RADIATION THERAPY ONCOLOGY GROUP

RTOG 0514

ESTABLISHMENT OF A HEAD AND NECK CANCER TISSUE/SPECIMEN REPOSITORY

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RADIATION THERAPY ONCOLOGY GROUP

RTOG 0514
ESTABLISHMENT OF A HEAD AND NECK CANCER TISSUE/SPECIMEN REPOSITORY

SCHEMA (4/14/08)

Registration—Step 1: (See Section 5.1)
Patient who is potentially eligible for an active RTOG treatment study signs consent for and is registered on RTOG 0514.

Patient will undergo or has undergone biopsy or surgical resection of head and neck tumor or pre-malignant lesions.

Patient specimen from biopsy or surgery (collected prior to initiation of treatment) is submitted according to RTOG 0514, Section 10.0. Optional specimens (see Section 10.2) also are submitted. Note: If the patient is found not to have head and neck cancer, specimens should not be submitted.

Registration—Step 2: (See Section 5.2)
A) Site informs RTOG Headquarters that the patient is registered on an active RTOG study and provides the study number and patient case number. Site submits case report forms according to the RTOG study on which the patient is registered.

OR

B) Site informs RTOG Headquarters that patient is not registered on an active RTOG study, and responds to questions on page 2 of the Eligibility Checklist.

When the RTOG Biospecimen Resource confirms receipt of appropriate specimens and the site has completed Step 2 of Registration, the site is reimbursed and case credit is assigned.

Patient Population: (See Section 3.0 for Eligibility) [4/4/06]
Patients must have a suspected or confirmed diagnosis of head and neck cancer. Patients with biopsy proven recurrent cancer at the primary site also are eligible. Patients must be ≥ 18 years of age.

Required Sample Size: N/A, Ongoing Prospective Tissue/Specimen Repository Research Study
RTOG Institution # __________

RTOG 0514

ELIGIBILITY CHECKLIST—Step 1 (4/14/08)

Case # __________

(page 1 of 2)

(Y) 1. Does the patient have a suspected or confirmed diagnosis of head and neck cancer?

(Y) 2. Is the patient potentially eligible for an active RTOG treatment study?

(N/Y) 3. Does the patient have biopsy proven recurrent cancer?

(Y) If yes, is the patient potentially eligible for an RTOG treatment study for patients with recurrent disease or has the patient failed on an RTOG treatment study which collects specimens at the time of recurrence?

(Y) 4. Is the patient’s Zubrod performance status 0-1?

(Y) 5. Is the patient ≥ 18 years of age?

(Y) 6. Was an informed consent signed for RTOG 0514 prior to submission of specimens?

The following questions will be asked at Study Registration:

1. Name of institutional person registering this case?

(Y) 2. Has the Eligibility Checklist (above) been completed?

(Y) 3. Is the patient eligible for this study?

4. Date the study-specific Consent Form was signed? (must be prior to study entry)

5. Patient’s Initials (First Middle Last) [May 2003; If no middle initial, use hyphen]

6. Verifying Physician

7. Patient’s ID Number

8. Date of Birth

9. Race

10. Ethnic Category (Hispanic or Latino; Not Hispanic or Latino; Unknown)

11. Gender

12. Patient’s Country of Residence

13. Zip Code (U.S. Residents)

14. Patient’s Insurance Status

15. Will any component of the patient’s care be given at a military or VA facility?

RTOG 0514
ELIGIBILITY CHECKLIST—Step 1 (8/28/06)

16. Registration Date (Step 1)

17. Has the patient consented to collection and storage of normal tissue from the cheek, blood, and/or saliva?

18. Has the patient consented to contact for future research?

The Eligibility Checklist must be completed in its entirety prior to web registration. The completed, signed, and dated checklist used at study entry must be retained in the patient’s study file and will be evaluated during an institutional NCI/RTOG audit.

Completed by ___________________________ Date _______________________
See Section 5.2 for details of Step 2 of Registration.

1. Name of institutional person registering this case?

2. Patient able to go on to Step 2?

3. Reason patient cannot continue to Step 2:
   - Progression of disease;
   - Patient refusal;
   - Physician preference;
   - Death;
   - Tissue not submitted;
   - Not head and neck cancer;
   - Other: _______________________

4. Patient’s Initials (First Middle Last) [May 2003; If no middle initial, use hyphen]

5. Verifying Physician

6. Patient ID number

7. Registration Date (Step 2)

8. Has the patient been registered on an active RTOG study?
   - If yes, specify the study number and patient case number.


10. Specify patient’s stage of disease.

Completed by ___________________________  Date ___________________________
1.0 INTRODUCTION (4/14/08)

1.1 Head and neck cancer continues to cause significant morbidity and mortality in the patients who develop these neoplasms. The methods of diagnosing incipient tumors and for predicting biologic behavior in pre-cancerous and invasive lesions remain substantially unchanged. Advances in head and neck tumor and pre-malignant lesion research have been made slowly. The application of advanced molecular biologic principles to this field should provide new information that may have a significant impact in the clinical setting relative to predicting tumor behavior and prevention. The identification of molecules associated with tumor invasion, treatment efficacy, and which may serve as prognostic markers is critical to the development of novel treatment strategies and are important to improve disease outcome. The proposed RTOG Head and Neck Cancer Tissue/Specimen Repository will maintain the resource material required for research studies in human head and neck cancers.

1.2 The RTOG Biospecimen Resource

The RTOG Biospecimen Resource at the University of California San Francisco acquires and maintains high-quality specimens from RTOG trials. Tissue from each block is preserved through careful block storage and processing. The RTOG encourages participants in protocol studies to consent to the banking of their tissue. The RTOG Biospecimen Resource provides tissue specimens to investigators for translational research studies. Translational research studies integrate the newest research findings into current protocols to investigate important biologic questions.

This study proposes an organizational structure that will support the collection, storage, and cataloging of head and neck tumor tissues and other specimens. The RTOG Biospecimen Resource will house high-quality specimens from patients with head and neck cancer enrolled on this trial or on other RTOG active studies. The specimens collected will provide investigators with essential materials for planned or future investigations. Such investigations will be separately considered as research protocols and will link results of specimen investigations with demographic, treatment, and outcome data provided by RTOG Headquarters.

1.3 Future Use of Tissue/Specimens (4/14/08)

Specimens collected on patients who are subsequently enrolled on an RTOG treatment study and for which follow-up data will be available (expected to be the majority of patients) will be used to address current scientific questions. Specimens collected on patients who are not subsequently enrolled on an RTOG treatment study (not ideal and expected to be a minority of patients) will be retained to address emerging scientific questions or assays. These dual objectives are important in view of rapid progress in biology and the inability to predict what questions will arise in the near future.

Tissue/specimens will be provided to collaborating investigators according to the written RTOG Biospecimen Resource guidelines for specimen use. Investigators interested in obtaining tissue/specimens must submit a full usage proposal and application request for approval by a designated committee (Appendix VI). Tissue/specimens only will be released after approval by the tissue banking committee in consultation with correlative science members according to strict RTOG Biospecimen Resource procedures. The investigator must return any tissue/specimens remaining after a research study is complete to the Biospecimen Resource. The tissue/specimens will be kept until expended or until requested to be returned to the donor institution. See Section 13.0 for further details of future studies.

