Feasibility Study for an Evaluation of the Small Animal Imaging Research Program

Final Report

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I. Introduction

Purpose of the Feasibility Study

The purpose of the Feasibility Study was to explore whether an Outcome Evaluation of the Small Animal Imaging Research (SAIR) Program is both warranted and feasible, and, if warranted and feasible, to make recommendations regarding the design of the Outcome Evaluation.

About the SAIR Program

The Small Animal Imaging Research (SAIR) program is one of several specialized initiatives administered through the National Cancer Institute (NCI) Division of Cancer Treatment and Diagnosis (DCTD) Cancer Imaging Program (CIP). Increasingly in cancer research, small animal models are used to better understand cancer. The SAIR program aims to facilitate scientific advances by increasing the availability of small animal imaging and its use by cancer researchers. The SAIR program began funding 5 institutions in 1999 and is currently funding a total of 10 institutions through a R24 mechanism with approximately $750,000 dollars going to each institution annually for a 5 year award period. Each SAIR spends one-half to two-thirds of its effort providing imaging-related services to cancer investigators and the remainder of the time developing small animal imaging technology. Total program funding FY1999-FY2006 was $45.8 million.

The current goals of the SAIR program are to to increase efficiency, synergy, and innovation of such research and to foster research interactions that cross disciplines, approaches and levels of analysis. The SAIRs carry out their goals through funding:

- Multiple imaging technologies for small animals, emphasizing, but not limited to, those technologies which can provide biochemical, genetic, pathological or pharmacological information related to malignancy in vivo.
- Technology research and development on innovative new imaging technologies appropriate for small animals, as well as refinement and development of technologies already established.
- Capabilities and personnel to assist in the development and/or production of necessary probes for the imaging technologies provided.

- Capabilities and personnel to aid in small animal anesthesia and care, as well as to consult on the optimal use of animals in connection with the cancer-related imaging experiments.
- Training for both professional and technical personnel in the techniques and methodologies of cancer-related small animal imaging.

Additional information concerning the current program mission and goals (an RFA released in 2006 is intended to change the program's implementation in future years) is available in RFA-CA-04-011.

II. Activities and Methods

In order to determine whether an Outcome Evaluation was warranted and feasible, the Science and Technology Policy Institute (STPI) engaged in the following activities:

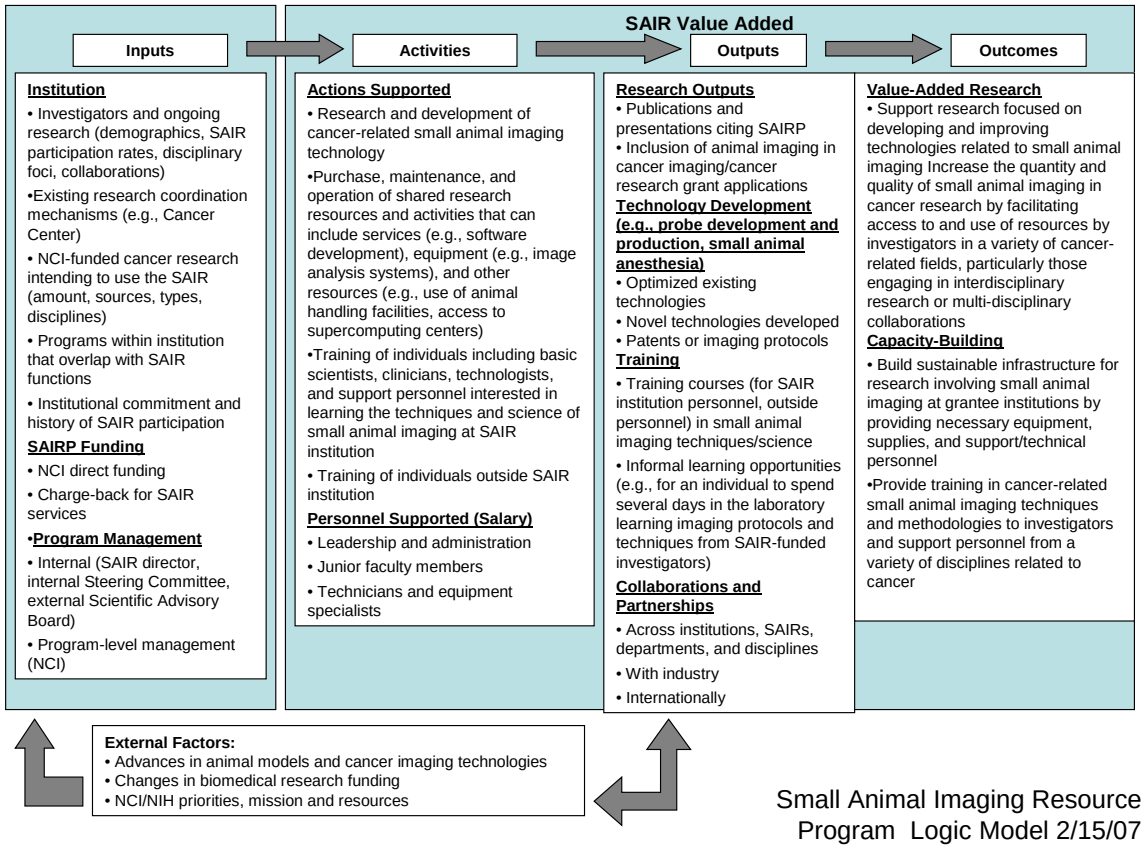
- **Consulting with Cancer Imaging Program staff,** including the SAIR program officer and the CIP director.
- **Developing a provisional logic model** that describes the inputs, activities, outputs, outcomes, impacts, and external influences of the SAIR program as currently understood. It is fully expected that the logic model will be further developed and refined as part of a SAIR Outcome Evaluation, should one occur.
- **Reviewing and analyzing existing data on the SAIRs and potential comparison groups,** including all of the following:
    - RFAs, application and award data, and other historical documentation
    - Publications attributed to the program, compiled through a MEDLINE search and from program records
    - Annual Progress Reports submitted by SAIR Principal Investigators
    - Patent searches for patents by SAIR-designated key investigators
    - Compilation of "imaging-related" clinical trials in the United States
- **Development of an outcome evaluation design.** Insights gained from the activities and analyses described above were used to decide that an outcome evaluation was feasible and warranted, and to develop recommendations for an Outcome Evaluation study design, including the following components:

