

# Topical problems of NLS-diagnosis (theoretical and clinical)

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## Computer Non-Linear Diagnosis

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The Non-linear Diagnosis Systems (NLS) have been extensively used lately and are gaining ever growing popularity. Even in the few cases, where the clinical symptoms look very typical, NLS diagnosis provides extra information about the extent of dysfunction and enables a better opportunity for a more comprehensive prognosis. In most cases it is of vital importance for diagnosis and consequently for the right choice of treatment.

In 2000 Theodore Van Hoven theory of quantum entropy logic (that underlies this method) had been in existence for 20 years. Non-linear diagnosis appears to be the most up-to-date of all methods of the hardware-based diagnosis. His discovery can be viewed as a significant landmark in diagnostic medicine.

Non-linear analysis was originally employed in organic chemistry to determine the composition of complex compounds.

Sviatoslav Pavlovich Nesterov, who introduced a trigger sensor in 1988 and thus framed the concept, is considered as the originator of the NLS-diagnosis device (metatron). Active work was immediately started to develop and improve the NLS-diagnostic systems. Clinical testing of the early equipment took the period from 1990 through 1995. The late 90s saw a fast growth of commercial production of the device and a sudden surge in the quality of the results produced.

The non-linear diagnosis method is still in its development stage. The diagnostic techniques are improving so fast that the system versions have to be updated every six months. Due to the introduction of some new devices, equipped with digital trigger sensors, the NLS-diagnosis has become not only far more time-efficient but also quite different in terms of quality. It is obvious that some routine techniques, for instance three-dimensional visualization of investigation results will soon become a daily practice. The vegetative testing aspect (testing of specific item signatures against the client) is just one example of the developments. NLS analysis is now becoming so widely employed that we should rather speak about a definite range of indications for its use than just about its popularization.

Research centers continue their quest for some new investigation methods based on the non-linear analysis systems. So far the results appear to be quite promising.

Unlike NMR and computer tomography, the NLS-analysis does not need strong fields. The method seems to have good prospects for metabolism studies, particular on a cellular level.

The NLS-method is advancing not only in technical innovation but also in new applications. Some minor surgical operations (e.g. biopsy) have long been monitored

using ultrasound, fluoroscopy or computer tomography. Today we have an opportunity to have biopsy monitored by NLS. Many surgeons now focus on using this method to assist major surgeries.

The cost of equipment for NLS-diagnosis is still very low as compared to some other hardware-based methods. This should help promote more extensive use of the method in countries with low living standards. Of all methods of hardware-based diagnosis the NLS provides representations most proximate to the pathologic-anatomic picture. The feature of the method along with its harmlessness, promotes rapid development of the NLS-diagnosis.

## Clinic Tech Inc. - Ascending In The XXI Century

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The development of a new generation of non-linear computer scanner (metatrons) which make use of multidimensional virtual imaging of the body area of interest, has facilitated substantially improved efficiency of the NLS-method and even expanded its fields of application (despite the MRT competition). The originally volumetric pattern of scanning is a distinctive feature of the multidimensional NLS imaging. The data thus acquired are an integral array, which facilitates reconstructing multidimensional virtual images of anatomical structures. In this connection the virtual NLS is widely used especially for angiographic investigations with a three-dimensional reconstruction of vascular formations.

Another promising field of application of the three-dimensional image reconstruction, based on the data acquired by means of multidimensional NLS, is the study of hollow organs with a "virtual NLS-scopy" involved. This kind of a system was developed by Medintech Company for their high-rate multidimensional Z-series non-linear scanners, and was called Hunter. The high resolution maintained during spiral scanning and the use of LAPP system (a system of parallel processors with a powerful computational capability and speed of operation) enables the implementation of the principal of "virtual NLS-scopy" on a Voxel Z multimodal DICOM-compatible work station, which is the basic system for imaging and subsequent data processing with Medintech scanners.

NLS images are made ready for visual analysis by means of the 4D Tissue, an original company-developed method, that enables not only virtual multidimensional images of anatomical structures but also selection of a particular biological tissue of interest to give it an extra dimension, and additionally visualize bones, soft tissues and vessels.

A specific feature of representing virtual data by the Hunter system is its simultaneous visualization of surfaces of cavatus and extramural formations located outside the lumen of the cavity under examination (e.g. lymph nodes, vessels). The acquired images form a natural sequence of virtual NLS shots, while a special navigation program automatically determines the path of the "virtual scanner" by center of the cavity under examination. The path of the motion can be chosen by operator using some other settings, which allow detailed NLS pictures by changing the view fields. A raised representation of the cavity surface is also achievable by shaping particular artificially shaded areas. The presulting sequences of NLS shots can be easily converted into a standard VHS video format by means of the epi-Client program and can be used in standard video systems, in particular for teleradiology.

The Hunter system is primarily designed for case detection of obstructive processes in the upper respiratory passages, bulky esophageal, gastric or colonic formations, atherosclerotic lesions of large vessels, and disorders affecting paranasal sinuses, urinary

bladder or spinal canal. The data gathered by “virtual NLS-scopy” facilitates selection of the optimum spot for biopsy and can define the extent of surgical intervention in good time.

This technique can be used both stand alone and as a useful linking element between tomographic, endoscopic and NLS investigations.

The Medintech’s latest development is its Pincers stereo tactic manipulator integrated into a computer scanner, which is a convenient tool for planning interventional procedures monitored by NLS. The Pincers comprises a controlled stereo tactic manipulator (“arm”), a flat gentry-mounted monitor, a cable system and software. The system provides the physician with the means of simulating and performing interventional procedures through an interactive link between the virtual NLS and the real operational field.

## Method Of Computer Non-Linear Analysis And Its Role In Diagnosis

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Computer-based non-linear analysis (NLS) as a dynamic non-invasive informative method is increasingly used to examine the status of health affected by pathologies of different origin. NLS can be applied both in vivo (to acquire an NLS-spectrum of one or another part of an organ or tissue), and in vitro (to obtain an NLS-spectrum of extracts from tissues, biological fluids or cells). Often both approaches can be combined for a more accurate data interpretation. The usage of NLS at a clinic requires devices producing an at least 20-30mT eddy magnetic field. The proceedings of the latest International Congress of Medical Doctors (2000 and 2001), that dealt with new methods of diagnosis, provides evidence of a growing number of NLS-investigations used for the diagnostic purposes - the 2000 summit heard 16 presentations on the subject, while in 2001 there were twice as many.

S.D. Tutin et al. reported on the possibility of using NLS to diagnose abscesses in the encephaloea. It appears that the presence of an abscess in the encephalon in the NLS-spectrum generates evaluation some signals from lactate and amino acids which can be detected using the biochemical homeostasis aspect of the program. These signals disappear in the course of treatment. The NLS data in vivo correlates well with the results of abscess sample tests made by means of MRC with a high resolution in vitro.

Using the NLS-method the dynamics of metabolic change in the encephalon when treating epilepsy can be traced. Some data are available, that indicate a possibility to register a decline in oxidative phosphorylation in the lower limbs muscles with construction of the vessels caused by ante-rioscclerosis. In the course of treatment the muscle metabolism appears to improve.

Another trend in the application of the NLS method is detection of metabolic disturbance of phosphoregic compounds at muscular atrophy related to a pathology in the musculoskeletal system.

Some promising prospects for myocardial infarction diagnosis by means of the NLS method were described by U.A. Shovkopylas et al., who studied the ATP exchange in the myocardium. At a myocardial infarction its level was proven to decrease. The NLSanalysis method was employed to study the dynamics of change in the metabolism of lipids in the liver affected by cirrhosis.

The NLS-investigation of the pancreas affected by malignant degeneration enables to diagnose tumor progression, judge of the efficiency of radiation- or chemotherapy and also adjust individual dosage schemes for inoperable patients.



Moreover, NLS use has been reported in the diagnosis of CNS disorders, cardiovascular diseases, muscular system disorders, prostate tumors, mammary gland tumors and in addition to monitor radiation and medicinal therapies. Researchers have demonstrated the diagnostic importance of NLS for arteriosclerosis, apoplexy, encephalomyelitis and vasculitis. NLS permits an estimate of the phase of a pathology and activity of the nidus (focus), determining a relationship between genetic characteristics, clinical symptoms and metabolic deviation in the encephalon. NLS helps to differentiate between benign and malignant tumors in the mammary gland. The studies of abnormal changes in the prostate gland by means of NLS showed that the method allowed identification of an incipient change in the gland tissue, thus enabling appropriate therapy selection.

K.A. Kvasov et. al. presented some data about diagnose of prostate diseases (including histologically confirmed benign hypertrophy and Aden carcinoma) by combining NLS and dynamic MRT with artificial "Magnevist" contrasting. According to the derived results, this kind of combination enables definition of the pattern of a prostate pathology and substantially increases the diagnostic accuracy.

Recently special attention has been focused on a study of the metabolism by means of NLS, necessitated by a growing number of organ transplants (in Europe the annual number of liver transplantations is around 2000 and in the USA it is 10000) due to this method's noninvasive evaluation of the liver function in the course of implantation. The results indicate appropriateness of using the NLS-analysis in these cases since the ATP level in the liver mirrors an integrated picture of cell homeostasis. There is a close correlation between the disturbed metabolisms of phosphorergic compounds and the extent of liver de-compensation.

Beyond diagnosing liver disorders in vivo, NLS facilitates a view on the state of the transplanted liver in vitro by acquiring special characteristics of the organ's metabolites. This is based on a good correlation between the pathological liver metabolism defined by means of NLS and the disease prognosis. The authors would like to emphasize that NLS enables not only definition of pathological change in the liver but also monitoring of the biochemical responses to treatment.

In summary it can be concluded that the ever growing use of NLS-analysis in different fields of clinical medicine, including its combination with MRT with contrast amplification involved, increases the efficiency and diagnostic accuracy and is indicative of a continuous progress in the field of internal organ visualization techniques based on the NLS-analysis phenomenon.

## Potential for the NLS Approach In Diagnosing Gastic And Colonic Cancers

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The non-linear diagnostic method (NLS) has been actively practiced lately at many medical institutions. The most tangible results were achieved by using the NLS method as a means of **idpensary** observation. In the course of its development and advancement the method has become a foremost tool for diagnosis and monitoring for a number of widespread digestive organ diseases: it facilitates rapid and detailed information about a lesion and its pattern and helps in assessing treatment efficacy. This has been found true in our studies for a range of diseases including gastro-duodenal ulcer, chronic gastritis, benign and malignant gastric and colonic tumors. The specific character and working conditions of the therapeutic and clinical institutions in Russia enables the extensive use of NLS methodology, not only for diagnosis with some symptoms present but also for medication monitoring. Importantly the speed and low cost enables many patients to avail themselves of the NLS information. Physicians can now assess patients with latent changes that can only be verified by means of NLS. Specifically, such patients include those having precancerous diseases or a mucous disturbance in the upper and/or lower sections of the digestive tract and patients who developed a tumor, which still remains latent in a certain phase.

According to the data acquired by some medical specialists, using the device for NLS-diagnosis, and based on annual research in thousands of cases, the frequency of detecting local or diffuse changes, typical for chronic atrophic gastritis in patients over 50 years old, is within 30-40%. The analysis of the spectral examinations of pattern-different sections of focal changes in stomach mucosa shows that different symptoms of diseases including intestinal metaplastic and epithelial dysplasia can be detected in them just as often. During NLS analysis symptoms of gastric ulcer were recorded in about 5% of cases, polyps in stomach in 7% and polyps in colon in 45% of cases. Thus, just the NLS analysis results alone (without other risk factors taken into account) indicates that most of the patients in the respective age group appear to be among those who need dynamic observation because of potential gastric cancer (GC) or colonic cancer (CC).

According to the cancer register for 1999-2000, the values of gastric and colonic cancer cases were 80.9 and 53.1 respectively per 100000 patients, and the death rate according to the mortality statistics was 47.35 and 19.5%. According to the conclusions of the therapy-diagnosis unit, with around 70% of patients under active medical observation, pathologies of that kind are likely to be detected as often as in 0.4-0.8% of cases. Therefore, the NLS screening would allow to detect GC or CC in about every 150<sup>th</sup>-200<sup>th</sup> examinee.

Considering that the emergency of clinical signs is one of the incentives for a patient to take medical advice and a reason for hardware-based examination, some clinical

implications and their pattern were evaluated in the cases of the above mentioned diseases. In 720 patients affected by GC or CC the condition appeared to be symptom-free in 42% of cases. In 32% of cases there were some signs characteristic of previous chronic digestive tract diseases. That was the case in 77% and 92% for the 1<sup>st</sup> phase, 56% and 68% for the 2<sup>nd</sup> phase, 23% and 32% for the 3<sup>rd</sup> phase, and 8% for the 4<sup>th</sup> phase of the disease. The clinical implications at a gastric cancer are of a pain-dyspepsis syndrome nature typical for the lesion in the upper section of the digestive tract. Colonic cancer subgroups were segregated with dominating signs of intestinal hemorrhage, disturbed evacuation or abdominal pain. A certain interrelationship was proven between the pattern of the clinical implications and the process localization. In more than 50% of cases the clinical implications lasted less than 3 months and in 26% of patients the CC developed acutely within a few days. It should be noted that the so-called "minor sign syndrome" corresponded to some later phases of the disease. The same was true for lab examination data where the change became evident during phases III and IV (2).

The results of NLS-diagnosis for the initial phases of gastric cancer in a series of 104 examinations showed that in 72% of cases the physician (on the assumption of a spectral similarity to the reference standard) regarded the lesion as benign and indicative of focal mucosa hyperplasia, polyp, an area of local inflammation, wall deformation or a small ulcer. The probability for detecting signs of malignant change found out in the elimination mode was under 1%. Of 134 cases of colonic cancer in phase 1 malignant adenomas were detected in 58% of patients. The rest of the patients were found to have the so-called "minor" forms of cancer, like polyps, atrophic gastritis or atrophic-hyperplastic gastritis. The endoscopic verification of GC and CC with reference to the diacrisis of phases II, III and IV of the diseases completely confirmed the results of the NLS-investigation.

172 patients were found to have GC or CC discovered by NLS-examination conducted within a less than a year interval. Among them 62% of patients had an initial phase of gastric cancer and 38% of the patients during previous observation were found to have some or other signs of chronic gastritis in the form of focal mucosa hyperplasia, local inflammation or wall deformation. According to morphological investigation, the sections were of a benign nature and cancer developed over the last year only. In the rest of the patients the macroscopic changes corresponding to malignant affection (spectral similarity to "gastric carcinoma" reference standard  $D < 0.425$ ) occurred in the span between the last two examinations. The preceding endoscopy detected atrophic gastritis free of focal changes in the area of the developed tumor. Similar NLS data were acquired for 38 patients who during a year's observation were diagnosed to have developed a tumor corresponding to phases II and III.

The NLS of the colon and straight intestine was performed a year before tumors were diagnosed in 21 patients affected by malignant polyps, of whom 17 had been under active observation because of polyposis, while no formation of that kind was in evidence during the initial examination. In addition, within the same time span 13 patients were examined who were diagnosed with a precancerous condition (spectral similarity to straight intestine carcinoma, reference standard  $D > 0.7$ ) and minor forms of cancer. In 6 of the

patients the tumor developed in the area of endoscopic polypectomy after they had a huge villous adenoma removed. Thus, in 34 (27%) of 121 patients, who were diagnosed to have a malignant polyp condition in phase I or a small size tumor, colonic cancer developed within a year. 36 patients examined within the same time interval were found to have the condition in phase II and III just as frequently. 28 of them were subjected to regular medical check-ups with no clinical signs of the disease in evidence in any of them. 8 patients, within 3-7 months prior to tumor diagnosis, began to show signs of growing anemia or progressive stool retention. The medical observation data for these patients, with the NLS method employed a year before the cancer was detected, had indicated no tumor.

There are two very essential factors known to be of paramount importance for malignant disease diagnosis: the quality of clinical and diagnostic techniques and the specific pattern of the disease progress which actually determine the dynamics of the disease progression. Considering the capabilities and working conditions in the therapeutic institutions, the data on gastric and colonic cancer diagnoses may to a certain extent be regarded as optimum. This implies, that even if all the patients were readily diagnosed with the disease during the medical observation (actually it is a matter of 60%), the phase I condition could have been detected only in 40% of them. The analysis of causes of the late diagnosis cases suggests that such cases could be prevented by improving organizational and methodical work.

Furthermore, the focus should be placed on the specific features of the disease progress which are of great and possibly of vital importance for tumor detection. The analysis of the available data prompts the assumption that a tumor may develop within a short time interval reaching the size of either "minor cancer" or extensive lesion. This confirms the idea that the tumor growth dynamics in different patients and in different phases of the disease is likely to vary and be of both continuous and discrete patterns. So a possible scenario of tumor development could be the emergency of "early" gastric cancer against the background of precancerous gastric diseases with a subsequent prolonged period of existence in the initial phase which enables its diagnosis after a year or a long time later. At the same time, this "benign" scenario of disease progress is not typical for some patients and based on rapid tumor growth we just fail to detect the initial phase of the condition in advance. Colonic cancer development through the benign phase and then through a malignant adenoma is not the only possible scenario. Tumors can develop de novo and here too, a variant of a comparatively slow or fast growth is possible. This provides an explanation of an "accidental" detection of patients with fairly large tumors during medical observation and a great number of patients with a short clinical anamnesis and late phases of the disease.

Thus, NLS can be considered as an adequate method for diagnosing gastric and colonic cancers. The difficulties in dealing with NLS interpretation largely concern the initial phases where the frequency of disease detection depends in the long run on how keen the physicians are on performing a spectral verification of any focal changes in the mucosa in the case of a chronic gastritis and on keeping the patients under dynamic observation at the given modes of elimination and NLS-analysis involved.

