The Sinai Robotic Surgery Trial in HPV Positive Oropharyngeal Squamous Cell Carcinoma (SCCA) (SIRS TRIAL)
Dr. Raymond Chai
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TITLE OF RESEARCH STUDY:

Title: The Sinai Robotic Surgery Trial in HPV Positive Oropharyngeal Squamous Cell Carcinoma

PRINCIPAL INVESTIGATOR (HEAD RESEARCHER) NAME AND CONTACT INFORMATION:

Name: Raymond Chai, MD

Physical Address: Mount Sinai Union Square, [redacted], New York, NY 10003

Mailing Address: Mount Sinai Union Square, [redacted], New York, NY 10003

Phone: office (212) 844-8775

Fax: (212) 844- 6976

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. Participating may not 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 within the Mount Sinai Health System.

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.

We will register 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 U.S. Food and Drug Administration (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 evaluate Transoral Robotic Surgery (TORS) alone or combined with either lower dose radiation or lower dose of chemotherapy and radiation in the treatment of early to intermediate stage HPV (Human Papillomavirus) related oropharyngeal cancer.

HPV (Human Papillomavirus) related Oropharyngeal cancer (HPVOPC) accounts for 80% of oropharynx cancer cases in the United States. HPVOPC has better prognosis than patients with oropharyngeal cancer that does not show the HPV virus. In many hospitals, the standard of care treatment for oropharyngeal cancer is (chemo) radiotherapy. Even though survival rate has increased because of chemoradiation therapy (CRT), the long-term side effects of radiation therapy are still problematic. The purpose of this study is to determine whether robotic surgery alone or with reduced doses of radiation or chemoradiotherapy can result in rates of cancer control and survival similar to those that have been previously reported with standard therapy. Our hope is that with this newer approach, the long term complications from chemotherapy and radiation can be reduced. You may qualify to take part in this research study because you have been diagnosed with early to intermediate stage oropharyngeal cancer, which has tested positive for HPV and carries an improved prognosis.

If you are an appropriate candidate Transoral Robotic Surgery (TORS) will be used to surgically remove cancers from the base of tongue or tonsil. This uses new technology to allow the surgeon to remove your cancer with a less invasive technique performed through your mouth with a system of special retractors and robotic instruments. Historically tumors of the tongue base and tonsils were removed with procedures such as splitting your lip and jaw, or via incisions in the neck to access the tumor. Robotic technology has allowed many of these tumors to be removed through the mouth, decreasing the side effects and morbidity of surgery.

Funds for conducting this research are provided by Icahn School of Medicine at Mount Sinai and the Mount Sinai Hospital.

LENGTH OF TIME AND NUMBER OF PEOPLE EXPECTED TO PARTICIPATE

Your participation in this research study is expected to last 5 years after completion of your treatment.

The number of people expected to take part in this research study at Icahn School of Medicine at Mount Sinai North Campus is 160, at Mount Sinai South and West Campus is 20, and Valley Hospital System is 20. The total number of people expected to take part in this research study is 200.

DESCRIPTION OF WHAT'S INVOLVED:

If you agree to participate in this research study, the following information describes what may be involved.

The sites where the research activities will take place are Icahn School of Medicine at Mount Sinai and Mount Sinai Beth Israel. ***Before the research starts (screening):*** *After signing this consent form, you will be asked to undergo some screening tests or procedures to find out if you can be in the research study. Many of these tests and procedures are likely to be part of regular cancer care and may be done even if it turns out that you do not take part in the research study. If you have had some of these tests or procedures done recently, they may or may not have to be repeated.*

