

# ISPY1

# Summary

[ACRIN 6657](#) was designed as a prospective study to test MRI for ability to predict response to treatment and risk-of-recurrence in patients with stage 2 or 3 breast cancer receiving neoadjuvant chemotherapy (NACT). [ACRIN 6657](#) was conducted as a companion study to CALGB 150007, a correlative science study evaluating tissue-based biomarkers in the setting of neoadjuvant treatment of breast cancer. Collectively, CALGB 150007 and ACRIN 6657 formed the basis of the multicenter **Investigation of Serial Studies to Predict Your Therapeutic Response with Imaging and moLecular Analysis (I-SPY TRIAL)** breast cancer trial, a study of imaging and tissue-based biomarkers for predicting pathologic complete response (pCR) and recurrence-free survival (RFS). **Participant Eligibility and Enrollment:** Criteria for inclusion were patients enrolling on CALGB 150007 with T3 tumors measuring at least 3 cm in diameter by clinical exam or imaging and receiving neoadjuvant chemotherapy with an anthracycline-cyclophosphamide regimen alone or followed by a taxane. Pregnant patients and those with ferromagnetic prostheses were excluded from the study. The study was open to enrollment from May 2002 to March 2006. 237 patients were enrolled, of which 230 met eligibility criteria.

## Acknowledgements





This shared data set was provided by David Newitt, PhD and Nola Hylton, PhD from the Breast Imaging Research Program at UCSF, in collaboration with ACRIN, CALGB, the I-SPY TRIAL, and TCIA. Many thanks are due to [The ACRIN 6657 trial team](#), [The I-SPY 1 TRIAL team](#), and all the patients participating in these studies

Funding sources include NIH grants to UCSF (R01 CA132870 and U01 CA151235), ACRIN (U01 CA079778 and U01 CA080098), and CALGB (U01 CA31964 and U01 CA33601).

### Data Access

#### Data Access

Click the **Download** button to save a ".tcia" manifest file to your computer, which you must open with the [NBIA Data Retriever](#). Click the **Search** button to open our Data Portal, where you can browse the data collection and/or download a subset of its contents.

| Data Type                                | Download all or Query/Filter   |
|--|--|
| Images and Segmentations (DICOM, 76.2GB) |   |
| DICOM Metadata Digest (CSV)              |   |
| Clinical and Outcome Data                |   |

The ISPY team has provided additional options for download. The significance and download links for these subsets are explained on the [Detailed Description](#) tab.

Click the Versions tab for more info about data releases.

## Third Party Analyses of this Dataset

TCIA encourages the community to [publish your analyses of our datasets](#). Below is a list of such third party analyses published using this Collection:

- SDTM datasets of clinical data and measurements for selected cancer collections to TCIA
- DICOM SR of clinical data and measurement for breast cancer collections to TCIA

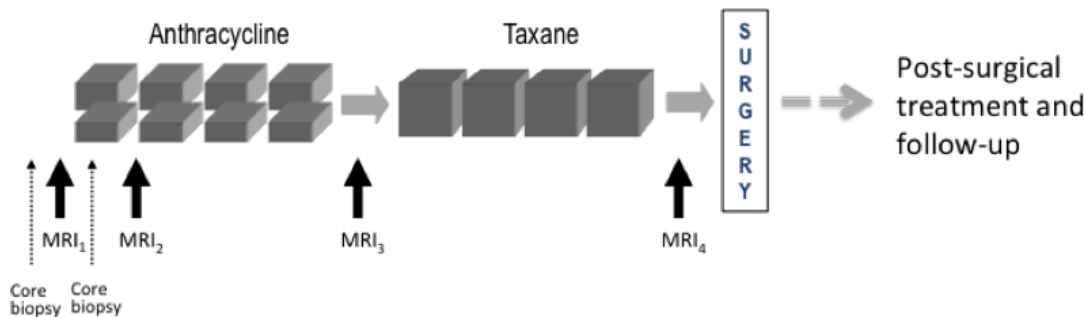
### Detailed Description

## Detailed Description

| Collection Statistics  |         |
|------------------------|---------|
| Modalities             | MR, SEG |
| Number of Participants | 222     |
| Number of Studies      | 847     |
| Number of Series       | 9032    |
| Number of Images       | 386,528 |
| Images Size (GB)       | 76.2    |

## Requirements for MR imaging (As specified in the ACRIN 6657 protocol )

Imaging time points: MRI exams were performed within four weeks prior to starting anthracycline-cyclophosphamide chemotherapy (T1, MRI<sub>1</sub>), at least 2 weeks after the first cycle of AC and prior to the second cycle of AC (T2, MRI<sub>2</sub>), between anthracycline-cyclophosphamide treatment and taxane therapy if taxane was administered (T3, MRI<sub>3</sub>), and after the final chemotherapy treatment and prior to surgery (T4, MRI<sub>4</sub>). The study schema is shown in Figure 1



