Appendix D: Access to Data and Aggregate Reporting

ReCKord Request Form for Use of Aggregate Data:

Eligibility Criteria for Participating Centers

- Enter > 50 patients into ReCKord annually
  (The Radiosurgery Society will not be held to this criterion)

Submission Requirements

Please attach each of the following with your Data Request Form:

- Copy of IRB approval letter for use of ReCKord at your institution
- Curriculum vitae of the principal investigator.

General Information

Submitted Data Request Forms (DRF) are posted on the Radiosurgery Society homepage under the Clinician Resource dropdown. Applications are reviewed twice/year (April & September). You will receive a letter from the ReCKord Registry Review Committee regarding the status of your request within 30 days. Accepted DRFs will be forwarded to Advertek[sm] by the RSS to generate the requested custom data report. Custom reports will require a minimum of 2 weeks to generate. Submit DRF to Nalani Brown at nbrown@therss.org. Applications are posted on the Radiosurgery Society website at www.theradiosurgerysociety.org.

Administrative Information

Date of Submission (mm/dd/yy):	10-1-13
Name of Organization:	**The Radiosurgery Society**
Project Title:	Stereotactic Body Radiotherapy for Central Lung Tumors
Principal Investigator:	Anand Mahadevan, M.D.
Co-Investigators:	Clinton Medbery, M.D., Joanne Davis, Ph.D.
Corresponding Contact Name:	Joanne Davis
Contact Title:	Consultant
Contact Telephone Number:	248-719-2998
Contact E-mail Address:	Davis.joanne@hotmail.com
Contact Address: **City, State, Zip:**	1315 Dell, Suite 105 Campbell, CA

Project Description

Project Start Date (mm/dd/yy):	10-15-13
Project End Date (mm/dd/yy):	2-1-14
Type of Research Project:	□ Prospective Study x Retrospective Analysis □ Technical Study □ Other
If "Other," please explain nature of project:	
What is the research question being asked?	The objectives of the analyses are to 1) describe the patient and lesion characteristics of central lung tumors in ReCKord 2) investigate the SBRT treatment patterns to

	identify optimal dose/fractionation schedule 3) assess toxicity and correlate with SBRT dose/fractionation schedules 4) investigate efficacy of SBRT treatment of central lung tumors by assessing overall survival, local control, and disease progression.
What is the background or rationale for the research question? (if needed, please attach as a separate page to application)	Please see attached publication plan "Stereotactic body radiotherapy for central lung tumors" for description of study, background, rationale and detailed plan.
Patient Inclusion/Exclusion Criteria:	All patients with centrally located lung tumors treated with SBRT

Data Requested

Description of patient population to be analyzed:	All patients with centrally located lung tumors treated with CyberKnife SBRT
Time frame to be studied:	All patients entered in ReCKord through September 1, 2013
List exact data variables requested (i.e. pathology, treatment planning information, outcome, reimbursement, etc.): If the request is not self-evident, write a summary of the request and/or instructions on data output (e.g., table specifications, sample tables).	All data variables from Screening, Treatment and Follow-up CRFs.
Deadline for receipt of data (mm/dd/yy):	11-1-13

Data Use

Are these data for internal research purposes only? (yes/no)	No
If requesting party will seek to share data with persons not already listed on this request, list the organizations with which data would be shared and in what capacity? (e.g., FDA for a clinical trial, NIH for a grant proposal, consultant for project development)	Accuray has provided a grant to fund this study. Accuray representatives will be provided a draft of publication for review prior to journal submission.
Peer-reviewed publications to which submission is anticipated (if	RED Journal; Radiation Oncology

National meetings at which abstract presentation is anticipated (if any)	Will submit abstract to RSS Scientific meeting

Additional Submission Requirements

Please attach each of the following:

- Copy of IRB approval letter for use of ReCKord at your institution
- Curriculum vitae of the principal investigator

Requestor Certification

In making this request, I certify that:

- All information provided on this form and attachments is accurate and complete.
- I have all requisite institutional authority to submit this Request for Use of Collaborative Data

Signature	Laura Dent
Print Name	Laura Dent
Title	Consultant
Date	10.1.13

Please submit Request for Use of Collaborative Data to nalan@theradsurgerysociety.org

For Internal Use Only:

Date application received:	October 15, 2013
ReCKord Registry Request #	2013_1015

The ReCKord™ Registry Publication Proposal: Stereotactic body radiotherapy for central lung tumors

Date: August 15, 2013
Contact: Kristine Gagliardi
Executive Director
The Radiosurgery Society®
1350 Dell Avenue, Suite 105
Campbell, CA 95008
Telephone: 408-370-1998
Email: kgagliardi@therss.org

Joanne Davis, PhD
Clinical Research Consultant
Telephone: 248-719-2998
Email: davis.joanne@hotmail.com

