Study ID #: HSM# 13-00865 **Form Version Date: November 14, 2013**

TITLE OF RESEARCH STUDY:

Title: Validating predictive models and biomarkers of radiotherapy toxicity to reduce side-effects and improve quality-of-life in cancer survivors (REQUITE)

PRINCIPAL INVESTIGATOR (HEAD RESEARCHER) NAME AND CONTACT INFORMATION:

Name: Barry S. Rosenstein, Ph.D.

Physical Address: Hess Center for Science & Medicine, 1470 Madison Avenue, 8th floor, Office S8-109.

Mailing Address: One Gustave L. Levy Place, Box 1236, NY, NY 10029

Phone: 347-306-4515

Email: barry.rosenstein@mssm.edu

WHAT IS A RESEARCH STUDY?

A research study is when scientists try to answer a question about something that we don't know enough about. However, participating may not necessarily help you or others.

People volunteer to be in a research study. The decision about whether or not to take part is totally up to you. You can also agree to take part now and later change your mind. Whatever you decide is okay. It will not affect your ability to get medical care at Mount Sinai.

Someone will explain this research study to you. Feel free to ask all the questions you want before you decide. Any new information that develops during this research study that might make you change your mind about participating will be given to you promptly.

It is up to you to decide whether to take part. Your research doctor or nurse will be happy to answer any questions you might have. You will be asked to sign a consent form and will be given a copy to keep together with this information sheet. Please keep these safe. If, at any time, you have any questions about the study you can contact Dr. Rosenstein.

Basic information about this study will appear on the website http://www.ClinicalTrials.gov. There are a few reasons for this: the National Institutes of Health (NIH) encourages all researchers to post their research; some medical journals only accept articles if the research was posted on the website; and, for research studies the FDA calls "applicable clinical trials" a description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

PURPOSE OF THIS RESEARCH STUDY:

The purpose of this study is to try to predict which patients who receive radiotherapy are more likely to have side effects than others. Approximately half of all cancer patients receive radiotherapy as part of their cancer treatment. The dose of radiation given, however, is limited because of a risk of damaging the healthy cells that surround the tumor. Patients vary in how they react to radiation. About 5% of patients (5 out of every 100) are sensitive and at risk of having side effects. In recent years,

researchers have developed predictive models and biological tests to try to identify before the start of treatment those patients who are very sensitive. However, these methods are not yet ready to use in the clinic so radiation doses for all patients are currently limited by the doses the most sensitive patients can have. The international REQUITE multi-center observational study is the largest study of its kind, and the information collected will allow researchers to thoroughly test these models and biological markers for future use. We hope that results from this study will confirm and/or improve current predictive models and biological tests to predict how a patient will respond to radiotherapy. If we are successful, then in the future we could identify the 'radiosensitive' patients before they start their radiotherapy. The sensitive patients could potentially be safely and effectively treated with less radiation and other patients with more radiation. This should reduce side effects for all patients, improve quality of life and potentially increase the number of patients successfully treated for their cancer.

You may qualify to take part in this research study because you were recently diagnosed with cancer and your doctor has recommended that you should receive radiotherapy. The REQUITE study needs 5,300 patients in total to take part. We want to include patients with breast, prostate or lung cancer. REQUITE is a worldwide study with patients from the USA, Belgium, France, Germany, Italy, Spain, UK and The Netherlands.

This study is being carried out by a network of medical doctors and scientists from across the world. This is an international study co-ordinated by Professor Catharine West at The University of Manchester in the UK. It is funded by the European Commission's FP7 HEALTH program. The study Sponsor is The University of Manchester. The local study leader in the United States is Dr. Barry Rosenstein at the Icahn School of Medicine at Mount Sinai.

LENGTH OF TIME AND NUMBER OF PEOPLE EXPECTED TO PARTICIPATE

Your participation in this research study is expected to last for at least two years. However, the blood sample you will donate and clinical data will be stored and used indefinitely. In addition, information will be obtained from your medical record through periodic review.