**Figure 1.** CALGB 150007 and ACRIN 6657 study schema.

Imaging protocol: MR imaging was performed on a 1.5 Tesla field strength scanner using a dedicated breast radiofrequency coil. The image acquisition protocol included a localization scan and T2-weighted sequence followed by a contrast-enhanced T1-weighted series. All imaging was performed unilaterally over the symptomatic breast and in the sagittal orientation. The contrast-enhanced series consisted of a high resolution (1mm in-plane spatial resolution) three-dimensional, fat-suppressed, T1-weighted gradient echo sequence with TR20 ms, TE = 4.5 ms, flip angle 45°, 16-18 cm field-of-view, minimum matrix 256x192, 64 slices, slice thickness 2.5 mm. Scan time length for the T1-weighted sequence was required to be between 4.5 and 5 minutes. The sequence was acquired once before contrast injection and repeated at least twice following injection.

Tumor diameter measurement and volumetric analysis: Tumor longest diameter (LD) was measured by the site radiologist as the greatest extent of disease on baseline MR images, including intervening areas of non-enhancing tissue. The same measurement direction was used on all subsequent MRI exams. The primary predictor variable, functional tumor volume (FTV) was measured from contrast-enhanced images using the signal enhancement ratio (SER) method. Volumetric analysis, including Quality Control assessment, was performed centrally at the Breast Imaging Research Program (BIRP) laboratory at University of California at San Francisco (UCSF).

Detailed information about the DICOM data is available in the [DICOM Dictionary](#).

### **Further information on these studies can be found at:**

- ACRIN 6657 Protocol [http://www.acrin.org/6657\\_protocol.aspx](http://www.acrin.org/6657_protocol.aspx)
- CALGB 150007 <http://www.cancer.gov/clinicaltrials/search/view?cdrid=69280&version=HealthProfessional>

# Imaging Data Transfer History

The processing of the MR image data for ACRIN 6657 consisted of the following steps between image acquisition and the creation of this shared data set on TCIA:

- MRI studies were sent from the study centers to the ACRIN Core Lab either via media (DVD) or the TRIAD program
- Image data were de-identified and centrally archived at the ACRIN Core Lab
- Archived data was sent to the Breast Imaging Research Program (BIRP) at the University of California, San Francisco (UCSF) for volumetric analysis.
- De-identified image data, derived analysis maps and segmentations, and ancillary data files were transferred from UCSF to TCIA for data sharing.

*While every effort was made to preserve the integrity of both the original image data and image meta-data (DICOM attributes, public and private), multiple file transfers and strict adherence to HIPPA guidelines for patient confidentiality may have resulted in loss of some data. If any questions arise, or patient PHI is found in any data on this collection, please contact the [UCSF Breast Imaging Research Program \(BIRP\)](#).*













# Curated Data Sets

In addition to the complete set of ACRIN 6657 imaging studies ("Level 0" data), the following curated data sets based on UCSF QC assessment, protocol compliance and data completeness are provided:

- Level 1: MRI Longest Diameter (LD)
- Level 2a: SER Volume Dataset for ongoing volumetric analyses (updated 9/17/16)
- Level 2b: SER Volume Dataset for pCR Analysis (Hylton, et al; Radiology 2012)
- Level 3: SER Volume Dataset for RFS Analysis (Hylton, et al; Radiology, 2016)

The image data sets are accompanied by Excel files with selected patient clinical and outcome data.

## Data subset Descriptions

| Data set                                       | subjects | All Series   | DCE +<br>Derived Only   | DCE Only   | Clinical and<br>outcome data  |
|--|----------|--|---|--|---|
| Level 0: Complete image data set               | 222      | <br>(76.2 GB) | NA  | NA   |  |
| Level 1: Studies with MRI LD measurements      | 219      | <br>(75 GB)   | NA  | NA   |  |
| Level 2a: Studies with SER Volume measurements | 207      | <br>(63 GB)   | <br>(43 GB) | <br>(24 GB) |  |
| Level 3: Studies used in primary aim analysis  | 162      | <br>(49 GB)   | <br>(34 GB) | <br>(18 GB) |  |

### Level 0: Complete I-SPY 1 / ACRIN 6657 MRI Dataset

This data set is comprised of all HIPPA compliant, DICOM compliant MRI series.

Level 0 image data set consists of 847 on-study MRI studies on 222 subjects in the UCSF image database.

One patient in the image data collection (I-SPY ID 1079 ) does not appear in the Feb. 2, 2011 I-SPY FINAL LOCKED clinical data dump. So no clinical or outcome data is available for this subject.

### Level 1: MRI exams for which longest diameter was measured

This data set is comprised of all studies with MRI measured longest diameter (LD) values reported.

