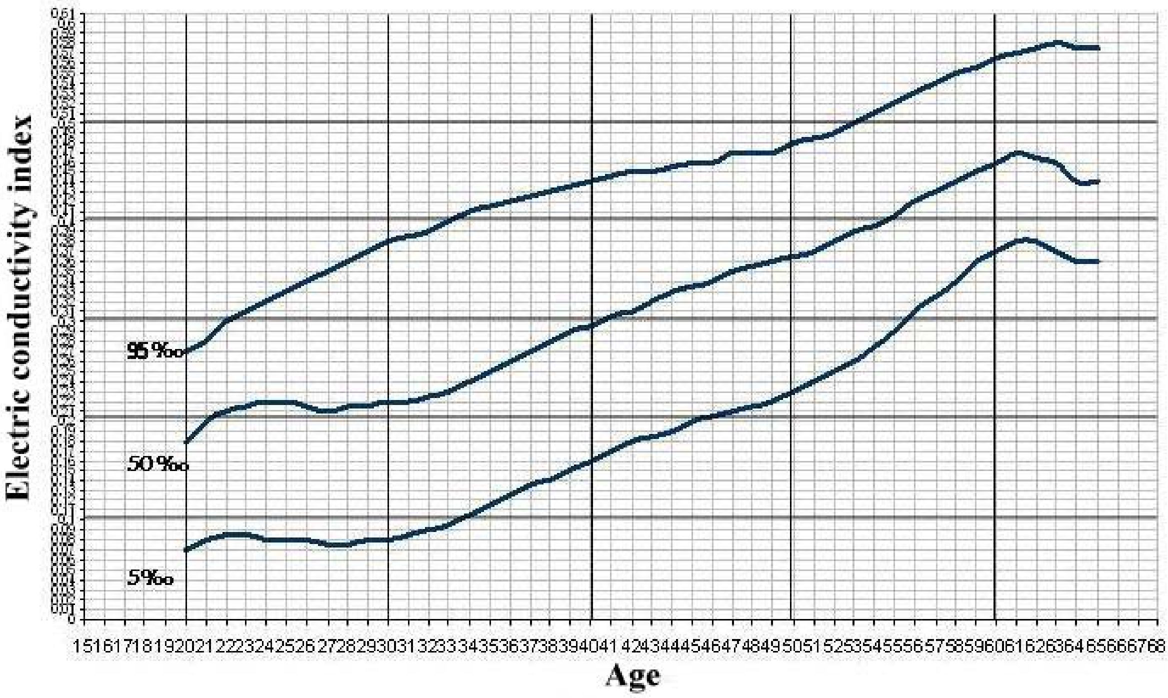



**Fig. 2.** Percentile curves of age-related electrical conductivity of the mammary gland. Mean electrical conductivity index (red marking) is lower than age norm (<5‰).

*High-Risk Group Formation*

To form a high-risk group the age-related electrical conductivity scale (Fig. 2) and anomalous divergence in electrical conductivity distribution histograms between left and right breast are used. To form the so-called high-risk group the age-related electrical conductivity scale and anomalous divergence in electrical conductivity distribution histograms between left and right breast (Fig. 3) are used.

The age-related electrical conductivity scale with distinguished percentile ranges (based on the examination of more than 2000 healthy women) serves to form the high-risk group. Patients with anomalously low age-related electrical conductivity of the mammary gland (less than 5th percentile) belong to the high-risk group. Such a value of age-related electrical conductivity of the mammary gland indicates that the density of the ductal component of the mammary gland is high (Fig. 2).

The indices showing the anomalous divergence in the histograms of the electrical conductivity distribution between the left and right breast are also used to form high-risk groups.

The histograms of the electrical conductivity distribution variance percent chosen with the help of the Kolmogorov-Smirnov nonparametric test (more than 40%) is highly informative, j>3.0 according to Kullback.

The example of electrical impedance diagnostic. Figure represents the comparison of two electrical impedance mammograms. The divergence between electrical conductivity distribution histograms is more than 60% (Fig. 3). This fact enables to consider the patient as belonging to the high-risk cancer group.