The number of people expected to take part in this research study at this site is 800.

The total number of people expected to take part in this research study is 5,300.

DESCRIPTION OF WHAT'S INVOLVED:

If you agree to participate in this research study, the following information describes what may be involved. You will be seen by a member of the research team at the beginning of your cancer treatment who will then ask you to complete some questionnaires asking about symptoms you may be experiencing before you start your radiotherapy treatment and about your general well-being. You will then be asked to complete the same questionnaires again when your radiotherapy is finished and once a year for a minimum of two years after your treatment. We would also like you to complete a questionnaire at all other follow-up appointments, but this is not required for participation in this study. This is a practical and reliable way for us to measure and record the effects of your radiotherapy treatment. These questionnaires should preferably be completed in the clinic (but could be done at home) and take no more than 20 minutes to complete each time.

We will also ask you to give a blood sample. We would like to take about 20 ml of blood, which is less than two tablespoons and similar to the amount taken for routine blood-testing. If possible, we will

collect the sample when you are already having blood taken as part of your standard treatment at your usual follow up appointments. Apart from the short time involved and the minimal discomfort associated with giving blood, there should be no pain, distress or inconvenience caused to you by taking part in the REQUITE study. Your blood sample will be coded using a unique study number so that no one outside the study can identify you from it. A portion of the sample will be stored in the REQUITE Biobank in Manchester, which is located in the United Kingdom, and ready for the subsequent research work including genetics analysis and the remainder will be stored locally at Mount Sinai. The results of these tests will not be given either to you or your doctor.

If you are receiving treatment for breast cancer, we may ask your permission to have digital photographs taken of your breasts (your face will not be included). This will take place at the start of your treatment, and will be repeated at your two year follow up appointment to assess any changes. Your research doctor or nurse will discuss this with you.

In addition to the genetic research for which your blood sample will be used for this study, it may be possible to use your blood sample for other tests in the future. We would like to store your sample for future medical research on this or a related project. The side effects information we collect about you could also be used anonymously in future studies. Future research may be carried out at academic institutions, hospitals or by commercial companies involved in cancer research worldwide. Please be aware that this could mean that doctors and scientists in other countries might use your blood sample and medical data. However, the data will not contain any personal information so you could not be identified.

The research team will also look at your medical data to collect information on your cancer and your treatment. The information will be used to test predictive models for radiotherapy toxicity.

Therefore, your blood sample is being given as a gift that may be used for future research. The blood sample and information could be made available for future research and that this may include researchers working abroad or in commercial companies. Any information transferred to a third party for future research will not contain your personal information. You are giving permission for these individuals to have access to your sample and information.

Each sample will be coded and the experimental results will never be associated with your identity. Therefore, neither you nor any other individual will ever be provided with this information. In addition, information from your medical record concerning your treatment and how you responded will be periodically reviewed.

Material derived from your blood sample will be stored indefinitely as part of a tissue repository. Your sample will be labeled only with a subject identification number and only Dr. Rosenstein, the Principal Investigator at Mount Sinai for this study, will be able to link this number with your identity. You may, at any time, withdraw your consent to allow storage and use of your blood sample, in which case your blood sample and any material derived from it will be discarded. If you wish, you may at any time ask that any remaining material from your blood sample be destroyed by making this request in writing to Dr. Barry S. Rosenstein, Box 1236, Department of Radiation Oncology, Icahn School of Medicine at Mount Sinai, New York, NY 10029.

The researchers would like to ask your permission to keep the blood and any materials derived from you're the blood sample collected from you during this study for use in future research studies. They would also like to know your wishes about how they might use your specimens in future research studies. You should also know that it is possible that products may someday be developed with the help of your specimens, and there are no plans to share any profits from such products with you.

