image accrual in clinical trials

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We need a lot of data

- “Numbers Are King, Quality Is Queen” (R. Gilles)
  - protection against spurious correlations and type I errors
- Most clinical data repositories are inaccessible
- 3% to 5% of cancer patients in the U.S. participate in clinical trials
- roughly 20% of phase II and III trials in the U.S. are funded by the federal government
Imaging data from NCI-sponsored clinical trials

• National Clinical Trials Network (NCTN)
• NCI Community Oncology Research Program (NCORP)
## Proposed List of EA Trial Data for Transfer to QIN

<table>
<thead>
<tr>
<th>Priority</th>
<th>Study Title/Short Title</th>
<th>Disease Site</th>
<th>Total Accrual</th>
<th>Response Endpoint/TX</th>
<th>Imaging Data</th>
<th>Clinical Data</th>
<th>Primary Endpoint Published</th>
<th>Special Requirements</th>
<th>Reason for Priority Level</th>
<th>What's to be transferred?</th>
<th>When will data transfer start?</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>ACRIN 652/DMIST</td>
<td>Breast</td>
<td>49529</td>
<td>Detection</td>
<td>Digital Mammogram</td>
<td>ACRIN</td>
<td>yes</td>
<td>Imaging data not available. FFDM images available for ~45,000 cases</td>
<td>Requested by Stanford QIN site, but otherwise probably more limited use.</td>
<td>mammography, pathology data detected tumors</td>
<td>Can start as soon as permissions worked out (perhaps right away?)</td>
</tr>
<tr>
<td>2</td>
<td>ACRIN 654/ALIST</td>
<td>Lung</td>
<td>18894</td>
<td>Detection</td>
<td>CT</td>
<td>ACRIN</td>
<td>yes</td>
<td>Imaging data and good radiomics dataset.</td>
<td>Data currently available through NC-IC</td>
<td>Imaging data and good radiomics dataset.</td>
<td>Can start as soon as permissions worked out (perhaps right away?)</td>
</tr>
<tr>
<td>1</td>
<td>ACRIN 659</td>
<td>Prostate</td>
<td>134</td>
<td>Detection</td>
<td>MRI</td>
<td>ACRIN</td>
<td>yes</td>
<td>MRI/MRIs highly specialized dataset but could be good for prostate QINs. Data on pathology available.</td>
<td>MRI/MRIs highly specialized dataset but could be good for prostate QINs. Data on pathology available.</td>
<td>prostate MRI/MRIs; pathology data</td>
<td>Can start as soon as permissions worked out (perhaps right away?)</td>
</tr>
<tr>
<td>1</td>
<td>ACRIN 667/ISP1 (CALGB 15007)</td>
<td>Breast</td>
<td>356</td>
<td>Pathologic Response/Chemotherapy</td>
<td>MRI (1273 studies)</td>
<td>ISPY-CALGB 15007</td>
<td>Pending</td>
<td>Key secondary aim available. Endpoint data must be requested from ISPY</td>
<td>Highly responsive patients with acceptable survival but not necessarily so within QIN site. UCSC QIN site played an active role. Very useful for breast MRI.</td>
<td>serial contrast breast MRI with limited time sampling, response data (pathologic response)</td>
<td>Should be used by all sites for publication in process</td>
</tr>
<tr>
<td>4</td>
<td>ACRIN 664</td>
<td>Colorectal</td>
<td>2600</td>
<td>Detection</td>
<td>CT</td>
<td>ACRIN</td>
<td>yes</td>
<td>Not clear if this is relevant to QIN</td>
<td>Data currently available through NC-IC/NCIC</td>
<td>Imaging data and good radiomics dataset.</td>
<td>Can start as soon as permissions worked out (perhaps right away?)</td>
</tr>
<tr>
<td>3</td>
<td>ACRIN 667</td>
<td>Breast</td>
<td>1007</td>
<td>Detection</td>
<td>MRI</td>
<td>ACRIN</td>
<td>yes</td>
<td>Detection study could be very good for breast radiomics. For reponse, all data in ACRIN and available.</td>
<td>Detection study could be very good for breast radiomics. For reponse, all data in ACRIN and available.</td>
<td>breast MRI; pathology data</td>
<td>Can start as soon as permissions worked out (perhaps right away?)</td>
</tr>
<tr>
<td>2</td>
<td>ACRIN 668</td>
<td>Lung</td>
<td>251 (185 eval)</td>
<td>Response, PFS, OS/Rad Therapy</td>
<td>MRI (840 studies)</td>
<td>RT0G 0235</td>
<td>yes</td>
<td>Outcome data must be requested from RTOG</td>