- **A medical history,** which includes questions about your health, previous surgery/ treatment, current medications, smoking history and any allergies. You will also be asked about existing alcohol and drug use. Active abuse of alcohol or drugs will exclude you from participating in the study for safety reasons.
- **Clinical assessment** will be performed by direct visualization and manual palpation
- **Endoscopic evaluation** with flexible endoscopy of the upper aerodigestive tract to evaluate the size and extension of your cancer.
- **Radiographic evaluation,** by high-resolution CT (Computerized Tomography) scan or MRI (Magnetic Resonance Imaging) or PET Scan (Positive Emission Tomography) or CT Scan w/contrast. These are ionizing radiation (CT and PET CT) and magnetic radiation (MRI) procedures that are used to define normal and abnormal structures in body and to measure the size of your cancer.
- **Examination under anesthesia (EUA) and biopsy:** With help of a scope your doctor will examine back of your mouth and deeper parts of throat in order to assess the exact extent of disease. This is done in operating room under sedation. Along with proper biopsy, this helps in planning of treatment and helps determine if you are a candidate for robotic surgery.
- **HPV and p16 tests-** tumor tissue either from your outside biopsy, or if unavailable from another biopsy performed here will be tested for both HPV and p16 antibodies.
- **TNM staging-** with help of information from physical, laboratory, pathology, radiological and surgery reports, your doctor will determine the extent of the tumor (T), whether cancer cells have spread to nearby (regional) lymph nodes (N), and whether distant (to other parts of the body) metastasis (M) has occurred.
- **Blood tests:** which will include measurements of:
  - Blood chemistry (tests to measure substances in the blood which tell us what is going on in your body) - approximately 2-3tsp (10-15ml) of blood is required
  - Complete blood count (tests to measure cells in blood) - approximately 1 tsp. (5ml) of blood is required.
  - Pregnancy testing will be performed prior to surgical interventions, anesthesia, and prior to initiation of radiation/chemotherapy. Active pregnancy will exclude you from entering the study. If you should become pregnant during the study, you will be withdrawn from the study.
  - Research studies (tests to obtain measurements of your immune system). This will involve collecting 46ml or 9 tsp before surgery.
- **European Organization for Research and Treatment of Cancer** Core **(EORTC) Performance status**, which includes completing questionnaire that will evaluate how you are able to carry on with your usual activities, this will help determine the affects of treatment on your overall function.
- **M.D. Anderson Symptom Inventory-Head and Neck (MDASI-HN) - M.D. Anderson Dysphagia Inventory (MDADI-HN)** these questionnaires provide brief measure of symptom distress you experience as a result of your disease or treatment to determine the effects of treatment on your swallowing and eating and other functional aspects.

- **Xerostomia/ Dysphagia assessment questionnaire-** which includes completing questionnaire that will evaluate your swallowing ability of food with different consistencies before and after treatment.

If these tests show that you are eligible to participate in the research study, and you choose to participate, you will then undergo robotic surgical resection of your tumor. If you do not meet the eligibility criteria, you will not be able to participate in this research study.

Surgical Intervention
Surgery will include transoral robotic resection of the tumor and neck dissection to remove at risk lymph nodes in your neck which may be likely to harbor early cancer spread. Same side neck dissection for tonsillar tumors and bilateral neck dissection will be performed for tongue base tumors. Additional lymph node sampling will be performed at the discretion of the operating surgeon if indicated on the size and location of the primary tumor. Appropriate reconstruction will be performed at the time of tumor resection as deemed necessary by the operating surgeon. No additional surgery will be performed outside of the standard of care as a result of participation in this study.

After your surgery you will be re-classified according to findings of the pathologists when your surgical specimens are examined, and the results of your surgical resection. Based on this review you will be assigned to one of three groups: Low risk, Intermediate risk and High risk. Each group will undergo different treatment plans as indicated below:

Group I: Low Risk

- **No radiotherapy**
- **Monthly clinical evaluation** during your first year.
- **PET or CT or CT w/contrast** at 4 months,12 months, 24 months,36 months, 48 months, 54 months and 60 months unless clinically indicated.
- **Questionnaires (EORTC, MDAASI-HN, and Xerostomia/Dysphagia)** will be performed 3 months, 6 months, 12 months and every year after therapy for 5 years.
- **Blood tests:** which will include measurements of:
  - Blood chemistry (tests to measure substances in the blood which tell us what is going on in your body) - approximately 2-3tsp (10-15ml) of blood is required. These will be performed quarterly during your first year and then semiannually through year 5.
  - Complete blood count (tests to measure cells in blood) - approximately 1tsp (5ml) of blood is required. These will be performed quarterly during your first year and then semiannually through year 5.
  - Research studies: test to obtain measurements of your immune system. This will involve collecting 46ml or 9tsp of blood 3 months and 24 months after surgery. 16ml or 3tsp of blood will also be collected at your 6 month, 12 months and 36 month visit post treatment.

