Title: TARGIT Collaborative Group Breast Quality Collaborative

Study Key Name **TCG Breast QC**

Protocol No: **1**

Protocol Date: 1/7/2019

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SITE INVESTIGATORS SIGNATURE PAGE

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Short Title	TCG Breast QC
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Protocol Version	V1
Version Date	1/7/2019

I confirm that I have read this protocol, I understand it, and I will participate in the quality collaborative according to the protocol.

Site Principal Investigator Name _____

Site Principal Investigator Signature _____

Date: _____

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ABBREVIATIONS AND DEFINITIONS OF TERMS

APBI	Accelerated partial breast irradiation
ASTRO	American Society of Therapeutic Radiation Oncology
BCS	Breast Conserving Surgery
IORT	Intraoperative Radiotherapy
TARGIT	Targeted Intraoperative Radiotherapy
TCG	TARGIT Collaborative Group
TCG Breast QC	TARGIT Collaborative Group Breast Quality Collaborative
TCGQC	TARGIT Collaborative Group Quality Collaborative
WBI	Whole Breast Irradiation

ABSTRACT

Context:

Targeted Intraoperative Radiotherapy (TARGIT) has recently emerged as an alternative to fractionated whole breast irradiation (WBI) for administration of adjuvant breast radiotherapy following breast conserving surgery (BCS). To facilitate access to high-quality breast cancer care, the TARGIT Collaborative Groups' Breast Quality Collaborative (TCG Breast QC) aims to enhance the outcome of patients treated with BCS and TARGIT through establishment of a national quality improvement initiative. The TCG Breast QC will also fulfill the ASTRO accelerated partial breast radiotherapy guideline recommending administration of low-dose IORT only with the context of a prospective cancer registry or trial.

Objectives:

- The primary objective of the TCG Breast QC is to use longitudinal outcomes analysis to improve the safety of patients receiving BCS and TARGIT.
- The secondary objectives are to:
  - Establish best practices for patients treated with BCS and TARGIT;
  - Develop care pathways to enhance patient care and safety for patients treated with BCS and TARGIT;
  - Provide a mechanism to enroll patients receiving BCS and TARGIT in a prospective registry to meet requirements of ASTRO APBI guideline for low-dose IORT.

Study Design:

- Basic design: Prospective data registry/quality improvement initiative
- Organizational Structure: Specialty society based registry
- Potential Future Use: Registry-based clinical trials

Setting/Participants:

- Academic and Community-based practices
- 30 Sites in initial 2 years
- Individuals with breast cancer undergoing BCS and TARGIT

1 BACKGROUND INFORMATION AND RATIONALE

1.1 Introduction

Intraoperative Radiotherapy (IORT) has recently emerged as an alternative to fractionated whole breast irradiation (WBI) for administration of adjuvant breast radiotherapy following breast conserving surgery (BCS). As a strategy for delivering accelerated partial breast radiation (APBI), the primary appeal of IORT to the patient is the ability to receive the entire course of therapeutic breast radiation in a single fraction at the time of tumor resection.

Three IORT approaches are currently in common usage in the U.S.: the **Targ**eted **I**ntraoperative radio**T**herapy (TARGIT) method using the Intrabeam System (Carl Zeiss Meditec, Inc., Oberkochen, Germany), the **EL**ectronic **I**ntraoperative **T**herapy (ELIOT method using the Mobetron System (IntraOp Medical Corporation, Sunnyvale, CA), and the Xoft method using the Axxent System (iCAD, Inc., Nashua, NH). Each method

Targeted **I**ntraoperative radio**T**herapy (TARGIT) method using the Intrabeam System (Carl Zeiss Meditec, Inc., Oberkochen, Germany) is the most commonly used methods of delivering intraoperative radiotherapy internationally. The TARGIT is also the only method of delivering IORT that has been evaluate by an international prospective randomized control trial. However, due to limited long-term follow-up and limited usage in the U.S., the TARGIT Collaborative Groups' Breast Quality Collaborative (TCG Breast QC) aims to facilitate access and enhance the outcome of patients treated with BCS and TARGIT through establishment of a national quality improvement initiative. Additionally, the TCG Breast QC will permit participating physicians and institutions to meet ASTRO guideline recommending TARGIT only when performed as part of a prospective trial or registry.