The results allow segregation into two principal variants of disease diagnosis. The first one suggests “accidental” tumor detection during NLS-investigation; neither clinical nor other familiar signs of disease are in evidence or their intensity is an insufficient reason for the patient to see a doctor. The second variant occurs when the patient develops clinical implications which impel the physician to carry out investigations for them. The results of diacrisis of gastric and colonic cancers indicate that for most patients the problem of early diagnosis can not be solved, not only because of certain organizational factors but also and primarily because of the specific pattern of the disease progress and its manifestations. However, the actual opportunities for improving the well-timed disease diagnosis in practical public health conditions lie, primarily, in increasing the number of patients to be examined by means of the NLS-method within the frameworks of a health survey and also in a timely and complete examination of the patients who are suspected to have the disease.

## New Potentials for NLS-Methods In Colonic Neoplasm Diagnosis

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### Introduction

Colonoscopy is successfully used today to diagnose colon new growths. Based on a number of indications endoscopic investigation provides reliable information about the colonic growth surface in order to correctly classify its pattern and take a sample for morphological identification. Yet, colonoscopy does not give an idea of the kind of internal structure the new growth has, nor does it allow an assess the depth of the invasion of the colon wall by a malignant tumor, determine its proliferation to adjacent organs or metastases to regional lymph nodes. Besides, colonoscopy does not provide information about extra intestinal new growths unless they have already permeated the intestinal wall.

The NLS-investigation of the colon using a 4.9 GHz high frequency nonlinear sensor can help clear up all of these issues.

The NLS-investigation provides information on intestinal wall layers and the adrectal cellular tissue.

This research aimed to define the potentials of the NLS-method in a more specific diagnostic of straight-and segmented intestine tumors.

### The matter and investigation methods

87 patients were examined in whom 91 new growths were investigated using NLS techniques. The examinees included 41 men and 46 women aged from 31 to 83 with most of them (82%) aged 50 and over. All the patients affected by colon new growths were subject to surgical treatment depending on the patient, size and location of the growth. In 23 cases endoscopic polypectomy was performed. In 61 cases a resection was undertaken on different parts of the colon and in 3 patients trans-anal endo-microsurgery was performed. All of the NLS investigation results were verified by a pathomorphological examination of macro preparations according to which the colonic new growths were represented by simple tumors in 30 cases and by glandular cancers with different degrees of differentiation in 61 cases.

The stages of the malignant process were defined according to TNM classification adopted by the International Anticancer Association in 1997 (the 5<sup>th</sup> revision). Phase T1 was diagnosed in 13 patients (21%), phase T2 in 26 patients (43%), phase T3 in 17 patients (28%) and phase T4 in 5 patients (8%).

According to a patho-morphological examination, metastases into regional lymph nodes were detected in 11 of 61 cases.

All the patients underwent NLS-investigation and ultrasound colonoscopy to diagnose and localize new growths, define their size, growth patterns and approximate morphological characteristics together with ultrasound scanning of the abdominal cavity and small pelvic organs to assess the condition of the organs adjacent to the colon and diagnose distant metastases.

The NLS-investigation used a 4.9 GHz nonlinear sensor. The endoscopic ultrasonography made use of the endoscopy ultrasonographic system UM-20 complete with the ultrasonic colonoscope CF-UM20 (Olympus, Japan). The echographica of the abdominal cavity made use of the diagnostic unit SSD-630 (Aloka, Japan) and Logiq-700 (General Electric, USA).

#### Discussion of results

We know from experience that every NLS-investigation should be preceded by diagnostic colonoscopy, which evaluates anatomic characteristics of the colon and defines the number, localization and macroscopic characteristics of the new growth, and by ultrasound scanning of the abdominal cavity as well. A thorough trans-abdominal ultrasound scanning is required to assess the condition of the organs adjacent to the colon and diagnose remote metastases.

A comparison of the NLS results with those of pathomorphological investigations was made in order to define the potential of the NLS-method in differential diagnosis of benign and malignant colonic new growths.

The results of the NLS-investigation coincided with the pathomorphological investigation in 87 of 91 cases. Most of the errors occurred in diagnosing colon adenomas. In 6 of 31 cases the patient was suspected of having cancer. The analysis of the observations noted that difficulties in diagnosis were related to the deformation of intestinal wall layers due to the pressure of a nodal villous tumor rather than to a genuine invasion. Two false-negative results were obtained in the case of malignant adenoma and cancer diacrisis.

Thus, the accuracy of the NLS method in differential diagnosis of malignant and benign colon tumors amounted to 81.3% of sensitivity to 79.8%, while the specificity was 76.4%.

The method of treatment to be chosen for patients affected by colon cancer depends on the tumor process phase. A comparison was made to the patho-morphological investigation data in 61 cases in order to assess the diagnostic efficiency of the NLSmethod in classifying the colonic cancer phase.

The correct definition of the phase of tumor process was possible in 68.4% of the observations. The best results were obtained in defining phases T3 and T4, where the diagnostic accuracy was 78.2% and 81.2% respectively. It should be noted that most of the errors occurred in determining phases T1 and T2, where the data of NLS and patho-

morphological investigations coincided only in 54.2% and 47.4% of the observations respectively.

In diagnosing phase T1 mistakes were made in 4 cases with 3 of the errors toward overstating the phase; in one case signs of intestinal wall invasion were not found and the tumor was taken for adenoma. In the analysis of phase T2 diagnostic errors in overstated phases were noted in 7 of 9 cases; an under-statement of phase of the tumor process occurred in one case and yet in one case no evidence of invasion proved to be found. The analysis of the post surgical morphological conclusions revealed that in 6 of 7 false positive results the patho-morphological investigation of a macro preparation detected a deeper infiltration into the intestinal wall. However, according to microscopic examination, the infiltration was of inflammatory rather than of a tumor kind. It should also be noted that in all of the cases it had to do with an infiltrative tumor process in the inferior ampullar section of the straight intestine free of serous membrane while the inflammatory infiltration area was located in adrectal cellular tissue.

To understand better where there is imprecision in diagnosis, the efficiency of the NLS method was analyzed in terms of the size, localization and form of germination of neoplasms. The best results were obtained in diagnosing new growths sized under 2 cm and over 5 cm.

Epithelial tumors over 5 cm in size is represented by phases T3 and T4 in 12 of 17 cases. It has to be noted for large neoplasms the data of NLS assay did not coincide with patho-morphologic data only in phase T2, where the process phase was overestimated because of the presence of inflammatory infiltration in deeper layers, than the layers where the tumor invasion occurred. Thus, at neoplasms larger than 5 cm in size the diagnosis of the invasion degree of the intestinal wall correlates in 78.2% of observations. High correlation was also obtained for depth of tumor invasion by neoplasms sized up to 2 cm. Most of them are represented by a tumor in phases T1 and T2. The results of ultrasonic colonoscopy coincided with those of patho-morphologic conclusions in 76.7% of the observations. It should also be noted, that tumors sized up to 2 cm are most convenient for examination since they have the least number of artefacts.

In this study the greatest group was the tumors sized from 2 to 5 cm, where the results proved to be lower, than in two first groups. The NLS data and those of the patho-morphologic essays coincided in 66.7% of cases. An appreciable error band (60%) occurred in phase T2, where the intestinal wall invasion depth was overestimated in all observations.

The great value has the fact, that according to pathomorphologic essay, in 5 of 6 cases of hyper-diagnosis apart from the tumor infiltration an expressed inflammation was detected in deeper layers of the intestinal wall. The relatively low accuracy of diagnosed depth of the intestinal wall invasion by a tumor sized from 2 to 5 cm is due to the fact that 24 of 30 observations of this group corresponded to phases T2 and T3. A differential diagnosis of the tumor infiltration depth in these phases is complex.



At the next research stage we made comparative analysis of the effect of the form of growth of the neoplasm for accuracy of defining the phase of tumor invasion in the intestinal wall. All neoplasms were classified into three groups. In function of the shape of the tumor growth: polypiform, saucer-shaped and infiltrative.

The highest results were obtained when diagnosing the phase of the saucer-shaped growth cancer process where the accuracy of defining the tumor invasion in the intestinal wall was 78.3%.

It seems however possible to fully estimate the accuracy of the NLS method in defining the depth of a tumor invasion at neoplasms with saucer-shaped growth because of its dismal occurrence among other forms of patients surveyed by us.

The polypiform of the growth was noted in 30 neoplasms. The growths had a distinct interface with unaltered sections of the intestinal wall and did not block the intestine lumen by more than half, which created favorable conditions for the survey. The accuracy of NLS method in defining the depth of tumor invasion in the intestinal wall was as high as 65%. It has to be noted, that half of all cases divergent with the pathomorphologic conclusions is due to the overestimated depth of tumor infiltration at defining the phase T2, which is connected with the presence of a perifocal inflammation.

This fact suggests difficulties in defining the phase of a cancer process in cases where the tumor invasion is compounded by the inflammatory component penetrating deeper layers of the intestinal wall and beyond its limits.

The neoplasms with an infiltrative growth shape have proved to be most difficult in defining the degree of the tumor invasion into the intestinal wall. In this group the results of NLS method and those of the pathomorphologic essays coincided only in 49.8% of observations. It was due to the fact that these neoplasms, as a rule, had a large size and occupied more than a half of the intestine wall circle.

In the next investigation phase we estimated the accuracy of the NLS method in defining the degree of the intestinal wall invasion depending on the tumor location in the colon.

In 40 cases the tumor was localized in the rectum and in 21 cases in the segmented intestine. The accuracy of diagnosing the phase of the tumor process in the colonic intestine is significantly higher, than at finding the tumor invasion depth with the neoplasms located in the rectum and amounts to 71 and 62.5% respectively. This high result can be most likely explained by the fact that this department of colon contains a serous membrane, which distinctly separates the muscular layer from the abenteric organs and tissues. Also it is noted, that the serous membrane of the intestine is less subject to penetration of the inflammatory infiltration, than the para-rectal cellular tissue. The majority discrepancy relates to over-estimated depth of the invasion at defining Phase T2.

These researchers have noted that the accuracy of diagnosing the phase of a tumor process was higher in colonic intestine, than in rectum. The greatest number of

discrepancies occurs in Phase T2, which is conditioned by the presence of abscesses, inflammatory infiltration or radial therapy in the neoplasm area.

Damaged regional lymph glands are an important prognostic factor in diagnosing rectum cancer. To define the capabilities of the method in diagnosing metastases in regional lymph glands, the results of the NLS method were compared with those of the pathomorphologic essay. In the latter the malignant damage to the regional lymph glands was detected in 11 observations from 22 cases.

The analysis of the derived data proved that the NLS essay had correctly defined the pattern of damage to the lymph glands in 63.6% of cases.

The metastatic pattern of damage to the lymph nodes was defined in 74.8% of cases, and in inflammatory changes the results of the ultrasonic colonoscopy and those of the pathomorphologic essay coincided only in 45.5% of observations. In 6 from 11 of cases the presence of metastasizes in lymph nodes was assumed (false-positive result). Such mistakes can be attributed to oneologic vigilance of the researcher and complexity of differential diagnosis of inflammatory and metastatically-altered lymph glands.

#### Conclusions

1. NLS diagnosis is a highly efficient method of diagnosing the neoplasms of the colon, allowing to diagnose neoplasms and regional lymph glands.
2. The NLS method enables to detect the colon adenoma and cancer by the presence or absence of the tumor invasions in the intestinal wall.
3. The diagnostic efficiency of NLS method in defining the phase of tumor process in the rectum is lower, than in segmented intestine.
4. The diagnostic accuracy of the cancer phase in colon depends as much on the size as on the anatomic shape of the tumor growth. The best results were obtained at defining depth of invasion of the intestinal walls by a tumor sized under 2 cm and over 5 cm.

## NLS-Method In Vascular Pathology Diagnosis

S.M. Patrushev,  
A.D. Sluzky, V.M. Vagulin

Today the world faces a constant trend of a growing rate of mortality caused by occlusive vascular diseases, especially by cerebro-vascular disorders which are in the third place among death causes. On the one hand the trend is caused by a growing number of elderly and aged patients. On the other hand many men even already at 45 have atherosclerotic damage of main head arteries, causing the need for a medical observation.

The most simple and at the same time informative method of non-invasive diagnosis of occlusive damage of peripheral vessels appeared to be the NLS-method which has been used in clinical practice for a short time. The first NLS devices equipped with analog trigger sensors, operating in 1.4 GHz frequency mode and used in clinical practice since the late 90-s have not lost their importance yet. They can help determine the condition of certain sections of the main vessels in the lower limbs and that of the brachio-caphalic vessels.

Not only the condition of the vessels but also that of the valve system within deep veins can be studied. 102 patients were examined in 1997-1998 to detect valve insufficiency of deep veins affected by varicosis. The patients were from 21 to 67 years old. The examined patients included 25 men (24.5%) and 77 women (75.5%). The study was carried out by means of a NLS device using a 1.4GHz analog trigger sensor. In 32 patients a valve insufficiency of the femoral vein was detected, in 44 patients failure of both femoral and popliteal veins. NLS enables to assess the condition of the valve system of deep veins in low limbs on a noninvasive and objective basis. This enables appropriate surgical intervention and can be used as an alternative to phlebography analysis.

The NLS-digital spectral analysis method has no contra-indications and in terms of informational content is comparable to angiography. It can be used to perform screening in the course of poly-clinical examination with a view to detect early or latent forms of vascular pathology and also as a preliminary method for selecting patients for angiographic treatment, since according to some specialists, angiography should only be performed on candidates for surgery picked out after a preliminary NLS investigation. However, this method does not assess the bulk index of the bloodstream, because NLS does not provide a vessel's image and thus is unable to measure the vessel's diameter. This kind of information may be acquired with the help of Doppler systems with 3D-imaging, that offer duplex and triplex scanning (the so-called Doppler chromatic charting).

The NLS-method was developed in the mid 90-s and played an essential role in vascular pathology diagnosis. The main advantage of the NLS-method was that it facilitated search and location of the vessels and facilitated rapid differentiation of vessels from nonvascular structures, arteries from veins and very accurate detection of signs of

disturbed vascular permeability caused by stenosis or occlusion of the vessel lumen by an atherosclerotic patch or a thrombus: both of which are generally not visible at scanning in B-mode alone.

In addition the NLS-method enables diagnose of portal hypertension, the extent of its intensity, and permeability of Porto systemic bypasses. NLS is very sensitive in defining the extent of peri-pancreatic vessel involvement with pancreatic cancer: essential in selecting the approach for surgical treatment. NLS facilitates detection of the damaged renal vessels (both veins and arteries): invaluable for the correct choice of a hypotensive drug at arterial hypertension.

Some efficient hypotensive drugs, i.e. inhibitors of angiotensin converting enzyme (ACE) such as capoten, enalapril, bezlipril, etc., have become very popular lately, but they have counter-indications at renal artery stenosis. So physicians should bear in mind that checking for stenosis is a must before prescribing this kind of medicine. The NLS-method is likely to be the choice method in such cases.

The NLS-method is indispensable for differential diagnosis of benign and malignant hepatic diseases. Its sensitivity is comparable with the potentials of conventional or digital angiography and computer-assisted amplified tomography. In addition, the NLSmethod is much cheaper, simpler and more intelligible. It can be employed directly at the patient's bedside if required. The NLS-method may be used in ophthalmology to check ocular hemodynamics before or after surgical intervention, in obstetrics to detect the disturbed blood current in umbilical cord arteries with a view to diagnose a retarded fetus development and predict a negative perinatal produce.

Yet another potential of NLS method lies in cranial scanning which enables to detect intracranial hematomas, aneurisms, cysts and tumors in the encephalon.

These are far from all potentials of the NLS method.

Summing up, the NLS-method is one of the most dynamic techniques and within the next few years it is bound to bring some new discoveries.

## NLS-Diagnosis Of Lung Abscess

S.N. Makarova

A screening NLS-investigation detected two causes of lung abscess in feverish patients who were complaining of pain in the right hypochondriac region. The patients were subjected to echography in order to preclude an abdominal cavity pathology.

The NLS examination was conducted by means of a NLS device equipped with a digital trigger sensor (1.4GHz).

Patient N., aged 57, was admitted to the therapeutic department. He was complaining of a week-long fever with a temperature of up to 40C, a moderate non-productive cough and pain in the right hypochondriac region as a result of catching a cold. He came to see a doctor ten days after falling ill. Clinical history included a bilateral pneumonia 14 years previous. The clinical blood analysis indicated an increased leukocyte content - up to  $18.7 \times 10^9$  with a flush left leukogram. The common urinalysis showed no deviations. Physical examination: vesicular pulmonary respiration, weakened in the lower sections on the right with no rhonchi.

The tongue was dry, white furred. The belly was soft, with significant pain in the right hypochondriac region. No symptoms of peritoneum irritation were in evidence. Pasternatski symptom was negative on the right and left.

The NLS-investigation of the abdominal cavity did not detect any signs of pathology in the liver, gall bladder or pancreas. On the right were visual blackenings in the diaphragmatic pleura (4-5 points according to Flandler's scale) and an image of voluminous formation in the right lung (5-6 points). On the dorsal thoracic wall there was an image of an enhanced chromogenic formation (6 points) of a heterogeneous internal structure, sized 8-x65x54 cm. The lung tissue around the nidus had a higher chromogenic density (4-5 points) on account of infiltration. A spectral similarity to the "lung abscess" reference standard ( $D=0.312$ ) was detected. The investigation of the left lung and pleural cavities did not detect any structural changes. NLS conclusion: certain signs of developing abscess in the right lung.

