WHAT IS BIOIMPEDANCE?

Bioimpedance is a measurement of how the cells in our body impede the flow of electric current. Otherwise, bioimpedance is about the electrical properties of biomaterials that are special conductors. Animal and human tissue consists of cells. The cell has a membrane, that is thin but has high resistivity and in terms of electricity behaves as small capacitor. The membrane surrounds the intracellular liquid consists from water, biological ions, enzymes, acids etc. In practice we using high frequency current which is able to pass through cell`s membrane capacitor. Direct and low frequency alternative currents cannot to pass through living cells. So, the current transition is dependent then on tissue and quality of liquids both inside and outside the cells.

WHAT IS THE PURPOSE OF MEIK MAMMOGRAPH?

Eletrical impedance computer mammograph MEIK ® is intended for mammary gland screening by means of eletrical conductivity distribution pattern visualization with the software to identify different changes in tissue structure of breast, pathologies such as cancer, cysts, scars, calcificates, fibroadenomas, mastitis, etc.

WHAT IS THE SAFETY CLASS OF THE DEVICE?

Electrical safety class: Russia…….. II,
EU…… IIa,
Canada…… II
Class of laser hazard for the sight……..…1
Weight of the unit with sensors, max……. 2 kg

CAN YOU TELL US SOME TECHNICAL PARAMETERS?

Electroimpedance computer mammograph MEIK® version 5.6 consists of:

- a microprocessor unit
- a probe cable

Microprocessor unit, controlled by the MEIK Software 5.6, is connected via a USB 2.0 port to a PC.

Power supply of a microprocessor unit …… 5 V,
Power, max ……. 400 mA,
Current used for breast scanning…… 0.5 mA,
Scanning current frequency…….. 50 kHz.

The array of microprocessor unit contains 256 cylindrical electrodes plated with galvanic gold (thickness - 2 micrometers). Gold coating allows stable contact and constant low resistance for the passage of electrical current during the stated period of operation of the device. In the middle of the

array there is a laser light that allows precise positioning of the microprocessor-based sensor on the breast.
Patient's coupling cable is fitted with push-button latches to attach self-adhesive EKG gel electrodes. This provides a stable contact with the skin of the patient during scanning.

Continuous work time: min. 8 hours,
Warranty: 2 years,
No-failure operation (ageing of electronic components), min: 10 000 hours

IS MAMMOGRAPH MEIK® A MEASUREMENT DEVICE?

Mammograph MEIK version 5.6 is not a measurement tool, but a device which operates with the calculated values of average relative conductivity of tissue, defined according to the potentials measured on the skin surface. Mathematical processing of data allows for reconstruction of seven computed tomographic slices up to 5 cm depth.

RESISTANCE AND NOISE IN MEASUREMENT, DEPTH OF SCANNING

The selected scanning current frequency (50 kHz) is optimal, because it allows to conduct examination of the skin which is moistened with tap water and does not require any special solutions with electroconductive additives. The electronic circuitry and software helps to reduce the level of external interference (noise) to less than 1%. However, **it is not recommended** to operate the device **close to powerful sources of electromagnetic radiation, because it can cause malfunctioning of the device or of the master computer.**

WHO MAKES THE CONCLUSION – THE OPERATOR OF THE DEVICE OR IS IT DONE AUTOMATICALLY BY THE SOFTWARE?

Oncomarkers embedded in the software allow the doctor to quickly and easily diagnose early forms of breast cancer.

WHAT IS THE APPLICATION OF THE DEVICE?

Oncology, mammology, obstetrics and gynecology, paediatrics

INDICATIONS FOR APPLICATION

— Evaluation of palpable lesions of the mammary gland.
— Evaluation of the impalpable changes which are not manifested clinically.
— Formation of groups of people with heightened risk of breast cancer development, using the percentile curves of the age-related electrical conductivity.
— Screening for oncopathologies.
— Additional examination of the dense tissue of the mammary gland.
— Examination in the age group under 50, including adolescents.

— Examination of pregnant and lactating women.
— Monitoring during hormonal contraception and hormone replacement therapy.
— Monitoring after pharmacotherapy or operative therapy.
— Examination of the women after cosmetic surgery.

HOW IS THE EXAMINATION OF THE BREAST DONE?

Positioning of the device

The examination is carried out on the massage couch, the patient lying on her back. Patients with small mammary glands may also be examined while sitting.