The TCG Breast QC is sponsored the TARGIT Collaborative Group, a national professional organization of surgeons, radiation oncologists, physicists, and other experts in intraoperative radiotherapy that are committed to improving cancer patient care through education, patient advocacy, mentorship, and collaborative research. The TARGIT Collaborative Group is a 501(c)(3) not-for-profit organization managed by a board of directors comprised of surgeons, radiation oncologist, or physicists.

The TCG Breast QC will be funded by the TARGIT Collaboration Group, which in turn will receive funding from medical device companies and members. The TCG Breast QC is modeled after the American Hernia Society Quality Collaborative which is primary supported by mesh device companies.

2 OBJECTIVES

The purpose of the TCG Breast QC is to provide a quality improvement initiative for patients treated with breast conserving surgery (BCS) and targeted intraoperative radiotherapy (TARGIT).

- Primary Objective (or Aim)

  The primary objective of the TCG Breast QC is to use longitudinal outcomes analysis to improve the safety of patients receiving BCS and TARGIT.

2.1 Secondary Objectives (or Aim)

- The secondary objectives are to:
  - Establish best practices for patients treated with BCS and TARGIT;
  - Develop care pathways to enhance patient care and safety for patients treated with BCS and TARGIT;
  - Provide a mechanism to enroll patients receiving BCS and TARGIT in a prospective registry to meet requirements of ASTRO APBI guideline for low-dose IORT.

3 INVESTIGATIONAL PLAN

3.1.1 Duration of Quality Collaborative

Data will be retained by the Targited Collaborative Group for at least 10 years.

3.1.2 Total Number of Study Sites/Total Number of Subjects Projected

The quality improvement initiative will be conducted at approximately 30 investigative sites in the United States. It is expected that approximately 300 patients will be entered in the TCG Breast QC database in the first 2 years.

3.2 Study Population

3.2.1 Inclusion Criteria

1) Females or male age 18 and older.
2) Individuals undergoing breast conserving surgery for breast cancer
3) Individuals receiving intraoperative radiotherapy for breast cancer

3.2.2 Exclusion Criteria

1) Individuals receiving IORT for non-breast related conditions
2) Age < 18

4 STUDY PROCEDURES

4.1 Medical Data Collection Procedures

4.1.1 Data Collection

Data will be collected from medical records that are generated in routine patient care. Data collection will be performed by the Participant (i.e., physicians and physicists, research coordinators, research assistants, and other pre-approved users) and then entered into the online TCG Breast QC Database. Printed case report forms will not be utilized.

4.1.2 Data Elements

Appendix A displays the electronic case report forms showing the data elements that will be captured in the TCG Breast QC Database. This information could come from medical history, physical examination, laboratory, radiological, pathology, procedure reports and consultations reports that was obtained in the routine care of the patients or specifically requested for the TCG Breast QC Database. Additional data might be requested for inclusion in a registry-based clinical trials that would require appropriate institutional review board approval and patient informed consent.

4.1.3 PHI Elements Collected

The following PHI will be recorded in the TCG Breast QC Database: geographical subdivisions (city, county, zip code, and their equivalent geocodes); all elements of dates (except year) for dates directly related to an individual, including birth date, date of death; age; and medical device identifiers and serial numbers.

The following elements that will be maintained at the local site by the Participant but not entered into the TCG Breast QC Database: patient name; medical record numbers, and account numbers.

5 QUALITY COLLABORATIVE ORGANIZATION

5.1 Quality Collaborative Organization

The TCG Breast QC will be managed by the TCG Breast QC Steering Committee under the direction of the TARGIT Collaborative Group's Board of Directors. Access to the TCG Breast QC will be restricted to active members of the TARGIT Collaborative Group or their pre-approved associates. The TCG Breast QC Steering Committee will be responsible for granting access to the Database only after Data Use Agreements have been completed by all potential users, and subsequently approved.