Group II: Intermediate Risk Protocol

- **Postoperative Radiotherapy** in a reduced dose **(5000 cGy).** You will receive daily radiation treatment with intensity-modulated radiotherapy (IMRT). Treatment will be given 5 days per week and, as per standard practice, will not be delivered on Saturday, Sunday or major holidays.
- **History and Physical Exam including neurological exam** will be performed weekly where you will be asked questions about your general health and specific questions about any problems you may be experiencing. After your treatment, this will be done monthly during your first year.
- **PET or CT or CT with contrast** at 4 months,12 months, 24 months,36 months, 48 months, 54 months and 60 months unless clinically indicated.
- **Questionnaires (EORTC, MDAASI-HN, and Xerostomia/Dysphagia)** will be performed 3 months, 6 months, 12 months and every year after therapy for 5 years.
- **Blood tests:** which will include measurements of:
  - Blood chemistry (tests to measure substances in the blood which tell us what is going on in your body) - approximately 2-3tsp (10-15ml) of blood is required. These will be performed weekly during your treatment, then quarterly during your first year and then semiannually through year 5.
  - Complete blood count (tests to measure cells in blood) - approximately 1tsp (5ml) of blood is required. These will be performed weekly during your treatment, then quarterly during your first year and then semiannually through year 5.
  - Research studies: test to obtain measurements of your immune system. This will involve collecting 46ml or 9tsp of blood 3 months (or pre radiation) and 24 months after surgery. 16ml or 3tsp of blood will also be collected at your 6 month, 12 month and 36 month visit post treatment.
- **Assessment of any adverse events** that may have occurred may be performed at every study visit until resolved or stable.

Group III: High Risk Protocol

- **Postoperative Chemotherapy** with **Cisplatin** weekly. You will receive Cisplatin as intravenous infusion mixed in normal saline or D5W (a solution of 5% dextrose in water) over 30 – 45 min. Rehydration with IV fluids is also required the day of your treatment. In the event you are unable to receive Cisplatin for medical reasons, Carboplatin may be administered as an alternative option to decrease complications and side effects associated with chemotherapy.
- **Postoperative Radiation** in a reduced dose (**5600 cGy**). You will receive daily radiation treatment with intensity-modulated radiotherapy (IMRT). Treatment will be given 5 days per week and, as per standard practice, will not be delivered on Saturday, Sunday or major holidays.
- **History and Physical Exam including neurological exam** will be performed weekly where you will be asked questions about your general health and specific questions about

any problems you may be experiencing. After your treatment, this will be done monthly during your first year.

- **PET or CT** at 4 months,12 months, 24 months,36 months, 48 months, 54 months and 60 months unless clinically indicated.
- **Questionnaires (EORTC, MDAASI-HN, and Xerostomia/Dysphagia).** The EORTC questionnaires will be completed on weeks 1, 3, 5, 7; and the MDASI-HN module will be completed on weeks 2,4,6,8. The adverse events assessments, the MDADI-HN (dysphagia) and Xerostomia questionnaires will be completed on a weekly basis during your treatment. After your treatment completion, they will be repeated at 6 months, 12 months and every year after therapy for 5 years.
- **Blood tests:** which will include measurements of:
  - Blood chemistry (tests to measure substances in the blood which tell us what is going on in your body) - approximately 2-3tsp (10-15ml) of blood is required. These will be performed weekly during your treatment, then week 4 and 8 after you treatment, then quarterly during your first year and then semiannually through year 5.
  - Complete blood count (tests to measure cells in blood) - approximately 1tsp (5ml) of blood is required. These will be performed weekly during your treatment, then quarterly during your first year and then semiannually through year 5.
  - Research studies: test to obtain measurements of your immune system. This will involve collecting 46ml or 9tsp of blood 3 months (or pre radiation) and 24 months after surgery. 16ml or 3tsp of blood will also be collected at your 6 month, 12 month and 36 month visit post treatment.
- **Hearing test:** Patients who receive chemotherapy with Cisplatin require monitoring for hearing loss related to the drug and audiomeric testing will be done for subjects receiving cisplatin at baseline and prior to each dose.
- **Assessment of any adverse events** that may have occurred will be performed at every study visit until resolved or stable.