The mammary gland visualization will be shown in 7 levels from frontal point of view. To achieve this, the patient's arm nearest to the examined breast is raised, her hand placed behind her neck. The nipple must be in the center of the array with 256 electrodes.

The breast is to be moistened with a wet cotton wool tampon. Formation of droplets should be avoided.

Put disposable gel electrodes at the forearm of the opposite arm. The arm should not be touching the patient's body.

The panel with electrodes is placed against the breast in such a way that the laser light is positioned on the nipple. It is necessary to achieve the state with as little number of poor contacts as possible (good contact areas are colored green).

WHAT ARE ADVANTAGES OF MEIK?

The advantages of MEIK compared to ultrasound

- MEIK meets all the requirements of screening.
- MEIK provides complete images of the breast
- MEIK generates a tomographic image of the breast.
- MEIK provides numerical evaluation and representation of the mammary gland with the help of electrical conductivity index.
- There are oncomarkers employed in MEIK to ensure early diagnostics of breast cancer.
- MEIK is a portable device which requires minimum consumables.

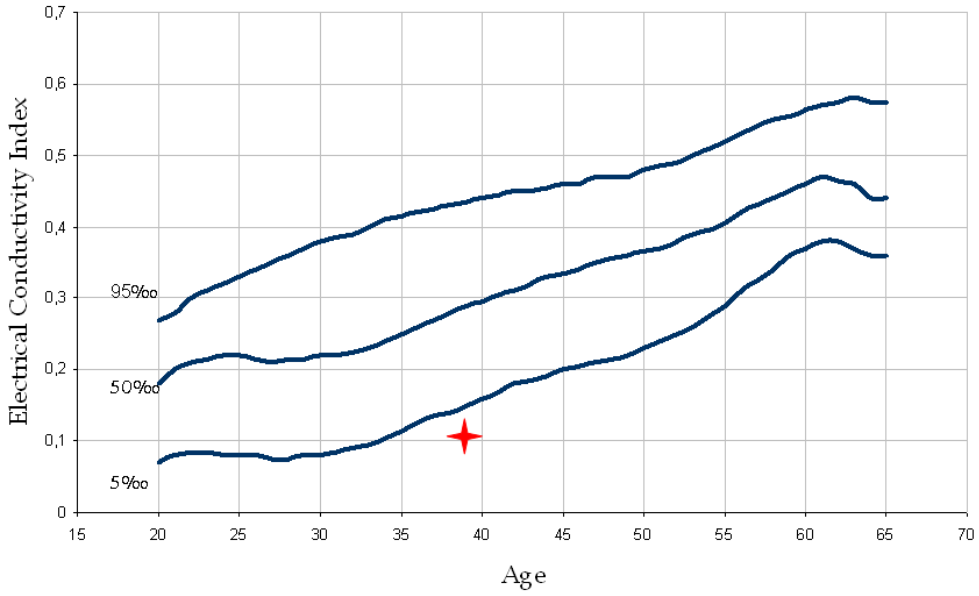
CAN MEIK DISTINGUISH BETWEEN BENIGN AND MALIGNANT TUMOURS?

Surely, since electrical conductivity of breast cancer at early stages is twice as high as electrical conductivity of benign tumours (such as cysts and fibroadenomas).

QUESTION CONCERNING LOCAL PHENOTYPE DATABASE

Creation of a local database in different phenotypes will help to develop percentile curves of age-related electrical conductivity. This would allow for primary prevention of breast cancer, namely for high risk group formation.

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 large population groups.



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

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

The groups of people with heightened risk of breast cancer development can be formed with the help of the percentile curves of the age-related electrical conductivity. The usage of percentile curves is habitual for many diagnostic techniques. For example, ultrasound specialists widely use percentile curves to assess growth and development of the fetus. The figure shows the percentile curves of age-related electrical conductivity, where each age group corresponds to a certain range of electrical conductivity. The values which fall into the first range (less than 5th percentile) should be considered as pronouncedly low and the values which fall in the fourth range (above 95th percentile) - as pronouncedly high. Patients with anomalously low age-related electrical conductivity of the mammary gland (less than 5th percentile, indicative of high density of ductal component) shall be considered as belonging to the high-risk group. High density of ductal component is potentially dangerous as it can be accompanied by insufficient trophic function of the connective tissue. It is well known that this function is performed by inoglia mainly. Dyscrasia may lead to dystrophic processes, in the basal membrane as well.

