Information for the Participant and Informed Consent Form for Participation in the Research Experiment

This Information for the potential Participant of the research experiment and the informed consent form for participation in the research experiment is addressed to men and women with a cancerous disease in whom there is a suspicion of lymph node involvement by the cancerous process.

Title of the Research Experiment: Comparison of the value of classifications: LN-RADS, RECIST 1.1, and Node-RADS in the assessment of lymph nodes in magnetic resonance imaging (MRI) and computed tomography (CT) in relation to histopathological results.

Name and Surname of the Principal Investigator: Cezary Chudobiński, MD, PhD

Center Details:

Sponsor Name: Copernicus Memorial Hospital in Łódź

Name and Surname of the Research Experiment Participant: .....

This informed consent form consists of two parts:

- **Information for the Participant (containing information about the research experiment),**
- **Statement of consent to participate in the study (to be signed if you agree to participate in the study) along with the attachments.**

You will receive a complete copy of the informed consent form.

PART I: INFORMATION FOR THE RESEARCH EXPERIMENT PARTICIPANT

Introduction

Whenever the term "Study" written with a capital letter is used in this document, it shall be understood as the research experiment titled: "Comparison of the value of classifications: LN-RADS, RECIST 1.1, and Node-RADS in the assessment of lymph nodes in magnetic resonance imaging (MRI) and computed tomography (CT) in relation to histopathological results".

Please familiarize yourself with the detailed information presented below regarding the goals and principles of conducting the study in which we would like to propose your participation.

Your participation in this study is entirely voluntary. The decision to participate is yours.

Regardless of your decision to participate in the research experiment, we will provide you with treatment in accordance with the scope of services provided by the Hospital.

One copy of the informed consent form will be provided to you.

This form consists of two parts:

- Information for the Participant (containing information about the research experiment),
- Statement of consent to participate in the study (to be signed if you agree to participate in the study) along with an appendix in the form of consent for the processing of the Research Experiment Participant's personal data.

If the document contains phrases that are unclear to you, the doctor will explain all incomprehensible terms.

If you have any questions later, you will be able to ask them to the Investigator.

The confidentiality of personal data will be maintained, and personal identifying data will be excluded from any Study report or scientific publication.

Every Participant of the Study is covered by insurance against harm arising in connection with participation in the Study.

The policy number covering the research experiment insurance will be provided by the Investigator upon request at any time.

Purpose of the Research Experiment

The assessment of cancerous changes in lymph nodes is a major diagnostic challenge and problem. Despite the dynamic development of imaging techniques, the criteria for lymph node assessment in radiology are highly imperfect. The common criterion RECIST 1.1 is the short-axis dimension of the lymph node with a cutoff point of 10 mm. This criterion is uncertain due to both false-negative and false-positive diagnoses (in cases

of non-rare reactive enlargement of lymph nodes). Another classification, Node-RADS, subjects the nodes to structural assessment and is a step forward, but it has numerous limitations, and in particular, it has not been unequivocally verified. The LN-RADS concept is inherently universal, applicable in ultrasound (USG), computed tomography (CT), magnetic resonance imaging (MRI), and what is particularly important, it takes into account small cancerous changes in lymph nodes in the range of 2-9mm. To date, promising results have been obtained in assessing the value of the LN-RADS scale during scientific Study based on USG images, and the work presenting its results on a material of 512 cases was recognized as the best in the field of oncological radiology at the European Congress of Radiology in 2022 in Vienna. The LN-RADS criteria, compared to the RECIST 1.1 criteria, allow for significantly more accurate classification of lymph nodes. A significant benefit for patients from the use of the LN-RADS scale is the improvement in the diagnosis of malignant lymph nodes, which according to the RECIST 1.1 scale would be classified as healthy, by approximately 20%. A group of such lymph nodes may constitute as much as ~20% of the entire material, which sheds light on how significant the phenomenon of underestimation of metastatic lymph nodes can be in clinical practice. As a result of applying old criteria such as RECIST 1.1, a large percentage of patients show false-negative results, and an incorrectly determined stage of cancerous disease may consequently lead to inadequate treatment and treatment failure.