- Framework and overall approach
- Study questions
- Recommended metrics
- Recommended data sources
- Appropriate analytic methods

III. Development of the Program Logic Model

Reviews of administrative documents (e.g., the program RFA) and discussions with CIP program staff were used to generate a program logic model (shown below as Figure 1) that was iteratively updated throughout the Feasibility Study. The logic model identifies critical inputs to the program (e.g., pre-existing capabilities at SAIR institutions, program management, funding for small animal imaging research), activities of awardees (e.g., purchase of equipment, research into new small animal imaging techniques or protocols), and ouputs and outcomes of those activities. Once the feasibility and necessity of pursuing an outcome evaluation was determined, the logic model served as the basis for generating study questions during the evaluation design phase.

Figure 1: Preliminary Logic Model for SAIR Program



Small Animal Imaging Resource Program Logic Model 2/15/07

IV. Findings

Key Feasibility Study Results

Publication Analysis

Publications were identified through two sources: A MEDLINE search based on SAIR and ICMIC award numbers, conducted on August 8th, 2006, and electronic lists of publications provided by the SAIR program officer in August 2006.[1] Lists were cross-checked to identify duplicates across lists, remove non-MEDLINE-indexed publications (e.g., presentations, book chapters), and to standardize information provided in the electronic lists (e.g., missing PubMed ID numbers or publication dates).

The information was compiled into two databases (schema for main publications database shown as Appendix A, schema of citation database shown as Appendix B) and analyzed the publication information to identify:

- Institution of corresponding author (determined from the MEDLINE "Affiliation" field)
- Identification of whether the institution was a SAIR institution or ICMIC or not (based on the list of SAIR and ICMIC grantees)
- Standardization of citation information (using Computer Retrieval of Information on Scientific Projects [CRISP] searches for award numbers as necessary)

Counts of Publications

Of those publications, 105 are review articles, comments, or reports from congresses/meetings. For the purpose of the publication counts, only the 689 journal articles are reported below. Table 1 shows that there are 450 SAIR publications, of which 336 (75%) are SAIR-only, and 114 (25%) cite at least one SAIR and one ICMIC grant. Of the publications, 370 (82%) were identified by the MEDLINE searches, while

[1] As many SAIR awards are co-located with in vivo Cellular and Molecular Imaging Center (ICMIC) awards and a substantial fraction of SAIR publications co-cite ICMICs, the SAIR-ICMIC linkage was incorporated into the FS analysis and a joint publication/citation database was created. The combined SAIR/ICMIC publications database includes 794 records.

an additional 80 publications were identified solely from the records provided by the SAIR program officer.