2.0 OBJECTIVES (4/14/08)

2.1 The aim of this study is to establish a Radiation Therapy Oncology Group Head and Neck Cancer Tissue/Specimen Repository to serve as a resource for current and future scientific studies. The RTOG Biospecimen Resource, under the direction of Fred Waldman, MD, PhD will maintain these materials for future utilization. In order for institutions to submit a patient’s specimens, the patient must be enrolled on this study, RTOG 0514, or be participating in an active RTOG treatment study. Multiple RTOG institutions will be the sources for the tissue and specimen repository. The Head and Neck Tissue/Specimen Repository will:

2.1.1 Collect, annotate, and store fresh frozen specimens of normal squamous mucosa, tumors, and pre-malignant lesions of the upper aerodigestive tract for biological investigation;

2.1.2 Collect, process, and store paraffin-embedded tissue sections from head and neck pre-malignant and malignant lesions;
2.1.3 Collect, process, and store serum, plasma and isolate lymphocytes from blood drawn from patients with head and neck cancer;
2.1.4 Collect, process, and preserve buccal scrapings and saliva samples from patients with head and neck cancer;
2.1.5 Establish a database to link materials acquisition, pathologic, and clinical information on patients who participate in protocols;
2.2 To utilize the Radiation Therapy Oncology Group clinical database to perform clinical-pathological correlation with the results of current and future scientific studies;
2.3 To test new hypotheses as they emerge.

3.0 PATIENT SELECTION
3.1 Conditions for Patient Eligibility (4/14/08)
3.1.1 Patients must have a suspected or confirmed diagnosis of head and neck cancer and must potentially be eligible for an active RTOG treatment study.
3.1.2 Patients with biopsy proven recurrent cancer at the primary site also are eligible if they are potentially eligible for an RTOG treatment study for patients with recurrent disease or if they fail on an RTOG treatment study which collects specimens at the time of recurrence.
3.1.3 Zubrod Performance Status 0-1;
3.1.4 Age ≥ 18;
3.1.5 Patient must sign a study specific informed consent for RTOG 0514 prior to submission of specimens.
3.2 Conditions for Patient Ineligibility
Not applicable for this study.

4.0 ADDITIONAL PRETREATMENT EVALUATIONS/MANAGEMENT
Not applicable to this study.

5.0 REGISTRATION PROCEDURES (11/1/05)
5.1 Registration—Step 1
5.1.1 Online Registration
Patients can be registered only after eligibility criteria are met.

Institutions must have an RTOG user name and password to register patients on the RTOG web site. To get a user name and password:
- The Investigator must have completed Human Subjects Training and been issued a certificate (Training is available via http://69.5.4.33/c01).
- The institution must complete the Password Authorization Form at http://www.rtog.org/members/webreg.html (bottom right corner of the screen), and fax it to 215-923-1737. RTOG Headquarters requires 3-4 days to process requests and issue user names/passwords to institutions.

An institution can complete Step 1 of the RTOG 0514 registration by logging onto the RTOG web site (http://www.rtog.org), going to "Data Center Login" and selecting the link for new patient registrations. The system triggers a program to verify that all regulatory requirements (OHRP assurance, IRB approval) have been met by the institution. The registration screens begin by asking for the date on which the Eligibility Checklist (page 1 of the Checklist) was completed, the identification of the person who completed the checklist, whether the patient was found to be eligible on the basis of the checklist, and the date the study-specific informed consent form was signed.

Once the system has verified that the patient is eligible and that the institution has met regulatory requirements, it assigns a patient-specific case number. The system then moves to a screen that confirms that the patient has been successfully enrolled. This screen can be printed so that the registering site will have a copy of the registration for the patient's record. Two e-mails are generated and sent to the registering site: the Confirmation of Eligibility and the patient-specific calendar. The system creates a case file in the study's database at the
DMC (Data Management Center) and generates a data submission calendar listing all data forms, images, and reports and the dates on which they are due.

If the patient is ineligible or the institution has not met regulatory requirements, the system switches to a screen that includes a brief explanation for the failure to register the patient. This screen can be printed.

Institutions can contact RTOG web support at websupport@phila.acr.org for assistance with web registration.

In the event that the RTOG web registration site is not accessible, participating sites can register a patient by calling RTOG Headquarters at (215) 574-3191, Monday through Friday, 8:30 a.m. to 5:00 p.m. ET. The Eligibility Checklist must be completed in its entirety prior to calling RTOG. The registrar will ask for the site’s user name and password. This information is required to assure that mechanisms usually triggered by web registration (e.g., drug shipment, confirmation of registration, and patient-specific calendar) will occur.

The completed, signed, and dated Checklist used at study entry must be retained in the patient’s study file and will be evaluated during an institutional NCI/RTOG audit.

5.2 Registration—Step 2 (4/14/08)
5.2.1 Online Registration
All institutions must complete Step 2 to inform RTOG Headquarters whether or not the patient registered on an active RTOG study. Note: RTOG 0514 was designed to collect specimens from patients who are potentially eligible for and who will be registered on an active RTOG study. It is anticipated that only a small minority of patients will not be registered on an active study.

An institution completes step 2 of registration by logging onto the RTOG web site (http://www.rtog.org), going to "Data Center Login" and selecting the link for new patient registrations. The registration screens begin by asking for the date on which the Eligibility Checklist was completed (page 2 of the Checklist) and the identification of the person who completed the checklist.

Note: Question #2 on the Eligibility Checklist-Step 2 asks if the patient met the eligibility requirements for tissue submission. If questions 1-6 on the Eligibility Checklist-Step 1 were answered “yes” (the patient had head and neck cancer confirmed by histology; the patient is potentially eligible for an active RTOG treatment study; the patient’s Zubrod is 0-1, the patient is ≥ 18 years old, and the patient signed an informed consent for RTOG 0514 prior to submission of specimens), then sites will answer “yes” to question 2, Step 2. If the patient did not meet the criteria (questions 1-6, Step 1), then sites will answer “no” and indicate the reason(s) why tissue was not submitted.

When the RTOG Biospecimen Resource confirms receipt of appropriate specimens and the site has completed Step 2 of registration, case credit will be assigned.

In the event that the RTOG web registration site is not accessible, participating sites can register a patient by calling RTOG Headquarters at (215) 574-3191, Monday through Friday, 8:30 a.m. to 5:00 p.m. ET. The Eligibility Checklist must be completed in its entirety prior to calling RTOG. The registrar will ask for the site’s user name and password. This information is required to assure that mechanisms usually triggered by web registration (e.g., drug shipment, confirmation of registration, and patient-specific calendar) will occur.

The completed, signed, and dated Checklist used at study entry must be retained in the patient’s study file and will be evaluated during an institutional NCI/RTOG audit.

6.0 RADIATION THERAPY
Not applicable if the patient is enrolled only on RTOG 0514. If the patient is enrolled on an active RTOG treatment study involving radiation therapy, the radiation therapy will be specified in that protocol.
7.0 DRUG THERAPY
Not applicable if the patient is enrolled only on RTOG 0514. If the patient is enrolled on an active RTOG treatment study involving drug therapy, the drug therapy will be specified in that protocol.

8.0 SURGERY (8/28/06)
Instructions for completing the surgery form (S1) are provided in Section 12.0. Guidelines for collection of each type of specimen are provided in Section 10.0. Also refer to specific studies for protocol-specific instructions.