839 MRI studies have LD reported in the I-SPY 1 clinical database, of which 5 studies are not present in either the UCSF or ACRIN image data collections (see Table 1).

Level 1 image data set consists of **834 MRI studies on 219 subjects** in the UCSF image database

**Table 1. Studies that have LD measurement but are missing from the UCSF and ACRIN TRIAD image data collections:**

|                            |                            |             |
|----------------------------|----------------------------|-------------|
| ID 1071, T1<br>ID 1138, T1 | ID 1101, T3<br>ID 1040, T4 | ID 1187, T4 |
|----------------------------|----------------------------|-------------|

## Level 2a: Good SER Volume Dataset – updated 9/3/14, 9/17/16

This data set is comprised of the patient studies which, following quality reviews in 2014 and 2016, were judged to have sufficiently good image quality and protocol compliance for volumetric DCE SER analysis. Rejection criteria included: incomplete volumetric DCE acquisitions, lack of a 2nd post-contrast acquisition, variability in fat suppression across the image, observed patient motion during the DCE acquisition, significant DCE protocol deviations such as changing scan parameters or image position during DCE acquisition.

Level 2a image data set consists of **706 MR studies on 207 subjects** in the UCSF image database. These include 7 studies not included in Level 1 (no MRI LD recorded) as listed in Table 2.

**Table 2. Studies in Level 2a (good volumetric analysis) that do NOT have LD measures:**

|   |                            |                            |
|---|----------------------------|----------------------------|
| ID 1059, T4<br>ID 1079, T2 *<br>ID 1104, T4   | ID 1192, T2<br>ID 1212, T4 | ID 1215, T1<br>ID 1238, T2 |
| <ul style="list-style-type: none"> <li>• Patient 1079 does not appear in the Feb. 2, 2011 I-SPY FINAL LOCKED clinical data set. So no clinical or outcome data is available.</li> </ul> |                            |                            |

## Level 2b: SER Volume Dataset Reported in Hylton et al. (Radiology, 2012) \*

This data set is comprised of the patient studies analyzed for pCR outcome and reported in the 2012 Radiology paper on ACRIN 6657 pCR results \*. This data set is not provided as a shared list, as it is not recommended for use in further analysis. It is described here because it is the data set from which the Level 3 (primary aim analysis) set was derived. Inclusion and exclusion was determined by quality and protocol reviews available at that time. In addition to the exclusion criteria listed for Level 2a, studies done with imaging in the axial plane, in violation of the sagittal orientation specified in the trial imaging protocol, were excluded due to processing limitations of the analysis software. Similarly, bilateral sagittal acquisitions (alternating left and right volumetric acquisitions) were excluded.

Level 2b image data set consists of **707 MRI studies on 207 subjects** in the UCSF image database.

- Hylton NM, Blume JD, Bernreuter WK, et al: *Locally advanced breast cancer: MR imaging for prediction of response to neoadjuvant chemotherapy--results from ACRIN 6657/I-SPY TRIAL*. Radiology 263:663-72, 2012

**Tables 3 and 4 show the specific inclusion/exclusion differences between Levels 2a and 2b:**

**Table 3. 16 studies accepted for SER analysis since 2008 (in Level 2a but not in 2b)**

|  |   |   |
|--|---|---|
| ID 1005, T3<br>ID 1043, T2<br>ID 1046, T4<br>ID 1057, T3<br>ID 1074, T3<br>ID 1084, T1 | ID 1110, T4<br>ID 1139, T4<br>ID 1159, T4<br>ID 1176, T2<br>ID 1201, T2 | ID 1203, T4<br>ID 1206, T4<br>ID 1225, T3<br>ID 1219, T3<br>ID 1228, T4 |
|--|---|---|

**Table 4. 17 studies rejected since 2008 (in Level 2b but not in 2a)**



| Study ID and TP  | Reason for rejection for volumetric SER analysis (level 2a)               |
|--|---|
| 1007 T4 *  | No fatSat; Different protocol from T1                                     |
| 1035 T4 *  | Only 1 post scan then acq. parameters changed                             |
| 1045 T1  | Alternating laterality acquisitions, 2 minute time gap                    |
| 1047 T1 *  | Image position changed during DCE   |
| 1053 T2 *  | Alternating laterality acquisitions, bad pre- acquisition                 |
| 1053 T4 *  | Alternating laterality acquisitions                                       |
| 1055 T1 *  | Alternating laterality acquisitions, 4 minute time gap                    |
| 1086 T1 *  | Alternating laterality acquisitions, time gap, different protocol from T4 |
| 1091 T1 *  | Changing acq. parameters during DCE                                       |
| 1095 T2 *  | Only 1 post scan then acq. parameters changed                             |
| 1173 T3 *  | Off protocol timing   |
| 1206 T1  | Bad DCE timing, 20 minute delay   |
| 1206 T2  | Bad DCE timing, 1'29" acquisition time                                    |
| 1224 T3 *  | Scan position changed during DCE  |
| 1230 T3 *  | Scan position changed during DCE  |
| #128 T1, T2  | 2 studies for ineligible patient: ACRIN ID 128 (no I-SPY ID)              |
| <ul style="list-style-type: none"> <li>• Subjects that <i>were</i> included in the primary aim analysis (Level 3)</li> </ul> |   |