Obligations Related to Participation in the Research Experiment

The Participant is obliged to: attend visits according to the planned visit schedule and undergo all procedures specified in the Study protocol. All medical procedures in the conducted Study will be performed with the Participant's consent. The Participant's refusal to undergo a medical procedure specified in the Study protocol will be equivalent to exclusion from further participation in the Study. The Participant is obliged to inform the research team about their well-being and observed symptoms. The Participant cannot participate in any other research experiment during the Study.

It is important that when deciding to participate in the Study, you accept its course and purpose and are ready to participate in it until its completion or until you withdraw your consent to participate in the Study. Until you complete and sign the informed consent form below, none of the Study procedures can be performed on you.

Selection and Number of Participants and Conditions for Participation in the Research Experiment

3000 Participants will take part in the study. This is assumed to be the necessary minimum number of Participants to perform statistical calculations in accordance with the research experiment protocol.

If, during the implementation of the research experiment, it turns out that events/factors preventing further participation in the Study (so-called exclusion criteria) occur in a potential Study Participant, the Principal Investigator may exclude the Participant from the Study, despite earlier qualification.

Voluntary Participation in the Research Experiment

Your participation in this Study is entirely voluntary. The decision to participate is yours. You have the right to withdraw from participation in the experiment at any stage without any consequences. Withdrawal from participation in the experiment does not affect the level and scope of healthcare services provided to you.

Types of Research Interventions

Lymph nodes are one of the key elements in oncohematological diseases, and in most cases, they are assessed based on old criteria from the 1990s. These criteria do not take into account small cancerous changes - macro-metastases, which means many patients with metastatic lymph nodes are classified as healthy. The application of a modern system for structural, multi-parametric assessment will improve the accuracy of radiologists' assessments, in particular, it will reduce the number of false-negative results. Within the Study, suspicious lymph nodes will be assessed using three available scales: RECIST 1.1, LN-RADS, and Node-RADS, both from CT and MRI images. The experiment will use for analysis computed tomography and magnetic resonance images, as well as histopathological test results obtained in the routine course of diagnostic and therapeutic activities. The assessment concerns lymph nodes visualized in computed tomography or magnetic resonance and the comparison of their consistency with the histopathological test result.

To obtain this data, you will go through three standard procedures detailed below:

- During the first medical visit, we will ask you a few questions about your general health and collect data on the results of tests preceding the planned surgery or biopsy. A clinical interview and physical examination will be conducted with you.
- During the experiment, we will collect data from available computed tomography or magnetic resonance results of the body area intended for treatment and containing the image of lymph nodes.
- Furthermore, we will collect data from available results of lymph node removal surgery or biopsy and the result of the histopathological assessment of the obtained tissue material.
- Finally, we plan to assess the images of lymph nodes visualized in the imaging study with a special structural analysis and classification into appropriate categories depending on the Study arm, which is the method of lymph node assessment that the radiologist will use.

In the event of obtaining important information that could affect the further treatment process in the center due to your underlying disease, the Investigator will inform you about the current test results.

Procedures and Protocol of the Research Experiment

The goal of the research experiment is to compare the effectiveness of the LN-RADS lymph node classification system with currently used systems, such as RECIST 1.1 and Node-RADS. For this purpose, we will divide the qualified lymph nodes into three groups. The assignment to groups is random, like flipping a coin, indicating to the radiologist the classification system according to which they are to assess the suspicious lymph node first.

However, eventually, every lymph node will be assessed according to all three classification systems. Participants' lymph nodes in one group will be assessed according to the LN-RADS system, while Participants' lymph nodes in the second group will be assessed according to the currently used RECIST 1.1 criteria, and in the third group according to the alternative Node-RADS criteria. Then we will compare the three classification systems in terms of their agreement with the histopathological test result. It is worth noting that this method of conducting the Study minimizes the risk of influence from our subjective assessments and expectations, while also enabling you to obtain diagnostic support for your treating physician.

Duration of the Medical Experiment

This Study will be conducted for a total of 5 years. In your case, participation in the study comes down to a one-time expression of consent.

After expressing consent, we will retrieve your radiological images with lymph nodes from the hospital database and subject them to above-standard radiological assessment in the context of clinical data and the histopathological result of the lymph node(s).

Risk

You will undergo an additional, above-standard radiological assessment of computed tomography or magnetic resonance images, which may provide additional diagnostic information not revealed during the standard assessment.