The check radiological investigation arrived at the conclusion: an abscess in the lower lobe of the right lung in progress.

A repeated NLS examination was conducted 10 days later. This revealed a rounded hypochromogenic formation with uneven outlines with some hypochromogenic zones inside, sized 81x60x51 mm.

The chromogenic density of the lung tissue around the nidus was somewhat higher (due to infiltration), and the folia of the visceral and parietal pleuras were blackened in the lower sections of the right lung.

The patient was offered a further therapy in a specialized surgical department, which he turned down. 3 weeks later, after some anti-inflammatory therapy a check NLS examination was performed. During the examination the patient complained of coughing with a profuse sputum discharge. His temperature was normal, the clinical blood analysis indicated a leukocyte count of  $8.6 \times 10^9$ , and the differential blood count was within the standard, and ESR grew up to 37 mm/h. The NLS-investigation revealed a rounded formation with even outlines, increased chromogenic density and heterogeneous internal structure sized 47x43. The chromogenic density of the lung tissue around the perimeter decreased (because of reduced infiltration).

At the patient's urgent appeal he was discharged from hospital for further outpatient treatment. Later he underwent two check examinations conducted.

Patient M., aged 63, was examined by means of the NLS-method in order to preclude a liver or gall bladder pathology.

An NLS-investigation of the lung and pleural cavities was carried out. In the left lung and pleural cavities there were no signs of pathology in evidence. In the right lung in the IX, X and XI hypochondria (from the paravertebral line to the scapular one) the analysis parietally displayed a formation having an increased chromogenic density and sized 85x60 mm with uneven outlines and heterogeneous structure (due to inclusions of a decreased chromogenic density) sized 3-4 mm. The chromogenic density of the lung tissue was not increased. NLS conclusion: signs of an abscess in the right lung.

Radiological conclusion: abscess in the lower lobe of the right lung.

The patient had check NLS-investigations conducted against the background of anti-inflammatory therapy.

With the NLS-investigation performed 10 days later the formation looked rounded, had even outlines, an increased chromogenic density (4-5 points) and a heterogeneous internal structure. Around the perimeter of the nidus the lung tissue had an increased chromogenic density (3-4 points) because of infiltration. The formation measured 73x50x60 mm.

The NLS-investigation 2 weeks later did not detect any positive dynamics from the administered anti-inflammatory therapy.

The submitted clinical observations once again confirm that the NLS-investigation with lung diseases is not used in clinical practice as often as it deserves.

Besides, the dynamic NLS-observation of the patients affected by lung diseases enables to assess the efficiency of the employed therapy and reduce the radiation load both on patients and on the medical personnel.

## NLS-Diagnosis Of Degenerative Changes In The Spine

A.G. Brusova, P.A. Manokhin,  
T.K. Puzanovskaya, T.A. Shyshkovets

Computer Nonlinear Diagnosis (NLS) is a new highly informative method provided to examine the spine and spinal marrow. The NLS advantages are non-invasiveness, scalability of the image field, a capability to obtain sections of any orientation and virtual imaging of radicular canals and paravertebral zone. Undoubtedly the use of NLS in diagnosis of degenerative spine diseases has apparent prospects.

### Subject and methods

The investigation was conducted by a 1.5 GHz NLS unit. 1217 patients affected by degenerative changes in the lumbar region of the spine were investigated. NLS analysis of the spine and spinal marrow was performed for all patients. 112 patients had NLS and CT, and myelography was performed for 10 patients.

### Analysis of results

In 87% of cases we found disks affected by degenerative changes. The earliest degenerative change in inter-vertebral disks (ID) was a hyper-chromous lesion (6 points on Flandler's scale) in zone between the pulpous nucleus and the fibrous annulus. Along with the degenerative changes NLS has detected an increased chromogenic density of the signal from the bone marrow in the adjacent regions of the vertebral bodies (4-5 points according to Flandler's scale). 3 degrees of degenerative changes could be distinguished depending on the process intensity.

Degree 1, a hyper-chromous zone appraised at 4-5 points on Flandler's scale, was detected in 90 patients. Conventional radiographs did not display any changes. Formation of fibro-vascular tissue followed by its penetration into the bone marrow is believed to underlie the changes. Some authors relate these changes to the lack of stability in this segment.

The histograms displayed a spectral similarity to the reference standard "intervertebral osteo-chondrosis" (D0.396 to 0.425).

Degree 2, a hyper-chromous response in the affected zone at 5-6 points on Flandler's scale was detected in 215 patients. Conventional radiographs did not show any changes. According to some literary evidence, in this phase the histology detects a substitution of the fat bone marrow for the red bone marrow often accompanied by enlarged trabeculae. This phase generally precedes an osteo-chondrosis development which can be diagnosed a little while later by conventional radiographs.

The spectral similarity was close to the reference standard "inter-vertebral osteochondrosis" (D 0.246 to 0.360).

Degree 3, a frank hyper-chromous response (6 points), which corresponds to a far advanced vertebral body sclerosis, was detected in 312 patients. Some secondary symptoms, like local bulging and vertebral osteophytes, were detected with far advanced degenerative lesion of the disks and a substantial similarity to the reference stand "osteochondrosis" (D from 0.152 to 0.218). NLS enables differentiation between a protrusion and prolapse of the disk and existence of rupture of the fibrotic ring and the condition of longitudinal and other ligaments.

A protrusion is defined as a bulging of the disk tissue beyond the posterior outline of the vertebral body into the spinal canal. The fibrotic ring tissue endures though becomes very thin and NLS only reveals a zone of slight destructive change in the structure (3-4 points). With compression it gives an acutely frank hyper-chromous response (6 points).

Protrusion may be accompanied by a slight caudal shift which is quite often defined by means of the NLS-method at L5-S1 inter-vertebral disk level. NLS detected protrusion in 729 patients.

The rupture of the fibrotic ring fibers results in the prolapse of the pulpous nucleus on a subligamentary level and the ligament rupture results in the prolapse inside the cerebrospinal canal. As can be seen from NLS, the longitudinal ligaments look well delimited and are represented as hyper-chromous band-like structures (5-6 points) which adjoin the bones and the fibrotic ring. The extra-ligamentary prolapse can shift either in a caudal or a cranial direction. The extra-ligamentary prolapses of the disk that lost contact with the host disk become sequestrers. Occasionally, we observed some very small extra-ligamentary sequestrers which shifted far into the cerebrospinal canal, which made it hard to detect them.

The NLS-investigation detected prolapse in 445 patients. In 68% of cases the hernia of intervertebral disk was combined with other degenerative dystrophic spinal changes on this level. The hernia of the intervertebral disk was detected at L4-5 level in 83%, and L5-S1 level in 15% and at L3-4 level in 2% of cases. A lesion of several disks was found in 50 patients. 196 patients underwent surgery, among them 114 had lateral hernia, 76 patients had median lateral hernia and 6 had median hernia. 5 patients had surgery for hernia recurrence. The NLS diagnosed extraligamentary sequestrated hernia in 38 patients, and intracanal hernia was diagnosed in 3 persons. Multiple sequestrers were detected in 5 patients.

The clinical symptomatology for the prolapse of intervertebral disks was variable and did not always depend on their size. In some cases we observed median protrusions which did not result in any clinical implications. The clinical symptomatology for small sequestrated hernia was no less than for large sequestrers.

In evaluating the NLS data not only the size of hernia but also the reserve area of the cerebrospinal canal and their repositions should be taken into account.



With a suspected hernia the NLS-investigation should be performed at least in two planes, sagittal and paraxial, i.e. parallel to the disk plane, and the sagittal investigation in T1W-SE can be combined with other sequences.

The median prolapses of intervertebral disks in sagittal shots could be seen quite clearly. The signal content of the hernia predominantly corresponded to the NLS signal content of the pulposus nucleus. The external part of the fibrotic ring, posterior longitudinal ligaments and the dura matter give a frank hyperchromous response and do not differentiate from one another. Thus, the NLS-method sometimes fails to present a direct proof of a rupture in the external part of the fibrotic ring.

It is largely a lesion of the pulposus nucleus on the side of the back edge of the vertebral body that speaks in favor of the protrusion in axial shots. Displacements and compression of the spinal marrow can well be seen in both sagittal and axial projections.

Sagittal shots have an advantage in deciding on the disk prolapse, the size of intervertebral foramina and the condition of the cerebrospinal canal and bones. These shots are not significant for detecting an intra-dural process with the cone especially poorly visible in them. Frontal shots have drawbacks in determining the condition of the pulpus nucleus and fibrotic ring. To that end paraxial virtual models are used, allowing to differentiate the process between the pulpus nucleus and the fibrotic ring and sometimes make it possible to differentiate between the fibrotic ring rupture and the protrusion free of the rupture. Thanks to virtual dimensional scaling sagittal shots allow to well delimit the subarachnoid space.

## NLS-Diagnosis of Diffuse Infiltrative Lung Diseases

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Among different kinds of lung disorders special attention has been paid over the last years to diffuse infiltrative lung diseases (DILD), which is largely accounted for by some problems in their timely diagnosis and treatment.

Most diffuse lung diseases involve in the pathological process both the interstitial tissue and the respiratory tract and alveoli. In this connection this type of pathological processes should be defined rather as diffuse infiltrative than as interstitial diseases. Despite of the polymorphism of clinico-morpholitis (in contrast to the exudative alveolitis in the case of a pneumonia) with fairly stereotyped changes in the lung interstice in the form of inflammatory infiltration with different degrees of intensity. Subsequently a fibrosis develops that can have different rates of progression. A 'cellular lung' pattern is the final phase of the development. It should be noted, that some infectious diseases of certain etiology (like tuberculosis, histoplasmosis, etc.) and particular malignant tumors (lymphogenous carcinomatosis, bronchioloalveolar cancer) do not directly belong to interstitial lung diseases but are similar to them in terms of manifestation.

The clinical evaluation of patients with a suspected DILD is a complex problem. Nonspecific symptoms and in some cases signs detected during chest examination may be characteristic of a multitude of acute or chronic lung diseases that involve the interstitial tissue, respiratory tract or alveoli. DILD are represented by an extremely heterogeneous group of diseases. The DILDs have been described in over a hundred possible versions, however in clinical practice only about 10 or 15 conditions are most common and it should be noted that sarcoidosis and various cases of lung fibrosis occur in clinical practice in 35-50% of all DILDs. Besides, acute diffuse lung processes in patients with reduced immunity (also in combination with HIV-infections) are likely to have a great number of infectious and non-infectious varieties, which X-ray evaluation is found to be difficult.

Unfortunately, the capabilities of conventional roentgenography for patients with a suspected DILD appear to be limited for the sensitivity and specificity of the method prove to be inefficient. The data on 458 patients with a histologically confirmed DILD were studied. The chest radiographs for 10% of the cases turned out to be normal. Among 86 patients affected by DILD no pathological change was detected in 50% of the patients with histologically proven bronchiectasia and in over 20% of the patients with emphysema shown on X-ray shots. Radiography may equally show false positive results of the investigation. We have discovered that in 10-20% of the patients with the x-ray confirmed signs of DILD no changes were detected during the lung biopsy.

The computer nonlinear diagnostixs (NLS) is one of the promising methods of diagnosing lung diseases of today. NLS appreciably improves the communication of the

fine morphological elements in the lung tissue and opens up new opportunities for recognizing interstitial diseases of the broncho-alveolar system. NLS has a high sensitivity in detecting the interstitial lesions of the parenchyma and small nodules.

The results of the investigations prove that NLS has a better sensitivity in detecting both acute and chronic diffuse lung diseases. The sensitivity of the NLS diagnosis in detecting lung diseases makes 85% as compared to 70% in chest radiography.

The accumulated experience too, gives additional grounds to assert that NLS is a highly efficient method for diagnosing a wide range of various diffuse lung diseases (DILD included) and excels the 'classic' chest radiography in sensitivity.

It should be noted that the high sensitivity of the NLS-method is achieved without sacrificing the specificity and diagnostic accuracy of the method. In patients affected by DILD the NLS specificity amounted to 86% as opposed to 76% in radiography. In particular, the high sensitivity (86-88%) and specificity (83-89%) of NLS were demonstrated in bronchietasia diagnosis.

Although NLS is a more sensitive method as compared to chest radiography, its sensitivity in lung disease diagnosis is not absolute and the fact that no radiological changes were detected by NLS may lead to precluding lung disease in patients who actually suffer from DILD. 100 patients were examined by means of the NLS with 86 of them affected by DILD and 14 having no pathological change in the lungs.

Despite a high value of NLS sensitivity and specificity, for 4% of the patients with biopsy-detected lung diseases the results were interpreted as being normal. On the other hand, the NLS was proven to be a high-accuracy technique for precluding acute lung diseases in patients with immunodeficiency. Some examination data were studied for patients with a bone marrow transplant and clinical symptoms of fever of obscure genesis. The authors demonstrated high reliability of the NLS in determining fungal infection in 20 of 24 cases. Besides, the fact that no changes were detected during NLS lung examination prompts the assumption that the fever was caused by bacterial or fungal infection of extra pulmonary genesis.

It is also a proven fact that the sensitivity with NLS is higher than with standard computer tomography. We examined 150 patients. Using conventional CT (10mm collimation) and NLS we found that NLS had a higher sensitivity in recognizing pathological changes in the lung tissue.

Due to its high sensitivity, NLS should be used to define lung diseases in patients with a normal or obscure aspect of disease who have a pulmonary disturbance or symptoms that suggest an acute or chronic diffuse lung disease.

Even with certain clinical signs in evidence the diagnostic accuracy of classic radiography in patients affected by DILD appears to be limited. The reason is both superposition of the image in the radiograph and low contrast of minute lung structures.

NLS is free of these aspects, which is why it is reputed to be a more efficient method for recognizing diffuse lesions of lung tissue as compared to both radiographic survey and conventional computer tomography.

Besides, having a higher sensitivity, specificity and diagnostic accuracy, the NLS method can become a determining factor in evaluating the activity of a pathological process in patients affected by DILD. In certain cases NLS can be used not only to define the presence or absence of a pathological process or the extent to which it has spread, but also to collect information about the reversibility of changes (in an acute or active phase) as compared to irreversible (fibrotic) changes in the lung tissue. Moreover, since NLS can accurately identify the imponderable activity of a pathological process in the lungs, it can be employed to evaluate the efficiency of the treatment given to patients.

The conventional methods for evaluating disease activity, such as trans-bronchial lung biopsy (TBLB), broncho-alveolar lavage (BAL), chest radiography, gallium lung scanning and functional lung tests are insufficiently reliable in evaluating the activity and in terms of prognostication. So the open lung biopsy (OLB) is still the choice method for both diagnosing and evaluating the process activity. We were able to prove, that signs detected in patients by means of NLS can provide some valuable information and be significantly important in defining the activity of a pathological process.

In terms of its prognostic value NLS is now advancing to the foreground leaving behind some functional lung tests BAL and even OLB, because it enables lesion assessment over the whole lung parenchyma as compared to a separate biopsy sample. Moreover, NLS can become an accurate noninvasive method for evaluating the efficiency of the administered treatment.

Sarcoidosis is one of the most interstitial lung diseases of unknown etiology. In typical cases granulomas are formed in fine lymph vessels or beside them, afterwards the granulomas self organize which causes lung tissue fibrosis.

A number of researchers considered the NLS potentials in defining the process activity in patients affected by sarcoidosis. The main activity indicator is the presence of small nodules and to a lesser degree their distribution and occurrence in the lung tissue. Unfortunately, despite the difference between reversible and irreversible changes detected by NLS for patients having sarcoidosis, the potentials of NLS in assessing the process activity have not been studied well enough.

Among different indications in favor of NLS application, the use of this method in lung biopsy is probably the most important one. Biopsy is a very essential diagnosis technique which enables to define the nosology of a lung diseases, its activity level and phase. The diagnostic value of biopsy to a certain degree depends on its method and the type of DILD. The authors proved that TBLB was diagnostically informative for only 20 patients of 53 (38%) who had DILD in evidence; in 33 such patients (62%) TBLB displayed normal lung tissue or nonspecific changes.

At the same time OLB made a specific diagnosis of DILD in 92% of cases. In DILD-affected patients TBLB proved to be the most informative for patients having sarcoidosis or lymphogenous carcinomatosis, because these lesions have largely peribronchial tissue involved and are therefore most accessible to TBLB. Diagnostically OLB appears to be more accurate, but it also has certain complexities because lung tissue is sampled from a small sector of the lung which might not reflect the changes occurring in the rest of the lung tissue. Many diffuse diseases affect lung tissue irregularly so the pathologically altered parts of lung parenchyma may be located among normal lung tissue. Besides, the same lung may contain both active manifestations of the disease and fibrotic changes of long standing. For an accurate diagnosis and assessment of the clinical progress of the disease the right choice of a biopsy sample is very important. During biopsy NLS helps to collect more accurate data indicating active areas of a pathological process. By using NLS, the areas affected by lung fibrosis in its final phase, with 'honeycomb' lung formed, could be skipped during biopsy sampling. In addition, NLS may prove to be vitally important for choosing the most effective technique (TBLB, BAL or OLB) for making a histological diagnosis.

Conclusion.

Radiography still remains the most accessible method for diagnosing DILD yet its informational content appears to be inadequate.

Making a correct diagnosis necessitates a combination of laboratory, functional and radiological investigations as well as some invasive methods, each of them having its own substantial limitations.

NLS-diagnosis is a method that greatly improves identification of diffuse infiltrative lung diseases and as such it should become a part and parcel of an integrated investigation.

