

## **Prospective Biospecimen Collection Protocol**

### **Breast Cancer**

**v1.2**

#### **Overview**

The Clinical Proteomic Tumor Analysis Consortium (CPTAC) sponsored by the NCI Office of Cancer Clinical Proteomics Research is a comprehensive and coordinated effort to accelerate the understanding of the molecular basis of cancer through the application of robust, quantitative, proteomic technologies and workflows. The overarching goal of CPTAC is to improve our ability to diagnose, treat and prevent cancer. To achieve this goal in a scientifically rigorous manner, the NCI launched CPTAC to systematically identify proteins that derive from alterations in cancer genomes and related biological processes, and provide this data with accompanying assays and protocols to the public.

CPTAC consists of a network of Proteome Characterizations Centers (PCC) and a Data Coordinating Center (DCC) serving as a hub and central repository for all CPTAC data. CPTAC will be expanded to include 1) a network of Tissue Source Sites (TSS) to obtain clinical specimens for proteomic and genomic analysis, 2) a Biospecimen Core Resource (BCR) to serve as a repository for tissue and associated, de-identified clinical data submitted to the program, and 3) a Genomic Characterization Center (GCC) dedicated to the genomic analysis of CPTAC specimens.

#### **Purpose**

The purpose of this protocol is to establish the minimum procurement parameters for ductal and lobular breast cancer stage IIA – IIIC specimens to be submitted to the CPTAC for proteomic and genomic analysis. The tissue source will be from newly diagnosed, untreated patients undergoing definitive surgery for breast cancer.

The protocol builds on CPTAC experience with human tissues obtained from the TCGA programs and specifically aims for:

- Minimized specimen processing and ischemia time with the ischemia time recorded.
- Sufficient total material from each patient divided into multiple samples suitable for independent processing for proteomic and genomic analysis.
- Independent samples suitable for histopathological analysis with frozen sections obtained at the BCR.
- Improved determination of weights of individual samples for improved estimates of protein yield.

#### **Scope**

The protocol applies to any samples submitted by a SAIC-F subcontractor to the CPTAC BCR.

## **Requirements**

### ***Patient Inclusion Criteria***

- Newly diagnosed patients with invasive breast cancer undergoing definitive surgery for breast cancer.

### ***Patient Exclusion Criteria***

- Prior history of other malignancies within the past 12 months other than treated basal cell carcinoma of the skin or treated DCIS of the contra lateral breast (as long as no tamoxifen was administered).
- Other malignancies at the time of surgery.
- Prior systemic chemotherapy for any cancer.
- Radiation or chemotherapy for the invasive breast cancer.
- Prior history of radiation therapy involving the breast such as mantle field radiation for Hodgkins Disease, radiotherapy for lung cancer, etc.
- Patients who are found to have a diagnosis other than invasive breast cancer as a result of the surgery.

### ***Regulatory (before procurement)***

- IRB approval received and documented with the CPTAC BCR.
- MTA/DUA agreement received and documented with the CPTAC BCR.

### ***Tissue Procurement and Shipping***

- Signed patient consent (maintained at the tissue source site, copy to CPTAC BCR not required).
- Cancer tissue per protocol.
- Normal tissue per protocol.
- Blood per SOP.
- Shipping Manifest completed and accompanying tissue shipment.
- CPTAC Tissue Submission Form (contains details regarding procurement such as warm ischemia times along with minimal patient information) completed and electronically submitted within 1-2 working days after tissue procurement.
- Adherence to BCR shipping instructions (the BCR will provide the shipping cryoport and cover the cost of shipping).

### ***Patient Data***

- CPTAC Baseline Case Report Form containing the patient's history and status at surgery along with diagnostic information (specific data to be collected to be determined) completed and electronically submitted prior to tissue shipment.
- Pathology Report (de-identified) including ER, PgR, and HER2 status submitted prior to tissue shipment.
- FFPE H&E diagnostic slides/images (at least one that is representative of the diagnosis in the pathology report; slides will be returned) submitted prior to tissue shipment.
- Ten 5 micron unstained FFPE slides from the definitive surgical specimen submitted.

- CPTAC One-Year Case Report Form with updated history and status one year after completion of the initial treatment regimen (data on neoadjuvant response if relevant and adjuvant/neoadjuvant treatment administered and other specific data to be collected to be determined).
- CPTAC Five-Year Case Report Form with updated history and status five years after completion of the initial treatment regimen (data on relapse and vital status along with other specific data to be collected to be determined).