Both the computed tomography and magnetic resonance images, as well as all clinical information, especially the histopathological results, will result from medical indications and will not be enforced by the needs of the research experiment. Thanks to this, you will not be exposed to any medical actions in connection with the conduct of the study.

Remuneration / Reimbursement of Costs

You will not incur any additional costs due to participation in this study. You are not expected to pay for procedures or tests required as part of this Study. You will be responsible for bearing the costs of your standard medical care, including procedures and medications not covered by the Study that your treating physician or primary care physician requires as part of standard medical care. You will not receive any remuneration for participating in this research experiment.

Data Confidentiality

Your personal data collected for the purpose of the conducted Study and processed by the Research Team will be secured and protected against unauthorized access. The information collected as part of the Study will be confidential, accessible only to the Investigators and the Research Team. Data enabling the identification of Participants will not be published anywhere.

Sharing the Results of the Experiment, Including the Provision of a Summary of the Research Experiment Results

After the completion of the Study, the results will be scientifically and statistically processed. The results of the experiment, containing conclusions and statistical summaries (without Participants' personal data), will be published in medical journals and at scientific conferences. Data enabling the identification of the Participant's identity will not be published. Participants will not be informed about the results of the Study.

Right to Refuse or Withdraw Participation in the Research Experiment

You do not have to participate in the Study if you do not want to. Refusal to participate will not affect your current treatment conducted at the Research Center in any way. You will still be able to use the benefits available at this Research Center. You may discontinue participation in the Study at any time and will not lose the benefits to which you are entitled as a patient. Such a decision will not affect the treatment received at the Center in any way.

Contact Opportunities

If you have any questions, you can ask them now or later, even after the Study has started and at any time during its duration. If you wish to ask something later, you can contact:

Investigating Physician at the Center	
Phone Number	
Center Coordinator	
Phone Number	

You can also contact the indicated persons if you wish to withdraw from the Study. In the event of any additional information about the research experiment that may affect the willingness to continue participation in the Study, the Investigator (the doctor conducting the Study) is obliged to immediately communicate it to the Participant. The design of this research experiment has been verified by the Bioethics Committee at the Regional Medical Chamber in Łódź and received a positive opinion. The bioethics committee is a group of people whose task is to protect research Participants from harms/injuries that may be associated with the study. If you wish to obtain further information about the Bioethics Committee, please contact the Secretariat of the Bioethics Committee by phone (+ 42 683 17 44) or email bioetyka@oil.lodz.pl. In the event of any adverse symptoms, depending on the clinical symptoms occurring, you should contact the Emergency Notification Center (CPR) at phone number 112 or report to the nearest Emergency Department (SOR).

PART II: Statement of Voluntary Consent to Participate in the Study

Statement of the Person Consenting to Participate in the Study

I have read or have had the above information read to me. I have had the opportunity to ask questions about this information and have received satisfactory answers to all my questions. I voluntarily give / do not give consent (strike out as appropriate) to participate in this study as a Participant. I am aware that by consenting to participate in the Study, I simultaneously consent to the disclosure of my medical records to the Investigator and the Research Team to the extent necessary for the conducted Study.

I give consent: **YES** **NO** *(strike out as appropriate)*

Participant's Name and Surname (in block letters) _____

Participant's Signature _____

Signature Date _____

Statement of the Investigator / Person Obtaining Consent

I declare that I have discussed the presented study with the potential Study Participant using understandable, possibly simple language, and provided explanations regarding the essence and significance of the Study. I confirm that the Participant had the opportunity to ask questions about the Study, and I answered the questions asked by the Participant truthfully and to the best of my ability. I confirm that the Participant was not coerced into giving consent, and the consent was given freely and voluntarily.

A copy of this informed consent form was handed to the Participant.

Name and Surname of the Investigator / Person Obtaining Consent (in block letters) _____

Investigator's / Person's Obtaining Concent Signature _____

Signature Date _____

INFORMATION CLAUSE CONCERNING THE PROCESSING OF PERSONAL DATA
of the Research Experiment Participant

The Information Clause concerning the processing of personal data of the Research Experiment Participant, hereinafter referred to as the Study.