## NLS-Diagnosis of Prostate Diseases

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S.N. Petrenko

An ever growing number of physicians enjoy an opportunity of a screening NLS diacrisis of prostate gland and urinary bladder. This article attempts to consider some particulars of morphological changes occurring in a prostate affected by pathology, based on the results of NLS-investigations.

In the West prostate cancer makes 20% of the total cancer diseases and ranks second to lung tumors as a death cause.

According to some autopsy findings with a histological investigation of the prostate, 12-47% of men aged over 50 appeared to have cancerous nidi. Clinically, cancer is diagnosed more rarely because a high percentage of that number corresponds to 'minor forms' of cancer that have low invasiveness, so the patients suffering from it die of another kind of pathology.

To enhance the quality of prostate diseases diagnosis it is important to comprehend the specifics of topographic and zonal anatomy of a particular organ.

The prostate gland is located in the small pelvis between the bladder and anterior abdominal wall, anterior rectum wall and secondary urogenital diaphragm. The gland has a chestnut shape and tightly envelops the bladder cervix and prostate urethra. The gland base is lightly connected with the bladder into a coherent mass. Its anterior surface is directed to the symphysis, and the posterior one - to the rectum ampulla. The posterior surface of the gland has an expressed sulcus, which enables to conventionally subdivide the gland into the left and right lobes. Besides, there is a protruding middle cone-shaped lobe confirmed anteriorly by the prostatic urethra and by the spermatic ducts posteriorly.

According to zonal anatomy theory usually 4 glandular zones are distinguished in the prostate. The correct interpretation of NLS data largely depends on the knowledge of their topical pattern. 20% of the glandular tissue correspond to the central zone (CZ). The peripheral zone (PZ) occupies 75%. The intermediate (transitory) zones (TZ) make up 5% of the total amount of the glandular tissue.

Perurethral glands (PUG) take a relatively small amount of the tissue, however exactly this area of the gland is very important for explaining the changes at a benign hyperplasia.

Apart from the glandular area, 4 fibro muscular zones can be discriminated:

1. Anterior fibro muscular stoma (AFS).
2. Unstriated muscular fibers of the urethra (UMFU).
3. Preprostatic sphincter (PPS), which is an extension of the musculature of the inferior part of the ureter and prevents inverse emission of seminal fluid.

4. Postprostatic sphincter (PPS), which is responsible for retaining urine in the bladder and blocks incontinent micturition.

The gland can be conventionally subdivided into 2 parts: -

- external part consisting of CZ, PZ, TZ and
- internal part comprising AFS, PPS and PoPS.

According to NLS-investigation, the external part looks like a structure of normal chromogenic density (2-3 points of Flandler's scale), and the internal one is hypochromogenic (1-2 points). The two parts are divided by a fibro muscular layer, the so called surgical capsule, along which an incision is made during surgical intervention, and calcium salts deposit (calcium incrustation of the gland). In the NLS-investigation those formations can well be seen as fairly hypochromogenic structures (3-4 points) of different size.

The analysis of the prostatic gland image on the NLS virtual model is made according to the following quantity and quality characteristics:

1. Size: from to back - 2-2.5 cm, across - 3-4.5 cm, from top to bottom - 2.5-4 cm;
2. Volume: up to 20 cm<sup>3</sup>;
3. Symmetry. The urethra is the reference point.

If any pathological changes are detected in the NLS-graph it is recommended to: - specify their exact location;

- perform histography of the pathological area and area of the tissue with a normal structure.

It will be helpful for the case follow-ups. At a benign hyperplasia NLS enables detection of the direction of the principal germination. In case of hyper-trophic transitory zones the gland proliferates inwards. Though darkened lateral zones are formed (4-5 points on Flandler's scale), the nodes can still be always visualized. The trans-rectal NLS offers the most detailed and authentic information.

Enlarged lateral lobes squeeze PZ and CZ causing their atrophy. With proliferation of the para-urethral zones a massive fibro muscular PPS layer restricts their hyperplasia, so with this kind of pathology the gland proliferates along the urethra forming a middle darkened zone pushing back the bladder wall. Virtual scanning makes this pathology clearly visible in longitudinal sections. At the beginning of the proliferation a relationship between the internal and external glandular parts is disturbed. Apart from some distinctions in the zones of principal proliferation, the clinical signs will be different as well. In the case where a globe-shaped gland is formed (TZ proliferation) the gland is chiefly hyper-chromogenic and the dysuric manifestations are minimal while with a 'middle zone' formed the gland is slightly darkened and dysuria appears to be frank. Sphincter decompensation leads to the development of urinary incontinence and dilation of the upper urinary tract followed by the atrophy of the cortical layer of kidneys, which gradually adds to frequent urination, nycturia, reduced pressure of the urine or reduced rate urination occurring in the initial phase of the disease.

In case of a squeezed cervix of the bladder a NLZ-graph provides visual signs of an infravesical obstruction that causes some morphological and functional changes in the lower and upper urinary tracts. Specifically, in the initial phases of benign hyperplasia a darkened wall in the bladder can be observed. Dark patches result from compensatory hypertrophy of the detrusor.

These 3 phases of benign hyperplasia of the prostate can be distinguished depending on the intensity of the changes:

1. hyperchromogenic density of the gland with no residual urine;
2. residual urine present;
3. all of the above-mentioned plus dilation of the upper urinary tract with the cortical layer of kidneys involved in the process.

Diagnosis of acute prostatitis is made on the basis of histograms (similarity to the reference standard process "prostatitis"  $D > 0.425$ ). Diagnosis should be done in combination with dactylar rectal examination (painfulness during palpation) with clinic lab data taken into account).

In the case of abscessed lesion a still higher hyperchromous area (6 points) is visible against the general dark patch (4-5 points according to Flander's scale). Areas of frank blackening correspond to necrotic changes. With an abscess in progress one can notice a reduced infiltration of the tissue around the cavity with the dark patch gradually getting lighter in the course of dynamic observation (up to 3-4 points). With adequate therapy employed the post inflammatory cyst may fall into regression.

As can be seen from NLS-investigation, chronic prostatitis does not give a common characteristic picture, however the morphological processes in different phases of the disease are reflected in histograms. With a long-lasting disease the chromogenic density tends to rise due to a post-inflammatory substitution for the glandular component and its histograms. In the 'organ preparations' mode destructuring of the fibrous component starts to predominate.

With an oncological pathology, analysis of the gland picture helps localize the process in different projections and assess the extent of prevalence and involvement of adjacent organs. The minimum size of tumor determinable by means of NLS-investigation is about 8-10 mm. 80% of the tumor nodes are presented by markedly hyperchromogenic structures (6 points on Flander's scale).

Analysis of histograms of the nidi help differentiate an onco-process. The method's sensitivity becomes higher with both 'elimination' and 'NLS-analysis' modes in use. Peripheral zones have first place as far as cancer incidence rate is concerned. They constitute 70-80% of cases. Transitory zones (TZ) are affected in 10-20% and CZ in less than 5% of cases. In transitory zones a tumor nidus should be looked for within 3-4 mm from the capsule. In case of an oncological alertness the symmetry in the lobe affection is assessed with respect to the sagittal axis and intensity of the black patch (4-5 points on



Flandler's scale), in the adjacent organs, especially seminal vesicles and bladder because in 25% of cases metastases occurs through the gland apex and seminiferous tracts. Considering the fact that cancer often develops with some diffuse changes occurring in the background, for example, with chronic prostatitis or adenomatosis, it is not always possible to visualize newly formed cancerous areas. In such cases the results of PSA level definition and digital rectal examination should be considered. The PSA level is defined considering the patient's age and gland volume.

Conclusions:

1. NLS-method enables diagnosis of most prostate diseases and being a screening diagnosis method, it should be supplemented by biopsy, should any pathological changes be detected.
2. The final diagnosis should be made on the basis of the clinic lab data and the results of digital rectal examination in combination with biopsy only.

## NLS Diagnosis Of Affected Regional Lymph Nodes At A Mammary Gland Cancer

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Mammary gland cancer is one of the most common women's oncologic diseases. Its annual growth rate in the developed countries is about 3%. In addition, this pathology proves to be the primary cause of mortality among females affected by oncologic diseases. The tactics of treatment and disease prognosis largely depend on the presence or absence of any regional metastases. In this connection the problem of competent diagnosis of affected regional lymph nodes becomes especially pertinent. With that end in view a number of methods have been used, from physical to hardware-based examinations. However, in 40% of the patients metastatic lesion of the lymph nodes in the axillary area is not determined clinically and false positive data were observed in 25% of cases. Instrumental diagnosis methods do not have a rich informational content either. The NLS investigation of regional lymph nodes has been more extensively used lately.

### Subject and methods of investigation

We have examined regional lymph nodes by means of a device NLS with a 4.9 GHz nonlinear trigger sensor in 25 patients affected by mammary gland cancer in Phases I-III. The obtained data were compared with the results of histological investigation of the macro-preparations removed during surgery.

### Investigation results

Of 25 patients examined prior to surgery as many as 1-3 affected lymph nodes were detected in 20 patients. The derived results were practically fully confirmed by histological investigation of the macro-preparations removed during surgery. Only in one case NLS analysis did not detect affected nodes which we account for their small size.

During the NLS investigation the metastatic lymph nodes were found to have pathological changes with quite a high degree of intensity. Flander's scale indicated 5-6 points in 80% of cases.

The fact that organo-saving surgery and in some cases tumorectomy are being more and more extensively used these days makes the NLS investigation even more important. Our own practical experience can confirm that. Patient B., 63 years old was admitted to the clinic with regard to right mammary gland cancer in its early phase IIa after an ischemic stroke in combination with ischemic heart disease and hypertension III. Palpation did not detect any lymph node enlargement. The NLS investigation did not detect metastasis-affect lymph nodes which allowed a tumorectomy for this patient at a low hazard to life.

Thus NLS investigation of regional lymph nodes with mammary gland cancer may become a sufficiently reliable method for assessing their metastatic affection which enables to pick out the most efficient tactics in treating patients with this kind of pathology.

# NLS-Investigation In Evaluating Knee Joints Affected by Osteoarthritis Deformans

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## Introduction

Primary osteoarthritis deformans of the knee-joint is one of the most pertinent problems in modern medicine due to its prevalence, great loss of working time and treatment expenses. In addition, in many cases an early or differential diagnosis of the knee-joint lesion is impeded, which complicates selecting the most efficient therapeutic and rehabilitation measures and evaluating the patient's disability.

Today diagnosis of knee-joint disorders comprises conventional radiography as well as sonographic evaluation of the joints, used to examine soft tissues of the locomotorium. The existing techniques used to examine the knee-joint allow determination of dominance of pathological process in the joint, including degenerative ones. However, the relationship between the intensity of patho-morphological changes and the severity and dynamics of the process have not yet been studied.

This article aims to demonstrate the efficiency of the NLS-investigation in diagnosing osteoarthritis deformans, especially in the early (sub-clinical) phase of the disease.

## Subjects and methods

To define a normal relationship of the knee-joint anatomical structures 10 healthy persons aged from 25 to 55 (test group) were examined. The main group consisted of 50 patients with clinical implications of osteoarthritis deformans of knee joints in different phases. The average duration of the disease was 7.0 + years. All patients were routinely radiologically examined in two interperpendicular planes.

The X-ray pattern analysis took into account the joint space amount of narrowing, existence of marginal osteophytes and deformation of osseous structures with cysts and fibrosis areas present in the sub-cartilaginous bone department.

The NLS investigation was carried out using a device equipped with a 1.5 GHz trigger sensor. Changes in the joint capsule were evaluated in virtual shots in sagittal planes above and below the kneecap and along the posterior surface of the joint. Frontal planes along the lateral surfaces of the joint were used to define the exact condition of menisci, articular cartilages and changes in the synovium.

It is traditionally believed that in the articular cartilage degenerative changes start with a rupture of the articular matrix and degeneration of chondrosites. Therefore during the NLS examination special attention was paid to changes in the articular cartilage. In the

examinees of the test group the articular cartilage looked like a hyperchromous strip (1-2 points according to the Flandler's scale). Two patients were found to have an articular cartilage of a heterogeneous chromogenic pattern, 3-5 points in the initial phase of the disease with small hyper-chromogenic nidi (1-2 points) present. No radiological changes in the joints were detected for this group of patients.

In 14 (28.0%) patients in the second clinical phase of the disease the chromostructure of the cartilage was heterogeneous and some high hyper-chromogenic structures (4-5 points) were detected as well as hyper-chromogenic inclusions (1-3 points) of a small diameter.

In 21 (42%) examinees in the third phase of the disease the hyaline cartilage appeared as a hyper-chromogenic strip (5-6 points).

In 10 (20.0%) patients in the same clinical phase of the disease the articular cartilage was visualized as a distinctly hyper-chromogenic linear structure (6 points) with vertical fissures present (4-5 points). In three patients the higher line cartilage was not visualized mostly in the middle departments of the joint.

Depending on the phase and duration of the disease a spectral similarity (D 0.189 to 0.621) occurred to the reference standard process 'osteoarthritis deformans'.

The X-ray pictures detected a moderate constriction and deformity of the joint space as a primary sign of the articular cartilage distractions in 22 patients and considerable constriction in 12 patients. Sub-cartilaginous osteophyte was very important for osteoarthritis pathogenesis. Formation of sub-cartilaginous and epiphyseal cysts were present in the initial phases of the disease (71.0% of the patients). According to NLS-investigation, the cysts were located sub-cartilaginously in the lateral regions of the bone, 1.0-3.0 mm deep and were as many as 4 to 12-15. Standard X-ray pictures of knee joints displayed some changes in the sub-cartilaginous regions of the bone, like cysts and fibrosis, only in the second phase of the disease.

A very important role in the osteoarthritis deformans development was attributed to the condition of the synovium and articular capsule. With the progress of the disease and changes in its phases, a cartilaginous detritus with antigenicity formed on the articular surfaces. That often led to the inflammation of the synovium and its fibrosis. As a result, the synovium produced an inadequate fluid, which in turn impaired the cartilage nutrition with its ensuing degeneration.

The synovium in healthy persons (test group) was visualized as a hyper-chromogenic linear structure (1-2 points). The first and second phases of the disease saw a steady rise in its chromogenic pattern in 14 (28%) patients (3-4 points). In 32 (62%) patients in the third phase of the disease the chromogenic density of the membrane reached 4-5 points throughout the phase with at most 3 or 6 hyper-chromogenic inclusions. In three patients with an aggravated form of the osteoarthritis deformans (the fourth clinical phase) the synovium looked like a distinctly hyper-chromogenic structure (4 points) with areas of a reduced entropic density (3-4 points).

Changes in the membrane structure were always concomitant with synovitis with a limited amount (mostly in the upper entrophe in 28.0% of the patients) or a great amount (in all regions of the joint - in 68% of the patients) of fluid free of sediment and additional inclusions.

Depending on the phase and extent of pathological changes in the joint affected by osteoarthrosis a change in the joint capsule structure also took place. Only in the first phase of the disease did the joint capsule structure remain normal.

In the second phase of the disease, especially with synovitis in evidence, the chromostructure was assessed at 4-5 points in 14 (28%) patients and in the third and fourth phases of the disease - up to 6 points in 34 (68%) patients.

Roentgenographic evidences of synovitis and changes in the para-articular soft tissues were detected in some patients only in the third and fourth phases of the disease.

Thus, the analysis showed that the NLS-investigation had an advantage over conventional roentgenologic methods in terms of early detection of degenerative changes in the articular cartilage.

On the whole, the NLS-method sensitivity in the early phase of the disease amounted to 82%, specificity to 85% and accuracy to 86%. The sensitivity of standard radiography in two projections was 68%, specificity 54% and accuracy 78%.

#### Conclusion

The extensive use of NLS-investigation of knee-joints in everyday clinical practice enables the diagnoses of osteoarthrosis deformans in its early phases.

## Potential of NLS-Investigation In The Pre-surgical Evaluation Of Intramural Invasion Of Gastric Cancer

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Gastric cancer in Russia as well as in some other countries all over the world remains one of the most acute medical problems. Most researchers engaged in the diagnosis and treatment of gastric cancer have concluded that a timely and early diagnosis can promote cancer treatments and improve prognostication for the patients.

For many decades radiology and endoscopy remained the principal methods for diagnosing gastric cancer. The main shortcoming of these methods of investigation is their inability to obtain a picture of the thick layers of the stomach wall and hence a more exact data about the extent of tumor invasion into the stomach wall, i.e., the phase of the tumor process in the pre-surgical period. The first attempts to establish phase gradation in stomach tumor were made when such investigation methods as computer tomography (CT), trans-abdominal ultrasound scanning (US) and the most recent NLS investigation were put into clinical practice. In today's medicine the NLS investigation may become an essential method for diagnosing abdominal cavity disease because of its extreme simplicity, accessibility and non-invasiveness. However, in view of the fact that this investigation method has been used in medical practice since the late 90, the amount of the published literature dealing with potentials of the NLS in diagnosing parenchymal organs is still insufficient.

Rather explicit methods of NLS stomach investigation have been already developed and some NLS signs of cancer, benign and malignant gastric ulcers have been described (V.I. Nesterova et.al., 2002). An attempt was made to establish phase gradation of gastric cancer by means of NLS investigation which resulted in a fairly high accuracy (75.8%) of the diagnosis mostly due to diagnosing much earlier phases of the tumor process. According to some authors, NLS offers some incontestable opportunities in defining phases of gastric tumor mostly located in distal regions of stomach.