***Tumor Specimen Inclusion Criteria***

- Greater than 500 mg total of all tumor samples obtained from a patient (including the weight of the cores).
- Greater than 60% tumor cell nuclei.
- Less than 20% necrosis.

**Tissue Procurement Procedure**

**Lumpectomy/Mastectomy (Two-Step Process)**

***Core Biopsies of Tumor before Devascularization of Tumor***

- Obtain core biopsies (minimum of 4) with a 14 gauge biopsy needle while the tumor is still in vivo.
- Place in pre-labeled cryovials and freeze in liquid nitrogen vapor. Pre-weighed cryovials will be supplied by the CPTAC BCR.

***Larger Sample Acquisition from Excised Tumor from the Same Patient***

- Record time when the tumor is surgically devascularized.
- Process through pathology within 30 minutes of removal from patient (specimen grossing must therefore be done as soon as possible after the tumor is removed).
- Accrue as much material possible while maintaining the integrity of tissue needed for clinical diagnostics.
- Divide the tumor specimen into at least two ~100 mg pieces for submission to the BCR. The size of the samples should allow them to fit into the cryovials with little to no compression.
- Additional samples may be obtained for local use.
- Place each piece destined for the BCR into a pre-labeled cryovial and freeze in liquid nitrogen vapor. Pre-weighed cryovials will be supplied by the CPTAC BCR.
- Record time when samples are placed in the liquid nitrogen vapor.

***Normal Breast Tissue from the Same Patient***

- Identify normal appearing breast tissue as far from the tumor as possible and excise without interfering with surgical-margin analysis. Alternatively, if a surgical procedure is to be performed on the contralateral breast for cosmetic reasons, collect normal-appearing breast tissue from that procedure.
- Divide the tissue into ~200 mg samples.

- Place each piece destined for the BCR into a pre-labeled cryovial and freeze in liquid nitrogen vapor. Pre-weighed cryovials will be supplied by the CPTAC BCR.

### **Large-Bore Percutaneous Coring During Port Placement for Neoadjuvant Treatment**

#### ***Tumor Tissue Cores***

- Obtain the large-bore (~10 ga.) samples to be submitted to the CPTAC BCR from the tumor (minimum of 3).
- Place each in a pre-labeled cryovials and freeze in liquid nitrogen vapor. Pre-weighed cyrovials will be supplied by the CPTAC BCR.
- Obtain at least one additional core and process for H&E staining.

#### ***Normal Tissue Cores from the Same Patient***

- Obtain the large-bore (~10 ga.) samples from the contralateral breast (minimum of 3).
- Place each piece destined for the BCR into a pre-labeled cryovial and freeze in liquid nitrogen vapor. Pre-weighed cryovials will be supplied by the CPTAC BCR.

Reference: Wilson, R and Kavin, S, Comparison of Large-Core Vacuum-Assisted Biopsy and Excision Systems *In* Brun del Re, R. (Ed.) Minimally Invasive Breast Biopsies, Springer, pp. 23-41, 2010.

([http://www.google.com/url?sa=t&rct=j&q=bard%20large%20core%20biopsy%20instrument%20vacuum&source=web&cd=4&sqi=2&ved=0CEcQFjAD&url=http%3A%2F%2Fwww.springer.com%2Fcda%2Fcontent%2Fdocument%2Fcda\\_downloaddocument%2F9783540314035-c1.pdf%3FSGWID%3D0-0-45-796504-p150492838&ei=EUI4UcgvLOq10QGgg4C4Cg&usg=AFQjCNGzx8IYPTog2SPF9e-T9Fd\\_ZhY6lw&cad=rja](http://www.google.com/url?sa=t&rct=j&q=bard%20large%20core%20biopsy%20instrument%20vacuum&source=web&cd=4&sqi=2&ved=0CEcQFjAD&url=http%3A%2F%2Fwww.springer.com%2Fcda%2Fcontent%2Fdocument%2Fcda_downloaddocument%2F9783540314035-c1.pdf%3FSGWID%3D0-0-45-796504-p150492838&ei=EUI4UcgvLOq10QGgg4C4Cg&usg=AFQjCNGzx8IYPTog2SPF9e-T9Fd_ZhY6lw&cad=rja))

#### **Blood Collection Procedure**

- Obtained pre-operatively.
- 10 ml lavender top vacutainer with the blood processed per SOP.