<td>High priority dataset for PET response assessment, with good outcome data. Only for priority 2 is data need to come from RT0G.</td>
<td>Imaging data quickly; need RT0G data sharing for data</td>
<td>Imaging data quickly; need RT0G data sharing for data</td>
</tr>
<tr>
<td>2</td>
<td>ACRIN 677</td>
<td>Brain</td>
<td>123</td>
<td>Response and Outcome/Chemotherapy</td>
<td>MRI (537 studies)/MRIs</td>
<td>RT0G 0625</td>
<td>yes</td>
<td>Might take some work to get data from RT0G</td>
<td>High priority dataset for brain response, with good outcome data. For priority 2, data need to come from RT0G.</td>
<td>Imaging data quickly; need RT0G data sharing for data</td>
<td>Imaging data quickly; need RT0G data sharing for data</td>
</tr>
<tr>
<td>1</td>
<td>ACRIN 668</td>
<td>Lung</td>
<td>96</td>
<td>Response and Outcome/Chemotherapy</td>
<td>MRI (194 studies)</td>
<td>RT0G 0625</td>
<td>no</td>
<td>No response to PET/CT, repeatability</td>
<td>Can release the test data based on PET/CT, repeatability</td>
<td>Imaging data now available, need to request clinical data</td>
<td>Imaging data now available, need to request clinical data</td>
</tr>
<tr>
<td>1</td>
<td>ACRIN 666</td>
<td>Brain</td>
<td>51</td>
<td>PFS, OS/Rad Therapy, Chemotherapy</td>
<td>FMISO (44), DCE MRI (47), DSC MRI (47), MRS (37)</td>
<td>ACRIN</td>
<td>no</td>
<td>No data available at ASCO, primary aim not met</td>
<td>Data not available at ASCO, primary aim not met</td>
<td>Imaging data quickly; need RT0G data sharing for data</td>
<td>Imaging data quickly; need RT0G data sharing for data</td>
</tr>
<tr>
<td>1 (when publication accepted)</td>
<td>ACRIN 668</td>
<td>Brain</td>
<td>60</td>
<td>PFS, OS/Rad Therapy, Chemotherapy</td>
<td>MRI (184 studies)</td>
<td>ACRIN</td>
<td>no</td>
<td>Waiting on RT0G for a data. Outcome data must be requested from RT0G.</td>
<td>Another good brain dataset, but no RT0G outcome data.</td>
<td>Imaging data quickly; need RT0G data sharing for data</td>
<td>Imaging data quickly; need RT0G data sharing for data</td>
</tr>
<tr>
<td>2</td>
<td>ACRIN 667 (BCS Study RCA 180-263)</td>
<td>Bone</td>
<td>18</td>
<td>PS-S, Skeletal Events, Suspected Value</td>
<td>PS-S, Skeletal Events, Suspected Value</td>
<td>BMS Study CA 180-263, F. Peck, PI</td>
<td>yes</td>
<td>Outcome data must be requested from PS-S, Skeletal Events, Suspected Value</td>
<td>Specialized data set with dynamic and static MRI data.</td>
<td>Imaging data quickly; we have some data, need sharing permission.</td>
<td>Imaging data quickly; we have some data, need sharing permission.</td>
</tr>
<tr>
<td>1</td>
<td>ACRIN 668</td>
<td>Breast</td>
<td>90 (54 complete)</td>
<td>Pathologic Response and Tumor KI-677 Chemistry</td>
<td>MRI (199)</td>
<td>ACRIN</td>
<td>yes</td>
<td>MRI/MRIs highly specialized dataset but could be good for prostate QINs. Data on pathology available.</td>
<td>MRI/MRIs highly specialized dataset but could be good for prostate QINs. Data on pathology available.</td>
<td>Imaging data quickly; we have some data, need sharing permission.</td>
<td>Imaging data quickly; we have some data, need sharing permission.</td>
</tr>
<tr>
<td>4</td>
<td>ACRIN 669</td>
<td>Ovarian</td>
<td>120 (76 complete)</td>
<td>Response, PFS, OS/Rad Therapy</td>
<td>MRI (199)</td>
<td>ACRIN</td>
<td>yes</td>
<td>MRI/MRIs highly specialized dataset but could be good for prostate QINs. Data on pathology available.</td>
<td>MRI/MRIs highly specialized dataset but could be good for prostate QINs. Data on pathology available.</td>
<td>Imaging data quickly; we have some data, need sharing permission.</td>
<td>Imaging data quickly; we have some data, need sharing permission.</td>
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### STATUS

- Images available now or within next 6 months.
- Images available now. Data available subject to additional review (may involve a collaborating entity).
- Primary aim data and images expected to be available within 1 year.
- Images available now. Data available subject to additional review (may involve a collaborating entity).