Table 1: Publications by Program (excluding review articles)

Number of SAIR publications that are	
Not ICMIC	336 (SAIR only)
ICMIC	114 (Both)
Total	450 (Any SAIR)

Table 2 shows publications by year of publication date. As would be expected, there is a "ramp-up" period associated with each program. It appears from the table that publication productivity of the SAIRs has approximately stabilized (approximately 100 publications per year).

Table 2 – Count of SAIR publications by year of publication

	1999	2000	2001	2002	2003	2004	2005	2006 (through 8/8)	Total
Publications citing SAIR (includes joint SAIR/ICMIC)	4	14	36	65	82	96	103	50	450
Number of SAIRs active in year	5	5	10	10	10	10	10	10	

Table 3 further subdivides publications by individual awardee. Table 3 suggests that the SAIR publication rates vary by institution. Thirty-four publications (8% of the total SAIR-citing publications) have corresponding authors from 28 distinct non-SAIR institutions (including seven international institutions). Also of interest is that for the two institutions that have "lost" SAIR funding (University of Pennsylvania, University of Arizona), there is a two-year "ramp-down" period, which appears reasonable given the lag between research occurring and its publication.

Table 3 – SAIR publications by awardee and publication year

SAIR Awardee	1999	2000	2001	2002	2003	2004	2005	2006	Total
CWRU								1	1
Duke				1	2	6	6	3	18
Harvard				7	9	17	14	12	59
Johns Hopkins				4	2	3	8	1	18
Michigan	3	6	2	3	3	7	11	8	43
MSKCC		1	7	4	15	10	8	1	46
Stanford		1	6	4	6	7	9	6	39
UCLA			2	13	11	11	5	5	47
University of Arizona			1	4	6	10	7	2	30
University of California Davis	0	0	0	0	0	0	0	0	0
University of Pennsylvania		2	6	5	6	6	4	1	30
Washington University	1	3	7	13	15	15	23	8	85
32 other institutions	0	1	5	7	7	4	8	2	34

Note: Highlighted years are the years SAIRs have been active

Table 4A shows journals in which SAIR-affiliated articles have most often been published. Top journals include a mix of imaging-specific journals (e.g., Magnetic Resonance Medicine, Molecular Imaging, Journal of Nuclear Medicine), cancer journals (e.g., Cancer Research, Neoplasia), and general science journals (e.g., Proceedings of the National Academy of Sciences). Table 4B shows SAIR-affiliated publications in "high-impact" biomedical journals. SAIR publications appear in five of the ten high-impact journals – with most articles in Proceedings of the National Academy of Sciences.

Table 4A – Publications by most common journal

Journal	Number of SAIR publications (includes joint ICMIC-SAIR)
Magn Reson Med	45
Cancer Res	34
Proc Natl Acad Sci U S A	23
Mol Imaging	22
J Nucl Med	21
Mol Ther	16
Neoplasia	15
Bioconjug Chem	13
Clin Cancer Res	12
Nucl Med Biol	10
Circulation	10
J Biomed Opt	9
Hum Gene Ther	7
Eur J Nucl Med Mol Imaging	7
114 other journals	251

Table 4B – Publications by "high-impact journal"

"High-Impact" Journal	SAIR
Nature	0
Science	2
N Engl J Med	1
Cell	0
Proc Natl Acad Sci U S A	23
J Biol Chem	1
JAMA	0
Lancet	0
Nat Genet	0
Nat Med	5

Note: List of "high-impact" journals taken from, Journal Status, Johan Bollen, Marko A. Rodriguez, and Herbert Van de Sompel, May 17, 2006. http://www.arxiv.org/PS_cache/cs/pdf/0601/0601030.pdf

Analysis of Awards Co-Cited With SAIR Awards in Publications

For the purpose of this section, all 794 published articles in the SAIR/ICMIC publications database were considered;[2] of the 794 publications, 707 cited one or more awards; nearly half of the publications identified through program officer-provided electronic lists (87 of 191 or 46%) did not cite any awards. One use of award citation data is to identify cross-citations between SAIR/ICMIC publications and other NCI programs. Table 5 shows cross-citations associated with the SAIR publications.