Yet, according to most researchers, until recently the NLS had been largely used as a method for specifying the extent of cancer proliferation, for defining metastases and malignant invasions beyond the stomach, in other words, the NLS investigation method enables the diagnosis of stomach tumors even in early phases of the disease.

Most literature dealing with the use of radiological computer tomography to diagnose stomach tumors provides a proof that this method can potentially be used to diagnose gastric cancer, especially its endophytic forms. However, most authors still believe that the principal role of this method lies in acquisition of certain very important information about the extent of stomach lesion and spread of the process to some adjacent organs. According to different researchers, the early gastric cancer, that only affects the mucosa and submucous layer can not be detected on the computer tomograms. In the authors' opinion, this is beyond 'the resolution capabilities' of this investigation method.

This work attempted to evaluate the potentials of the noninvasive radiation methods of investigation (trans-abdominal ultrasound scanning and radiological computer tomography) in detecting intramural invasion of gastric cancer, and to draw their comparison characteristics.

The analysis included 72 cases of gastric cancer. All the cases were compared with the surgical intervention data and the morphological studies of post surgical evidence. According to the latest gastroenterological TNM classification of tumors (1997), the group of gastric cancer carriers in phase T1 was 9 (12.5%) cases, T2 8 (11.1%) cases, T3 22 (30.6%) cases and T4 33 (45.8%) cases. Computer linear diagnosis (NLS) and radiological computer tomography (CT) of the stomach were performed as supplementary investigation methods deliberately after a preliminary integrated radio-endoscopic investigation.

Computer tomography of the stomach was done after expanding the stomach walls with a gas (pneumo-scanning) in standard projections (lying on the back and belly); the trans-abdominal NLS-investigation of the stomach was performed using the standard procedure.

In order to more clearly comprehend the NLS and CT signs underlying the pre-surgical diagnosis of the T-phase of gastric cancer (i.e. invasion degree) one needs to have a clear idea of the image of a 'normal' cancer stomach wall visualized by means of the investigation method.

Thus, in CT investigation the stomach walls (adequately expanded) were at most 0.3 cm thick in normal conditions (test group of 50 persons) in all regions with few exceptions in cardiac and prepyloric regions where the walls were 0.4 cm thick, whereas at an intramural tumor effect the stomach wall authentically thickened over 0.6 cm ( $p > 0.01$ ). In most cases it proved to be impossible to differentiate the lamellar structure of the stomach wall by computer tomography. Changing the section thickness, pitch of the table and the patients' posture in the course of scanning facilitated visualization of all the regions of the stomach very well. The location of the tumor infiltrate to the stomach wall layers was assumed as a principal criterion whose analysis provided a guide to the extent of the intramural invasion of the gastric cancer during NLS-investigation, while in computer tomography the main point was to define the thickness and elasticity of the stomach wall at the lesion spot.

The point is that NLS-investigation allowed to differentiate tumor quite clearly with respect to the layers of the stomach wall, while in computer tomography the most diagnostically important factor was the degree of the stomach wall thickening at the lesion spot with respect to the neighboring unaffected areas (thickening ratio) along with some other signs (rigidity, roughness, unevenness). Based on the analysis of the results of the surgical intervention and morphological investigation of post surgical material as well as their comparison with NLS and CT data the following conclusions were reached: both methods are quite potent in pre-surgical determination of the extent of intramural



invasion of gastric cancer, however the NLS investigation demonstrates a higher specificity as compared to computer tomography in detecting early phases of gastric cancer due to visualization of lesion zones in the stomach wall.

Analysis of the investigations enabled discrimination in the NLS-signs that allowed to define the extent of intramural invasion of gastric cancer.

1. T1 phase: presence of tumor infiltrate within the first layer of the stomach wall, which is accompanied by hyper-chromogenic density of the wall at the lesion spot (5, less often 6 points on Flander's color scale).
2. T2 phase: tumor infiltrate within the first and second layers of the stomach wall accompanied by hyper-chromogenic density of the first two layers (5-6 points at the lesion spot).
3. T3 phase: a frank chromogeneity of the inner layers of the stomach wall (6 points) except for the serous layer, which is evaluated at 4 or more often 5 points.
4. T4 phase: lesion of all layers of the stomach wall accompanied by chromogeneity of the serous membrane (6 points) and signs of tumor invasions into the neighboring anatomical structures accompanied by a frank chromogeneity (4-5 points) of the adjacent organs.

Detection of some affected perigastric (regional) lymph nodes and distant metastases in the course of investigation enabled analysis of the N and M criterion as well.

With respect to the potentials of computer tomography in pre-surgical determination of the extent of intramural invasion of gastric cancer, it should be admitted that it had a less specific pattern and was essentially based on the extent of the stomach wall thickening at the lesion spot.

Thus, since the CT signs are indicative of one or another degree of gastric cancer invasion, they could be conditionally classified in the following manner:

- It proved practically impossible to distinguish between tumors in T1 and T2 phases. So diagnosis was based on the analyses of non-multiple stomach wall thickenings from 0.3 to 0.5 cm, with the external outlines being clear and smooth.
- The T-3 phase typically had integer multiple thickenings of the stomach wall over 0.5 cm not accompanied by deformed external outlines of the stomach wall and with no signs of the tumor spreading beyond the stomach wall.
- The T-4 phase had multiple thickenings of the stomach wall (two, three or more times as thick) over 0.1 cm with a disturbed integrity of the external outlines of the stomach wall at the lesion spot and with some signs of tumor invasion into the adjacent anatomical structures.

According to our information, the NLS-investigation proved to be the most accurate and specific method of investigation in pre-surgical diagnosis of gastric cancer in its early phases (T-1, T-2) while CT results appeared to be more convincing in detecting later phases of tumor lesion (T-3, T-4). It should be noted, that, in our opinion NLS is the most

accurate method of investigation in detecting remote metastases ( $p > 0.05$ ). Based on the statistical analyses, the specificity of the NLS method of the investigation in detecting the T-phase of gastric cancer (with calculations made with reference to T-1, T-1 phases) amounted to 76%, sensitivity to 74.3% and accuracy to 78.2%, w.r.t. the computer topography the specificity, sensitivity and accuracy were 70% each (in this case calculations were made w.r.t. T4-phase of gastric cancer, because differentiating the lamellar structure of the stomach wall was found impossible in CT investigation).

Thus, as compared to computer tomography, the NLS investigation proved to be a more specific method for diagnosing cancer in its early phases although in a number of cases it was found difficult to differentiate between T1-T3 phases of a tumor lesion. In CT investigation T1-T2 phases were defined conventionally based on the degree of stomach wall thickening the lesion spot. NLS did not succeed in imaging anatomical structures beyond the stomach wall as distinctly as CT investigation did, but NLS was more efficient in evaluating such characteristics as M and N.

So, an integrated approach to the use of NLS investigation and radiological computer tomography has proved to be more preferable for more accurate pre-surgical diagnosis of intramural invasion of gastric cancer, however the order of priority and efficiency in their use somewhat depend on the results of primary radio-endoscopic investigation of the stomach. In addition it should be noted, that contra-distinction of these methods of investigation in diagnosing and phasing of gastric cancer against each other would be a mistake and delusion.

In conclusion, it should be emphasized that despite their subordinate use with reference to radiological and endoscopic methods of gastric cancer investigation, the NLS investigation and radiological computer tomography should be brought into line with primary methods of stomach investigation.

The conclusion is based on the facts that unlike some conventional radiological and endoscopic methods of investigation they allow to evaluate the internal structure of the stomach wall, which is a major factor in the pre-surgical detection of intramural invasion.

This enables to work out the proper approach for treating patients affected by gastric cancer, and based on the well-founded data reject the explorative laparotomy in case of an obvious process. Considering general accessibility, lack of radiation exposure and application simplicity it appears more appropriate to use NLS investigation as the most preferable of the above mentioned methods.

## Potential for NLS-Scopy In Adrenal Tumor Diagnosis

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Adrenal tumors do not occur very often: still they are known to be the most hormoneactive and even if small sized cause various glandular disorders. However in practice adrenal tumors often clinically develop with no symptoms in evidence or are accompanied by vague complaints.

Both documentary evidence and our experience show that 6 months to two years may elapse from primary disease manifestations to forming a diagnosis. Early detection of adrenal tumors has become an important clinical problem, which is now conventionally solved by means of ultrasound investigations (US) along with computer tomography (CT), magnetic resonance tomography (MRT) and angiography (AG).

Today NLS-scopy is one of the most advanced informative hardware-based methods of diagnosis. The NLS method will allow a substantially increase in the early and accurate diagnosis of adrenal tumors. The implementation of the latest devices equipped with digital trigger sensors made it possible to detect any growth sized around 1 cm in adrenals, which is comparable to computer tomography in terms of diagnostic accuracy.

This our research aimed to study the NLS-scopy potentials in adrenal tumor diagnosis and to provide an evidence that with a proper procedural approach and advanced equipment in place, bulky growths could be diagnosed as successfully as if by using computer-aided and magnetic resonance tomography.

### Subject and methods

Clinical data: from June 2000 through May 2001 23 patients aged 25-64 were examined who were suspected to have developed adrenal tumors based on careful complaint analysis and clinical and lab data. For all the patients kidney and adrenal investigation was conducted under a regular procedure using a 4.9 GHz NLS unit. The device has an automatic focusing, that can self adjust both when emitting and receiving echo signals, and it ensures high definition of the spectrogram, which is very important, for example, for differential diagnosis. As a result of using high frequency sensors in combination with virtual imaging equipment, a high spatial resolution is provided which is very important for patient examination.

According to the analysis of our observations, the correct diagnosis was made for 22 patients of 23 (95.6%). In one female patient with Itzenko-Kusching syndrome in clinical evidence the NLS-scopy detected in the superior pole area of the right kidney a small (30-35 mm) hyperchromous growth which had a mono-chromous internal structure and a spectral similarity to the 'adrenal adenoma' reference standard ( $d=0.217$ ) and was regarded as a benign adrenal tumor. Because of typical clinical presentation of Itzenko-Kusching syndrome and concomitant changes in blood and urine in clinical and lab

evidence, computer tomography was not performed. The surgery detected a focal macronodal hyperplasia of the adrenal, which was confirmed by the histological investigation of the removed growth.

Generally a distinction is made between the diffuse and focal hyperplasia. Focal hyperplasia can be subdivided into micro- and macro-nodal hyperplasia. As a matter of fact, focal hyperplasia can not be easily discriminated from adrenal tumors by means of NLS evidence, so in this particular case our conclusions cannot be considered to be diagnostically wrong.

Of 23 cases computer tomography was undertaken for 17 with its data matching the NLS investigation results. 9 patients of 23 underwent surgery to have an adrenal tumor removed, and the NLS data were confirmed by surgery and histological investigation results.

The size of detected tumors varied in diameter from 6 to 10 cm. All of them had a capsule, smooth surface and rounded or oval shape. Small tumors had a monochrome structure and in 4 cases with the tumor size over 8 cm, the internal structure was represented by an irregular alternation of areas having different color saturation on account of necrotic zones, degenerative changes and decalcification, which was confirmed by a histological investigation of the removed tumors.

According to the literature and our information the different diagnosis of benign and malignant adrenal tumors is an extremely difficult process. A malignant pattern of the detected growth can be suspected only in the presence of an irregular internal structure of the growth, restricted kidney mobility at forced breathing, enlarged regional lymph nodes and metastases in other organs.

Thus, diagnosis of adrenal tumors is complicated because of diverse clinical implications in place. The potentials of the NLS-diagnosis could scarcely be overestimated, for the simplicity of the investigation procedure, its harmlessness and rich informational content allowed us to make a correct and prompt diagnosis in 78% of cases. The investigation showed that NLS-scopy may become as efficient method of adrenal tumor examination as computer tomography and US. Patients having complaints typical for adrenal tumors should be examined by means of the NLS-method the first. Patients with symptoms indicative of adrenal tumor should be referred to specialized endocrine surgery departments where they would be thoroughly investigated using US, CT and MRT which will enable a substantial reduction in the investigation time and thus a more appropriate and early treatment.

## Diagnosing Rare Instances of Mammary Gland Diseases Using NLS-Investigation

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This article deals with some clinical observations of rare cases of mammary gland diseases detected by means of nonlinear diagnosis method (NLS) during clinical diagnostic prophylactic investigations performed in October 2001 with the purpose of an early diagnosis. In the course of the activity the patients were found to have different diffuse or nodal mammary gland diseases among which of particular interest are some rare diseases like liposarcoma (1 case), colloidal cancer (1 case), phyllode cystosarcoma (1 case), phyllode fibroadenoma (2 cases), hemanglomma (1 case) and Mondore's syndrome (1 case).

According to some literary evidence, colloidal cancer and lipo-sarcoma do not occur very often among malignant tumors: colloidal cancer in 2.4% and lipo-sarcoma in 0.001-0.03% of cases respectively. Among benign tumors hemanglomma occurs in 0.12%, phyllode fibroadenoma in 5.4% and phyllode cystosarcoma in 2.5-5.4% of cases. The investigation was done using A NLS device with a 4.9Ghz nonlinear sensor under the program of virtual tissue representation of panoramic scanning (Panoramic NLS Imaging).

### Mammary gland lipo-sarcoma

Patient G., aged 28, was admitted having complaints of a nodal formation in her left mammary gland. During the examination an umbilication symptom in the upper outside guardant of the left mammary gland was discovered. The palpation detected a small-sized painless sluggish node of a dense elastic consistency that had a dotted structure and adhered to the skin. By means of a detailed imaging the investigation ascertained a node of 15-20 mm in diameter and detected its spectral similarity to the reference standard 'mammary gland lipo-sarcoma' ( $D=0.204$ ). The investigation of the regional lymph nodes did not detect any metastatic lesion.

Based on the NLS-investigation data a surgery (medical mastectomy according to Maden's method) was performed. The histological diagnosis was liposarcoma.

### Colloidal mammary gland cancer

Patient K., aged 49 was admitted as having complaints of a node in the left mammary gland.

The examination did not produce any visible evidence of changes in the mammary glands. A sluggish roundish formation with a diverse consistency and vague outlines was palpated on the border between the upper quadrants of the left mammary gland.

The NLS-investigation detected a roundish formation (6 points according to Flander's scale). The graph examination showed spectral similarity to the reference standard 'solid cancer'.

The patient underwent surgery, a radical mastectomy was performed according to Moden's technique. The histological conclusion was colloidal cancer.

#### Phyllode mammary gland cystosarcoma

Patient G., aged 46 was admitted as having complaints of a slow growth dense node in the right mammary gland.

Palpation detected in the upper outside quadrant of the right mammary gland a painless motionless formation with a diverse density and heterogeneous surface that adhered to the skin.

The NLS-investigation detected an irregular 3x6x4 cm formation. A spectral similarity to the reference standard 'mammary gland sarcoma' ( $D=0.412$ ) was found. Its small size allowed to completely visualize the involvement of lymph nodes.

The patient underwent surgery - radical mastectomy according to Moden's technique. The histological diagnosis was phyllode cystosarcoma.

#### Phyllode mammary gland fibroadenoma

Patient Z., aged 43 was admitted as having complaints of a large node in the right mammary gland.

The examination showed asymmetry of the mammary glands.

On the border between the outside quadrants of the right mammary gland a mobile node of a large node with distinct outlines and smooth surface and tight elastic consistency was palpated. The skin above the tumor was very thin.

The NLS-investigation detected some hyper-chromous structures corresponding to intranodal vessels. The analysis of the graphs detected a similarity to the reference standard 'fibroadenoma' ( $d=0.384$ ).

On the strength of the NLS-investigation subcutaneous amputation of the right mammary gland and omento-mammoplasty on a vascular pedicle were performed. The histological diagnosis was phyllode fibroadenoma.

After the plastic surgery (one month later) a repeated NLS-investigation was carried out.

## Mammary gland hemangioma

Patient C., aged 42 was admitted as having complaints of a large size node in the right mammary gland.

During the examination it was found out that the skin over the node had a cyanotic cast. On the border between the upper quadrants a mobile formation with a soft consistency was palpated. The graph analysis detected a similarity to the reference standard 'hemangioma' ( $D=0.414$ ).

The patient underwent surgery i.e. a sectoral resection was performed. The histological diagnosis was cavernous hemangioma.

The presented clinical observations showed that the continuous improvement of NLSsystems and the modern technologies made it possible to introduce a morphological picture of the neoplasm which helps devise the optimal tactics of surgery with further morphological verification of the derived results.

## Diagnosis of Toxoplasmosis (Serologic Examination, CT, MRT and NLS)

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A.S. Sosnovskaya

Toxoplasmosis is a parasitic disease whose causative agent is toxoplasma (*Toxoplasma condii* Nicolle et Manceaux), which belongs to protosa. The disease typically has a chronic course, nervous system lesion, lymph-adenopathy and enlarged liver and spleen. Quite often myocardium, muscles and eyes are affected.

The infection is mostly transmitted through the alimentary tract. Yet there are some instances recorded where contagion occurred through the injured skin and mucous membranes. Toxoplasma is apt to form cysts in tissues causing a latent infection condition. The parasite becomes active in the conditions adverse to the macro-organism and with its immune responsiveness going down. In the pathogenesis of the toxoplasmodial lesion of the central nervous system of importance are local inflammatory occurrences, dis-circulatory disturbances related to vasculitis and blocked liquor tracts leading to hydro- or micro-cephaly.

Clinically, the lesion of the central nervous system manifests itself as meningitis, encephalitis, meningeoncephalitis and encelphalomyelitis.