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To do more powerful research, it is helpful for researchers to share information they get from studying human samples. They do this by putting it into one or more scientific databases, where it is stored along with information from other studies. Researchers can then study the combined information to learn even more about health and disease. If you agree to take part in this study, some of your genetic and health information might be placed into one or more scientific databases. There are many different kinds of scientific databases; some are maintained by the REQUITE study, some at the Icahn School of Medicine at Mount Sinai, some are maintained by the federal government, and some are maintained by private companies. For example, the National Institutes of Health (an agency of the federal government) maintains a database called "dbGaP." A researcher who wants to study the information must apply to the database. Different databases may have different ways of reviewing such requests. Researchers with an approved study may be able to see and use your information, along with that from many other people. Your name and other information that could directly identify you (such as address or social security number) will never be placed into a scientific database. However, because your genetic information is unique to you, there is a small chance that someone could trace it back to you. The risk of this happening is very small, but may grow in the future. Researchers will always have a duty to protect your privacy and to keep your information confidential.

(1) Will you allow the researchers to store your specimens and information for use in future research studies? **Please initial your choice:**
Yes_____ No_____ If no, please stop here since you cannot participate in this study. If yes, please continue to the next question.

(2) Will you allow the researchers to keep your specimens and information stored in a way that it is linked to your identity (through the use of a code that can indicate the information came from you personally). **Please initial your choice:**
Yes_____ No_____

(3) Do you give the researchers permission to contact you in the future to collect additional information about you, discuss how your specimens might be used, or to discuss possible participation in another research project? **Please initial your choice:**
Yes_____ No_____

(4) Do you give the researchers permission to keep the specimens and information indefinitely and use them for future studies that are directly related to the purpose of the current study? **Please initial your choice:**
Yes_____ No_____

(5) Do you give the researchers permission to keep the specimens and information indefinitely and use them for future studies that are not related to the purpose of the current study (for example, a different area of research)? **Please initial your choice:**
Yes_____ No_____

(a) If the future research in a different area can be done without having to know that the specimens and clinical information came from you personally, that will be done.

(b) If the future research in a different area requires that it is known specifically who the specimens and clinical information came from, then one of the following will be done:

(i) If you allowed the researchers to contact you in the future, they will be able to contact you to explain why your specimen is needed and what will be done with it. Your permission will be asked to use your specimens and clinical information in that research project.

(ii) If you do not give permission to be contacted in the future, or if it is found that contacting you is not practical, for example, because you have moved, your specimens and clinical information may still be used. Either all links to your identity will be removed from the specimens and clinical information, or an Institutional Review Board will be asked for permission to use the specimens and clinical information linked to your identity. The Institutional Review Board (IRB) is a committee of doctors and scientists and non-scientists and people not associated with this hospital or medical school whose job it is to protect people who participate in research. The IRB can give permission for researchers to use and share health information connected to specimens and clinical information that are linked to people's identities, but only if it determines that doing this will not be more than a minimal risk to people or their privacy.

(6) Do you give permission to have portions of the specimens and clinical information given to other researchers at Mount Sinai or other institutions for use in research that is either related or not related to the purpose of this study? **Please initial your choice:**
Yes_____ No_____

To summarize, you are giving permission for a person from the research team to look at your medical records to get information on your medical history, diagnosis, treatment and progress following treatment. This includes all scans taken in standard practice. This information will be kept confidential. You are also giving permission for your medical notes and study information to be looked at by research staff working on this study or the regulatory authorities where it is relevant to the research. In addition, you are giving permission for your family doctor to be informed about your participation in this study.

YOUR RESPONSIBILITIES IF YOU TAKE PART IN THIS RESEARCH:

If you decide to take part in this research study you will be responsible for the following things:

At recruitment:	Donate a blood sample (20 ml, about 2 tablespoons)
At start of radiotherapy:	Complete Questionnaire
At end of radiotherapy:	Complete Questionnaire
After 12 months:	Complete Questionnaire
After 24 months:	Complete Questionnaire

In addition, we would like you to complete a questionnaire every time you come in for a follow-up appointment at other times, not specified above, but this is not required for participation in this study.