Tables 6A and 6B show co-citations of non-NCI awards for the SAIR publications in the database. Table 6A suggests that SAIR/non-NCI award co-citation is quite broad, whether in terms of the number of publications that cite non-NCI awards (174 of 396 SAIR publications which had award citations, or 44%) or the number of individual awards and citations cited. Table 6B considers co-citations by individual Institute or Center (IC). The table shows that NHLBI, NCRR, NIBIB, and NINDS awards are most likely to be co-cited with SAIR awards.

[2] Note that 87 of the 105 review articles did not include citations; it was not feasible, however, to separate the citations of the remaining 18 from the citation analysis, and so they are included in the following section.

Table 5 – Award Co-citations between SAIR and other NCI awards

Program	Award co-citations between SAIR and:	Comments:
SPORE	1	
Cancer Center Support Grants	37	27 of SAIR-Cancer Center co-citations are Washington University
EDRN	0	None identified
NTROI	2	New program – both co-citations are University of Pennsylvania
Mouse Models	3	3 of 5 total co-citations are UCLA
Cancer Nanotechnology	0	New program
Training (T32)	18	Primarily Harvard/MGH and UCLA
Training (K-series)	3	
Research (R01)	199	Primarily UCLA, MSKCC, Harvard/MGH
Research (P01)	70	Primarily Harvard/MGH and Michigan
Research (R21)	20	Often Harvard/MGH
The Washington University radiolabeling R24	18	13 WU SAIR – WU R24 co-citations
Multiple awardees within program	2	1 Michigan-Stanford, 1 WU-UCLA
Number of individual SAIR publications with citation data	396	
Total individual NCI awards cited	459	

Note: Such analyses likely understate collaboration, as not all publications include award citations and not all PIs are consistent in citing grants.

Table 6A: Award Co-Citations between SAIR and non-NCI awards summary

Measure	Number
Publications citing any non-NCI awards	174
Distinct awards cited	215
Number of non-NCI award citations	358

Table 6B: Award Co-citations between SAIR and non-NCI awards by non-NCI Institute or Center

IC/HHS Unit	Number of individual awards from IC co-cited with SAIR	Number of times those awards are co-cited with SAIR
FDA (not NIH IC)	1	2
NCRR	21	48
NEI	4	4
NHGRI	0	0
NHLBI	45	85
NIA	5	7
NIAAA	1	1
NIAID	12	18
NIAMS	7	9
NIBIB	20	47
NICHD	11	15
NIDA	4	4
NIDCD	1	1
NIDCR	11	13
NIDDK	21	27
NIEHS	3	3
NIGMS	12	15
NIMH	2	3
NINDS	34	56

Table 7 adopts a different perspective, looking at award co-citation patterns from an institutional perspective, focusing on the publications of individual SAIRs. Washington University St. Louis, Stanford, University of Pennsylvania, and Duke often co-cite between SAIRs and non-NCI awards, while MSKCC, UCLA, and University of Arizona were less likely to do so. Progress reports were read to identify the extent to which these co-citation trends are replicated in the written descriptions.

Table 7: Non-NCI Award Co-citation patterns of SAIR awardee institutions

SAIR	Number of times non-NCI awards are co-cited with SAIR	Total SAIR publications (from Table 3)	Non-NCI citations per SAIR publication
Duke	23	18	1.3
Harvard/MGH	50	59	0.8
Johns Hopkins	16	18	0.9
Michigan	28	43	0.7
MSKCC	3	46	0.1
Stanford	57	39	1.5
UCLA	11	47	0.2
University of Arizona	12	30	0.4
University of Pennsylvania	33	30	1.1
Washington University	94	85	1.1

Progress Report Analysis

Identification of Participants – Key Personnel, Total Participation, and Trainees

SAIR progress reports for the last two available fiscal years were mined to identify named personnel, which were collected into a participant database. The SAIRs vary substantially in their definition of "key" personnel: the number of co-PIs, project leaders, and co-investigators, for example, ranges from 1 to 11 in the SAIRs. Furthermore, it is difficult to define the boundary of "all" personnel involved in a SAIR – in addition to the key personnel and the personnel (e.g., technicians) directly employed using the SAIR award, many investigators across institutions use SAIR facilities. Some individual SAIR progress reports (e.g., UC Davis SAIR) do list all personnel affiliated.