9.0 OTHER THERAPY
Not applicable to this study.

10.0 TISSUE/SPECIMEN SUBMISSION (4/14/08)
For patients who have consented to submission of tissue/specimens for RTOG 0514 or an active RTOG treatment study (For RTOG 0514, see Appendix I)

10.1 Required Specimens (4/14/08)
The following specimens are required for each patient enrolled on 0514:

<table>
<thead>
<tr>
<th>Required Specimens: Collected prior to initiation of treatment</th>
<th>Per case reimbursement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fresh, flash frozen tumor or premalignant leisional tissue</td>
<td>$300 for the first sample, $100 for second sample Å</td>
</tr>
<tr>
<td>Fresh, flash frozen grossly normal tissue</td>
<td>$300 Å</td>
</tr>
<tr>
<td>If unable to submit fresh, flash frozen tissue, sites should submit a paraffin-embedded tissue block of tumor</td>
<td>$200 Å</td>
</tr>
<tr>
<td>Nodal tissue: Fresh and paraffin-embedded block</td>
<td>$100 Å</td>
</tr>
</tbody>
</table>

Å Institutions submitting the required fresh, flash frozen specimens (tumor or premalignant tissue and normal tissue) also will be assigned 1.0 case credit.

B Institutions submitting fresh, flash frozen normal tissue and a paraffin-embedded tissue block of tumor (versus fresh, flash frozen tumor tissue) also will be assigned 0.5 case credit.

C For patients undergoing lymphadenectomy as part of their primary surgery resection

10.2 Optional Specimens (8/28/06)
Sites submitting the required specimens also may submit the following specimens for each patient, if available, but these are not required. Note: Sites should not submit optional specimens without the required specimens or in place of the required specimens.

<table>
<thead>
<tr>
<th>Optional Specimens: Collected prior to initiation of treatment</th>
<th>Per case reimbursement, if required specimens are submitted</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-30 cc’s of anticoagulated blood (EDTA) [purple top]—Spun and processed for lymphocytes (buffy coat)</td>
<td>$50</td>
</tr>
<tr>
<td>5-10 cc’s of whole blood (red-top)—Spun and processed for serum</td>
<td>$50</td>
</tr>
<tr>
<td>1 saliva sample</td>
<td>$50</td>
</tr>
<tr>
<td>Buccal scrapings</td>
<td>$50</td>
</tr>
</tbody>
</table>

A collection kit including a shipping container, cryovials, and forms is available through the RTOG Biospecimen Resource to participating institutions upon request (see Appendix IV).

10.3 Tissue: Fresh and Fixed
10.3.1 Fresh tissue from patients suspected of having head and neck cancer to be confirmed by biopsy or those patients with or pre-malignant lesions (i.e., eligible for an RTOG
chemoprevention trial) will be harvested by the designated surgeon at each participating institution and confirmed by frozen section. Harvest must not interfere with margin assessment or with patient care priorities. Note: If frozen section confirms that the patient does not have head and neck cancer, specimens should not be submitted.

10.3.2 Tissue Harvest
Tissue will be obtained in two ways: 1) At the time of diagnostic examination/biopsy where cup forceps will be used to harvest tissue from the primary tumor or pre-malignant lesion; 2) At the time of resection when the specimen has been removed from the patient, transported to the institution’s pathology department, and harvested as soon as possible.

10.3.3 Surgery
If the patient is enrolled on an active RTOG treatment study involving surgery or requiring a biopsy, the operation will be specified in that protocol. The surgical procedures (including biopsy collection) described below will be performed according to the established standard of care or per protocol-specific guidelines. At the time of diagnostic biopsy, when extirpative surgery is not performed, or at the time of surgery, the following will be collected:

10.3.3.1 Tumor or Premalignant Lesion: Two 5 mm³ tumor samples will be obtained from the center of the tumor (two large cupped forceps of tumor tissue) OR two 5 mm³ samples of premalignant lesion.

10.3.3.2 Grossly Normal Mucosa: One sample of grossly normal mucosa will be harvested from the uninvolved squamous mucosa by a 5 mm³ dermatologic punch prior to initiation of treatment.

10.3.3.3 Metastatic Lymph Node: For patients undergoing lymphadenectomy as part of their primary surgical resection, a portion of a metastatic lymph node (if present) should be submitted.

10.3.3.4 Uninvolved Lymph Node: For patients undergoing lymphadenectomy as part of their primary surgical resection, a portion of a histologically normal lymph node should be submitted.

10.3.4 Pathology
Properly labeled tissue specimens are to be received fresh (without fixative) in the participating institution’s dissection room immediately after removal from the patient. The pathologist responsible for the study must be alerted to be present in the dissection room to handle the specimen.

10.3.5 Fresh Tissue: Collection Instructions
Fresh tissue should be harvested directly by punch biopsy or from the surgical specimen and snap frozen in liquid nitrogen without preservatives. Tissue samples must be frozen immediately after receipt in order to minimize deterioration of RNA and labile protein.

10.3.5.1 Tumor or Premalignant Lesion: One 5 mm³ sample of tumor or premalignant lesion will be snap frozen. One 5 mm³ sample of tumor or premalignant lesion will be bisected. One half of the bisected sample will be snap frozen.

10.3.5.2 Grossly Normal Mucosa: The entire sample will be snap frozen.

10.3.5.3 Metastatic Lymph Node: The portion of the lymph node with obvious metastatic tumor will be bisected. One half of the bisected specimen will be snap frozen.

10.3.5.4 Uninvolved Lymph Node: The portion of the uninvolved lymph node also will be bisected and as in the lymph node with tumor, one half will be snap frozen.

10.3.6 Fixed Tissue: Collection Instructions
Fixed tissue should be harvested by biopsy or from the surgical specimen and placed in cassette for formalin-fixation and paraffin embedding, with the specimen oriented on edge; a paraffin-embedded tissue block of the tumor will be submitted.

10.3.6.1 Tumor or Premalignant Lesion: The remaining half of the bisected sample will be placed in formalin for paraffin embedding. The sample will be oriented on edge in the paraffin-embedded block.

10.3.6.2 Metastatic Lymph Node: The remaining half of the specimen will be fixed in formalin and submitted as a paraffin-embedded block, which will be used for histological evaluation.

10.3.6.3 Uninvolved Lymph Node: The remaining half will be fixed in formalin and submitted as a paraffin-embedded block.

10.3.7 Fresh and Fixed Tissue Summary

<table>
<thead>
<tr>
<th>Surgical</th>
<th>Pathologic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grossly normal mucosa from uninvolved squamous mucosa</td>
<td>Harvest by 5 mm³ punch into single cryovial</td>
</tr>
<tr>
<td>One 5 mm³ of tumor or premalignant lesion</td>
<td>Harvest by punch biopsy or from center of tumor</td>
</tr>
</tbody>
</table>
## Fixed Tissue

<table>
<thead>
<tr>
<th>Surgical</th>
<th>Pathologic</th>
</tr>
</thead>
<tbody>
<tr>
<td>At least 2.5 mm$^3$ of tumor or premalignant lesion</td>
<td>Half of a bisected specimen (the other half is fixed; see table below); put into separate cryovial</td>
</tr>
<tr>
<td>*Metastatic lymph node</td>
<td>Half of a bisected specimen (the other half is fixed.)</td>
</tr>
<tr>
<td>*Uninvolved lymph node</td>
<td>Half of a bisected specimen (the other half is fixed.)</td>
</tr>
</tbody>
</table>

*For patients undergoing lymphadenectomy as part of their primary surgery resection*

**Paraffin Blocks:** All specimens should be fixed in 10% buffered formalin. The method of fixation is dependent on feasibility at the local institution. Immersion of the serially sliced sections in formalin is acceptable provided that slices are no more than 1 cm in thickness. Specimens are to be placed in adequate-sized containers with a 10-fold excess of fresh (non-bloody formalin). Whatever method is chosen, good penetration of tissue by fixative is essential. After overnight fixation, the specimen is to be carefully dissected, and the tissue blocks are to be removed from the specimen for embedding in paraffin, orienting the specimen on edge.

