Aims

ACRIN 6657 is a multi-site clinical trial evaluating the use of quantitative single-voxel breast MRS. Ensuring that the spectroscopic measurements can be performed with sufficient accuracy and precision to address the clinical goals of the trial is a difficult challenge, especially considering that field strength, scanner manufacturer, breast coil, and sequences will vary between sites.

The goal of this abstract is to describe the design of the study and its quality control measures and present initial findings from the quality control phantom scans.

Methodology

The ACRIN 6657 Trial

The American College of Radiology Imaging Network (ACRIN) is supporting a multi-site trial using single-voxel spectroscopy (SVO) for characterizing breast cancer. ACRIN 6657, titled Contrast-Enhanced Breast MRI and MRS for Evaluation of Patients Undergoing Neoadjuvant Treatment, was designed to examine the role of MR spectroscopy (MRS) and imaging in selecting and monitoring breast cancer patients treated with neoadjuvant chemotherapy. The trial is conducted as part of the I-15 P multi-center trial (along with CALGB 150007) evaluating imaging- and tissue-based biomarkers for assessing response to neoadjuvant chemotherapy.

The original trial, which used only breast MRI, completed accrual of 237 patients in 2006. In 2007 a trial extension was approved to add breast MRS and enroll an additional 140 patients. The ACRIN 6657 extension opened in September 2007.

Schema

The trial aims to measure early response to therapy using quantitative estimates of the total choline concentration (tCho). The study includes a baseline MRI study, repeated shortly after beginning therapy (either 2-28 weeks or 48-96 weeks), and again prior to surgery. Additionally, a subset of patients (25%) will receive 2 pre-therapy baseline scans to evaluate reproducibility.

Rationale

A previous single-site pilot study showed that an acute decrease in [Cho]c, measured one day after the administration of the first dose of adriamycin/cytotoxic chemotherapy, was predictive of overall clinical response.

Trial Participation

The study design includes a baseline MRI study, repeated shortly after beginning therapy (either 2-28 weeks or 48-96 weeks), and again prior to surgery. Additionally, a subset of patients (25%) will receive 2 pre-therapy baseline scans to evaluate reproducibility.

Quality Control Phantoms

To measure consistency within and between the sites, several quality control measurements are required using a pair of standard phantoms. The phantoms were produced at a control lab and distributed to all participating sites. The normal phantom consists of a 2 liter leak-proof bottle containing vegetable oil and a 2 plastic sphere mounted on a post that allows the phantom to be imaged in the standing position. The abnormal phantom consists of a 1 cm plastic sphere, a small amount of Gd-DTPA, 10 mM deuterated TSP as a frequency reference, and 0.1% sodium chloride. The control phantom is identical except it contains no phosphocholine. Each site was provided with a normal and control phantom.

Quality Control Regimen

Two types of QC scans are performed. The Entry QC scan is used to identify artifacts, determine if a sequence/scanner/coil combination is acceptable, and set a baseline for follow-up QC scans. This scan needs to be performed for each MR scanner prior to scanning subjects and must be repeated after any major upgrades of the scanner or change of breast coil. A shorter QC measurement, the Week QC scan, must be performed weekly during the patient study period or at minimum within one week of each patient scan.

Discussion

The quality control strategy for the MRS acquisitions in this trial is to set performance criteria and monitor compliance with those criteria, rather than dictate specific acquisition sequences and hardware that must be used. This enables sites to use the best scanner, pulse sequence variation, and breast coil available provided it performs acceptably.

Although this leads to a variety of MRS acquisition methods, there are controls built in to the study design that correct for the primary sources of variation across sites. The table on the right outlines the various approaches used to control many of the potential problems and sources of variation in the trial design.

Primary tests for maintaining consistency are the use of water as an internal reference, regular quality-control scanning, centralized data analysis, and a relatively rapid acquisition-analysis feedback cycle to alert sites that have data problems.

Current Status

Seven of the ten sites have successfully completed their Entry QC scans and are eligible to scan subjects. The trial opened for enrollment in September 2007, with over a dozen subjects enrolled to date. Acquisitions of both QC and patient data are ongoing and expected to continue throughout 2008-2009.

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