Participants will also have continuous access to their own patient data. Participants will have to aggregated, de-identified TCG Breast QC Data of other Participants in the TCG Breast QC Database through a formal data request submitted to the TCG Breast QC Steering Committee. See section 6.8 (Confidentiality) and the Data Use Agreement (Appendix B) for procedures and policies for accessing/sharing Data.

6 QUALITY COLLABORATIVE ORGANIZATION

6.1 Data Collection and Management

All patient data will be entered at the local level by Participant directly into the online TCG Breast QC Database utilizing electronic case report forms that which will be maintained on a secure remote server. Print case report forms will not be utilized. Data will be entered directly from source documents that will be retained by the Participant. Data entered into the TCG Breast QC Database will be audited periodically by the TCG Steering Committee for data completeness and accuracy.

6.2 Computer Systems

Participants will use their own password-protected computers to access the TCG Breast QC online.

6.3 Confidentiality of Subjects:

Confidentiality of patients will be minimized through the use of password-protected accounts, Data Use Agreements with Participants and subcontractors that obligate them to maintain the confidentiality of passwords associated with each account and for all activity that occurs through Participant's accounts, and the sharing of only de-identified data among TCG, Participants, and agents or subcontractors. Confidentiality will be facilitated by a policy in which all patients are assigned a unique identifier that is maintained at the local site which will be used to access and enter patient-specific data, thereby eliminating the need for entry of the patient's name into the TCG Breast QC Database.

The TCG Breast QC will be accessible to Participants on a secure, password-protected, U.S.-based server maintained by Amazon Web Services located in Seattle, Washington, in compliance with the requirements as stated in the standard: ISO/IEC 27001:2013, certificate number 2013-009.

6.4 Regulatory and Ethical Considerations

6.4.1 Risk Assessment

There is minimal risk of physical harm for participating in the TCG Breast QC. The main risk of participation is a potential breach of confidentiality arising from unintentional disclosure of PHI to persons who are not authorized to receive the information.

6.4.2 Potential Benefits of Participation

There is no direct benefit to patients whose data are entered into the TCG Breast QC Database. However, there is a society benefit that has the potential to improve the safety and quality of care of future breast cancer patients through development of best practices regarding the use of BCS and TARGIT. The TCG Breast QC will also benefit society by

facilitating the conduct of registry-wide clinical trials related to breast conserving surgery and targeted intraoperative radiotherapy.

6.5 Recruitment Strategy

Patients data entered into the TCG Breast QC Database will be obtained from TCG members who voluntarily agree to participate in the TCG Breast QC. It is expected that data will come from the member's patients that are candidates that are recipients of BCS and/or TARGIT. The TCG Breast QC will also meet ASTRO accelerated partial breast radiation guideline recommendations for patients receiving low-dose IORT to receive treatment within a prospective clinical protocol. This recommendation should promote physician participation in the TCG Breast QC since no nationwide prospective protocol currently exists for targeted intraoperative radiotherapy.

6.6 Informed Consent

In most instances, informed consent is not required as the TCG Breast QC is not primarily a research endeavor but rather a quality improvement effort. Nonetheless, it is recommended that individual physicians comply with local and institutional regulations regarding the need for informed consent.

6.7 Payment to Physicians/Patients

No payments will be paid by TCG to Participants or their patients for participating in the TCG Breast QC. However, physician or patient payments may be permitted if the TCG Breast QC is utilized to conduct a registry-based clinical trial. Registry-based clinical trials would require appropriate institutional review board approval and patient informed consent which would specify the amount of be paid to the physician and/or patient.

6.8 Confidentiality

Access to the TCGQC Web Site and TCG Breast QC Database will be controlled through a password protected account or accounts. Participants must agree that they are responsible to maintain the confidentiality of passwords associated with each account and for all activity that occurs through their accounts. A unique account will be created and assigned for each Participant. A participants shall notify TCG promptly if Participant is aware of any unauthorized activity under its accounts.

