Purpose:

To provide researchers with a tissue microarray of formalin fixed paraffin embedded samples of human breast cancers. Cases from a variety of tumor stages (T1-T4) are represented including those with and without nodal metastases at presentation and cases with metastasis. Clinical follow-up is provided. This TMA may detect strong trends in differential gene expression among cancer types; it is intended for pilot surveys and generation of hypotheses. This TMA is not designed by itself to prove the utility of a marker for clinical prognosis.

Tissue samples:

The following tissue types are represented in the original TMA design:
- Category A: 60 cases of node-negative invasive breast carcinoma
- Category B: 60 cases of node-positive invasive breast carcinoma
- Category N: 20 cases of lymph nodes involved by metastatic breast carcinoma
- Category M: 20 metastatic breast carcinomas

Notes:

1) The metastasis cases (category M) may have been collected at the time of initial breast cancer presentation or later in the disease course. The time from initial diagnosis is provided in years. Metastases are collecting from a variety of sites including brain, lung, and bone.

2) Cases in Category N and M may overlap with patients in Category B. Cases with patient overlap are designated as such on the excel sheet as "redundant," with designation of the specific B case with which they overlap.

TMA design:
Each cancer case was sampled four times with a 0.6 mm needle cores in the original array design. Two TMA blocks were required to hold the entire cohort of samples (designated BRCaStg1-1 and BRCaStg1-2). Four duplicates of each block were made, designated A, B, C and D. Each array block is serially sectioned at 4 micron thickness. The histologic sections are placed on charged glass slides (Superfrost Plus, Fisher Scientific). At intervals, sections are stained and examined by a pathologist for quality assurance (QA) purposes.

The TMA also contains control tissues:
- Normal spleen
- Normal liver
- Normal myometrium
- Normal placenta

Quality assurance procedures:

Due to the variability inherent to tissue samples and histologic methodology, *most of the tissue microarray sections will not contain all of the tissue spots in the original design.* The number of tissue spots in which the desired tissue types resides will vary from section to section.

The following guidelines are used during histologic quality assessment:
A tissue spot is defined as being present if tissue occupied at least 25% of the possible surface area OR if at least 10 cells of target tissue are present. Target tissue is defined as being present if at least 10 cells were present in a tissue spot.

TMA slides are being released up to the histologic level in which there at least 45 cases present for the two primary tumor categories (A and B) and 15 cases present for each of the two metastatic categories (N and M). Thus, at a minimum, 120 cases will be represented on the TMA. Copies of the QA scoring sheets are also available upon request. THE TISSUE SAMPLES HAVE BEEN ANONYMIZED, NO FURTHER DATA ON THE DONORS IS AVAILABLE OTHER THAN THAT FOUND IN THE ACCOMPANYING GUIDE SHEETS.

Guide sheets in Microsoft Excel format and H&E stained whole-slide images representative of the array are available on the CHTN TMA website: http://chtn.sites.virginia.edu/.

If despite our efforts there are fewer than the minimum number of target tissue samples on your array sections, please contact the CHTN Mid-Atlantic Division at (434) 924-9879.

Frequently asked questions:
Why aren't all there as many tissue spots on my section of the array as are listed on the TMA key?
The key represents the original TMA design. Tissue cores are of various lengths, hence at deeper sections, some cores have been exhausted while others remain. In addition, some tissue spots may be lost during the process of transferring the TMA section to the glass slide.

Why isn't the target tissue type present in the tissue spot?
Although TMA manufacture is guided by a histologic section that represents the surface of the donor tissue, this target tissue may not be uniformly represented in the deeper sections of the tissue. This problem is greatest with small structures (e.g. breast ducts and lobules).

Why doesn't the representative microscopic image of the target tissue exactly match the tissue spot on my TMA?
The representative images or digital slides have been taken from a single QA section from a single array. Three different replicate TMA blocks were made for this series, each of which has different tissue cores. Even the same tissue core at a deeper section would not exactly match a more superficial section due to the variability inherent in tissue architecture.

Can I use antigen retrieval methods (boiling, microwave, pressure cooker, etc) on these sections?
Yes.

Can I perform in situ hybridization on these sections?
Yes.

Definitions and abbreviations:
Donor block: a tissue paraffin block (see below) that contains tissue of the desired type to be placed into the tissue microarray.

Histologic section: a flat sheet of paraffin and embedded tissue cut from a paraffin block on a microtome. The thickness of the section can vary, but a typical thickness is 4 microns (micrometers).

QA: quality assurance

Recipient block: The blank paraffin block into which tissue cores are inserted to form the tissue microarray.

Tissue core: the cylindrical tissue sample removed from the donor block, which is placed in the recipient block.

TMA: tissue microarray. A recipient paraffin block into which tissue cores have been inserted in a gridded array.

Tissue paraffin block: a sample of tissue that has been fixed in formalin, processed to remove water, then infused with molten paraffin, which is allowed to harden within and around the tissue in a square mold. This is the standard method of preparing tissue for clinical histologic analysis. The paraffin block is subsequently cut on a microtome to produce thin histologic sections which are placed on glass slides. In the manufacture of TMAs, these become the donor blocks.

Tissue spot: the tissue sample present on a histologic section of a tissue microarray that corresponds with a tissue core.