Reassessment evaluation will take place between 8-10 weeks at the completion of the chemotherapy. You will be assessed as follows:

- **Physical Exam including neurological exam,** will be performed.
- **Nasopharyngoscopy**
- **Dysphagia assessment questionnaire**
- **CT or MRI of the neck and PET CT scan** will be performed at 12-16 weeks to assess complete response.

Contraception
For Women:

Since you are participating in a study that involves drugs or investigational treatment with potential risks to a developing fetus, it is recommended, for your protection, that you not become pregnant for the duration of the study. Also, you should not participate if you are breastfeeding. Therefore, practicing effective contraception is important. No individual contraceptive is 100% effective. Recommended methods of birth control are:

- The consistent use of an approved hormonal contraception (birth control pill/patches, rings),
- An intrauterine device (IUD),
- Contraceptive injection (Depo-Provera),
- Double barrier methods (Diaphragm with spermicidal gel or condoms with contraceptive foam),
- Sexual abstinence (no sexual intercourse) or
- Sterilization.

Hormonal contraceptives, implants, and injections are only considered effective if used properly and started at least one month before you begin the study, continuing throughout the study and for one month after the end of the study. You should ask your study doctor if you should continue birth control for longer than 30 days after the end of the study. If you are unsure whether the method of birth control you use is acceptable to use while participating in this study, you should ask your study doctor before you begin the study. If you are less than one year post-menopausal, there is the potential that you could become pregnant. If you or your partner becomes pregnant or thinks either of you may be pregnant at any time during the trial (or in the “month” following it), it is important that you tell your study doctor immediately. The trial drug may be stopped and a referral will be made to an obstetrician/gynecologist for follow-up. If you plan to become pregnant in the year following a clinical trial, speak with your study doctor.
If you have any questions about birth control, your study coordinator or study doctor will be able to answer your questions and give you advice.
Should you become pregnant, regardless of the outcome, the sponsor may ask for information on your pregnancy, even if you are withdrawn from the study. Your written consent will be obtained separately in the case that this happens.

For Men:
Since you are participating in a study that involves drugs or treatment with potential risks to a developing fetus, it is recommended that you use a condom and not father a child or donate sperm while you are taking the study drug. Also, it is recommended that you use a condom and not father a child and/or donate sperm for 90 days after you stop taking the study drug. This is because levels of the study drug may be present in the sperm and/or seminal fluid even after you stop taking the study drug. Continuing to use a condom and not donating sperm during this 90 day period may allow time for any study drug that is still present in sperm and/or seminal fluid to be eliminated from your body before you attempt to father a child or donate sperm. You are encouraged to tell your female partner(s) and/or their doctor(s) that you are participating in a clinical trial.

Correlative Studies

In this clinical trial we are investigating reduced radiation therapy in patients with HPV related cancer. The purpose of correlative studies are to study cancer in order to better understand cancer processes, to learn about interaction between cancer cells and immune system, to study patterns of cancer, health-characteristics, to identify and better understand risk factors associated with cancer, to develop predictive biomarkers or blood tests to measure presence or severity of disease and effects of treatment to be examined in future studies. For these tissues, unstained slides, plasma, sera, whole blood DNA, and cells will be collected and stored in the Investigators Laboratory.

Genetic testing:

Over the past few years, there has been an enormous increase in our knowledge about the important role that hereditary factors (genes) play in a number of diseases. Genes are made up of DNA, which may be found in your blood cells, plasma and tumor tissue. We now have some indication of how the genetic 'makeup' of an individual and an individual's tumor may influence the reaction to a specific drug, both in terms of wanted and unwanted effects. The number of genes we choose to analyze may vary from a few to a very large number of genes depending on how much knowledge is available regarding your disease and the drugs used in this study at the time of the analyses. We may also choose to study the expression of your genes.

Compared to healthy tissue, the genetic material in cancer cells is often altered. The genetic changes in the tumor may influence the reaction to a drug and determine whether the treatment of a particular patient is effective.

The genetic changes in the tumor may result in an increase or decrease in gene activity. These changes can be measured by analysis of the gene products (RNA and proteins). It is possible that analysis of genes and their products may be used in the future to identify those patients that will benefit from the treatment.