### 10.4 Optional Specimens: Peripheral Blood, Saliva, Buccal Scrapings (8/28/06)

Peripheral blood, saliva and buccal scrapings will be collected as deemed appropriate by the patient’s physician and should be collected after patient consent and prior to biopsy/surgery or treatment. All specimens will be processed according to written protocols and stored at the appropriate temperatures until transported to the RTOG Biospecimen Resource. In addition, specimens will be labeled with the date and time of collection. **Note:** Sites should not submit optional specimens without the required specimens or in place of the required specimens.

#### 10.4.1 Peripheral Blood Samples

The following peripheral blood will be collected:

- Two or three tubes (total of 20-30 cc’s) of anticoagulated blood (EDTA) [purple top] will be obtained for lymphocyte isolation.
- Five to ten cc’s of whole blood (red-top tube) will be collected for serum.

##### 10.4.1.1 Processing: Purple top tube for buffy coat

- Using three (3) 1 mL cryovials, label them with the RTOG study, 0514, and patient’s case number, procedure date, and clearly mark cryovials “buffy coat”.
- Spin EDTA (purple top) tube in a standard clinical centrifuge at ~2500 RPM at 4°C Celsius for 10 minutes. **Centrifuge within one hour of collection.**
- If the interval between specimen collection and processing is anticipated to be greater than one hour, keep specimen on ice until centrifuging is done.
Remove plasma close to the buffy coat and set plasma aside (can be used to send EDTA plasma samples – see above instructions).

Remove the buffy coat cells carefully and place into the 1 mL cryovials labeled “buffy coat” (it is okay if a few packed red cells are inadvertently collected in the process).

Place cryovials into biohazard bag.

Label bag with RTOG study, 0514, and patient’s case number.

Store serum frozen at –80° Celsius until ready to ship.

10.4.1.2 Processing: Red top tube for serum

- Using four (4) 1 mL cryovials, label them with the RTOG study, 0514, and patient’s case number, procedure date, and clearly mark cryovials “serum”.
- Allow one 5 mL red top tube to clot for 30 minutes at room temperature.
- Spin red-topped tube in a standard clinical centrifuge at ~2500 RPM at 4° Celsius for 10 minutes.
- Aliquot serum into the four 1 mL cryovials labeled with the RTOG study and case numbers, procedure date, and marked “serum”.
- Place cryovials into biohazard bag.
- Label bag with the RTOG study, 0514, and patient’s case number.
- Store serum frozen at –80° Celsius until ready to ship.

10.4.3 Saliva

The patient should rinse his/her mouth with water several times prior to collection. The patient should allow saliva to flow in the mouth and should empty saliva by spitting into an empty airtight screw-top container. The specimen will be divided and a minimum of 1 mL will be placed into the screw-top container filled with Saccomanno’s fixative or an equivalent alcohol-based fixative. Once collected and placed into fixative, ship at room temperature.

10.4.4 Buccal Scrapings

A simple brushing or swab of the oral mucosa will serve to collect the specimens. The swab with the specimen will then be placed into a cup with RNAlater solution. The specimen should then be stored frozen for shipment. RNAlater can be obtained from the Biospecimen Resource upon request; see RTOG Biospecimen Resource contact information in Appendix IV.

10.5 Documentation of Tissue/Specimen Submission (4/4/06)

Sites must submit the following documentation with all tissue/specimens:

10.5.1 A Pathology Report documenting that the submitted tissue specimen contains tumor. The report must include the RTOG protocol number and patient’s case number. The patient’s name and/or other identifying information should be removed from the report. The surgical pathology numbers and information must NOT be removed from the report. In addition, the pathology report must include the following:

- Tumor localization;
- Maximum size of the tumor;
- Histologic type and grade;
- Percent of tumor necrosis;
- Site from which normal tissue was collected (as concisely as possible).

10.5.2 A Specimen Transmittal Form clearly stating that tissue is being submitted for the RTOG Biospecimen Resource for translational research. If serum is collected: the Specimen Transmittal Form must document the date of collection of the serum and method of storage, for example, stored at -20° C. The Specimen Transmittal Form must always include the RTOG protocol number and patient’s case number. Note: Institutions must clearly indicate on the form the “Type” of specimen (e.g., pre-treatment or post-treatment) and collection time frame (“Procedure Date”).

10.5.3 (4/14/08) Submit specimens as follows:

Mailing Address: For Non-frozen Specimens Only
RTOG Biospecimen Resource
University of California San Francisco
Campus Box 1800
1657 Scott Street, Room 223
San Francisco, CA 94143-1800

Courier Address (FedEx, DHL, etc.): For Frozen Specimens
RTOG Biospecimen Resource
University of California San Francisco
10.6 Pathology Review of Specimens (4/14/08)

10.6.1 Pathology review will be done on three levels:

1. All specimens submitted to the RTOG Biospecimen Resource are reviewed when received by Richard Jordan, DDS, PhD, FRCPATH, the Head & Neck Tissue Repository Director, or his associate pathologists to assure that tumor tissue is present in the submitted specimen. The squamous histology of the sample also will be confirmed in this review. Unusual tumor types will be separately reviewed as described below.

2. All rare and unusual head and neck tumor specimens will be reviewed by Adel El-Naggar, MD, PhD, the Head & Neck Tissue Repository Co-Director.

10.7 Reimbursement (4/4/06)

RTOG will reimburse submitting institutions $300 per case for the first sample of fresh or flash frozen tumor/pre-malignant lesional tissue and for 1 sample of fresh or flash frozen grossly normal tissue; $100 for the second sample of fresh or flash frozen tumor/pre-malignant lesion; $200 per case for a block or core of material; $100 per case for nodal tissue; $50 per case for serum, plasma, saliva, or buccal scraping. It is strongly recommended that a significant percentage of the per-case reimbursement in this study be earmarked for the surgeon who harvests and for the pathologist who processes the specimens.

After confirmation from the RTOG Biospecimen Resource that required, viable materials have been received (i.e. ≥ 80% viable cells [non-necrotic or crushed specimens] in non-cancerous and cancerous samples), RTOG Administration will prepare the proper paperwork and send a check to the institution. Pathology payment cycles are run twice a year in January and July and will appear on the institution’s summary report with the institution’s regular case reimbursement.

10.8 Confidentiality/Storage (8/28/06)

(See the RTOG Patient Tissue Consent Frequently Asked Questions, http://www.rtog.org/tissuebank/tissuefaq.html for further details.)

10.8.1 Upon receipt, the specimen is labeled with the RTOG protocol number and the patient’s case number only. The RTOG Biospecimen Resource database only includes the following information: the number of specimens received, pathology and block numbers, the date the specimens were collected, documentation of material sent to a qualified investigator, type of material sent, and the date the specimens were sent to the investigator.