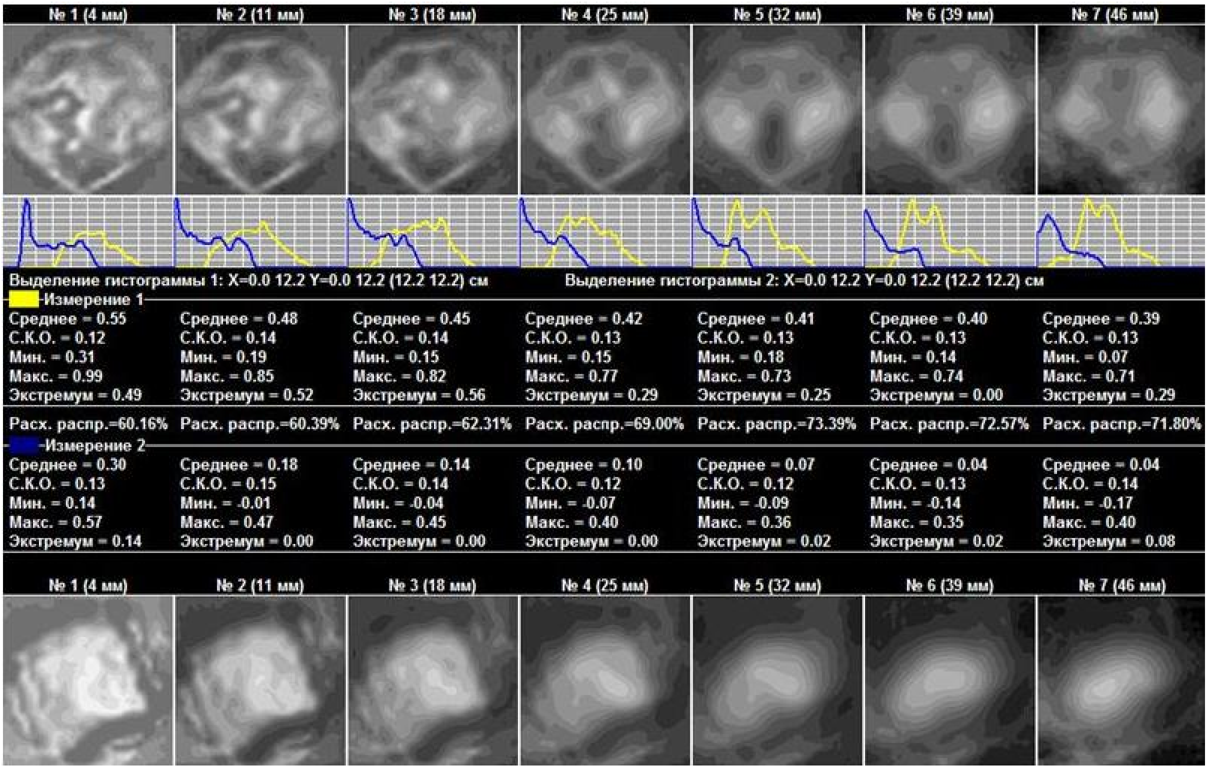



**Fig. 3.** Comparison of electrical impedance mammograms of the left and the right mammary gland.
The fourth line represents the percentage of divergence between electrical conductivity distribution histograms.

# AFTERWORD

«Beauty will save the world». This famous quotation can be applied to woman breasts. However, there is no doubt, that only the healthy mammary gland can be beautiful. Thus, our work is devoted to save this beauty.

Breast cancer is one of the most important problems of modern medicine. Currently, it is still X-ray mammography which is considered as the “golden standard” in the diagnostics of malignant diseases of the mammary gland. However, working for the benefit of patients, we offer to use all the available diagnostic methods in order to detect the disease as early as possible, when it can be surely treated and even fully overcome. The stages of oncologic process development, which have been described in the book, testify that the disease appears well in advance of we are trying to detect it, but even earlier – when we are not even thinking about if. It seems to be unethical to employ the diagnostic techniques which can harm a patient in any way without compelling. During the first stage, it is reasonable to use the available radiation-free diagnostic methods such as impedance mammography, which has been introduced in the book. High operational performance, user-friendliness, portability, relatively low price, well reproducibility enable to recommend impedance mammography as the first-link method in the chain of diagnostic techniques for benign and malignant diseases of the mammary gland. Impedance mammography is now at the beginning of its development and the authors hope that the book will make it possible for practicing doctors and scientists to inherit the helm. It will undoubtedly bear fruits and will result both in early and accurate diagnostics and the ability to prevent mammary gland diseases.

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