In the course of this study, alterations to genes and gene products in your cancer may be analyzed. Furthermore, your heritable genetic make-up may be studied.

A new Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

• Health insurance companies and group health plans may not request your genetic information that we get from this research.
• Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.

• Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.
All health insurance companies and group health plans must follow this law by May 21, 2010. All employers with 15 or more employees must follow this law as of November 21, 2009. Be aware that this new Federal law does **not** protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

When you provide your consent to take part in research studies, your whole blood (DNA) will be collected for genetic testing and some of your blood (plasma, serum) and tumor biopsy material will be collected for non-genetic biomarker testing (i.e., not involving DNA or RNA).

We would like your permission to obtain and store specimens (serum/ plasma, blood, tissue) collected during this study for optional research studies and future research. We would also like to know your wishes about how we might use your specimens in future research studies. While no current plans exist, you should also know that it is possible that products may someday be developed with the help of your specimens, and there are no profits from such products will be shared with you as a result of your participation in the study.

Your samples will be stored using a unique code that does not identify you by name or address. Researchers with access to your samples will not be able to identify you. The code linking the sample to your name would be stored at Mount Sinai and known only to your doctor and a limited number of research personnel at Mount Sinai.

(1) Will you allow the researchers to store your specimens to use in future research studies?

Yes_____ No_____

If no, please stop here. If yes, please continue to the next question.

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

Yes_____ No_____

(3) Do you give the researchers permission to keep the specimens 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_____

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_____"

(a) If the future research in a different area can be done without having to know that the specimens 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 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 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 may still be used. Either all links to your identity will be removed from the specimens, or an Institutional Review Board will be asked for permission to use the specimens 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 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.

(4) Do you give permission to have portions of the specimens **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_____

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.

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*:* taking prescribed medications, using birth control methods as described in the Description of What's Involved section, and attendance at study visits. At each visit, you will be asked about any symptoms you have experienced since the previous visit. And, you will be asked to provide the names of any medication you took since the last visit– whether prescribed or bought. If you are unsure about taking a particular drug, please check with your doctor first. We recommend you keep a list of drugs you are taking and bring it with you to each visit. At each visit you should also let your doctor know of any changes in your health/condition including possible drug side effects.

You must also let your doctor know immediately if there are any major changes in your health/condition between visits because your doctor may need to adjust the dosage of your medication. If you think you are having a severe allergic reaction, please seek medical attention immediately**.** If you have any concerns regarding the study, you should also contact your doctor. If you see another doctor/nurse/health care person you are encouraged to tell them you are taking part in this study and that they can contact us for information. If you are admitted to a hospital between study visits you must inform your study doctor as soon as possible.

COSTS OR PAYMENTS THAT MAY RESULT FROM PARTICIPATION:

You will not be paid for participating in this research study. You will not be reimbursed for your travel or time that may be required for study visits.
Taking part in this research study may lead to added costs to you. You or your insurance company will be responsible for the costs of all items and services during the research study, which you would have received for your condition if you were not enrolled in this research study. You or your insurance company will also be responsible for the costs of all services that occur during the research study that your physician believes are medically necessary to treat you. You or your insurance company will not be responsible for the costs of the items and services associated with this research study, which are provided to you only for research purposes and not to treat your condition.

POSSIBLE BENEFITS:

It is important to know that it is possible that you may not get any benefit from taking part in this research. However, possible benefits may be that by receiving a reduced dose of radiation therapy, or no radiation at all, you may experience fewer long-term side effects with no reduction in your cure rate.

REASONABLY FORESEEABLE RISKS AND DISCOMFORTS:

Risks/Benefit Associated with Reduced Therapy

Group 1: If you are assigned to Group 1, it means you have favorable features related to your cancer, and therefore are a candidate for observation after surgery. Current standard of care often involves radiation after your surgery. By not receiving radiotherapy or chemotherapy, you may run a higher risk of local and regional recurrence of cancer, which will lead to additional treatments with chemoradiotherapy and possibly surgery. The purpose of the study is to find a balance between treatment that is too aggressive and results in uncessessary functional disturbances and decreased quality of life, while emphasizing the ability to cure your cancer. We cannot estimate what your risk that the cancer will recur without routine radiotherapy or chemoradiotherapy after surgery, however we predict that those patients who do recur will be curable if they receive a full course of treatment and will have an excellent survival outcome equivalent to what they would have had with standard therapy. If you do not recur then you will have been spared the long term consequences of uncessessary chemotherapy and radiation. It is possible that by not having radiotherapy after surgery that your cancer may require more intensive therapy then originally planned. The purpose of the study is to establish that risk.