10.8.2 Specimens for tissue banking will be stored for an indefinite period of time. Specimens for future translational research components of this protocol will be retained until the study is terminated or until the specimens are completely consumed during research. If at any time the patient withdraws consent to store and use specimens, tissue(s) or materials containing tissue will be returned to the submitting institution and serum, lymphocytes, saliva, and buccal scrapings will be discarded/destroyed.

11.0 PATIENT ASSESSMENTS

Not applicable to this study.

12.0 DATA COLLECTION

12.1 Summary of Data Submission to RTOG Headquarters

Data should be submitted to:

RTOG Headquarters
1818 Market Street, Suite 1600
Philadelphia, PA 19103

Patients will be identified by initials only (first middle last); if there is no middle initial, a hyphen will be used (first-last). Last names with apostrophes will be identified by the first letter of the last name.
12.2 Summary of Data Submission to the RTOG Biospecimen Resource (4/14/08)
Data should be submitted to:

RTOG Biospecimen Resource
University of California San Francisco
Campus Box 1800
1657 Scott Street, Room 223
San Francisco, CA 94143-1800
415-476-RTOG (7864)/FAX 415-476-5271
RTOG@ucsf.edu

<table>
<thead>
<tr>
<th>Item</th>
<th>Due</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specimen Transmittal Form (ST)</td>
<td>Within 2 weeks of study entry</td>
</tr>
<tr>
<td>Pathology Report (P1)</td>
<td></td>
</tr>
</tbody>
</table>

When the patient has consented to tissue/specimen submission (for this study or for an active RTOG treatment study), the site will complete a surgical form (S1) with all relevant information including: institution, patient case number, tumor site, disease stage, surgical procedure, and date of surgery. The RTOG study for which the patient is a candidate will be included on the data sheet when applicable. In addition, the name of the physician who has assisted in acquiring the sample for the study will be noted for appropriate study credit.

The site Clinical Research Coordinator will notify all relevant personnel and the pathologist that a patient has consented to tissue/specimen submission and provide the date of tissue/specimen harvest. The surgical form (S1) requires that the Surgical Pathology Requisition slip specify that the attending pathologist, who will be trained in tissue specimen procurement as per protocol, be paged. On the date of harvest, the institution’s Clinic Research Coordinator will fax/email the data form to the RTOG Biospecimen Resource (contact information above), notifying the Biospecimen Resource that a specimen will be sent in the near future.

13.0 Statistical Considerations

13.1 The establishment of the Head and Neck Cancer Specimen Repository for RTOG should be considered as a long-term, ongoing project. Prior to the use of any specimens from this repository, a formal study proposal will be written and approved by the Head and Neck Cancer Committee, the RTOG Translational Research Committee, and the NCI and appended to this protocol as an amendment. Proposals for the use of specimens will contain specific objectives, plans, and statistical considerations.

13.2 Patient Accrual

Patient accrual will come from patients whom RTOG clinicians identify as potentially eligible for an active (accruing) RTOG treatment protocol. The vast majority (85%+) are expected to be subsequently entered onto the RTOG treatment studies. There is no information available within RTOG to estimate the percent of such candidates who will not be enrolled onto treatment studies. The accrual criteria for the Head and Neck Cancer Specimen Repository will be based on the percentage of specimen entries that are enrolled onto the treatment protocols. The percentage of patients in past treatment protocols that submitted tissue will be used to generate the baseline data. In the last four RTOG head and neck protocols, the mean percentage of such patients was 32%. This specimen repository protocol will be considered successful if it increases that rate to at least 55% of all patients entered onto active RTOG treatment studies during its second and subsequent years. However, a rate below 40% will be considered unsatisfactory and the specimen repository protocol would be discontinued unless there are extenuating circumstances, such as the major head and neck protocols being closed to patient enrollment.
13.3 **Interim Monitoring of Study Progress**

Interim reports will be prepared twice each year and will provide the percent of patients entered on the specimen repository protocol from the each treatment studies (once both trials are open to patient accrual). The reports also will provide information about the progress of approved translational research (TRP) projects using patient specimens from specimen repository protocol.

In addition, NCI determines the reporting requirements for each RTOG protocol and for each amendment to the RTOG Head and Neck Specimen Repository protocol. The reporting may be by the Clinical Data Update System (CDUS) version 3.0. Cumulative CDUS data may be submitted quarterly by electronic means. Reports are due January 31, April 30, July 31, and October 31.

13.4 **Gender and Minorities**

These figures will be generated for specific active study proposals.
REFERENCES


This is a clinical trial, a type of research study. Your study doctor will explain the clinical trial to you. Clinical trials include only people who choose to take part. Please take your time to make your decision about taking part. You may discuss your decision with your friends and family. You can also discuss it with your health care team. If you have any questions, you can ask your study doctor for more explanation.

You are being asked to take part in this study because you have head and neck cancer or tissue that is suspected of being cancerous.

Why is this study being done?

The purpose of this study is to find better ways to find and treat head and neck cancers by collecting and storing tissue (and bodily fluids such as blood and saliva) for future research. Research using tissue is an important way to try to understand human disease.

Doctors and other medical scientists want to (1) find better ways to find cancer early; (2) determine how cancer spreads and resists current types of treatment; and (3) treat and, if possible, (4) cure patients who have cancer. To do these things, they need more information about the causes of cancer. Doctors and scientists want to study samples of cancer cells (tumor tissue) from people who have been diagnosed with cancer or with pre-cancerous tissue.

How many people will take part in the study?

This will be an ongoing study. It is not limited to a particular number of patients.

What will happen if I take part in this research study? (8/28/06)

You have had or you will have a biopsy or surgery to see if you have cancer. Your doctor has removed or will remove some of your tissue to do some tests. The results of these tests will be given to you by your doctor and will be used to plan your care.

If you agree to participate in this study, you must agree to collection and storage in a central tissue bank of the following:

- A small sample of the tumor or suspected tumor tissue that has been removed in your biopsy or surgery
- A small sample of normal tissue from the area close to the tumor or suspected tumor tissue for comparison to the tissue removed in the biopsy or surgery

It is not required, but you also can give your permission for the collection and storage of the following:
- A small portion of normal tissue from inside your cheek taken after you agree to participate in this study and before biopsy, surgery, or treatment
- About 2 tablespoons of your blood drawn after you agree to participate in this study and before biopsy, surgery, or treatment
- A sample of your saliva taken after you agree to participate in this study and before biopsy, surgery, or treatment

The tissue placed in the tissue bank will not be needed to plan your care (or manage your tumor if you are found to have cancer). The tissue and bodily fluids (blood and saliva) obtained for this research study may be tested immediately or may be frozen and examined later for cancer-related research.

If you are found to have cancer, your doctor or institution will give us information on the location and size of the tumor. If you also agree to receive treatment in an RTOG clinical trial, your doctor or institution will give us information about how you and your tumor responded to treatment. In addition, you will be asked some questions about your smoking and alcohol use and any previous treatment you have had. We may need to contact your doctor or institution for more information in the future and will ask for your permission to do that.

At the tissue bank, your tissue, bodily fluids, and information will be given a number. Your name will not be used at any time. All of the information will be stored in a computer and used for research purposes. Only the staff of the tissue bank can get into the computer.