The most typical form of toxoplasmosis of the central nervous system is meningeoncephalitis, which clinical picture contains general cerebral and meningeal symptoms, paresis and limb paralyzes, tonic and clonic spasms, opticokinetic-(diplopia) and coordination disturbances. The blood test reveals a left-shifted leukocytosis and increased ESR: the cerebrospinal fluid contains lymphocytic pleocytosis and a moderately increased protein content.

In diagnosing toxoplasmosis of importance are cranial radiography, serological investigation, pneumoencephalography, CT and MRT. However, it is the NLS-investigation of cerebral structures that plays the most important part in the diagnosis. Of great diagnostic importance is a substantially increased spectral similarity to the reference standard '*tomoplasma gondii*' ( $D < 0.425$ ).

The toxoplasmosis should be discriminated from viral encephalitis, encephalomyelitis and meningitis.

In the MRT-investigation toxoplasmosis is manifested by a progressive multi-focal encephalopathy. With toxoplasmosis the typical cases have to do with granulomatous fields which are small: 2.0 cm or less in diameter. On NLS image these formations look like hyperchromatic areas (6 points on Flandler's scale) with the central necrosis zone in ring-shaped structures being visible as an area of lower chromogenic density (4-5 points). Hemorrhage areas of small size are quite typical. The above-mentioned changes are



localized peri-and para-ventricular, often in the region of bordering cortico-medullary structures as well as in the regions of basal ganglia.

#### Clinical observation

Patient K., born in 1974. The preliminary diagnosis when admitted into the neurological department as acute cerebral circulation disturbance in the spinal artery basin.

The patient complained of weakness in left limbs, speech impediment, asthena and loose cough. According to her wording she fell ill (Feb. 06.01) when she stopped talking, developed weakness in left limbs, diplopia and disturbed swallowing. The anamnesis read a developed right-side hemiparesis, that passed off by itself within two weeks.

The patient is in grave condition. Neurological status: conscious, understands when she hears people speaking to her, but doesn't speak. Cranial nerves: equal palpebral fissures, nystagmus not present, the right nasolabial fold smoothed out. Slight deviation of the tongue to the right. High tendon and periosteal extremity reflexes, weakness in right limbs. Reduced pharyngeal reflex on both sides. Rigidity of occipital muscle is moderately frank. Kering's symptom on both sides. Babinski's reflex on the left.

#### Laboratory investigation:

Clinical blood analysis: erythrocytes -  $3.96 \times 10^{12}/l$ , hemoglobin - 127 g/l; -0.9: L -  $5.6 \times 10^9/l$ , ESR - 32 mm/g. - 1; - 74; - 21; - 2; -2.

Biochemical blood test: glucose - 4.6 mmol/l; urine - 6.6 mmol/l, bilirubin - 13.38; - 5.5; - 7.85 mmol/l; creatinine - 0.066 mmol/l, total protein 70.0mg/l; albumin - 5.5; globulins - 44.8; L2 - 4.8; L2 - 7.7, B - 11.8; J - 20.5; - 1.24; - 0.29 mmol/l; - 0.31 mmol/l.

Test for toxoplasmosis detected antibodies with rising antibody titer in dynamics (1:21 - 1:400).

Cerebrospinal - 2.5 mmol/l; chlorides 0 1.24 mmol/l, protein - 0.2 g/l, sugar 0 4.1 mmol/l. Cellular composition: cytosis 0 213, L - 1.2; erythrocytes - 4.5.

MRT-investigation of the encephalon (of 16 Feb.01) in T-2 picture on both sides, detected paraventricular and subcortically multiple unequal-sized roundish nodi (from 0.5 to 2.0 cm) producing an unevenly increased MR-signal. Similar nodi were detected in the dorsal part of the pons on the left and in the basal regions of the frontal lobes. In the frontal lobe the examination subcortically detected an ellipsoidal cyst 1.2x0.5 cm. In the T-1 picture of the field the nodi detected in the T-2 picture produced a slightly diminished MR-signal and was clearly outlined. Upon administration of magnevist some nodi, not visualized in the T-1 picture, manifested themselves by uniform amplification of the MR-signal, the others produced an amplification in the form of a thin ring or a small amplification in the center.

The cyst did not respond to administration of the contrasting agent. The central regions of the granulomatous fields represented by necrotic zones were more hyperintensive in the T-2 picture and after the contrasting agent administration did not accumulate it, signal amplification occurred in the peripheral regions in the form of a thin ring. The lateral ventricle bodies were not quite clearly enlarged. The median structures did not appear to be shifted.

In the frontal lobe on the right NLS picture shows subcortically detected hyperchromatic areas (6 points) surrounded by a perifocal edema zone (3-4 points) detected in the dorsal part of the encephalon on the right. A spectral similarity to the standard reference process "toxoplasma gondii" ( $D < 0.183$ ) was found, which allowed to confirm the diagnosis of toxoplasmosis.

# Nonlinear Diagnosis of Thyroid Gland Pathology

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## Introduction

The morphological diagnosis of thyroid gland pathology during surgery is rightfully considered one of the most important and complicated tasks faced by anatomist and surgeon. This research aimed to choose an optimum surgical tactics with tumors and tumor-like lesions of the thyroid gland, which is achieved by accurate verification of the process as well as by determining its spread in the organ and/or beyond it. The experience in the use of nonlinear computer diagnosis (NLS) in surgical clinics covers quite a short period of time, during which quite conflicting opinions with respect to its efficiency were formed. Among the prime considerations against an extensive use of NLS we should mention the possibility to preclude in some instances malignant pattern of a new growth because of a morphological similarity of follicular tumors. Without down-grading this problem and based on our own experience in the use of NLS we have attempted to assess the importance of this method for choosing the optimum surgical tactics and working out some methodical techniques enhancing efficiency and accuracy of the NLS investigations.

## Subject and investigation methods

We analyzed the results of 682 patho-histological investigations of the thyroid gland carried out in 2000-2001 in patients operated on for solitary nodes, diffuse and multinodal hyperplasia and autoimmune thyroid diseases. 326 of all surgeries were accompanied by NLS. NLS data were compared with the final results of pathohistological investigations.

## Result analyses

Of 682 surgical operations of the thyroid gland, 326 (47.8%) were accompanied by NLS investigation. According to our information, there is an increased demand for NLS, which has to do with a growth of surgical operations for nodular goiter from 70% to 85% and also with a growing thyroid cancer incidence including hyper-plastic and autoimmune lesions of the thyroid gland.

We did not succeed in specification of the pattern of the process in the course of 3.6% of all the surgical operations. In 65% of cases for which diagnosis was postponed, a malignant process was detected in the final phase of the investigation. An erroneous intra-operative diagnosis was made in 4.8% of cases with hyper-diagnosis of thyroid cancer recorded in 5 cases. Carcinoma was not identified during 38 operations, in 23 cases of the surgery the tumor did not exceed 2.5 cm nor did it spread beyond the thyroid gland. 17 (2.3%) patients needed correction of the amount of the thyroid gland resection,

which was done on the 4-5<sup>th</sup> day after the first surgery. The NLS sensitivity was 76.4%, specificity - 87.6% and accuracy - 78.6%.

The submitted data generalizing the experience in the use of NLS in a specialized surgical clinic are indicative of extensive opportunities for choosing the optimum surgical tactics to treat the goiter using this method, and also of a growing recognition of NLS despite some recent publications questioning the efficiency of consultations during the surgery. Apart from some evidence of a high efficiency rate, another advantage of NLS method is indisputably the low percentage of delayed diagnoses, which in our cases was under 1.4%. The advantages of the method include quickness (10 or 15 min) and relative technical simplicity of the investigation.

According to our research and some literary evidence, the problems in the course of NLS investigation are caused by differential diagnosis between cellular follicular adenomas and minimum invasion follicular cancer. These very cases account for the major share of delayed and erroneous results. In the series of our investigations in 48 cases of tumors with a micro follicular or trabecular structure (among which 21 were benign and 27 malignant) drawing a final conclusion on their pattern was impossible. In 5 cases it was false negative. At the same time 257 follicular adenomas and 30 cases of follicular cancer were correctly verified in the course of surgery.

It is known that the problems of differential diagnosis of follicular adenoma and follicular cancer are closely related to histo-typical and cylo-typical similarity of the two processes, that are so much expressed that it is impossible to diagnose a carcinoma without apparent manifestations of a malignant potential in the form of the tumor germinated capsule with the tumor invasion into its vessels. With cancer having minimum invasion the nidi of infiltrative growth appear to be isolated. In addition, being microscopically invisible these diagnostically important areas may escape observation in case of a limited number and random choice of investigation targets in the course of surgery.

We have considered a number of clinical and microscopic characteristics in terms of their potential use in NLS differential diagnosis of follicular tumors of the thyroid gland. A comparison was made considering age and gender of patients as well as the size of the tumor nodes in 61 cases of follicular cancer and 162 cases of follicular adenoma. This study of the parameters didn't detect any difference between these two patient groups. The male/female ratio in both groups was the same -1:9, the average age of the patients operated on for adenoma was 42.36±13.76 and was not different from that of the patients in the follicular cancer group (41.40±16.14). Follicular cancer is known to be more common with elderly people and very rare with children and teenagers. The latter circumstance could be a supplementary reference point for investigating solitary nodes of the thyroid gland in junior patients. The investigation analysis of 89 cases of follicular tumors in patients operated on at the age of 30 showed that in one third of cases the new growth was of a malignant nature.

Some differences were found in the average diameter of the tumor nodes: 3.05±1.45 cm for adenoma and 3.89±1.77 for follicular cancer ( $p < 0.05$ ). At the same time, the

coincident size limits (from 1.5 to 8 cm) in patients in both groups made this evidence an unreliable indication in the differential diagnosis of tumors. Both kinds of neoplasms equally often (approx. in 80% of cases) were not accompanied by morphologically significant changes in the thyroid gland being a solitary node. Some frank secondary changes such as sclerosis, petrification, cystic changes, hemorrhages, etc., were more often observed in follicular adenomas, however these distinctions were not authentic enough.

In our opinion the difficulties in the clinical morphological interpretation of the follicular tumors pattern need more than anything else improvement in the methodical techniques, which is especially important considering certain time and hardware-related limitations of the NLS-method. When faced with diagnostic difficulties we investigate series of nidi in every 30-60 mm. Conducting investigation on such a large scale consumes additional time (30-45 min) and yet in many instances it enables to specify the pattern of a follicular tumor. If the investigation of some additional nidi doesn't produce the desirable result, the diagnosis is performed after the surgery. According to our observations, in 65% delayed cases the tumor proved to be malignant yet had minimal manifestations of invasive growth into the node capsule or its individual vessels. Absence of palindromium in 95-99% of cases, following the surgery for follicular cancer with minimal manifestations of invasive growth into the capsule and with some individual vessels (up to 5) involved, gives solid grounds to classify these tumors as clinical "boundary" processes whose malignant potential remains conditional and justifies the tissue-sparing amount of the thyroid resection (lobectomy with isthmectomy and subtotal thyroidectomy) similar to the one recommended for surgery for follicular adenoma.

Thus, the NLS-investigation of follicular thyroid tumors can be regarded as an efficient method for choosing the optimum surgical approach, because with sufficient experience and proper performance it enables the diagnosis of some clinically adverse forms of follicular thyroid cancer that actually need radical surgery and post surgical treatment.

Papillary cancer is the most common form of thyroid gland carcinoma. It was correctly diagnosed by means of the NLS-method in 63.2% of cases, was a diagnosis failure in 26.3% and was responsible for delayed diagnosis in 0.6% of the observations. Unlike follicular tumors, most versions of papillary cancer typically have frank histo-typical differences from benign proliferate processes, clear manifestations of infiltrative germination in the tumor-surrounding tissues and frequent metastatic lesion of the lymph nodes by the time of surgery, which enables the diagnosis of a malignant process without difficulty even with inadequate practical experience. The difficulties we confronted mostly concerned papillary micro carcinoma, which made 71% of cases non diagnosed during the surgery, and also a follicular encapsulated version of papillary cancer that was responsible for the rest 29% of diagnostic errors.

The problem of NLS papillary micro carcinoma lies in a macroscopic search for a cancer nidus in the removed fragment of the thyroid gland, which creates difficulties because of concomitant changes in the thyroid gland at a multi-nodal form of the goiter or autoimmune processes. At the same time in 45 cases micro-carcina was diagnosed intra-

operatively, including 15 cases, where the tumor size was below 0.4 cm. In 23 cases of papillary micro carcinoma unidentified by NLS, the surgery was performed for multinodal goiter (15 cases) and autoimmune thyroiditis (8 cases), which determined the required amount of surgical intervention (subtotal or total thyroidectomy). The undiagnosed micro cancer nidi sized from 0.4 to 0.9 cm did not spread beyond the thyroid gland and afterwards none of the patients affected by latent carcinoma required another surgical operation to extend the amount of thyroid gland resection.

Papillary micro carcinoma is known to localize quite often in the thyroid gland, especially in elderly people and it does not always display its malignant potential in the form of clinical implications (I.L. Avetisyan, 1999). The progress of the great majority of such tumors is entirely favorable. Meanwhile, a direct relationship was established between the size of a papillary micro carcinoma nidus and the frequency of its metastasizing into the cervical lymph nodes. According to our information and some evidence obtained from other clinics, a tumor in excess of 0.5 cm incurs a higher risk of potential palidromium and requires a more radical approach to its treatment, than a microscopic cancer nidus. In this connection, it is recommended to take a series of parallel shots of the thyroid tissue in different projects in the course of macroscopic search for cancerous nidi. According to our observations this technique may be effective in diagnosing 52% of papillary micro carcinomas sized up to 0.4 cm and 68.6% of tumors over 0.4 cm, and in most cases will ensure the right choice of a surgical approach.

According to most pathologists, diagnosis of follicular version of papillary cancer is considered to be one of the most difficult problems in NLS-investigations. Erroneous verification of this neoplasm often leads to another surgical operation. Among the difficulties in diagnosing this kind of tumor, we should first mention some artificial histogram changes in tumor cells, which hamper identifying diagnostically significant cytological criteria of papillary cancer. In our series of observations follicular version of papillary cancer was reported in 43 cases, in 2 of which diagnosis was postponed until after final investigations and in 5 (3.2%) cases the diagnosis was false negative. None of the cases showed any metastatic lesions of cervical lymph nodes. Considering the spectral similarity of follicular encapsulated version of papillary cancer to adenomatous goiter, the cytological differences in differential diagnosis are the decisive criterion in differential diagnosis. In order to assess them in doubtful cases we have additionally investigated some impression smears, which in most cases helped detect some changes in the nuclei characteristics of papillary thyroid cancer, such as irregular shape, jagged boundaries, deep nucleolemma invaginations, outlines of intranuclear sulci and inclusions marked off by marginally condensed chromatin, fine chromatin dispersion, etc., as well as to indirectly assess some cohesive properties of tumor cells and the inflammatory infiltrate pattern. Among some cancer-suspicious histological signs observed on a frozen section, we can note polymorphism of follicles lined with high cubical epithelium with intensely tinged colloid (if fixed in ethanol!) and/or its marginal vacuolation, close adherence of follicles to one another owing to scarce stroma in the central part of the node, hemorrhage in the follicle lumen at abundance of siderophages, multinuclear cells, etc.

The recent years publications have extensively debated expediency of NLS-investigations of the thyroid gland in the cases with the available results of aspiration biopsy. The cytological investigation is known to be the most extensively applicable method of pre-surgical diagnosis of nodular forms of the goiter because of its accessibility, comparatively low cost, lack of traumatism and most importantly, high accuracy. The progress in the diagnosis of thyroid tumors using the cytological investigation technique has induced some researchers to become result-oriented in choosing a surgical approach.

In this connection we made an attempt to define to what extent this approach is justified after having analyzed our own observations and the practical experience of specialists in a number of well-known clinics of the world.

Among some major problems of fine needle aspiration biopsy (FNAB) performed under the control of ultrasound scanning (US) we can mention an amount of aspirate inadequate for diagnosis as well as some situations that do not allow to preclude a malignant process in the node under the investigation. While in the former instance a repeated procedure may prove efficient for 30% of the patients, the other problem needs to be solved by a surgical removal of the tumor with a subsequent histological verification of its pattern. According to some publications, the number of tumors, which malignant potential cannot be excluded based on FNAB results, exceeds 11%. In the majority of cases (about 70%) this kind of diagnostic problems is caused by follicular adenoma.

According to our information of 338 patients who had surgery after preliminary FNAB the malignant process was not cytologically ruled out in 41 cases. In 26 of these observations follicular adenoma and in 15 thyroid cancer were verified (2 follicular, 3 medullary and 10 papillary carcinomas). In all cases the NLS allowed to specify the diagnosis and avoid errors in defining the amount of resection.

The problem of FNAB accuracy is no less pertinent. According to some recent reports, the sensitivity and specificity of thyroid FNAB has approached 100%. At the same time, it proves to be difficult to interpret the data due to different approaches to their analysis. For instance, specialists in some clinics, where the results were highly accurate, consider only specific cytological conclusions ignoring a category of tumors, which cytological picture gives grounds only to suspect malignant change. In analyzing the FNAB accuracy some researchers consider follicular adenoma in the same category as malignant tumors. Though this kind of approach may be justified in terms of indications for surgery, by no means it can be justified in terms of a surgical approach to be chosen. The analysis of some publications shows, that FNAB can ensure the right surgical approach only in 70-75% of cases. The FNAB efficiency data-evaluated after classifying cancer-suspicious conclusions as malignant tumors and adenoma as a benign tumor, were as follows: sensitivity - 92.1%, specificity - 94.4%, accuracy - 93.45. Thus, the FNAB data could help decide on the proper amount of surgery for 90% of the patients, which in terms of specialized clinic cannot be a sufficient reason and is an argument in favor of supplementing FNAB with NLS-investigation.