ClinicalTrials.gov Identifier: NCT01563549

I. Specific Aims

Stereotactic body radiotherapy (SBRT) is now considered a standard treatment option for stage I non-small cell lung cancer in patients who are not candidates for surgery. SBRT may also be considered for select patients with metastatic and recurrent lung tumors and is used in both the curative and palliative setting for lung tumors. In general, SBRT doses with a biological equivalent dose (BED) greater than 100 Gy must be given to improve tumor control, but such doses pose a risk of harmful side effects to nearby normal tissues. The goal of lung SBRT is to maximize the dose of radiation to the tumor and to spare normal tissues, including normal lung, heart, esophagus, pleura, skin and spinal cord to prevent radiation-induced side effects. Patients with centrally located lung tumors are even more at risk of radiation-induced side effects because of the close proximity of centrally located lung tumors to the critical normal structures. Some studies have suggested that patients with central lung tumors have more severe toxicities when treated with SBRT compared to patients with peripheral tumors. Efforts to decrease the toxicity risk factor by decreasing the dose may result in increased local failure. The optimal SBRT fractionation schedule for treatment of central lung tumors is not known. Studies are needed to define the optimal patient/lesion characteristics and SBRT dose and fractionation schedule for patients with centrally located lung tumors.

The ReCKord Registry™ is an ongoing, observational, multi-center registry collecting patient demographics, lesion characteristics, treatment plan and treatment delivery information, toxicity, and outcome data from patients treated with stereotactic radiosurgery (SRS) and stereotactic body radiotherapy (SBRT) by the CyberKnife Robotic Radiosurgery System. Initial analysis identified 155 patients with centrally located lung lesions treated with CyberKnife SBRT with a median follow-up of 10

months (range 1 - 90 months). CyberKnife SBRT treatment was delivered with a median dose of 48 Gy (range 18 – 60 Gy) over a median number of 4 fractions (range 1-5). The purpose of this proposal is to investigate the patient demographics, lesion characteristics, treatment management practices, toxicity and efficacy of CyberKnife SBRT for centrally located lung tumors from patients entered in ReCKord.

The objectives of the analyses are to 1) describe the patient and lesion characteristics of central lung tumors in ReCKord 2) investigate the SBRT treatment patterns to identify optimal dose/fractionation schedule 3) assess toxicity and correlate with SBRT dose/fractionation schedules 4) investigate efficacy of CyberKnife SBRT treatment of central lung tumors by assessing overall survival, local control, and disease progression.

II. Background and Significance

Despite increased knowledge of SRS/SBRT technology and clinical outcomes from single institutions, information on physician practice patterns of SRS and SBRT in the daily clinical practice is limited. A registry provides a systematic and inclusive database of information which can reveal and evaluate the effectiveness of management practices. In contrast to a clinical trial, where patient enrollment is defined by specific inclusion and exclusion criteria, treatment is dictated by protocol guidelines, and treatment evaluation is measured at specific follow-up time intervals, a registry documents actual care, representing a broad spectrum of patients where treatments are not specified by protocol guidelines and patient follow-up schedules are conducted in a real-life setting. A registry can provide information as to whether clinicians are adhering

to practice guidelines, may complement randomized clinical trials and/or identify new clinical applications and treatment benefits.

The ReCKord Registry was conceptualized and designed by a board of ReCKord Clinical Advisors in 2005. The ReCKord Clinical Advisory Committee is comprised of radiation oncologists, neurosurgeons, surgeons, medical oncologists, and medical physicists to create and oversee the scientific conduct of the registry. The goals and objectives of the registry are to provide a method to collect standardized data on the use of SRS/SBRT treatment practices and outcomes to help determine the most effective clinical use of SRS/SBRT in management of patients with life threatening tumors and other diseases.

Through a grant provided by Accuray Incorporated (Sunnyvale, CA), a third-party medical software and web management company, Advertek Inc. (Louisville, KY), was contracted to provide services to design, store, and maintain the web-based database. The database meets all requirements to maintain HIPAA compliance and patient confidentiality. No patient identifying information is recorded in ReCKord. The ReCKord Registry is currently managed by The Radiosurgery Society®, a multi-disciplinary non-profit organization aimed at advancing the science and clinical practice of radiosurgery (see www.therss.org for additional information).

All centers treating patients with SRS/SBRT clinically are offered and encouraged to participate in the ReCKord Registry. Participation is voluntary and no compensation is provided for participation in the ReCKord Registry, either to patients or participating centers. Each principal investigator is provided a copy of the ReCKord Registry protocol, case report forms, sample patient informed consent, and web-based training for data entry and database navigation. Institutional Review Board (IRB) approval is

required at all participating centers. All patients who are screened for potential SRS/SBRT treatment are eligible to be included in the ReCKord Registry. All prospective patients are required to sign an informed consent prior to the patient's data entered into the ReCKord Registry. Entry of retrospective patient data may be approved by a Waiver of Authorization per the approval of the participating center's IRB. Retrospective data in ReCKord are identified from prospective data.