Group 2 and 3: If you are assigned to groups 2 and 3, it means that you have intermediate or high risk factors related to your cancer, however your chances of cure are still high as you have the more favorable viral related squamous cell carcinoma. In order to reduce long term side effects and decreased quality of life, Groups 2 and 3, will receive a lowered dose of radiation compared to current standard doses. By reducing this dose of radiotherapy or chemotherapy you may run a higher risk of local and regional recurrence which will lead to additional treatments with chemoradiotherapy and possibly surgery. We cannot estimate your risk that the cancer will recur when the radiation dose is reduced and it is possible that you can recur. The recurrence may not be curable or require intensive and damaging therapy were it to occur in the radiated areas. We have carefully selected the patients and defined the groups based on your pathologic findings and historical results in HPV oropharyngeal cancer, in order to optimize your dose of radiation to limit side effects while providing cure rates which we believe will compare to current standards. This study represents the first of many investigations into the ability to customize therapy base on knowledge gained with your surgical specimens, rather than broad statisitcal data which may not apply to you.

Risks Associated with Transoral Robotic Surgery

Transoral Robotic surgery is a minimal invasive procedure with a low rate of complications. Complications include, but are not limited to infection, bleeding, salivary fistula (abnormal passage in a salivary gland), velopharyngeal insufficiency (improper closing of the muscle in the mouth during speech) that causes speech disturbances, nasopharyngeal stenosis (narrowing of your nasal airway) as well as motor or sensory disturbances as a result of the neck dissection. There is also some risk of damage to your teeth, lips, cheeks and tongue due to the robotic retractor system used to open your

mouth during surgery. Occasionally, robotic surgery of the tongue leads to significant swelling, which may require placement of a temporary breathing tube in your neck (tracheostomy). There is also a risk of effects on your ability to swallow requiring temporary or permanent feeding tubes. Your surgeon will review specific risks relative to your case with you personally, prior to surgical intervention.

Risks Associated with Radiation therapy

Radiation therapy procedure is in itself painless. However the side effects with radiation therapy can vary depending on type, dose and organs receiving radiation.

Radiation of neck and head may cause acute side effects during treatment such as skin irritation, fatigue, mouth and throat sores, damage to the salivary glands resulting in a lack of saliva which can cause mild to severe malnutrition, swelling of soft tissues (edema), significant low levels of thyroid hormone (weigh gain, depression, constipation, brittle nails, hair loss and tiredness).

Long term side effects that can occur months to years after treatment include: dry mouth, dry eyes which may reduce patients' quality of life, diffuse scarring, decline in cognitive function (thinking, reasoning and remembering abilities) and a low risk of of developing secondary cancers related to the radiation itself.

Risks Associated with Cisplatin/Carboplatin Chemotherapy

Some common side effects of Cisplatin and Carboplatin (chemotherapy agents used in the study) are anaphylactic like reactions (Anaphylactic-like' means a severe drug reaction resulting in the following:
* Skin reactions, including hives along with itching, and flushed or pale skin (almost always present with anaphylaxis)
* Constriction of the airways and a swollen tongue or throat, which can cause wheezing and trouble breathing
* A weak and rapid pulse
* Nausea, vomiting or diarrhea
* Dizziness or fainting), damage to the kidneys, damage to the nerves, nausea and vomiting, hearing loss which is currently not treatable, hair loss, electrolyte imbalance – (various problems with body's cell operation), decrease of blood cells in bone marrow, decrease in blood platelet count, decrease in white blood cell count, decrease in bone marrow effectiveness, changes in how food tastes ,frequent diarrhea, constipation, stomach pain, loss of appetite, joint pain, cough, numbness, tingling or burning sensation in the extremities, extreme fatigue and allergic reactions. It should be noted that Cisplatin and Carboplatin are agents used in the current standard treatment of head and neck squamous cell carcinoma.

