The establishment of a diagnostic classification system for narrow-band imaging of bladder tumors Prospective, multicenter clinical studies

Informed consent form

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Informed consent notification page

Dear Ms./Mr.

You are invited to participate in a study entitled "Development of a Diagnostic Classification System for Narrow Band Imaging of Bladder Tumors". Before you participate in this study, please read this informed consent form carefully and make a careful decision whether or not to participate in this study. You may ask your study doctor/researcher about anything you do not understand and have him/her explain it to you until you fully understand it. You can have a full discussion with your family and friends before you make the decision to participate in this study. If you are participating in another study, please let your study doctor or researcher know. The main points of this study are listed below.

I Why the study was conducted

1. Background of the study.

Bladder cancer is the most common malignant tumor of the urinary system in China, with the 6th highest incidence rate of all malignant tumors and a growing trend year by year. Among them, 75%-80% are non-muscle invasive bladder cancer (NMIBC), and the recurrence rate of NMIBC is high. Early detection and treatment can significantly improve the prognosis of patients with bladder cancer. At present, white light cystoscopy (WLC) is the main diagnostic method to examine early bladder tumors and the presence or absence of recurrence, and is widely used in clinical practice, but its accuracy still needs to be improved. Therefore, in order to further improve the sensitivity and accuracy of cystoscopy, different optical imaging techniques have emerged as an adjunct to WLC to improve the visualization of tumors by contrast enhancement. Narrow-band imaging (NBI) is a diagnostic endoscopic illumination technique developed by Olympus and integrated

into the camera of the cyst/ureteroscope, and studies have shown that NBI-based transurethral resection of bladder tumors (TURBT) demonstrates diagnostic advantages compared to other adjunctive impact techniques. Although the NBI technique has been clinically applied for more than 20 years and clinical studies have confirmed that it can improve the sensitivity and specificity of bladder tumor diagnosis, there is no uniform classification standard for the performance of different bladder tumors under the NBI modality, and the microscopic diagnosis mostly relies on the clinician's experience, with the possibility of misdiagnosis and missed diagnosis.

2. Purpose of the study.

This study was conducted to develop NBI classification criteria for bladder lesions based on pathological findings and to assess their sensitivity and specificity in order to guide clinical work for a more standardized and accurate diagnosis of bladder tumors and early recurrence, thus improving patient prognosis.

II. Time frame of the study and research process, methodology.

1. Duration of the study.

The study was organized by the Department of Urology, Qilu Hospital, Shandong University (Qingdao), and the trial was expected to include a total of 1064 study cases, conducted at six medical institutions, starting and ending in January 2021 to December 2022.

The trial is broadly divided into two parts: in the first step, the Center will compete for enrollment of cases in parallel with the collaborators according to the inclusion and exclusion criteria, with an expected inclusion of 500 cases in the study, with an expected start and end date of January 1, 2021 to December 2021. The second step will continue with the inclusion of 564 cases, with an expected start and end date of January 2022 to December 2022.

2、Research process, methodology

2-1. Main entry and exit criteria.

(1) You may participate in this study only if you meet the following conditions.

① Your age is between 18 and 75 years old .

② Patients who require cystoscopy for definitive diagnosis due to hematuria or bladder occupancy; or patients who are routinely reviewed by cystoscopy after elective urinary bladder tumor resection (TURBT) for non-muscle invasive bladder cancer (NMIBC).

③ You are able to understand the study and sign an informed consent form, and are able to actively cooperate and follow the study process.

Also, you need to not be one of the following.

① Coagulation disorders.

② Complicated acute urinary tract infection or postoperative infusion of BCG.

③ Urethral stricture or bladder volume too small to perform cystoscopy.

④ Severe cardiopulmonary impairment unable to tolerate local anaesthetic surgery.

⑤ Women who are menstruating or more than 3 months pregnant.

⑥ The investigator is deemed unfit to participate in this clinical trial for any reason.

If you need to know more details about the entry requirements for participation in this study or if you have words or information that you do not clearly understand, please consult your study doctor.

2) The screening period physician will ask and take a detailed history of your medical and treatment history, perform a complete physical examination, and evaluate your physical status to determine if you are ready to participate in the study.

- Demographic information
- History of allergies, surgical history, past medical history, etc.
- Vital signs such as blood pressure, heart rate, and respiration, as well as a thorough examination of signs and symptoms.
- Collect your blood and urine samples for laboratory tests.
- An electrocardiogram may be performed if necessary.
- Imaging evaluation and measurement of disease status in different parts of the body including the chest, abdomen, pelvis and, if necessary, head and neck, may be done using ultrasound, CT or MRI scans, as determined by

your supervising physician, depending on your own physical condition.

- It is necessary to retain your blood sample, fresh tissue biopsy specimens, or you will be required to provide tissue wax blocks/pathology slides (15-20 white slides), histopathological diagnostic information.

Your doctor will tell you if you meet the requirements for enrollment in this study after all test results are available. If you need more details about the inclusion criteria or have any questions about the inclusion criteria, please ask the study doctor.

After reviewing all of these evaluations and tests, you may not be able to participate in this study. However, it will not affect your treatment of your disease and your doctor will discuss other diagnostic and treatment options with you.

2-2. Other important matters requiring your cooperation

- It is important that you come to the hospital for the follow-up appointment that your doctor has agreed with you. It is important that you are followed up in a timely manner because your doctor will be able to tell if the treatment you are receiving is actually working.
- Your doctor will ask you about the medications and treatments you are currently taking. Please be sure to tell your doctor, including any medications you have to continue taking for other co-morbidities. This is important.
- Be sure to tell your doctor if you experience any discomfort during this trial.
- In addition to yourself, it is expected that at least one of your family members will be aware of the clinical study you will be participating in and will be able to take an interest in your condition, as well as give feedback to your doctor on your health status during follow-up visits.