WHAT IS THE PRINCIPLE OF OPERATION?

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 array and two-dimensional mathematical conductivity reconstruction algorithms in the array of the electrodes. Electrical impedance mammograph belongs to the class of 3D tomography systems.

Thus, all the measurements are made on the surface of the investigated object. The change of surface potential difference (compared with the homogeneous case), as a rule, is caused by the presence of a local heterogeneous area in the object. It is mainly concentrated in the area which is a projection of the local heterogeneous area on the surface of the object.

Therefore, the main objective of electrical impedance mammography is to visualize the reconstructed three-dimensional electrical conductivity distribution of the object, basing on the results of electrical measurements on its surface.

For this purpose various modifications of mathematical method of “back projection” are employed (Dunaeva O.; Gerasimov D., Karpov A., Machin M., Tchayev A., Tsofin Yu., Tsyplyonkov V. Using Backprojection Algorithm for 3D Image Reconstruction in EIT. *World Congress on Medical Physics and Biomedical Engineering*, Munich, Germany, 2009). Mathematical methods provide also cross-sectional slices of conductivity.

AT WHICH MARKETS IS MEIK USED GLOBALLY?

MEIK mammograph is used worldwide, namely in: Russia and CIS countries, countries of European Union, Croatia, Turkey, Malaysia, Indonesia, Hong Kong, South Africa and Australia. Currently, it is being registered in Canada and South Korea.

IT IS POSSIBLE TO MAKE 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 when screening for early stages of breast cancer (the dimensions of a tumour less than 1 cm) is the following: high electrical conductivity areas (above 0.95 cu) outside the lactiferous sinus zone – the so-called animpedance areas, which differ markedly from electrical conductivity of healthy mamma’s areas. 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. The membrane permeability of cancer cells during intraductal and early extraductal stage increases both for chemical compounds and electric charges. This process results in increase of electrical conductivity.

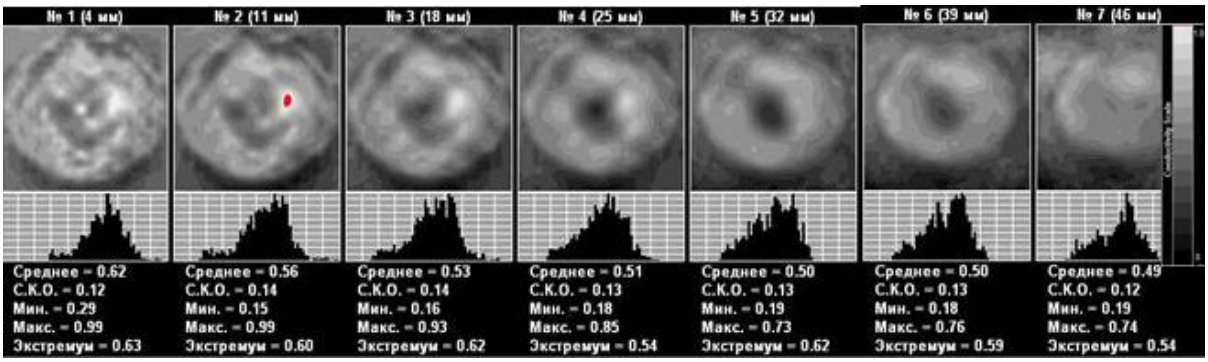


*Fig. **1.** EIM. Amorphous type of mammary gland structure. In the outer segment of the left mammary gland, at 3 o'clock position there is observed an an-impedance area, which is highlighted with red in the second scan plane, less than 10 mm in size.*

The example of electrical impedance diagnostics. Figure 1 represents the electrical impedance mammogram of a patient. There can be distinguished a focal lesion, in the form of an-impedance area, highlighted with red, with electrical conductivity index over 0.95 conditional units. This is the criterion for early diagnostics of breast cancer. Roentgenogram and US image of the same mammary gland are represented below (Fig. 2, 3).