Before your information, tissue samples, and/or bodily fluids can be used for research, the doctors and scientists doing the research must get approval from the Institutional Review Board (IRB) of RTOG and your institution’s IRB. An IRB is a committee made up of doctors, researchers, and members of the community. The IRB is responsible for protecting patients taking part in research studies and making sure all research is done in a safe and ethical manner.

Your tissue and bodily fluids will not be used for non-cancer research (to learn about, prevent, or treat other health problems like diabetes, Alzheimer’s disease, or heart disease) unless you give your permission.

**How long will I be in the study? (8/28/06)**

Your tissue and bodily fluids may be kept until no cells remain or until you request that your samples, if any remain, be returned to your hospital or your doctor or that the tissue bank dispose of the samples.
Can I stop being in the study?

Yes. You can decide to stop participating at any time. If you decide now that your tissue and bodily fluids can be kept for research, you can change your mind at any time. Contact your doctor/institution and let them know.

What side effects or risks can I expect from being in the study?

The greatest risk to you is the release of information from your health records. We will do our best to make sure that your personal information will be kept private. The chance that this information will be given to someone else is very small. Donating tissue for these research purposes will not add any additional risks to your biopsy or surgery, which your doctor will discuss with you before the biopsy or surgery.

Trained research technicians or research nurses will obtain the blood and saliva samples. Your doctor will be checking closely to see if bruising, swelling, and/or infection due to the drawing of blood samples occur and will treat you if needed.

Are there benefits to taking part in the study?

The benefits of research using tissue include learning more about what causes cancer and other diseases, how to prevent them, and how to treat them. You may or may not benefit directly from the research.

What other choices do I have if I do not take part in this study?

Your other choices may include:
- Getting treatment or care for your cancer without being in a study
- Taking part in another study

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

Will my medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:
- The Radiation Therapy Oncology Group;
- The National Cancer Institute (NCI) and other government agencies, like the Food and Drug Administration (FDA), involved in keeping research safe for people
What are the costs of taking part in this study? (8/28/06)

Since your tissue was/will be removed at the time of biopsy or surgery, your permission to use this tissue will not lead to any additional procedures or expense. Also, since blood will be drawn while you are in the operating room or when blood is drawn for laboratory tests and normal tissue from inside your cheek and saliva may be collected then as well, your permission to use this tissue and these bodily fluids will not lead to any additional procedures or expense. Storage of your tissue and bodily fluids and the research involving them will not result in cost to you.

You will not be paid for taking part in this study.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute’s Web site at http://cancer.gov/clinicaltrials/understanding/insurance-coverage. You can print a copy of the “Clinical Trials and Insurance Coverage” information from this Web site.

Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

What happens if I am injured because I took part in this study?

It is important that you tell your study doctor, __________________ [investigator’s name(s)], if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call him/her at __________________ [telephone number].

You will get medical treatment if you are injured as a result of taking part in this study. You and/or your health plan will be charged for this treatment. The study will not pay for medical treatment.

What are my rights if I take part in this study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

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

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.
Who can answer my questions about the study? (4/14/08)

You can talk to your study doctor about any questions or concerns you have about this study. Contact your study doctor _________________ [name(s)] at __________ [telephone number].

For questions about your rights while taking part in this study, call the _________________ [name of center] Institutional Review Board (a group of people who review the research to protect your rights) at _________________ (telephone number).

Please read the information sheet called "How is Tissue Used for Research" to learn more about tissue research. This information sheet is available to all at the following web site: http://www.rtog.org/tissue%20for%20research_patient.pdf

Making Your Choice About Collection of Normal Tissue, Blood, and Saliva, and Being Contacted (8/28/06)

Please read each sentence below and think about your choice. After reading each sentence, circle "Yes" or "No". If you have any questions, please talk to your doctor or nurse, or call our research review board at IRB’s phone number.

No matter what you decide to do, it will not affect your care.

1. A small portion of normal tissue from inside my cheek, my blood, and my saliva may be collected and kept for use in research to learn about, prevent, or treat cancer.
   Yes   No

2. Someone may contact me in the future to ask me to take part in more research.
   Yes   No

Where can I get more information?

You may call the National Cancer Institute’s Cancer Information Service at:

1-800-4-CANCER (1-800-422-6237) or TTY: 1-800-332-8615

You may also visit the NCI Web site at http://cancer.gov/

- For NCI’s clinical trials information, go to: http://cancer.gov/clinicaltrials/
- For NCI’s general information about cancer, go to http://cancer.gov/cancerinfo/
You will get a copy of this form. If you want more information about this study, ask your study doctor.

Signature

I have been given a copy of all _____ [insert total of number of pages] pages of this form. I have read it or it has been read to me. I understand the information and have had my questions answered. I agree to take part in this study.

Participant ________________________________

Date ________________________________
# APPENDIX II

## KARNOFSKY PERFORMANCE SCALE

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>Normal; no complaints; no evidence of disease</td>
</tr>
<tr>
<td>90</td>
<td>Able to carry on normal activity; minor signs or symptoms of disease</td>
</tr>
<tr>
<td>80</td>
<td>Normal activity with effort; some sign or symptoms of disease</td>
</tr>
<tr>
<td>70</td>
<td>Cares for self; unable to carry on normal activity or do active work</td>
</tr>
<tr>
<td>60</td>
<td>Requires occasional assistance, but is able to care for most personal needs</td>
</tr>
<tr>
<td>50</td>
<td>Requires considerable assistance and frequent medical care</td>
</tr>
<tr>
<td>40</td>
<td>Disabled; requires special care and assistance</td>
</tr>
<tr>
<td>30</td>
<td>Severely disabled; hospitalization is indicated, although death not imminent</td>
</tr>
<tr>
<td>20</td>
<td>Very sick; hospitalization necessary; active support treatment is necessary</td>
</tr>
<tr>
<td>10</td>
<td>Moribund; fatal processes progressing rapidly</td>
</tr>
<tr>
<td>0</td>
<td>Dead</td>
</tr>
</tbody>
</table>

## ZUBROD PERFORMANCE SCALE

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Fully active, able to carry on all predisease activities without restriction (Karnofsky 90-100).</td>
</tr>
<tr>
<td>1</td>
<td>Restricted in physically strenuous activity but ambulatory and able to carry work of a light or sedentary nature. For example, light housework, office work (Karnofsky 70-80).</td>
</tr>
<tr>
<td>2</td>
<td>Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours (Karnofsky 50-60).</td>
</tr>
<tr>
<td>3</td>
<td>Capable of only limited self-care, confined to bed or chair 50% or more of waking hours (Karnofsky 30-40).</td>
</tr>
<tr>
<td>4</td>
<td>Completely disabled. Cannot carry on self-care. Totally confined to bed or (Karnofsky 10-20).</td>
</tr>
<tr>
<td>5</td>
<td>Death (Karnofsky 0).</td>
</tr>
</tbody>
</table>
APPENDIX III
HEAD & NECK
(AJCC STAGING SYSTEM, 6th Edition)

STAGING-PRIMARY TUMOR (T)

TX Primary tumor cannot be assessed
T0 No evidence of primary tumor
Tis Carcinoma in situ

PHARYNX

Nasopharynx
T1 Tumor confined to the nasopharynx
T2 Tumor extends to soft tissues of oropharynx and or nasal fossa
  T2a without parapharyngeal extension
  T2b with parapharyngeal extension
T3 Tumor invades bony structures and/or paranasal sinuses
T4 Tumor with intracranial extension and/or involvement of cranial nerves, infratemporal fossa, hypopharynx, orbit, or masticator space.