Participant will have continuous access to Participant's own site-specific data in its original inputted format as detailed in a Data Use Agreement. Participant will also have access to aggregated, de-identified data of other Participants through a formal data request process in a manner that does not identify or permit identification of the other Participants or their respective patients and is presented for the purpose of comparison to other treatment outcomes for BCS and TARGIT.

Participants will not be permitted to give any third party access to the TCG Breast QC Web Site, TCG Breast QC Database or the accounts assigned by TCG under its Data Use

Agreement. TCG will not release Participant Data in any format or circumstance that identifies Participant or any patient PHI as the source of its specific data, except to the Participant, as required by legal process, or as specifically authorized by Participant. If any legal demand for Participant Data is made upon TCG, TCG will (a) promptly notify Participant so that Participant may, at its option, challenge the validity of the legal process and (b) reasonably cooperate with Participant in the event that Participant wishes to take action to challenge such claim or disclosure. However, this provision does not apply to requests for de-identified, aggregated data.

For purposes of this Protocol, patient PHI includes electronic PHI ("EPHI") and PHI and limited data sets refer only to PHI and limited data sets transmitted from or on behalf of Participant to TCG or an agent or subcontractor of TCG, or created by TCG or its agent or subcontractor on behalf of Participant. The parties agree that TCG is a business associate of Participant and Participant is a covered entity under HIPAA.

Except as otherwise specified in the Data Use Agreement, TCG may use or disclose PHI both to provide services to Participant to the extent such use or disclosure is reasonably necessary to facilitate Participant's participation in the TCG Breast QC, to aggregate Participant Data with other Participant Data as part of the TCG Breast QC and to further the health care operations and research purposes of the TCG Breast QC, provided that such use or disclosure of PHI would not violate HIPAA.

See Data Use Agreement (Appendix B) for specific details regarding the use and sharing of data contained with the TCG Breast QC.

7 SAFETY MANAGEMENT

7.1 Clinical Adverse Events

As a quality improvement initiative, anticipated and unanticipated adverse events will be monitored throughout the study by the TCG Breast QC Steering Committee to identify patterns and practices that may contribute to improvements in safety and reduction of complications. These findings will be utilized to establish best practices that will be communicated to TCG members in oral presentation and publication format. Serious adverse events related to medical device performance will be communicated in a de-identified manner to device manufacturers so that appropriate steps can be taken to minimize future device-related complications.

8 PUBLICATION

The primary intent of data collected by the TCG Breast QC is for quality improvement and not research. However, it is recognized that the prospective information contained within the TCG Breast QC offers a rich resource of information that could be disseminated via publications for the benefit of the general public. Publication of data obtained from the TCG Breast QC can occur via three approaches and would need appropriate institutional review board approval:

8.1. Individual user or user group publications—Participants can download and publish their own individual information. Groups of registered TCG Breast QC Participants can pool their information for multi-institutional publications.

8.2. Collaborative-wide publications—Publications performed using the entire dataset requires approval from the TCG Breast QC Steering Committee.

8.3. Registry-based clinical trials—A novel methodology to greatly improve the efficiency and speed at which formal prospective studies are performed are registry-based trials. In this type of research, high volume sites experienced with a particular technique or patient population are identified and recruited for involvement in a sponsored study. The infrastructure of the TCG Breast QC is used to markedly simplify data collection with key variables by individual sites for quality improvement. Appropriate institutional review board approval and patient informed consent would need to be obtained for this type of research. Data collection for quality improvement would proceed in the usual manner. A small amount of information particular to the study would be entered into a separate study-specific module to supplement the comprehensive TCG Breast QC Database. Leveraging the existing Database and its infrastructure could transform the efficiency and speed with which BCS and TARGIT research is performed.

APPENDIX

Appendix A: Electronic case report forms data elements
Appendix B: Data Use Agreement