### Priority scheme used

1. Looks like it will be useful to QIN with imaging components (e.g. response) and data is ready or close to ready
2. Like Priority 1, but need permissions that may take time
3. Good data, but probably less relevant for QIN (e.g. MRIs)
4. Not sure these are relevant for QIN at all or primary publication not close to done
EA->QIN data transfer dashboard
EA QIN Priority data sets

6657 Treatment Monitoring with Dynamic MRI (ISPY1)
Data have been loaded to TCIA (for BMMR)

6688 FLT PET in Invasive Breast Cancer
Approved for transfer to TCIA

6684 Assessment of Tumor Hypoxia with FMISO PET, DCE MRI and MRS
Revised manuscript scheduled for submission
Current process flow

Data resource support
(EA U01, TCIA, DART, ITCR, CIP)

QIN PI or QIN team

Intent?

Cooperative project
No correlatives needed

Cooperative project
Clinical correlatives needed

Evaluating methods with challenge projects

Submit QIN challenge proposal

Sign QIN data use agreement

E-A data use?

Y

Submit E-A data request

N

Transfer to TCIA or DART

N

on TCIA or DART?

Y

ready for QIN use

QIN projects and priorities
NCI Molecular Analysis for Therapy Choice (MATCH) Trial EAY131

- Analyzes patients’ tumors to determine for genetic abnormalities using a ‘basket’ or ‘umbrella’ approach
- Is there a targeted drug (i.e. an ‘actionable mutation’)?
- Assigns treatment based on the abnormality
- Each treatment is used in a unique arm
- trial opened Aug 2015 with 10 arm
- reopened May 2016 with 24 treatment arms
- Each arm expected to enroll a max of 35 patients
- Eligibility: solid tumors and lymphomas not responding to standard therapy
NCI MATCH Trial EAY131

- Coordinated by ECOG-ACRIN and open to NCTN and NCORP sites (expecting 2,400 or more)
- Utilizes advanced DNA sequencing
- “the largest and most rigorous precision oncology trial in history”
- primary endpoint is RECIST response rate (target ≥ 25%)
- secondary end-point is PFS at 6 months (target ≥ 25%)
NCI-MATCH Patients and Sites

- 795 patients enrolled for screening in the first 3 months
- Far surpassing original estimate of 50/month
- Plan to enroll 5,000 patients

- 192 active sites (at least 1 patient)
  - 2/3 community
  - 1/3 academic

- 796 approved sites
MATCH Imaging Concept

ECOG-ACRIN: Susanna Lee
NCI: Frank Lin

Objective:
To assess whether radiomic phenotypes obtained from pre-treatment imaging and changes from pre- through post-therapy imaging can predict OR and PFS and to evaluate the association between pre-treatment radiomic phenotypes and targeted gene mutation patterns of tumor biopsy specimens.
MATCH Trial Flow

Refactory tumor

Enroll → Biopsy & mutation analysis

Actionable mutation?

yes → Treat with study agent

SD → SD
PR → PR
CR → CR

PD

no → Off trial

PD

Additional actionable mutation?

yes → 3 year followup

no → Biopsy & mutation analysis

Off trial
Post Re-activation Imaging Statistics

- Blue line: Subjects Enrolled (Post Re-activation)
- Green line: Subjects Collected
- Red line: Sites Submitting Imaging
STUDY MODALITIES

*data as of 21-Sept-2016*
Diagnostic Imaging for Submission

• All screened subjects
• All imaging visits
  – Pre-biopsy exam demonstrating progression
  – Followup on MATCH therapy
  – Progression on MATCH therapy
• All body parts
• Modalities for collection: CT, MRI, FDG PET-CT
• Modalities not for collection: plain film, fluoroscopy, ultrasound, non-PET nuclear medicine
Summary

- Legacy imaging trial data available through EA->QIN transfers
- Prospective data with genomic analysis should be available though imaging add-on to MATCH trial
Acknowledgements

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