Oropharynx
T1 Tumor 2 cm or less in greatest dimension
T2 Tumor more than 2 cm but not more than 4 cm in greatest dimension
T3 Tumor more than 4 cm in greatest dimension
T4a Tumor invades the larynx, deep/extrinsic muscle of tongue, medial pterygoid, hard palate, or mandible.
T4b Tumor invades lateral pterygoid muscle, pterygoid plates, lateral nasopharynx, or skull base or encases carotid artery.

Hypopharynx
T1 Tumor limited to one subsite of hypopharynx and 2 cm or less in greatest dimension.
T2 Tumor invades more than one subsite of hypopharynx or an adjacent site, or measures more than 2 cm but not more than 4 cm in greatest diameter without fixation of hemilarynx.
T3 Tumor measures more than 4 cm in greatest dimension or with fixation of hemilarynx.
T4a Tumor invades thyroid/cricoid cartilage, hyoid bone, thyroid gland, esophagus or central compartment soft tissue.
T4b Tumor invades prevertebral fascia, encases carotid artery, or involves mediastinal structures.

LARYNX

Supraglottis
T1 Tumor limited to one subsite of supraglottis with normal vocal cord mobility
T2 Tumor invades mucosa of more than one adjacent subsite of supraglottis or glottis or region outside the supraglottis (e.g., mucosa of base of tongue, vallecula, medial wall of pyriform sinus) without fixation of the larynx.
T3 Tumor limited to larynx with vocal cord fixation and/or invades any of the following: postcricoid area, pre-epiglottic tissues, paraglottic space, and/or minor thyroid cartilage erosion (e.g., inner cortex).
T4a Tumor invades through the thyroid cartilage and/or invades tissues beyond the larynx (e.g., trachea, soft tissues of the neck including deep extrinsic muscle of the tongue, strap muscles, thyroid, or esophagus).
T4b Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures.
APPENDIX III (Continued)

Glottis
T1 Tumor limited to the vocal cord(s) (may involve anterior or posterior commissure) with normal mobility
   T1a Tumor limited to one vocal cord
   T1b Tumor involves both vocal cords
T2 Tumor extends to supraglottis and/or subglottis, or with impaired vocal cord mobility
T3 Tumor limited to the larynx with vocal cord fixation, and/or invades paraglottic space, and/or minor thyroid cartilage erosion (e.g., inner cortex).
   T4a Tumor invades through the thyroid cartilage and/or invades tissues beyond the larynx (e.g., trachea, soft tissues of neck including deep extrinsic muscle of the tongue, strap muscles, thyroid, or esophagus).
   T4b Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures.

Subglottis
T1 Tumor extends to the subglottis
T2 Tumor extends to vocal cord(s) with normal or impaired mobility
T3 Tumor limited to larynx with vocal cord fixation
   T4a Tumor invades cricoid or thyroid cartilage and/or invades tissues beyond the larynx (e.g., trachea, soft tissues of neck including deep extrinsic muscles of the tongue, strap muscles, thyroid, or esophagus).
   T4b Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures.

REGIONAL LYMPH NODES (N) Excluding Nasopharynx

NX Regional lymph nodes cannot be assessed
N0 No regional lymph node metastasis
N1 Metastasis in a single ipsilateral node, 3 cm or less in greatest dimension.
N2 Metastasis in a single ipsilateral node, more than 3 cm, but not more than 6 cm in greatest dimension, or in multiple ipsilateral lymph nodes, none greater than 6 cm in greatest dimension, or bilateral or contralateral nodes, none more than 6 cm in greatest dimension.
   N2a Metastasis in a single ipsilateral node more than 3 cm, but not more than 6 cm in greatest dimension.
   N2b Metastasis in multiple ipsilateral nodes, none more than 6 cm in greatest dimension.
   N2c Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension.
N3 Metastases in a lymph node, more than 6 cm in greatest dimension.

DISTANT METASTASIS (M)

MX Distant metastasis cannot be assessed
M0 No distant metastasis
M1 Distant metastasis
### STAGE GROUPING Excluding Nasopharynx

<table>
<thead>
<tr>
<th>Stage</th>
<th>T, N, M</th>
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<tbody>
<tr>
<td>Stage 0</td>
<td>Tis, N0, M0</td>
</tr>
<tr>
<td>Stage I</td>
<td>T1, N0, M0</td>
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<td>T4a, N0-2, M0</td>
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<tr>
<td>Stage IVB</td>
<td>T4b, Any N, M0</td>
</tr>
<tr>
<td></td>
<td>Any T, N3, M0</td>
</tr>
<tr>
<td>Stage IVC</td>
<td>Any T, Any N, M1</td>
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### STAGE GROUPING Nasopharynx

<table>
<thead>
<tr>
<th>Stage</th>
<th>T, N, M</th>
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<tbody>
<tr>
<td>Stage 0</td>
<td>Tis, N0, M0</td>
</tr>
<tr>
<td>Stage I</td>
<td>T1, N0, M0</td>
</tr>
<tr>
<td>Stage II</td>
<td>T2a, N0, M0</td>
</tr>
<tr>
<td>Stage IIA</td>
<td>T1-T2a, N1, M0</td>
</tr>
<tr>
<td></td>
<td>T2b, N0-1, M0</td>
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<tr>
<td>Stage IIB</td>
<td>T1-T2b, N2, M0</td>
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<tr>
<td></td>
<td>T3, N0-2, M0</td>
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<tr>
<td>Stage IVA</td>
<td>T4, N0-2, M0</td>
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<tr>
<td>Stage IVB</td>
<td>Any T, N3, M0</td>
</tr>
<tr>
<td>Stage IVC</td>
<td>Any T, Any N, M1</td>
</tr>
</tbody>
</table>
Specimen Kit Description and Shipping Instructions

Appendix IV (4/14/08)

Participating institutions can request specimen collection/shipping kits from the RTOG Biospecimen Resource, by fax or e-mail (contact information is below).

Each kit contains:
- Ten (10) 1mL cryovials (for peripheral blood);
- Three (3) 5mL cryovials (for fresh tissue);
- Two screw-top containers, 1 filled with Saccomanno’s fixative for saliva collection;
- Biohazard bags;
- Absorbant shipping material;
- Styrofoam container (inner);
- Cardboard shipping (outer) box;
- Pre-paid return shipping label.

Note: An additional collection cup containing RNAlater and buccal brush/swab will be added to this kit upon request (Not provided with standard kit).

Fresh Specimens: Cryo tubes with frozen tissue, buffy coat cells, serum, and buccal scrapings must be wrapped in an absorbent material (e.g., paper towels) and placed in an airtight plastic freezer bag (i.e., re-sealable bag). Serum specimens may be sent in batches, if within 30 days of collection. Pack the frozen specimens in a heavy grade Styrofoam box with dry ice (4-5 lbs. minimum). Seal the box with plastic tape. All paperwork (see Section 10.4) should be placed in a plastic bag, sealed, and taped to the outside top of the Styrofoam box. Pack the Styrofoam box in a cardboard box.