COSTS OR PAYMENTS THAT MAY RESULT FROM PARTICIPATION:

There will be neither a cost nor a reimbursement to you for your participation in this study.

POSSIBLE BENEFITS:

You are not expected to get any benefit from taking part in this research study. Others may not benefit either. However, possible benefits to others include the use of the results of this study to form the basis of a clinical test through which it will be possible to predict which patients are most likely to suffer complications from a radiation treatment for cancer. For these people, either the use of a lower dose of radiation or the avoidance of radiation treatment entirely, if surgery, chemotherapy or active surveillance represent an acceptable alternative, could be the preferred course for treating their cancer.

REASONABLY FORESEEABLE RISKS AND DISCOMFORTS:

The risks of a blood draw include pain, bruising, a slight possibility of infection at the place where the needle goes in or extremely rarely impairment of nerves. Some people feel dizzy or may faint during or after a blood draw. There always exists the potential for loss of private information; however, there are procedures in place to minimize this risk.

There is a Federal law called the Genetic Information Nondiscrimination Act (GINA). In general, this law makes it illegal for health insurance companies, group health plans, and most employers of over 15 people to discriminate against you based on your genetic information. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Group Risks:
Although we will not give researchers your name, we will give them basic information such as your race, ethnic group, and sex. This information helps researchers learn whether the factors that lead to health problems are the same in different groups of people. It is possible that such findings could one day help people of the same race, ethnic group, or sex as you. However, they could also be used to support harmful stereotypes or even promote discrimination.

Privacy Risks:
Your name and other information that could directly identify you (such as address or social security number) will *never* be placed into a scientific database. However, because your genetic information is unique to you, there is a small chance that someone could trace it back to you. The risk of this happening is very small, but may grow in the future. Since the database includes genetic information, a break in security may also pose a potential risk to blood relatives as well as yourself. For example, it could be used to make it harder for you (or a relative) to get or keep a job or insurance. If your private information was misused it is possible you would also experience other harms, such as stress, anxiety, stigmatization, or embarrassment from revealing information about your family relationships, ethnic heritage, or health conditions.

OTHER POSSIBLE OPTIONS TO CONSIDER:

You may decide not to take part in this research study without any penalty. The choice is totally up to you.

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IN CASE OF INJURY DURING THIS RESEARCH STUDY:

If you believe that you have suffered an injury related to this research as a participant in this study, you should contact the Principal Investigator.

ENDING PARTICIPATION IN THE RESEARCH STUDY:

You may stop taking part in this research study at any time without any penalty and without giving a reason. This will not affect your ability to receive medical care or to receive any benefits to which you are otherwise entitled.

If you decide to withdraw, your coded blood samples and information will be retained for use in this study and for future medical research unless you specifically request otherwise. If specifically requested, your samples will be destroyed and your medical information removed from the REQUITE database.

If you decide to stop being in the research study, please contact the Principal Investigator or the research staff.

You may also withdraw your permission for the use and disclosure of any of your protected information for research, but you must do so in writing to the Principal Investigator at the address on the first page. Even if you withdraw your permission, the Principal Investigator for the research study may still use the information that was already collected if that information is necessary to complete the research study. Your health information may still be used or shared after you withdraw your authorization if you should have an adverse event (a bad effect) from participating in the research study.

Withdrawal without your consent: The study doctor, the sponsor or the institution may stop your involvement in this research study at any time without your consent. This may be because the research study is being stopped, the instructions of the study team have not been followed, the investigator believes it is in your best interest, or for any other reason. If specimens or data have been stored as part of the research study, they too can be destroyed without your consent.

CONTACT PERSON(S):

If you have any questions, concerns, or complaints at any time about this research, or you think the research has hurt you, please contact the office of the research team and/or the Principal Investigator at 347-306-4515.