### Level 3: Subset of Level 2b used in primary aim analysis, reported in Hylton et al. (Radiology, 2016) \*

This data set is comprised of the patient studies analyzed for RFS outcome and reported in the 2015 Radiology paper on ACRIN 6657 survival results (Hylton et al, Radiology \*). Table 5 shows the 45 patients excluded from the level 2a cohort for this analysis. Please see the publication for specific information on exclusions of patients from this group.

Level 3 image data set consists of **586 MRI studies on 162 subjects** in the UCSF image database. This is also the study cohort used as the Test Phase data in the QIN BMMR Challenge.

**Table 5. 45 subjects excluded from Level 2b set**

|         |         |         |         |         |             |
|---------|---------|---------|---------|---------|-------------|
| ID 1027 | ID 1079 | ID 1157 | ID 1182 | ID 1210 | ID 1234     |
| ID 1040 | ID 1084 | ID 1159 | ID 1185 | ID 1212 | ID 1235     |
| ID 1045 | ID 1103 | ID 1160 | ID 1187 | ID 1214 | ID 1237     |
| ID 1046 | ID 1110 | ID 1167 | ID 1189 | ID 1215 | ID 1238     |
| ID 1048 | ID 1120 | ID 1171 | ID 1192 | ID 1219 |             |
| ID 1054 | ID 1137 | ID 1176 | ID 1194 | ID 1221 | ineligible: |
| ID 1063 | ID 1139 | ID 1177 | ID 1203 | ID 1222 | Case #: 128 |
| ID 1067 | ID 1152 | ID 1180 | ID 1206 | ID 1228 |             |

- Hylton NM, Gatsonis CA, Rosen MA, et al: Neoadjuvant Chemotherapy for Breast Cancer: Functional Tumor Volume by MR Imaging Predicts Recurrence-free Survival-Results from the ACRIN 6657/CALGB 150007 I-SPY 1 TRIAL. *Radiology* 279:44-55, 2016.

### Citations & Data Usage Policy

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Users of this data must abide by the [Creative Commons Attribution 3.0 Unported License](#) under which it has been published. Attribution should include references to the following citations:

#### Data Citation

David Newitt, Nola Hylton, on behalf of the I-SPY 1 Network and ACRIN 6657 Trial Team. (2016). **Multi-center breast DCE-MRI data and segmentations from patients in the I-SPY 1/ACRIN 6657 trials**. The Cancer Imaging Archive. <https://doi.org/10.7937/K9/TCIA.2016.HdHpgJLK>

#### Publication Citation

Hylton NM, Gatsonis CA, Rosen MA, et al. (2016) **Neoadjuvant Chemotherapy for Breast Cancer: Functional Tumor Volume by MR Imaging Predicts Recurrence-free Survival-Results from the ACRIN 6657/CALGB 150007 I-SPY 1 TRIAL**. *Radiology* 279(1):44-55. <https://doi.org/10.1148/radiol.2015150013>

#### TCIA Citation

Clark K, Vendt B, Smith K, Freymann J, Kirby J, Koppel P, Moore S, Phillips S, Maffitt D, Pringle M, Tarbox L, Prior F. **The Cancer Imaging Archive (TCIA): Maintaining and Operating a Public Information Repository**, *Journal of Digital Imaging*, Volume 26, Number 6, December, 2013, pp 1045-1057. <https://doi.org/10.1007/s10278-013-9622-7>





## Other Publications Using This Data

TCIA maintains [a list of publications](#) that leverage our data. At this time we are not aware of any publications based on this data. If you have a publication you'd like to add please [contact the TCIA Helpdesk](#).













## Altmetrics

### Versions

#### Version 2 (Current): Updated 2016/09/28


| Data Type                   | Download all or Query/Filter  |
|-----------------------------|---|
| Images (DICOM, 76.2GB)      |  <br>(Requires the <a href="#">NBIA Data Retriever</a> .) |
| DICOM Metadata Digest (CSV) |    |
| Clinical and Outcome Data   |    |

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Data publicly released and new "level-specific" download options provided.

#### Version 1: Updated 2015/06/18

| Data Type              | Download all or Query/Filter  |
|------------------------|---|
| Images (DICOM, 76.2GB) |  |