III. Possible risks and discomforts.

This study will specify that cystoscopy will be performed if necessary depending on your condition and that there is a low probability of haematuria or risk of urinary tract infection after the examination and we will give haemostatic or anti-infective treatment. Any queries encountered during the

study can be referred to the study doctor or ethics committee.

IV. Possible benefits.

The NBI modality may improve the detection of bladder tumor lesions, leading to early detection of tumor lesions, early intervention, and improved prognosis, while the analysis of your samples by testing or medical data will help to make a definitive diagnosis or effective treatment of the disease in the future. We would like to express our gratitude for your participation in scientific research and your contribution to the development of medicine!

五、Costs and compensation for injury.

Cost: Participation in this study will not add any additional cost to you; in addition, to compensate you for the inconvenience of participating in this study, you will be provided with a travel allowance of $200 for visits during the study.

Injuries and Compensation: Physicians will make every effort to prevent and treat injuries that may occur as a result of this study during the course of the consultation. If an adverse event occurs during a clinical study, a committee of medical experts will determine whether it is related to the study methodology. Damage related to the study will be treated in accordance with clinical practice and will be compensated in accordance with insurance procedures.

六、Will our information be kept confidential?

1、 When we have collected your data, we will establish a special database, the sample will be collected in the process of **personal identification data de-identified processing**, in order to protect the privacy of the subject patients: patients are enrolled in the group using the project uniform number, personal data and case information by the sample management of the special person to enter, save, the user sees only the individual number, no longer contact the participants' names and other information.

2、 Confidentiality of Personal Information: Your medical records will be kept at the hospital and will be accessible only to research personnel; if necessary, with your understanding and assistance and that of other subjects, the results of research through this program may be

published in medical journals, but we will maintain the confidentiality of your research records as required by law. The personal information of research subjects will be kept strictly confidential and your personal information will not be disclosed except as required by relevant laws. If necessary, government authorities and hospital ethics committees and other relevant researchers may have access to your information as required.

3、 USE OF STUDY RESULTS: Study results will be published as statistically analyzed data and will not contain any identifiable patient/participant information.

七、Refusal to participate or withdrawal from the study.

Your participation in the trial is completely voluntary and you may withdraw from the trial at any time without reason and will in no way affect your relationship with the medical staff or your future consultations.

viii. general things you should also know

- If you are going to participate in another clinical trial study, you must let the doctor in charge of that study know that you are participating in this study. You should ask that doctor to contact your supervising physician to discuss other necessary treatment measures.
- Your case information, collected blood samples, tissue biopsy specimens, tissue wax block specimens, or pathology sections will likely be used directly or secondarily for further scientific research, i.e., tissue specimens collected during the course of the study will be preserved at the end of the study for possible future retrospective studies. You have the right to make decisions about future use (refuse to preserve or request destruction).

IX. How can I get more information?

You may ask any questions about this study at any time. Your study doctor will leave you his/her phone number so that you can contact him/her.

Your physician will promptly notify you if there is any important new information during the course of the study, including but not limited to adverse events

and significant findings, that may affect your willingness to continue to participate in the study. You will be asked to re-sign an informed consent form to document the updated news you have received and your willingness to continue to participate in this study.

X. If you have questions, who do you contact?

If you personally have any questions about this study, you can contact Dr. Yang directly at 18561815850.

It is up to you to decide whether or not to participate in this study. You can discuss it with your family or friends before making a decision. Before you make the decision to participate in the study, ask your doctor as many questions as possible until you fully understand the study.

Thank you for reading the above material. If you decide to participate in this study, please let your doctor know and he/she will make all the arrangements for you to participate in this study.

Please keep this information to yourself.

Patient (subject) and/or legal representative consent statement

I have been given a copy of this informed consent form (signed name and date). Have read and fully understood the above description of this study and have had the opportunity to discuss and ask questions about this study with the investigator. All questions I have asked have been answered to my satisfaction, I am fully aware of the possible risks and benefits of participating in this study, and I voluntarily participate in this study.

I agree☐ or refuse☐ to utilize my medical records and pathology specimens for studies other than this study.

Patient's (subject's) signature._____ Date of signature._____

Telephone._____

Legal representative (where applicable)

[Informed consent should be obtained from (or simultaneously with) the subject's legal representative when the subject is incapable of giving informed consent, or is unable to give adequate informed consent (e.g., a minor, or a severely demented patient), and in emergency situations. When a minor is able to make a decision to consent to participate in the study, his or her consent must also be obtained]

Signature of legal representative (if required) Relationship to subject._____

Date of signature: (if necessary) Tel.____

Witnesses (where applicable)

[If the subject or his/her legal representative is illiterate, informed consent must also be given in detail to the subject or his/her legal representative and signed by a witness who will witness the process,

and if the subject or his/her legal representative can sign, they are also required to do so]

I certify that the information in this informed consent form has been accurately explained by the investigator to the subject or his or her legal representative and that the subject or his or her legal representative has fully understood the information. I also certify that my signature herein as a witness confirms that the patient or his/her legal representative has given his/her full and voluntary consent to participate in this study in my presence.

Signature of witness: Date of signature._____

Contact number._____

Witness ID number (or provide copy of ID)._____

Researchers' statement

I confirm that I have explained the details of this study, including its powers and possible benefits and risks, to the subject and/or legal representative, giving the subject the opportunity to ask and answer questions about the nature, risks and benefits of participating in this study. I will provide a copy of this signed and dated consent form to the patient and/or certifying person, legal representative.

Signature of the researcher Date of signature Month and year