This research has been reviewed and approved by an Institutional Review Board. You may reach a representative of the Program for Protection of Human Subjects at Mount Sinai School of Medicine at telephone number (212) 824-8200 during standard work hours for any of the following reasons:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You are not comfortable talking to the research team.
- You have questions about your rights as a research subject.
- You want to get information or provide input about this research.

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DISCLOSURE OF FINANCIAL INTERESTS:

None.

MAINTAINING CONFIDENTIALITY – HIPAA AUTHORIZATION:

All information will be kept strictly confidential and your name will not appear on any publications resulting from the study. Your medical notes will be seen by authorized members of the research team at your local hospital so that they can collect information needed for the REQUITE study. You will be given a unique REQUITE study number, which will be used together with your initials and date of birth on any forms that the research staff fill in. Samples will be coded with the unique REQUITE study number and kept anonymously which means that the laboratory researchers who are carrying out any tests on your sample cannot identify you. All information about you will be treated as strictly confidential and nothing that might identify you will be revealed to any third party.

Selected scientific and medical employees of the study coordinator at the University of Manchester and those conducting the study with them, may need to examine your medical records to ensure the study is being run properly and that the information collected on the forms is correct. Your confidentiality will be protected at all times.

The researchers running this study would also like to be able to combine information we collect about patients in REQUITE with information collected from other studies, if in the future it is a useful way of advancing our knowledge of the treatment of cancer. If this happens, information about you may be passed to other researchers but they would not be able to identify you from the information provided.

We would like to be able to make your blood sample and information available to other researchers to use in future medical research beyond the end of the REQUITE study. Any other research study planning to make use of your sample or information must be approved by an independent research protection of human subjects committee before it is allowed to go ahead. Any samples and information transferred to other researchers will not contain your personal information, so they will not be able to identify you from the information provided.

As you take part in this research project it will be necessary for the research team and others to use and share some of your private protected health information. Consistent with the federal Health Insurance Portability and Accountability Act (HIPAA), we are asking your permission to receive, use and share that information.

<u>What protected health information is collected and used in this study, and might also be disclosed (shared) with others?</u>

As part of this research project, the researchers will collect your Name, Address, Telephone number Birth Date, Admission and Discharge Dates, Telephone Number, Social Security Number and Medical Records Number.

The researchers will also get information from your medical record and any records sent by other doctors that are included in your chart

During the study the researchers will gather information by:

- completing the tests, procedures, questionnaires and interviews explained in the description section of this consent
- reviewing genetic tests

Why is your protected health information being used?

Your personal contact information is important to be able to contact you during the study. Your health information and the results of any tests and procedures being collected as part of this research study will be used for the purpose of this study as explained earlier in this consent form. The results of this study could be published or presented at scientific meetings, lectures, or other events, but would not include any information that would let others know who you are, unless you give separate permission to do so.

The Principal Investigator may also use and share the results of these tests and procedures to treat you.

The research team and other authorized members of The Mount Sinai Hospital and Icahn School of Medicine at Mount Sinai (together, "Mount Sinai") workforce may use and share your information to ensure that the research meets legal, institutional or accreditation requirements. For example, the School's Program for the Protection of Human Subjects is responsible for overseeing research on human subjects, and may need to see your information. If you receive any payments for taking part in this study, the Mount Sinai Medical Center Finance Department may need your name, address, social security number, payment amount, and related information for tax reporting purposes. If the research team uncovers abuse, neglect, or reportable diseases, this information may be disclosed to appropriate authorities.

Who, outside Mount Sinai, might receive your protected health information?

As part of the study, the Principal Investigator, study team and others in the Mount Sinai workforce may disclose your protected health information, including the results of the research study tests and procedures, to the following people or organizations: (It is possible that there may be changes to the list during this research study; you may request an up-to-date list at any time by contacting the Principal Investigator.)