From comparison of the FNAB and NLS results it was found that 27 false negative results of punch biopsy 21 nidi of malignant growth were detected during surgery among multiple benign goiter nodes. The latter, being prevalent in clinical implication, became the object of FNAB leaving some latent cancer nidi sized 0.2-1 cm undiagnosed before the surgery. The insufficiently accurate cytological interpretation of the pattern of a cystic cavity in the 111G also requires an intra-operative verification. In our series in 2 cases of encapsulated papillary cancer with cystic generation wrongly interpreted as a benign process during FNAB the diagnosis was rectified by means of NLS.

Another equally important task of intra-operative investigation is leveling possible false positive conclusions of FNAB. In our series of 497 patients having benign new growths according to FNAB results, papillary cancer was suspected in 2 cases and a malignant process was not excluded in 26 cases. The rectification of the process pattern in the course of surgery facilitated selection of the most efficient surgical approach in all cases.

### Conclusions

1. The NLS-investigation of thyroid tumors is an efficient method for choosing surgical approach in surgery for nodal and diffuse forms of goiter.
2. The NLS performed for the patients following FNAB, considerably enhances the accuracy of morphological investigations at the preliminary phase, and optimizes the surgical approach in surgery for the thyroid gland.
3. This is a very important reason in favor of the appropriateness of using NLS-investigation together with FNAB.



## Nonlinear Computer Diagnosis and the Problem of Pathology in the Hepatopancreatoduodenal Area

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The problem of pathology in the hepatopancreatoduodenal area still remains urgent and explains why researchers are keen on the search for improved diagnosis methods, since the diagnosis proper is the starting point for determining the approach to treatment. Today the basic methods for diagnosing a pathology in this region are traditionally methods of direct artificial contrasting of the pancreatobiliary system, such as endoscopic retrograde cholangiopancreatography (ERCPG) and percutaneous transhepatic cholangiography (PTCG), well established in both diagnosis and treatment of a number of diseases such as cholelithiasis, cysts and tumors in the head of pancreas, tumor and corrosive strictures of the biliary ducts, tumors of Vater's papilla, etc.

At the same time, the padioendoscopic methods of investigation of the biliary ducts, though characterized by a rich diagnostic informational content owing to their invasiveness, still do not eliminate the danger of serious complications, such as acute pancreatitis, hyperamylasemia, cholangitis, sepsis, and allergic reactions, biliary flux into the abdominal cavity with developing biliary peritonitis, hemorrhages, etc.

Their incidence rate varies from 0.8 to 36%. Besides, in the course of ERCPG different technical problems may arise (failure in the cannulation of Vater's papilla, the impossibility to enter the duodenoscope at esophagus diseases, such as strictures, achalasia, etc.). In addition ERCPG requires involvement of certain specialists like radiologic diagnosticians, surgical endoscopists and anesthesiologists.

The advent of new diagnostic techniques in radiology and first of all ultrasound scanning (US) and computer tomography (CT), did not produce a great limiting impact on the use of ERCPG so far as these methods were not successful in solving a number of diagnostic issues related to pathologies in the biliary system and pancreas.

The development of nonlinear computer diagnosis (NLS) as a method for diagnosing abdominal pathology, opened up new opportunities for detecting diseases in the hepatopancreatoduodenal region, with obstructive jaundice being one of their main clinical implications. With the development and adoption of a number of speedy programs for obtaining NLS images, specifically NLS- cholangiopancreatography, which enables to obtain an integrated virtual picture of the biliary system and pancreatic ducts without administration of contrasting agents and intervention into the biliary system, the method was attempted to put into active use as an alternative to ERCPG.

Some published works dealing with NLS have some distinct trends to pay more attention to this issue with a view of obtaining sufficiently convincing information, that

would allow to draw a final conclusion about a new relationship between integrated X-ray endoscopic examination and in the first place between ERCPG and NLS, when detecting a pathology in the hepatopancreatoduodenal region. Some of the works suggested that NLS be used as a method preceding endoscopic cholecystectomy.

With all the above in view, this paper aims to present our data on the role and significant of NLS at certain diseases in the hepatopancreatoduodenal region.

To achieve this aim the following tasks were performed:

1. Examination of the test group to study different versions of a standard NLS-picture of the biliary tract;
2. Description of the principal NLS semiotics in the patients with a pathology in the hepatopancreatoduodenal region;
3. Cross-comparison of MRT, ERCPG and NLS for a more objective assessment of the collected data;
4. Definition of clinical indications and diagnostic potentials of the NLS method for the patients with obstructed biliary ducts.

## Subject and methods

The NLS investigation was performed on 54 patients, of them 19 made a test group and 35 had different pathologies in the hepatopancreatoduodenal region, with 89% of these patients showing signs of obstructive jaundice. The patients were from 36 to 77 years old. There were 20 women and 15 men in the group of 35. As a primary method of investigation all the patients had a sonography which acted as a screening tool for performing NLS. A relative comparison of the results of MRT, ERCPG and NLS was made for 18 patients.

The NLS investigation was carried out using a unit equipped with a 4.9 Ghz trigger sensor.

We assessed the condition of the lymph nodes, especially in the portal fissure projection, and the hepaticoduodenal ligament on the virtual images. We used the "Metapathia IT", a special computer program for acquisition of a virtual image of the biliary system and Wirsung's duct.

## Analysis of results

The virtual model distinctly visualized the common bile duct, common hepatic duct, right and left lobar ducts and gall bladder (GB). The segmentary and sub-segmentary intra-hepatic ducts are not actually visualized even in a poly-projection examination. The normal lumen of the common bile duct is 0.6 cm; the NLS-signal coming from it is homogeneously normo-chromatic (1-2 points according to Fandler's chromatic scale).

The anatomical variations and abnormal developments occur very seldom, yet we observed 3 cases of this kind, of them 2 contained an abnormal drainage of the cystic duct

and 1 an atypically high point of entry of the cystic duct into the common hepatic duct. An insufficient detailing of the papillo-sphincter region is the basic limitation of NLS in our investigation was.

Calculi are known to be the most frequent cause of the bile duct obstruction. According to our investigations, cholecysto-choledocholithiasis comprised 34% of all diagnosed pathologies in the hepatopancreatoduodenal region. Regardless of their location, the concrements in the biliary ducts were visualized on the NLS images as individual or multiple hyperchromogenic zones (5-6 points), rounded or oval-shaped. The sizes of the concrements detected in the hepaticocholledochus and lobar hepatic ducts varied from 5 to 20 mm. 6 patients had single concrements, and 4 had multiple concrements, and the entire lumen of the hepaticocholledochus “stuffed” with concrements was found in 1 patient.

The localization of the concrements was variable. In 2 observations the concrements only localized in the gall bladder and in 5 cases they did in the hepaticocholledochus; in 1 case the clinic laboratory evidence of obstructive jaundice was not found, and in 2 cases the concrements were visualized in both the cholledochus and lobar biliary ducts. In 5 cases we observed a concurrence of concrements in the gall bladder and cholledochus.

In the course of our observations we arrived at a conclusion that the NLS-diagnosis of concrements in the gall bladder depended on their size. So, as compared to the US data, the concrements under 5 mm in diameter were largely not visualized on NLS shots, because the signal from them was overlapped by a hyperchromogenic signal from the mucous membrane. Small multiple concrements in the gall bladder that produce a low entropy density signal (3-4 points according to Fandler’s scale) on NLS-shots hamper their differential diagnosis because of sediment and putty-like bile. We agree with some authors who consider the ultrasound scanning to be the “golden standard” in detecting gall bladder concrements which should not be replaced by NLS.

The major NLS disadvantages in diagnosing concrements in the hepaticocholledochus are associated with certain difficulties in assessing the cholledochus condition, when the cholledochus is fully filled with concrements.

In one observation the concrement localized in some distal areas of the hepaticocholledochus, and on NLS shots it looked like a hyper-chromogenic oval-shaped defect with the upper outline looking like a concrete lens. The combination of NLS-shots with conventional MR-tomograms in axial plane allowed us to specify the spatial relationship between the cholledochus and head of pancreas and the duodenum, in other words. It enables to detail the localization of the concrement in the ampullar region of the common biliary duct.

Papillosphincterotomy was done during ERCPG with concrement extraction.

The genesis of benign strictures of biliary ducts was related to their surgical lesion or inflammation caused by lithiasis, chronic pancreatitis or papillostenosis in 90-95% of

cases. The number of iatrogenic lesions of the biliary system ducts grew up with the extensive application of the laparoscopic cholecystectomy; because the intraoperative investigation of the common bile duct is more complicated during laparoscopy than during open surgery. In this connection, in terms of preoperative preparation for endoscopic cholecystectomy, it is necessary to specify the anatomy of the pancreatobiliary system and assess its condition in order to prevent potential iatrogenic lesions of the biliary ducts.

So, owing to its noninvasiveness and high resolution, NLS can be a diagnosis-determining method for this kind of patient. Unlike ERCPG, NLS enables to visualize the bile ducts above and below the obstructive level, which is displayed on both MRT and NLS shots. The latter method gives a virtual physiological picture of the condition of hepatic and pancreatic ducts as compared to ERCPG, in which the administration of a contrasting agent overstates the extent of duct dilatation.

In all of our observations NLS allowed to define the accurate extent of the arctation, its length and cause. In 2 cases the arctations localized at the cystic duct level, which was indicative of their iatrogenic genesis. In 1 case it was an arctation hepaticocunoanastomosis. In 5 observations the arctations from 1.5 to 2.0 cm long were located at the confluence and in the proximal region of the hepaticocholledochus.

In assessing the arctation extent in the case where the lumen was not visualized on NLS-shots, we always analyzed the native MRT scans and supplemented the investigation with thin sections, which allowed forming a more exact opinion about the arctation extent. At the same time, comparing the results of nonlinear diagnosis to ERCPG one must admit that the latter method is more exact in determining the extent of duct affection.

However the essential criterion in deciding on the surgical correction method enables not only to detect the level and length of a structure, but also clearly specify the pattern of cholledochus deformation in presence of an arctation, which also determines the surgical approach to the reconstructive operations.

The combination of conventional MRT and NLS considerably enhances the diagnostic potential of this method as opposed to ERCPG in diagnosing chronic or acute pancreatitis, because it enables not only to investigate the condition of the ducts of the pancreatobiliary system, but also to assess both the pancreas proper and the adjacent organs and structures. Of 4 our observations of chronic pancreatitis in 1 case we had a frank contraction of the intrapancreatic part of the cholledochus cause by a chronic inflammatory process, in 3 patients the constriction of the distal part of the cholledochus was caused by a cyst in the head of pancreas. On the NLS-shots the obstruction of the biliary duct looked cone-shaped, and its affected part could be visualized all the way along the head of the pancrease including Vater's papilla area, and was assessed at 5-6 points according to Flandler's chromatic scale.

In all the cases a moderate chromogenic density of dilated biliary ducts and a heterochromous response of Wirsung duct occurred. The cysts, where they existed, were

depicted on MRT and NLS shots and the constricted area of the common biliary duct had an arc-shaped route because of being forced back by the cyst. The NLS allowed detection of a relation between the Wirsung duct and pancreatic cysts.

The most common and well-known causes of the biliary tract obstruction are the tumors localised in different organs: liver, biliary extra hepatic ducts, head of pancreas, major duodenal papilla, as well as metastases into the hepatoduodenal ligament and portal fissure. The tumors concentrated in these locations are conventionally called the “tumors of the hepatopancreatoduodenal region”. The reason for that is common clinical implications relate to the obstruction of biliary and pancreatic ducts. In patients affected by malignant tumors localized in this area the primary symptom of the disease is generally obstructive jaundice. A decision on the expediency of surgery for this kind of patients necessitates an assessment of a clinical prognosis depending on the tumor state according to the TNM system. So, if a malignant pattern of obstructive jaundice was suspected, then together with the elimination analysis, which is a special program, we always carried out standard investigations in the AUTO TUNE mode which enabled localization of the tumor and assessment of its spread to the adjacent structures as well as defining hematogenic and lymphogenous metastases.

We observed 4 cases of cholangiocarcinoma with obturation of intra- or extrahepatic ducts including 2 cases with a tumor localized at the common hepatic duct level and 2 cases with affected intrahepatic ducts and liver parenchyma. In all of the 4 cases the NLS allowed to precisely localize the lesion level and define its length. Both cases of cholangiocarcinoma displayed a spectral similarity to the reference standard process “liver carcinoma” (D from 0.213 to 0.418).

Researchers observed an increased chromogenic density (5-6 points) in intra-hepatic ducts more proximal to the arctation. In one of the observations, in the projection of the constriction of the common biliary duct, the MRT scans displayed a soft tissue structure, up to 3 cm in diameter with a medium intensity signal, which enveloped the duct in a sleeve-like manner at the lesion level and was indicative of a tumor etiology of the structure. Another observation at stenosis of the common biliary duct with no imaging of the tumor tissue, detected enlarged lymph nodes in the lesser omentum region and a single metastasis into the liver which allowed us to correctly interpret the pattern of the lesion confirmed by histological investigation of the biopsy material acquired during trans-hepatic drainage for decompressing the biliary ducts. In 1 of the 2 observations of cholangio-carcinoma of intra-hepatic ducts also histologically confirmed later, we drew an erroneous conclusion, because the pattern of MR-changes, i.e. a small ectasia of the intra-hepatic ducts by a varicose type above the moderately constricted common hepatic duct and unaffected hepatic duct more distal from the structure, a rather long anamnesis of the disease (the patient had had itching fits, occasionally icteric integument, de-colored feces and dark urine for ten years) and the obscure clinical presentation were interpreted by us (and during ERCPG) as manifestations of a primary sclerogenic cholangitis.

In all three our observations of pancreas head cancer the obstruction of the biliary duct looked on NLS shots like a progressively growing chromogenic density of the ecstatic

biliary duct at the level of its intra-pancreatic area. A frank hyper-chromogenic pattern of the intra-hepatic ducts was concurrently noted. The Wirsung duct was unevenly hyper-chromatic too. The standard AUTO TUNE shots allowed us to evaluate the spread of the tumor to the adjacent structures and determine some hematogenic and lymphogenous metastases. The structure of the tumor itself could be better visualized on the front shots. In one of the cases we also detected both metastases into the liver, and enlarged lymph nodes in the supra-pancreatic cellular tissue. The histological investigation confirmed the adenocarcinoma in all three cases.

Differential diagnosis of pancreas head cancer and chronic pseudotumor pancreatitis is a very complicated task and until now has been a problem yet to be solved. Integrated abdominal NLS-investigation with visual simulation of changes in the head of pancreas (not always pathognomonic for a tumor) and its spectral similarity to blastic process ( $D < 0.425$ ) allowed us to produce a more defined opinion about the tumor pattern of the process. In addition, the value of the NLS consists in its capability to assess the spreading of the tumor to the cystic duct which is very essential for making a decision on the expediency of cholecystodigestive anastomosis.

According to some literary evidence, differential diagnosis of diseases of the papillosphincter region by means of NLS investigation is very difficult. In one of our observations of a patient which clinical lab manifestations of obstructive jaundice the US detected a distal block of cholledochus with dilated superjacent regions of the biliary system. The duodenoscopy detected signs of frank papillate of the major duodenal papilla and suspected infiltration of the longitudinal fold of the duodenum. The percutaneous transhepatic cholangiography (PTCG) that was performed additionally showed a picture of stenosed papillosphincter region. The NLS displayed hyperchromatic intrahepatic ducts and hepaticocholledochus, with the latter traceable as far as the level of entering the duodenum. The NLS investigation performed in a sagittal projection allowed to detect an additional structure with a moderately chromogenic signal in the ampullar region of the cholledochus. It allowed a supposition about a tumor lesion of the major duodenal papilla. The patient died of DVS syndrome. In section: poorly differentiated adenocarcinoma of the major duodenal papilla. We would like to use this example to stress the importance of a correct methodical approach for carrying out an investigation in a specific diagnostic situation.

Thus, our results were able to show that NLS had great prospects for diagnosing a number of diseases with such a common anatomic-functional concept as a pathology in the hepatopancreatoduodenal region. So, thanks to its noninvasiveness, no need for administering contrasting agents and intervening into the biliary system as well as the ability to combine with conventional MRT, which substantially increases the diagnostic importance of the method, in quite a lot of cases the NLS investigation can replace radio-endoscopic methods of investigation (ERCPG and PTCG) as a primary diagnosis method although the other methods can retain their therapeutic functions. NLS may also become a method of diagnosis choice for patients who have some counter indications to X-ray-endoscopic investigation. We believe it necessary to actively expand the use of NLS with a view to making an ultimate decision on its clinical diagnostic importance.

## MECT and NLS in Diagnosing Myocarditis of Mild or Medium Gravity

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### Introduction

The diagnosis of non-rheumatic myocarditis remains a complicated and pertinent problems, which is conditioned by lack of pathognomic clinical signs and similarity to the semiotics of the disease to other kinds of cardiac pathology.

The notion of myocarditis brings together inflammatory myocardium conditions, different in terms of etiology and patho-geneisis both at isolated affects of myocardium (primary myocarditis) and at some infectious diseases and systemic pathological processes (secondary myocarditis). The disease may develop with a focal or diffuse lesion of the myocardium.