Patient demographics are captured during the screening process and include gender, ethnicity, age, weight, height, smoking history and Karnofsky performance score. Information on referral sources, primary and secondary payer information, previous treatments, and comorbidities are also captured during the screening process. SRS/SBRT treatment locations are classified using the World Health Organization (WHO) International Classification of Diseases (ICD), version 9 codes. Lesion characteristics including TNM staging, histology, pathology, lesion size, tumor markers, data from diagnostic imaging (ex. SUV uptake on PET/CT) and markers used as surrogate endpoints are recorded and available for analysis. Both manual and automatic Multiplan upload capabilities are available in ReCKord to capture treatment planning and delivery information. The automatic Multiplan upload tool allows the user to automatically upload treatment planning and delivery data directly into ReCKord without having to manually input the data, saving time for the end user and eliminating data entry errors from manual input. Treatment planning data fields include treatment planning system version, method of dose calculation (Monte Carlo vs. ray tracing), dose optimization method, number of fractions, number of fiducials, path set, tracking method (Synchrony), number of monitor units, prescription dose, maximum dose, number of nodes, collimator type and size, doses to organs at risk, treatment times, set-up times, and

delivery times and are captured for each treated lesion. ReCKord easily and accurately captures treatment planning and delivery information for multiple lesions treated in the same patient.

ReCKord also has an extensive outcome and follow-up data section that captures multiple follow-up visit information for each patient. For each follow-up visit, data fields are designed to capture toxicity, lesion response, disease-progression, tumor markers, surrogate endpoint markers, survival, information from post-treatment imaging, and additional treatments. Toxicity reporting utilizes the Common Toxicity Criteria for Adverse Event Reporting, version 3. All aggregate data can be exported from ReCKord and analyzed using statistical software programs.

III. Preliminary Results

Between October, 2004 and June, 2013, 155 patients with central lung lesions from 25 centers in the US were treated with CyberKnife SBRT. The median follow-up was 10 months (range 1-90 month). Thirty-nine percent of lesions were primary malignant, 30% metastatic and 31% recurrent. Ninety-three percent of the primary malignant lesions had pathological diagnosis, with non-small cell lung cancer as the most prevalent histology. The median tumor volume for all lesions was 20 cc (range 0.3 – 1751 cc) and median size was 27.5 mm (range 1.6 – 76 mm). CyberKnife SBRT treatment was delivered with a median dose of 48 Gy (range 18 – 60 Gy) over a median number of 4 fractions (range 1-5). Outcome data on toxicity, overall survival, and progression-free survival (local and distant metastases) are available for patients with central lung lesions treated with CyberKnife SBRT to conduct statistical analysis.

IV. Research Design and Methods

The Radiosurgery Society® currently manages and owns the data in ReCKord. The goal of the Society is to expand the knowledge of radiosurgery treatment practices to the medical community. We believe the ReCKord Registry houses a vast amount of clinical information describing the treatment management practices and efficacy of SRS/SBRT in a community clinical setting and will be a key resource to reporting outcomes of radiosurgery treatments. To conduct the analysis, the RSS will identify a Principal Investigator (PI), who is an expert in lung cancer, to oversee the conduct of the analysis and publication. The RSS will be responsible for conducting the quality assurance of the data in ReCKord, will coordinate with participating centers to complete quality assurance processes, and will coordinate with the PI to identify person(s) to conduct the statistical analysis, writing of the publication and submission to peer-reviewed journals. Once the project begins and participating sites are contacted to verify data entry completeness and accuracy, we expect the sample size to increase. Additional patients with central lung lesions that meet the project criteria may be included in the final analysis. All statistical calculations will be performed using InStat® (La Jolla, CA), GraphPad Prism® (La Jolla, CA) or SPSS (Armonk, NY) statistical software.

Patient demographics, referral sources, payer information, lesion characteristics, treatment planning and delivery information will be reported using descriptive statistics. Acute and late toxicities will be reported as symptoms that developed within or after 90 days of treatment completion, respectively. Common Toxicity Criteria for Adverse Events v3.0 (CTCAE) are used for toxicity scoring. Overall survival will be calculated from the date of registration using the Kaplan-Meier method and median values will be reported. Disease progression-free survival will also be measured from the registration date to the date of local progression, distant metastasis, or both using Kaplan-Meier

analysis. We will also conduct statistical analysis to identify any associating factors including lesion characteristics, dose/fraction scheme, and BED that correlate with clinical outcomes.