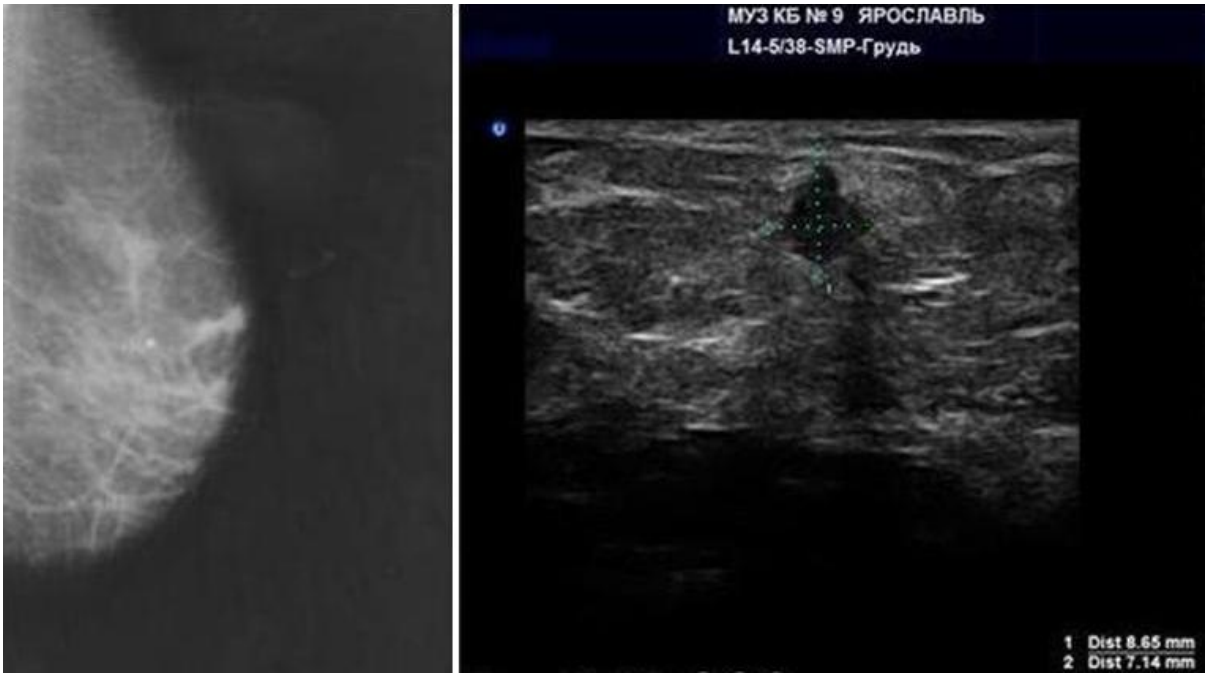


Fig. 2. Roentgenogram: Fibro-fatty involution. In upper-outer segment there is observed a lesion up to 1 cm in size with a radiant contour.

Fig. 3 Ultrasound: The structure of parenchyma with adipose lobules and connective tissue layers. An inhomogeneous 8x7 mm lesion of irregular shape is located at 28 mm distance from the nipple and at 12 mm depth.

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 data issued by different authors).

WHICH STANDARDS WERE USED IN REGISTRATION PROCESS?

LIST OF STANDARDS

Rules and Regulations applied during the design and manufacture of MEIK

Number	Title	Date of approval or status of the document
International legal and regulatory documents		
93/42/EEC MDD	Council Directive 93/42/EEC of 14 June 1993 concerning medical devices.	Effective
SOR/98-282	Medical Devices Regulations.	Effective
ISO 9000-2005	Quality management systems -- Fundamentals and vocabulary.	Effective
ISO 9001-2008	Quality management systems - Requirements.	Effective
ISO 9004-2009	Quality management systems. Guidelines for performance improvements.	Effective
ISO 13485:2003	INTERNATIONAL STANDARD. Medical devices – Quality management systems - Requirements for regulatory purposes.	Effective
ISO 14971:2007	INTERNATIONAL STANDARD. Medical devices – Application of risk management to medical devices.	Effective
ISO 13485:2003 & CMDR.	ISO 13485:2003 quality management system meeting the Canadian Medical Device Regulations (CMDR)	Effective
GHTF/SG3/N17R9:2008/	GUIDANCE DOCUMENT. Quality Management System - Medical Devices - Guidance on the Control of Products and Services Obtained from Suppliers. Global Harmonization Task Force (GHTF) Number: GHTF/SG3/N17R9:2008/	Effective
MEDDEV 2.12-1 Rev 6	Guidelines on a Medical Devices Vigilance System	Effective
GD210: ISO 13485:2003	GUIDANCE DOCUMENT. Quality Management System. Audits Performed by Health Canada Recognized Registrars.	Effective
EN 980:2008	Graphical symbols for use in the labeling of medical devices.	Effective
IEC 60601-1:2005-Ed.3.0	Medical electrical equipment – Part 1: General requirements for basic safety and essential performance IEC 60601-1:2005/Cor.1:2006	Effective