Risks Associated with Radiological Scans and X-Rays:

You will be exposed to radiation from the CT scans and PET scans that are done in the study. In the first year of the study you will have 3 CTs of the neck (or MRIs instead if possible) and up to 3 or 4 PET scans.

You will have a number of radiation procedures or examinations that are part of the regular care for your condition and you would have them whether or not you participate in this research. You will not be exposed to any additional radiation because you are participating in this research.

The study team will discuss radiation exposure with you.

The study team will always try to use tests that involve the lowest amount of radiation exposure possible. The radiation from the tests and treatments in this study would be in addition to any radiation you might receive from other medical tests or treatments. If you are going to have any other tests or treatments that involve radiation, please inform the study team. We can compare this possible extra cancer risk to other risks (over a lifetime) that everyone is subject to in everyday life. For example, the chances of a person dying of cancer with no extra radiation exposure are about one in 4. The chances of dying in a car crash are about one in 82, and the chances of being killed by a car while crossing the street are about one in 730.

In the long term, over many years, there is a very low risk of developing a new cancer as a result of the radiological evaluation and treatment for your cancer.

There is a small risk with using the contrast agent that is injected into a vein during the scan. It may worsen kidney function in people who already have decreased kidney function. Therefore, we will monitor your kidney function closely while you participate in this study. If there is any change in your kidney function, we may have to remove you from the study.

Uncommonly, some people have allergic reactions (such as hives and itching) to the contrast agent. Serious reactions (for example, drop in blood pressure, difficulty breathing or severe allergic reaction and death) are rare.

When having an MRI (Magnetic Resonance Imaging) scan, you will lie still on a table that slides into a tunnel slightly wider than your body. People who feel uncomfortable in confined spaces (claustrophobia) may feel uncomfortable in the narrow cylinder. If you feel uncomfortable in confined spaces, please tell your doctor. Your doctor may give you a medication to make you feel more comfortable. As images are taken, a loud banging noise will be produced. Earplugs or headphones will be available if needed. The MRI can be stopped at any time at your request, but the scan may not be complete.

Reproductive Risks:

The drugs used in this research study may affect a fetus. You should not become pregnant or father a baby while on this research study. Please read the acceptable methods of birth control found under the Description of What's Involved section of this document. Privacy risks**:** There always exists the potential for loss of private information; however, there are procedures in place to minimize this risk.

Unknown Risks: In addition to these risks, this research may hurt you in ways that are not known. The unknown risks might be minor or might be major (death).

Risks of Blood Draws

The risks of drawing blood include bleeding, bruising, infection, clotting within the vein (thrombophlebitis),

Risks of examination under anesthesia (EUA), endoscopy and biopsy: In some cases you will require a general anesthetic and biopsy in order to accurately diagnose or stage your cancer, or to determine if you have a recurrence. The risks of anesthesia include drug reactions, cardiac arrest, stroke, allergic reactions to medication, coma, and death. Endoscopy involves using cameras and scopes to evaluate your tumor. The risks for endoscopy involve damage to the lips, tongue, cheek, mouth, teeth. If biopsy is performed, bleeding may occur at the biopsy site. Some pain and discomfort is associated with biopsy procedures and you may have temporary difficulty speaking and swallowing immediately after the procedure.

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.

We will tell you about new information or changes in the study that may affect your health or willingness to continue in the study.

Instead of being in this research study, your choices may include:

- Having treatment or care for your cancer without being in a research study. Receiving high dose radiation therapy with or without chemotherapy. Radiation therapy is standard of care available for this study. Side effects are described earlier in risk section. Chances of recurrence are increased if receiving radiation therapy alone. If you are a candidate for

Transoral Robotic Surgery (TORS) your surgeon will discuss this with you. It should be noted that you do not need to participate in this study in order to be a candidate for robotic surgery.

- Taxotere, Cisplatin and Fluorouracil are the standard of care chemotherapy drugs. You may receive them with or without radiation therapy. You can discuss with your doctor what is good for you. The risks of those therapies might include nausea, vomiting, decrease in cells providing immunity increasing risk of infection, bleeding. Please see risk section for more detail.
- Taking part in a different study with another research drug. Your study doctor for that study will discuss the benefits and risks of the drug that is being offered.
- Having no treatment. This may or may not worsen your existing condition.