The clinical diagnosis of primary myocarditis presents great difficulties, so because of the lack of direct signs of the inflammatory lesion of the myocardium, the diagnosis is based on indirect clinical hardware-based syndromes that become apparent within 2 or 3 weeks after the administered infection. The related syndromes are as follows:

1. Any newly detected pathological changes in ECG;
2. An increased level of cardio selective enzymes and proteins in blood (troponin T and I);
3. Cardiomegaly as per radiography or echocardiography data;
4. Congestive heart failure;
5. Changed immunologic indexes (a higher CD4/CD8 and circulating immune complex ration, "yes" response to inhibition of lymphocyte migration
6. Tachycardia, reduced first sound and gallop rhythm.

The needle biopsy of the myocardium is one of such diagnostic techniques. Meanwhile, the basic morphological sign of the disease in this context is presence of an inflammatory reaction (lymphocytic and histiocytic infiltration) in the myocardium with damaged cardiomyocytes and capillary endothelium. However, the endomyocardiac biopsy does not ensure an exhaustive diagnosis because of a chance to pick up a sample from the unaffected section of the myocardium and obtain a false negative result. According to most authors, the endomyocardiac biopsy confirms the clinical diagnosis only in 17-37% of cases.

In this connection the development and extensive use in clinical practice of noninvasive method of diagnosis of myocarditis that allow to visualize myocardium inflammation and determine its intensity and evolution in the course of treatment, arouse active interest.

We have accumulated some experience in non-invasive diagnosis of myocarditis and dynamic control of the myocardium condition in the course of treatment. In the integrated diagnosis of inflammatory cardiac lesion, additionally to conventional methods of clinical, laboratory, immunologic and ultrasound investigation, we have used the methods of monophoton emission computer tomography of the myocardium (OEI, tomoseintigraphy of the myocardium) with autoleukocytes tagged by  $^{99m}\text{Tc}$ -hexamethylpropyleneaminooxym (HMPAO), and NLS-investigation of the heart.

## Material and methods

The tomoscintigraphy of the myocardium was performed on the monophoton emission computer tomograph 'Eleinct-Apex-SP-6' (Israel) every 1-2 and 24 hours after the autoleukocytes reentered the bloodstream. The leukocytic suspension was extracted from 500ml of the whole blood by centrifugation and leukocytapheresis. The leukocyte count was 37,000-45000 cells per 1 microlite. Before its administration the leukosuspension was incubated in a flask with  $^{99m}\text{Tc}$ -HMPAO (500) for 15 minutes at room temperature. For better visualization of myocardium inflammation and a perfusion study the tomosintigraphy was performed once again using  $^{44}\text{Tc}$ -tetrathosmine. During processing of the results the tomographic 'sections' of the heart were drawn along the short axis every 0.8 cm from top to bottom and the outward outlines of the aortic ventricle were encircled. The inflammation areas were visualized on the scans as foci of hyper-fixation of tagged leukocytes in at least three adjacent sections.

The NLS-investigation was carried out using a device equipped with a 1.4 GHz digital trigger sensor. In analyzing the obtained virtual shots special attention was paid to the emerging zones of the increased chromogenic value of the signal from the myocardium (5-6 points according to Flandler's scale). All in all 49 patients affected by myocarditis of mild or medium gravity were examined (25 women and 24 men aged 15-47). All the patients underwent a primary clinical hardware-based investigation including MECT with tagged leukocytes. 9 patients had check examinations of the myocardium condition carried out during the therapy using tomoscintigraphy of the myocardium and NLS. Six patients underwent an NLS investigation of the heart within 2-8 months after the primary radioisotope investigation and three patients had MECT performed repeatedly 1.5-8 months later.

Depending on the variant of the primary accumulation of leukocytes in the myocardium, all the patients with clinic-lab signs of myocarditis were divided into three groups. The first group included patients with a diffuse accumulation of tagged leukocytes in the myocardium (n=16), the second one comprised patients with a focal accumulation (n=20) and the third one did not have any distinct accumulation of tagged autoleukocytes in the myocardium (n=13). The groups were comparable by age and gender. The average age of the patients in the group with a diffuse accumulation of leukocytes was  $32.1 \pm 1.8$ , in the group with a focal accumulation -  $35.2 \pm 2.1$  and in the group without a distinct accumulation -  $36.6 \pm 2.2$ .



## Result analysis

The analysis of intracardiac distribution of tagged auto leukocytes showed that all the patients in the first group had a diffuse lesion of the cardiac walls in at least two regions: the atrium 94% of cases (n=15), left ventricle (LV) 63% (n=10), right ventricle (RV) 63% (n=10) and interventricular partition (IVP) was visualized most often - in 65% of cases (n=15), and in the other regions of the heart inflammatory infiltration was detected with certainty less often than in the first group and was less frank (atrium - 30%, n=6, RV - 25%, n=5 and LV -20%, n=4).

One of the factors possibly related to the pattern of auto leukocyte accumulation in the myocardium was an extra cardiac spot of leukocyte fixation in the nasopharynx, gall bladder and uterine appendages regions, which could be regarded as an obscure foci of chronic infection. It was established that at a diffuse pattern of auto leukocyte accumulation in the myocardium (which could be interpreted as a sign of diffuse myocarditis) the extracardiac foci of the infection were visualized in 100% of cases.

With a focal pattern of leukocyte accumulation in the myocardium the foci of chronic infection were determined in 70% of cases. In the group of patients without a clear accumulation of the leukocytes in the myocardium the foci of chronic infections were only detected in 40% of cases. Extra cardiac foci of tagged auto leukocyte fixation were more often detected in the nasopharynx, however there were no authentic distinctions among the groups.

Another factor related to the pattern of the auto leukocyte distribution in the myocardium was the duration of the disease which consecutively increased from group 1 to group 3. So, in the first group the average duration of the disease (from the initial signs of myocarditis to MECT performance) was 8+4 months, which is authentically shorter than in the second group, 16+ (P.2 < 0.05) and in the third group, 28+10 (P.3 < 0.05).

The initial integrated investigation of the patients affected by myocarditis showed that in 75% of the patients (36 cases of 49) the accumulation of auto leukocytes occurred in the thick layers of the myocardium, either diffuse or focal, which together with some clinical signs of myocarditis confirms the inflammatory lesion of the cardiac muscle. Typical for a diffuse myocarditis proved to be the moderately increased activity of cardio selective enzymes and indexes of the cell section of immunity as well as some changes in ECG, such as disturbed conductivity (A-V blocades of 1-II degrees). Increased diastolic size of the left atrium and left ventricle and increased indexes of the humoral section of immunity were typical for a focal inflammatory process. The minimum clinical implications of myocarditis were found in 25% of the examined patients, whose tomoscintigraphy did not display a distinct accumulation of leukocyte in the myocardium. All the patients were put on medication based on anti-inflammatory and metabolic drugs for 6 months and their walking regime was restricted for a month. As required, some antiarrhythmic, antiviral or antibacterial drugs were administered. 1.5-3 months after the

medication was started actually all of the patients began to feel better and the clinical signs that had made them call in medical aid disappeared.

Three patients had tomoscintigraphy of the myocardium performed repeatedly during the medication. Meanwhile, 2 patients with a diffuse pattern of tagged leukocyte accumulation, 1.5-3 months later during check tomoscans still showed some foci of auto leukocyte fixation in the myocardium, though fewer than at the primary examination. One patient with fixed accumulation of tagged leukocytes at a repeated MECT procedure 8 months after the medication did not show any foci of intracardiac leukocyte accumulation.

An NLS-investigation performed on three patients affected by diffuse myocarditis within 1.5-5 months after the medication was started, confirmed zones with an abnormality hyperchromatic NLS-signal, which fully corresponded to the foci of tagged auto leukocyte fixation in the myocardium. Our results are in conformity with some literary evidence on a possible noninvasive diagnosis of myocarditis using computer nonlinear investigation. Still in another instance of NLS investigation we obtained a doubtful or false negative result which was accounted for by some technical problems (increased signal deviation connected with a convulsion of ciliary arrhythmia that occurred during the investigation). Two patients with a focal leukocyte accumulation had NLS carried out 6 and 8 months after MECT and the shots did not display any pathological changes.

Thus, the repeated investigations using tomoscintigraphy of the myocardium and NLS proved, that a clinical improvement in the patients' condition that could be seen 1.5-3 months after the medication, was not indicative of a recovery, because the "morphological sanitation of the myocardium" even at a myocarditis of medium or mild gravity, arrives much later. The tomoscintigraphy of the myocardium with tagged auto leukocytes proved to be a more sensitive and informative method of diagnosing myocarditis in such cases (especially during the primary investigation) than the NLS investigation. MECT allowed detection of lesions of both ventricles and also atria despite their small thickness. The inflammatory tissues in thin-walled cardiac chambers were well visualized though it proved difficult to visualize them during NLS. In addition, rhythm disturbances rather often occurring in myocarditis patients did not affect the quality of the MECT scanning images, but they did affect the images obtained during the NLS examinations. Another negative factor of MECT examination was an inevitable admixture of erythrocytes in the leuko concentrate, which increased the general background radiation of organs and tissues and in some cases effaced the boundary between the organs under investigation and its background. The NLS-investigation can be probably used as a means of the myocardium condition control during therapy, but not as a method of primary diagnosis.

As an example we would refer to the data obtained during one of the observations. Patient K., 32 years old came to the clinic with complaints of a persistent dull heart pain experienced at rest, irregular heartbeat and respiratory distress at a moderate physical activity, pasty legs and feet in the evening, fatigue and general weakness. The anamnesis showed that two months before the patient had had an acute rhino-pharyngitis without

confinement to bed. For 5 days the patient had a fever with a temperature rising up to 38.5°C and algors in the evenings and in addition developed herpes labialis. The patient took biseptol, remantadinum and aspirin on her own accord, and gradually started to feel better; however 3 weeks later the complaints reappeared.

When she was hospitalized her condition was satisfactory. According to the physical examination the patient had pasty talocrural joints, moderate tachycardia (pulse rate 90 beats per minute), and frequent extra systole (about 5 beats per minute), muted first sound and third sound on the apex of the heart. The blood test detected moderate leukocytosis up to  $8.8 \times 10^9/l$ , stab cell shift within 9%, accelerated ESR within 20mm/h slightly increased within 12.8 U/L (with the norm being 12.5), LDG within 510 U/L (within 450), fibrinogen within 5.5 (4.0), immunoglobulin M within 4.5 g/L (2.5), immunoglobulin G within 24.2 g/l (16.0), within 96 units (66). The reaction to inhibited lymphocyte migration made 174% (with the norm being 90%). The ECG recorded some episodes of migration of the pacemaker and frequent ventricular extra systoles. The chest X-ray pictures detected a stronger lung pattern due to the vascular component. The heart shadow was not enlarged. The echocardiography did not detect any changes in the heart cavities and valve system, or any disturbed systolic or diastolic functions of the left ventricle.

Based on the clinical and instrumental investigations the patient was diagnosed to have an infectious-allergic myocarditis of medium gravity.

A performed tomoscintigraphy of the myocardium detected a diffuse accumulated of tagged leukocytes in the right atrium region, posterior and lateral walls of the left ventricle and interventricle partition. The NLS-spectral similarity to the reference standard process "Infectious-allergic myocarditis" ( $D=0.202$ ) allowed objectification of the clinical diagnosis and determination of the localization and spread of the inflammatory process. The patient was prescribed an antiviral, anti-inflammatory and metabolic treatment. 1.5 months later the patient's general condition improved: heartache, irregular heartbeat, shortness of breath and feebleness did not trouble her any longer and her legs were not pasty any more. The laboratory and ECG changes became smaller though did not disappear completely. 2.5 months later a check NLS examination of the heart was performed. Check shots displayed some areas with a higher chromogenics of the NLS signal (4-5 points). The increased chromogenics zones completely corresponded to the fixation areas of tagged autoleukocytes in the myocardium.

A peculiarity of this clinical example is that in this particular case the diagnosis of myocarditis was confirmed by several noninvasive methods; the spread of the process was determined and physical control over the myocardium condition was set in the course of treatment. In summing up it should be stressed that the MECT with tagged autoleukocytes and NLS are noninvasive methods of visual diagnosis of inflammatory diseases of the myocardium. That gives reasons to recommend using MECT and NLS for diagnosing myocarditis, for making a differential diagnosis of some other diseases of the

myocardium of a non-inflammatory pattern, and also for evaluating the condition of the cardiac muscle in the course of treatment.

## Importance of the NLS-Method for Diagnosing Timorous Diseases of the Segmented Intestine

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We made use of the computer nonlinear diagnosis method (NLS) to identify early phases of malignant growths in the colon. The results indicated that this method could evaluate the infiltration depth of the tumor within the intestine wall and allow to diagnosis of malignant adenopathy which was necessary to make a prognosis and determine tumor resectability.

The average detection rate of tumors in the colon at the NLS-investigation is around 63%. The sensitivity of NLS in diagnosing malignant lymphadenopathy and segmented intestine disease is about 65%. It is higher for rectal tumors because a visualizable lymph node in the adrectal region can be regarded as a malignant one. The detection of lymph nodes during the NLS investigation may be connected to the existence of an inflammatory process. However, pericolonc lymph nodes can be more often diagnosed in patients affected by colonic cancer (71%) than in cases of inflammatory lesions (45%).

The NLS-method can be useful in evaluating the spread of tumor to neighboring organs and tissues as well as metastatic lesions of the liver, adrenals, lungs, etc. The NLSinvestigation can be used to:

- Determine resectability and need for presurgical radiation therapy
- Plan radiation field
- Detect complications caused by the tumor such as perforation at a formed abscess or preobstructive ischemia in patients with fully tumo-occluded intestine lumen.

The NLS-method enables to distinguish tumor and ischemic changes in the wall in 75% of cases ( $D < 0.425$ ). In most cases the ischemic area is located beside (in closer proximity) the tumor area, however occasionally an intermediate zone with normal mucous membrane may be detected. The tumor is mostly defined as an unevenly chromogenic area of the intestine wall (from 0.8 to 4.5 cm, 2.0 cm on the average). The ischemic section is largely detected due to a concentric zone of a higher chromogenic pattern (5-6 points according to Flandler's scale), with the zone thickness varying from 0.6 to 1.5 cm (1.0 cm on the average). The timorous area is mostly heterochromatic (4 to 6 points) whereas the ischemic area is generally found to be homochromatic (in 70% of cases).

NLS is very important for diagnosing multiple colonic cancers and has considerable advantages over colonoscopy because it enables to detect changes more proximal to the tumor and exactly localize the process in the colon and outside of it. NLS is the only method to diagnose tumor relapses external to the colon.

It should be taken into account that colon tumor may be mimicked during the colonoscopy by ileocecal valve, fecal masses, respiratory artifacts or feces-filled

diverticulum, which is eliminated in the NLS-diagnosis. Colonoscopy does not discriminate whether a soft tissue formation in the tumor bed is a relapse, so it is very important that NLS be performed 4 months after the surgery and be repeated every 6 months. A scar tissue, even though it may slightly enlarge initially, should shrink some time later (about a year after) with its outlines becoming more distinct. Enlarged scar tissue and lymph nodes should be regarded as an indication for biopsy.

The computer NLS diagnosis method enables to judge the condition of the mesocolon that can be found by locating mesocolon vessels as a reference point. Some pathological changes in the mesocolon are related in the first place to organs with which the mesocolon is linked, such as colon and pancreas.

Computer non-linear diagnosis is a very promising tool for differentiating between malignant and precancerous colon diseases and some other changes. The NLS-diagnosis method makes it very easy to detect adenomatous polyps over 0.7 cm in diameter. However single polyps lower than 2 mm as measured from the colon surface are hard to detect. Although NLS-diagnosis does not allow to differentiate between hyperplastic and adenomatous polyps well enough, it can be very reliable in diagnosing lipomas.

In some typical cases detection of colonic cancer does not require any special preparation, however to make the diagnosis of colon diseases more reliable, it is advisable to evacuate the bowels by giving the patient an enema a day before and immediately before the examination.

We performed NLS-investigation of the segmented intestine in the cases of a suspected colon disease, where it was found difficult to carry out conventional methods of colon investigation such as irrigoscopy and colonoscopy (because of acute painfulness, enema incontinence, impossibility of investigating the right regions of the colon or some suspected early post-surgical complications) and also in the cases of massive extra organic growth in order to determine the spread of the process and extra organic relapses in tumor.

In 10 cases we found some signs characteristic of segmental intestine cancer, like unevenly chromogenic walls of the segmental intestine sized 1.5 to 3.5 cm (4-6 points on Flandler's scale) and a spectral similarity to the reference standard process, 'colon carcinoma' ( $D < 0.425$ ). In 2 cases segmental intestine cancer was accompanied by signs of ileus. In one case a massive tumor originated from the right kidney and involved the ascending intestine. In other cases we diagnosed a tumor largely located extra organically with respect to the descending intestine. In one case the dimensional scaling imaging of the segmented intestine gave reason to suspect a cancerous lesion of the splenic angle of the colon. To confirm it we repeated the investigation after vegetal testing 'colon adenocarcinoma' which resulted in diagnosing a polyp ( $D = 0.213$ ). In two cases the NLS-investigation did not produce a convincing evidence of a cancerous lesion of the segmented intestine ( $D > 0.425$ ) although the colonoscopy data were indicative of a cancerous disease or a malignant polyp.

## Conclusions

1. Computer nonlinear diagnosis should be used in the cases where a colon disease may be suspected or where it appears difficult to carry out particular conventional methods of colon investigation, such as irrigoscopy and colonoscopy, and also in the cases of a massive extra organic growth in order to define the spread of the process, extra organic relapses of the tumor and complications caused by tumor or surgical intervention, which helps solve the issue of tumor operability and therapy approach choice.
2. Using the NLS-method to diagnose single polyps does not appear efficient, because for the most part they are hard to detect, and differentiation between hyper-plastic and adenomatous polyps is impossible.