IEC 60601-1-1:2000	Medical electrical equipment – General requirements for safety – Collateral standard: Safety requirements for medical electrical systems	Effective
IEC 60601-1-2:2007-Ed.3.0	Medical electrical equipment – Part 1-2: General requirements for safety – Collateral standard –Electromagnetic compatibility – Requirements and tests	Effective
IEC 60601-1-4:1996-Ed.1.1	Medical electrical equipment – Part 1-4: General requirements for safety – Collateral standard: Programmable electrical medical systems IEC 60601-1-4:1996-Ed.1.1/Amd.1:1999	Effective
IEC 60601-1-6:2006-Ed.2.0	Medical electrical equipment – Part 1-6: General requirements for safety – Collateral standard: Usability	Effective
IEC 60825-1:1993	Safety of laser products – Part 1: Equipment classification, requirements and user's guide Amendment 1 (1997) Amendment 2 (2001)	Effective
IEC 60529:1989	Degrees of protection provided by enclosures (IP Code) Amendment 1 (1999)	Effective
IPC-A-610D RU	Acceptability of Electronic Assemblies	Effective
National legal and regulatory documents		
№ 184-FZ	Federal Law "On Technical Regulation".	dated January 11, 2010
№ 102-FZ	Federal Law "On Assurance of Measurement Uniformity"	dated June 26, 2008
GOST R ISO 9000-2008	Quality Management Systems. Fundamentals and vocabulary.	Effective
GOST R ISO 9001-2008	Quality Management Systems. Requirements.	Effective
GOST R ISO 13485-2004	Medical devices. Quality Management Systems. System requirements for regulatory purposes.	Effective
GOST R ISO / IEC 16085-2007	Risk Management. Application for system and software life cycle processes.	Effective
GOST R ISO 14155-1-2008	Clinical investigation of medical devices for human subjects. Part 1: General requirements	Effective
GOST R ISO 14155-2-2008	Clinical investigation of medical devices for human subjects. Part 2. Clinical investigation plans.	Effective

GOST R ISO 15223-2002	Medical devices. Symbols to be used with medical device labels, labelling and information to be supplied.	Effective
GOST R ISO 19011-2003	Guidelines for quality and/or environmental management systems auditing.	Effective
GOST R 1.5-2002	Standardization in Russian Federation. Standards. Rules of structure, drafting, presentation and indication.	Effective
GOST 2.501-88	Unified system for design documentation. Registration and storage rules.	Effective
GOST 2.503-90	UNIFIED SYSTEM FOR DESIGN DOCUMENTATION. Amendment rules.	Effective
GOST 2.601-95	UNIFIED SYSTEM FOR DESIGN DOCUMENTATION. Exploitative documents.	Effective
GOST 2.114-95	Unified system for design documentation. Specifications	Effective
GOST 3.1102-81	Unified system for technological documentation. Stages of designing and types of documents.	Effective
GOST R 6.30-2003	Unified system of managerial documentation. Requirements for presentation of documents.	Effective
GOST R 8.568.-97	State system for ensuring the uniformity of measurements. Verification of testing equipment. General principles.	Effective
GOST 9.302-88	Unified system of corrosion and ageing protection. Metal and non-metal inorganic coatings. Control methods.	Effective
GOST 9.303-84	Metal and non-metal inorganic coatings. General requirements for selection.	Effective
GOST R 15.013-94	System of product development and launching into manufacture. Medical devices.	Effective
GOST R 15.201-2000	System of product development and launching into manufacture. Products of industrial and technical designation.	Effective
GOST 15.309-98	Test and acceptance of produced goods.	Effective
GOST R IEC 60825-1: 2009	Federal Standard of the Russian Federation. Safety of laser products. General requirements for safety in the design and operation of laser products.	Effective
GOST R IEC 60601-1-1-2007	Medical electrical equipment. Part 1-1. General requirements for safety. Safety requirements for medical electrical systems	Effective
	Medical electrical equipment. Part 1-1. General requirements for safety. Safety requirements for medical electrical systems.	