- The United States Food and Drug Administration
- The United States Department of Health and Human Services and the Office of Human Research Protection.
- The University of Manchester

In all disclosures outside of Mount Sinai, you will not be identified by either name, social security number, address, telephone number, or any other direct personal identifier unless disclosure of the direct identifier is required by law. Some records and information disclosed may be identified with a unique code number. The Principal Investigator will ensure that the key to the code will be kept in a locked file, or will be securely stored electronically. The code will not be used to link the information back to you without your permission, unless the law requires it, or rarely if the Institutional Review Board allows it after determining that there would be minimal risk to your privacy. It is possible that a sponsor or their representatives, a data coordinating office, a contract research organization, will come to inspect your records. Even if those records are identifiable when inspected, the information

leaving the institution will be stripped of direct identifiers. Additionally, the monitors, auditors, the IRB, the Food and Drug Administration will be granted direct access to your medical records for verification of the research procedures and data. By signing this document you are authorizing this access. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

For how long will Mount Sinai be able to use or disclose your protected health information? Your authorization for use of your protected health information for this specific study does not expire.

Will you be able to access your records?

During your participation in this study, you will not be able to access your medical records. This will be done to prevent the knowledge of study results from affecting the reliability of the study. Your information will be available should an emergency arise that would require your treating physician to know this information to best treat you. You will have access to your medical record and any study information that is part of that record when the study is over or earlier, if possible. The investigator is not required to release to you research information that is not part of your medical record.

Do you need to give us permission to obtain, use or share your health information?

NO! If you decide not to let us obtain, use or share your health information you should not sign this form, and you will not be allowed to volunteer in the research study. If you do not sign, it will not affect your treatment, payment or enrollment in any health plans or affect your eligibility for benefits.

Can you change your mind?

You may withdraw your permission for the use and disclosure of any of your protected information for research, but you must do so in writing to the Principal Investigator at the address on the first page. Even if you withdraw your permission, the Principal Investigator for the research study may still use your protected information that was already collected if that information is necessary to complete the study. Your health information may still be used or shared after you withdraw your authorization if you should have an adverse event (a bad effect) from being in the study. If you withdraw your permission to use your protected health information for research that means you will also be withdrawn from the research study, but standard medical care and any other benefits to which you are entitled will not be affected. You can also tell us you want to withdraw from the research study at any time without canceling the Authorization to use your data.

If you have not already received it, you will also be given the Mount Sinai Hospital - Mount Sinai School of Medicine Notice of Privacy Practices that contains more information about how Mount Sinai uses and discloses your protected health information.

It is important for you to understand that once information is disclosed to others outside Mount Sinai, the information may be re-disclosed and will no longer be covered by the federal privacy protection regulations. However, even if your information will no longer be protected by federal regulations, where possible, Mount Sinai has entered into agreements with those who will receive your information to continue to protect your confidentiality.

- Family members of an individual who provided a stored tissue sample will not be contacted for clinical, research, or other purposes without your consent.
- Information about you derived from genetic tests will not be released to anyone else without your explicit written consent.

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If as part of this research project your medical records are being reviewed, or a medical history is being taken, it is possible that HIV-related information may be revealed to the researchers. If that is the case, the information in the following box concerns you. If this research does not involve any review of medical records or questions about your medical history or conditions, then the following section may be ignored.

Notice Concerning HIV-Related Information

If you are authorizing the release of HIV-related information, you should be aware that the recipient(s) is (are) prohibited from re-disclosing any HIV-related information without your authorization unless permitted to do so under federal or state law. You also have a right to request a list of people who may receive or use your HIV-related information without authorization. If you experience discrimination because of the release or disclosure of HIV-related information, you may contact the New York State Division of Human Rights at (888) 392-3644 or the New York City Commission of Human Rights at (212) 306-5070. These agencies are responsible for protecting your rights.