Talk to your doctor about your choices before you decide if you will take part in this study.

IN CASE OF INJURY DURING THIS RESEARCH STUDY:

If you are injured or made sick from taking part in this research study, medical care will be provided. Generally, this care will be billed to you or your insurance in the ordinary manner and you will be responsible for all treatment costs not covered by your insurance, including deductibles, co-payments and coinsurance. This does not prevent you from seeking payment for injury related to malpractice or negligence. Contact the investigator for more information.

ENDING PARTICIPATION IN THE RESEARCH STUDY:

You may stop taking part in this research study at any time without any penalty. This will not affect your ability to receive medical care at any of the Mount Sinai Health System hospitals or to receive any benefits to which you are otherwise entitled.

If you decide to stop being in the research study please contact the Principal Investigator or the research staff. At that point tests needed at the end of the study could be performed.

If you stop being in the research study, already collected information may not be removed from the research study database and will continue to be used to complete the research analysis. You may be asked whether the investigator can collect information from your routine medical care. If you agree, this data will be handled the same as research data.

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 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 phone number *(212) 844-8775*

If you experience an emergency during your participation in this research, call 911; go to the emergency room and contact Principal Investigator at phone number *(212) 844-8775*

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 the Icahn School of Medicine at Mount Sinai at telephone number (212) 824-8200 during standard work hours for any of the reasons listed below. This office will direct your call to the right person within the Mount Sinai Health System::

- 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.

DISCLOSURE OF FINANCIAL INTERESTS:

Sometimes, physicians/researchers receive payments for consulting or similar work performed for industry. Effective September 2014 Mount Sinai reviews only payments to an individual totaling more than $5,000 a year per entity when determining potential conflicts of interest. If you have questions regarding industry relationships, we encourage you to talk your physician/researcher or visit our website at http://icahn.mssm.edu/ where Mount Sinai publicly discloses the industry relationships of our faculty.

None.

MAINTAINING CONFIDENTIALITY – HIPAA AUTHORIZATION:

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.

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

As part of this research project, the research team at the hospital(s) involved in the research will collect your name, address and telephone/fax numbers.

The researchers will also get information from your medical record which will come from Mount Sinai Health System and your private doctor.

During the study the researchers will gather information by:

- Taking a medical history (includes current and past medications or therapies, illnesses, conditions or symptoms, family medical history, allergies, etc.)
- doing a physical examination that generally also includes blood pressure reading, heart rate, breathing rate and temperature
- Completing the tests, procedures, questionnaires and interviews explained in the description section of this consent.
- Reviewing mental health records
- Reviewing alcohol and/or substance abuse records
- 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 in collaboration with others in the Mount Sinai Health System..

The research team and other authorized members of the Mount Sinai Health System ("Mount Sinai") workforce may use and share your information to ensure that the research meets legal, institutional or accreditation requirements. For example, the Icahn School of Medicine at Mount Sinai and the Mount Sinai Hospital 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.)

- Other collaborating research center(s) and their associated research/clinical staff who are working with the investigators on this project: TBD
- A Data Safety Monitoring Board or other committee that will monitor the study on an ongoing basis for safety.
- The United States Food and Drug Administration
- The United States Department of Health and Human Services and the Office of Human Research Protection.

In all disclosures outside of Mount Sinai, you will not be identified by name, address and telephone number 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, may 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, when applicable, 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 have access to your medical record and any study information that is part of that record. 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 Hospital's Notice of Privacy Practices that contains more information about how The Hospital 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.

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.

Signature Block for Capable Adult

Your signature below documents your permission to take part in this research and to the use and disclosure of your protected health information. A signed and dated copy will be given to you.

Signature of subject	Date

Printed name of subject	Time

Person Explaining Study and Obtaining Consent

Signature of person obtaining consent	Date
Printed name of person obtaining consent	Time

Witness Section: For use when, a witness is required to observe the consent process document below (for example, subject is illiterate or visually impaired, or this accompanies a short form consent) :

My signature below documents that the information in the consent document and any other written information was accurately explained to, and apparently understood by, the subject, and the subject freely gave that consent.

Signature of witness to consent process	*Date*
Printed name of person witnessing consent process	*Time*