Saliva can be shipped at ambient temperature with the fixed specimens in a separate container or in an ambient compartment within a separated shipping container. Note: Specimens requiring specific infectious precautions should be clearly labeled, with specific sources of infectious concerns listed, if known. Mark the outer cardboard box “biohazard”.

Send specimens by overnight express to the address below. Specimens only should be shipped Monday through Wednesday to prevent thawing due to delivery delays. Saturday or holiday deliveries will not be accepted. Samples received thawed will be discarded, and a notification will be sent immediately to the Principal Investigator and Clinic Research Assistant of the submitting institution. The institution should send a subsequent sample, collected as close as possible to the original planned collection date.

Fixed Specimens: Generally, paraffin-embedded tissue or fixed tissue should be shipped at ambient temperature, not on wet or dry ice, in appropriate shipping containers with adequate packing to protect specimens. During periods of extremely hot weather, paraffin-embedded tissue should be shipped on ice. All paperwork (see Section 10.4) should be included in the shipping container. Send specimens to the address below. Saturday or holiday deliveries will not be accepted.

Shipping/Mailing:
- Include all RTOG paperwork in pocket of biohazard bag.
- Place frozen specimens and the absorbent shipping material in the Styrofoam cooler and fill with dry ice (if appropriate; double-check temperature sample shipping temperature). Ship ambient specimens in a separate envelope/cooler. Place Styrofoam coolers into outer cardboard box, and attach shipping label to outer cardboard box.
- Multiple cases may be shipped in the same cooler, but make sure each one is in a separate bag.
- Notify Biospecimen Resource personnel before you send specimens via Fed-ex.
APPENDIX IV (Continued)

Specimen Kit Description and Shipping Instructions

For questions regarding collection/shipping please contact the RTOG Biospecimen Resource:

415-476-RTOG (7864)/FAX 415-476-5271
RTOG@ucsf.edu

All specimens must be labeled with the RTOG protocol number, 0514, and the patient's case number. Sites must submit the required documentation (see Section 10.4) with specimens. All specimens will be shipped as follows:

Mailing Address: For Non-frozen Specimens Only
RTOG Biospecimen Resource
University of California San Francisco
Campus Box 1800
1657 Scott Street, Room 223
San Francisco, CA 94143-1800

Courier Address (FedEx, DHL, etc.): For Frozen Specimens
RTOG Biospecimen Resource
University of California San Francisco
1657 Scott Street, Room 223
San Francisco, CA 94115
I. Application process:

Information about the RTOG Translational Research Program (TRP) can be accessed on the RTOG web site (no password needed) at http://www.rtog.org/tissuebank/main.html, including the TRP Project Application Form, instructions for completing the form, and a description of the review/approval process. Investigators should send completed applications to the RTOG TRP Coordinator, dmalone@phila.acr.org, 215-574-3236.

Proposals will be reviewed promptly by the Head and Neck Cancer Tissue/Specimen Repository Utilization Committee, the RTOG Biospecimen Resource, and RTOG Statistics via conference call with the Investigator.

Key components of the application will be critically reviewed by the committee directorship and will include, but not be limited to, the following: skill of investigators, pilot data, scientific merit, disease site, tissue/specimen availability, and application completion. Applicants may be asked to submit additional documentation addressing specific concerns of both the directorship and the committee. Questions should be directed to the RTOG TRP Coordinator, dmalone@phila.acr.org, 215-574-3236.

II. Application review process:

Each application is reviewed by the committee directorship or ad hoc reviewers as appropriate once it is determined that the application is complete. The RTOG Head and Neck Cancer Committee is composed of radiation oncologists, surgical oncologists, pathologists, medical oncologists, basic scientists, statisticians, and other medical/scientific professionals. The committee meets by conference call as needed.

Members of the directorship will be assigned to review each request. Applications will be assessed for scientific merit, the potential value to new or developing protocols in Head and Neck Cancer, and regulatory and/or HIPAA compliance. In addition, the directorship will determine the effect of the proposed study on the overall tissue/specimen resource. If warranted, the applications will be submitted for full review by the committee at the semi-annual meeting. A written summary of critiques will be maintained by the committee.

III. Process of application approval/notification of investigator:

If upon review by the committee, approval is denied, the investigator will be given a written summary of the reviewer critiques detailing why the decision was made. If final approval is granted, a letter will be sent to the investigator from the Head and Neck Group Chair stating that the investigator is can access the tissue/specimen repository.

If any changes are requested before approval can be given, the investigator has one month from the date of the critique to re-submit. The application then will go through an expedited review by the Chairman of the committee or designee, and the final approval letter for tissue/specimen repository utilization will be sent to the investigator.
APPENDIX VI (8/28/06)
PATHOLOGY TEMPLATES (SAMPLE)

**Squamous Cell Carcinoma Template**

- **Specimen Type:** Biopsy
  - **Site:**
  - □ Hyperplasia and hyperkeratosis
  - □ Verrucous hyperplasia
  - □ Dysplasia
    - Hyperkeratosis / Parakeratosis: Yes [ ] No [ ]
      - □ Mild [ ] □ Moderate [ ] □ Severe [ ]
  - □ Chronic inflammation
    - □ Mild [ ] □ Moderate [ ] □ Marked [ ]
  - □ Squamous carcinoma
    - Depth: □ > 1 mm [ ] □ ≥ 3 mm [ ]
    - Differentiation: □ Well [ ] □ Moderate [ ] □ Poor [ ]
  - □ Subtypes:
    - □ Verrucus carcinoma [ ] □ Basaloid [ ] □ Undifferentiated [ ]
    - □ Papillary [ ] □ Sarcomatoid [ ]

OK  |  Cancel
### Squamous Cell Carcinoma Template

#### Specimen Type: Resection

- **Site:**

### SQUAMOUS CELL CARCINOMA:

- **Differentiation:**  
  - Well
  - Moderate
  - Poor

- **Variants:**
  - Verrucous
  - Basaloid
  - Papillary
  - Sarcomatoid

---

**APPENDIX VI (Continued)**
### Squamous Cell Carcinoma Template

**From Patient:**
- Negative: O
- Positive: O
- Location: 

**Additional:**
- Negative: O
- Positive: O
- Location: 

**From Specimen:**

**Mucosal Margin:**
- En-face: O
- Negative: O
- Positive: O
- Radial: O
- Negative: O
- Positive: O
- Closest (<2mm): O

**Deep Margin:**
- En-face: O
- Negative: O
- Positive: O
- Close <2 mm: O
- Radial: O
- Negative: O
- Positive: O
- Close <2 mm: O

**Dysplasia:**
- Present: O
- Absent: O
- Degree: O
- Mild
- Moderate
- Severe

---

APPENDIX VI (Continued)
APPENDIX VI (Continued)

Squamous Cell Carcinoma Template

<table>
<thead>
<tr>
<th>Bypass only</th>
<th>Resection Diagnosis</th>
<th>Tumor Features</th>
<th>Margins</th>
<th>Lymph Nodes</th>
</tr>
</thead>
</table>

Pick Level:
Level I ○ Level III ○ Level V ○
Level II ○ Level IV ○ Level VI ○

Level VI
Left ○ Right ○ Ipsi ○ Contra ○
Total # Nodes: [ ] # Positive Nodes: [ ]

Extracapsular Extension:
Absent ○ Present ○
Minimal (≤1mm) ○ Extensive (≥1.0mm) ○