GOST R 50267.0.4-99 (IEC 60601-1-4:1996)	Medical electrical equipment. Part I. General requirements for safety. 4 Collateral standard. Programmable medical electrical systems.	Effective
GOST R 51901.5-2005 (IEC 60300-3-1:2003)	Risk Management. Guide for application of analysis techniques for dependability.	Effective
GOST R 51901.5-2005 (IEC 60300-3-1:2003)	Risk Management. Guide for application of analysis techniques for dependability.	Effective
GOST 14192-96	Marking of cargoes.	Effective
GOST 16504-81	The state system of testing products. Product test and quality inspection. General terms and definitions.	Effective
GOST 23592-96	Electrical wiring of radio-electronic equipment and devices. General requirements for three-dimensional wiring of electronic and electrical devices.	Effective
GOST 24297-87	Input inspection of products.	Effective
GOST R 50326-92	Basic aspects of the safety philosophy of electrical equipment, used in medical practice.	Effective
GOST R 50444-92	Medical instruments, apparatus and equipment. General specifications.	Effective
GOST R 51293-99	Identification of products. General principles.	Effective
GOST 51474-99	Packaging. Pictorial marking for handling of goods.	Effective
GOST R 51609-2000	Medical products. Classification in accordance with potential risk of using.	Effective
GOST R 51672-2000	Metrological ensuring of product testing for the assurance of conformity. General principles.	Effective
GOST R 51897-2002 (ISO / IEC 73:2002)	Risk Management. Terms and definitions	Effective
GOST R 51901-2002	Dependability management. Risk management of technological systems.	Effective
Internal regulatory documents		
TU 9442-001-018100676-2003	Technical specifications. Electrical impedance computer mammograph MEIK for breast cancer screening by the means of electrical conductivity distribution pattern visualization with modifications 1, 2, 3.	Effective
PK 1-2011	Quality manual. Part 1.	19.01.2011
	Quality manual. Part 2 Processes book.	19.01.2011

STP 01-2009	Company specification. Records management.	21.10.2009
STP 02-2009	Quality Management System. Document management.	02.09.2009
STP 03-2009	Company specification. Project management. Project management and new product development and launch.	12.10.2009
STP 04-2009	Company specification. Project document management.	14.10.2009
STP 05-2009	Company specification. Technological documentation management.	04.09.2009
STP 06-2009	Company specification. Production process design	09.09.2009
STP 07-2009	Company specification. Products and processes monitoring and measurement (evaluation).	09.09.2009
STP 08-2009	Company specification. Measurement (assessment), analysis and refinement. Monitoring and measurement devices control.	28.08.2009
STP 09-2009	Company specification. Measurement (assessment), analysis and refinement. Corrective action	29.10.2009
STP 10-2009	Company specification. Measurement (assessment), analysis and refinement. Preventive action	15.10.2009
STP 11-2009	Company specification. Production.	27.10.2009
STP 12-2009	Company specification. Measurement (assessment), analysis and refinement. Nonconforming product management	02.09.2009
STP 14-2009	Company specification. Procurement management.	21.09.2009
STP 15-2009	Company specification. Equipment management.	17.09.2009
STP 17-2009	Company specification. Occupational safety and health management.	27.11.2009
STP 18-2009	Company specification. Statistical technology.	04.09.2009
STP 19-2009	Company specification. Identification and traceability.	25.09.2009
STP 20-2009	Company specification. Measurement (assessment), analysis and refinement. Internal audit (inspection).	30.06.2010
STP 21-2009	Company specification. Measurement (assessment), analysis and refinement. Technical discipline control	03.09.2009
STP 22-2009	Company specification. Management responsibility. Analysis of quality management system.	19.10.2009
STP 23-2010	Company specification. Human Resources Management.	27.09.2010

I 01-2009	Instruction on designing, manufacturing and managing of technological equipment.	15.10.2009
I 02-2010	Instructions on elimination of incidents involving medical products in the domestic market.	20.12.2010
I 03-2011	Instruction. Application of risk management to medical devices.	19.01.2011
I 04-2011	Instruction on customer satisfaction survey.	19.01.2011
I 05-2009	Technical file. Administrative procedures.	14.09.2009
I 06-2011	Instruction. Processes efficiency expert evaluation.	19.01.2011
I 07-2008	Instruction on software validation.	15.10.2009
I 08-2009	Instruction on special processes validation.	18.11.2009
I 09-2009	Instruction on warehouse management.	17.09.2009
I 10-2011	Instruction. Supervision over medical products in the global market.	23.05.2011