To ensure transparency in the processing of personal data in connection with participation in the scientific Study, we would like to inform you that:

Data Administrator Details

- The Administrator of the personal data of the Study Participant is M. Kopernik Provincial Multi-Specialist Center of Oncology and Traumatology in Łódź, hereinafter referred to as the Hospital.
- Hospital contact details: 93-513 Łódź, ul. Pabianicka 62, tel.: +48 42 689 5000, e-mail: szpital@kopernik.lodz.pl.
- If you have questions about data processing, please address them by post to the Hospital address or by email to the Data Protection Officer, Mr. Tomasz Zdzienicki (iod@kopernik.lodz.pl).

Purpose of Data Processing

The personal data of the Study Participant will be processed for the purpose of:

- conducting the scientific Study titled: "Comparison of the value of classifications: LN-RADS, RECIST 1.1, and Node-RADS in the assessment of lymph nodes in magnetic resonance imaging (MRI) and computed tomography (CT) in relation to histopathological results".

Legal Basis for Data Processing

The personal data of the Study Participant are processed with the Participant's consent based on:

- Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation), hereinafter referred to as the GDPR,
- the Act of 5 December 1996 on the profession of doctor and dentist,
- the Act of 14 July 1983 on the national archival resource and archives.

Sources of Data Acquisition

The Hospital may obtain the personal data of the Study Participant:

- directly from the Participant,
- from other healthcare entities that obtain appropriate consent from the Participant to participate in the Study.

Data Recipients

Recipients of the Participant's data may include:

- entities authorized to obtain them on the basis of legal provisions (courts, police, authorities conducting proceedings and controls),
- entities providing services for the Hospital:

- legal,
- support for IT systems used by the Administrator.

Storage Period

The personal data of the Study Participant contained in the Study files will be processed for a period of 20 years from the end of the calendar year in which the final resolution on the issuance of an opinion on the Study by the Bioethics Committee was issued. The data contained in the scientific Study files cannot be deleted before the expiry of the above-mentioned period. The Study documentation will be archived in accordance with art. 5 of the Act of 14 July 1983 on the national archival resource and archives.

Rights of Individuals

In connection with the processing of personal data, the Participant can:

- obtain access to the content of their data,
- demand their rectification,
- demand the restriction of processing or deletion of certain data if the Study documentation storage period has expired,
- object to processing,
- demand all information concerning the processing of the Participant's data.

If you believe that the processing of personal data violates the provisions of the GDPR, you have the right to lodge a complaint with the supervisory authority, i.e.: to the President of the Personal Data Protection Office, 00-193 Warsaw, ul. Stawki 2.

Consequences of Not Providing Data

Participation in the scientific Study is voluntary. If the Participant agrees to participate in the Study, it is necessary to obtain their personal data contained, among others, in the medical records. Refusal to provide the personal data of the Study Participant will result in the exclusion of the Participant from participation in the Study. Refusal to participate in the scientific Study does not affect the process of providing medical assistance to the patient.

Automated Decision-Making

The Participant's data will not be processed in an automated manner, including in the form of profiling.

Transfer of Data to a Third Country

We do not plan to transfer the Participant's data to third countries that do not guarantee an adequate level of data protection.

Consent to the Disclosure of Medical Records for Scientific Purposes

If the Participant agrees to participate in the scientific Study, they thereby consent to the disclosure of their medical records to the Research Team to the extent necessary for the conduct of the Study.

Below we provide the exact legal basis for the processing of the Study Participant's data:

Action / Scope of Data	**Additional Information**
Scope of processed data:	Range of data: - identification data contained in medical records, - special categories of data: health information contained in the medical records used for the purposes of the Study. Range of medical records used in the scientific Study: - descriptions from diagnostic imaging (CT, MRI), - histopathological test results.
Acquisition and processing of personal data for the purpose of the Study	art. 6 sec. 1 lit. c) and art. 9 sec. 2 lit. j) of the GDPR in connection with: - art. 25 of the Act of 5 December 1996 on the professions of doctor and dentist
Defense against claims	art. 6 sec. 1 lit. f) and art. 9 sec. 2 lit. f) of the GDPR in connection
Archiving of Study files	art. 6 sec. 1 lit. c) and art. 9 sec. 2 lit. j) of the GDPR in connection with: - art. 29 point 21. of the Act of 5 December 1996 on the professions of doctor and dentist, - art. 5 of the Act of 14 July 1983 on the national archival resource and archives

Participant's Name and Surname (in block letters) _____

Participant's Signature _____

Date of Signature _____