Lists of participants in training activities (e.g., workshops, informal training) were identified from the progress reports, where available. Documentation of SAIR trainees and training activities in progress reports was highly variable; it would be necessary to collect additional information (likely from PIs directly) to identify participants in these activities.

As the SAIR goals include multidisciplinary research, collecting discipline/department information will be necessary; much initial data can be gleaned from the progress reports and Internet searches of institutions' directories, but additional information (e.g., CVs) would be required for a full assessment of the degree to which interdisciplinary/multi-disciplinary research occurs.

Identification of Resources Generated

Lists of products and resources generated were compiled from the progress reports. SAIR progress reports are variable in their description of the resources or technologies that have been generated through their projects and institutions. Assessment of translational products of SAIR research (e.g., new models, imaging protocols) would require data collection and analysis in addition to the progress reports.

Identification of SAIR-Supported Infrastructure and Capabilities Provided

A list of SAIR-supported imaging systems (e.g., microPET scanners, SPECT systems) was created using SAIR progress report information. While progress reports appear to provide complete listings of physical infrastructure supported, they are more variable in discussing the capabilities provided by those systems and how they are used by SAIR investigators. Assessment of what facilities are available, the capabilities they provide, and their use by investigators would require supplementary data collection.

External Data Collection

Patent Searches

Patent searches (using PatentLens) were performed for SAIR key investigators as described above, identifying all patents with one more SAIR key investigator listed as inventors. Patents were coded to determine whether they appeared to be SAIR-related (e.g., application filed after SAIR award, related to small animal imaging). Patent searches can identify inventions by SAIR investigators during the timeframe awards were active– but were not able to identify which resources were specifically "SAIR-influenced", as few patents cite the SAIR award in their application. The patent searches revealed that imaging agents, diagnostic techniques, and new imaging tools/instruments were more likely to be idenitifed through the patent searches identifying software algorithms or protocols for using/optimizing imaging tools.

Clinical Trials Searches

Imaging-related clinical trials with one or more sites open in the United States (both currently accruing patients and closed to accrual) were downloaded from clinicaltrials.gov.[3] Trials were coded further to identify whether the lead institution was

[3] "Imaging-related" defined by searching clinicaltrials.gov for all trials mentioning, "imaging", which STPI then coded to assess whether the trial truly used imaging, and the nature of the trial (e.g., new imaging agent, imaging for diagnosis/staging/guide to treatment/assessor of treatment success).

a SAIR institution, the trial PI was a SAIR key investigator, and used trial descriptions to identify whether small animal imaging was listed in the protocol rationale or design or whether a SAIR-generated resource or finding was directly incorporated into the trial.

The clinical trials search was successful in identifying whether SAIR institutions/key investigatorss were involved in leading trials. One SAIR key investigator (Mitchell Schnall, University of Pennsylvania) was identified as an imaging trial PI. As might be expected given the design of the SAIR program, this method proved wholly unsuccessful in identifying resources, techniques, or protocols that have been incorporated into the design of clinical trials. Assessment of the integration of SAIR-developed tools into clinical research would require additional data collection (e.g., through interviewing of SAIR PIs and key investigators), rather than through this approach.

Identification of Other Small Animal Imaging Infrastructure at SAIR and non-SAIR Institutions

Multiple sources were assembled to identify small animal imaging infrastructure and research at SAIR and non-SAIR institutions, including:

- NIH database searches (e.g., CRISP) for core facilities in the Cancer Center and SPORE programs and "translational" P01 awards
- Downloads from the NCI Cancer Research Portfolio (CRP) identifying awards with "small animal imaging" character, and
- Internet site reviews of leading academic medical institutions

NIH database searches provided the names of institutions and awards with one or more "small animal imaging" related core facilities as of FY 2004; such facilities were generally funded through Cancer Center Support Grants. Three Cancer Centers at SAIR institutions (MSKCC, UCLA, Washington University) support "animal imaging" cores through their Cancer Centers in addition to through their SAIRs. Two Cancer Centers at non-SAIR institutions (MD Anderson, Vanderbilt) fund "animal imaging" cores through their Cancer Center Support Grants. Nevertheless, with only the names of core facilities – and no information about their size, capabilities, or use – this information represents a starting point in identifying small animal imaging infrastructure funded outside the SAIR program rather than as a complete list of capabilities or facilities.

The CRP search identified several SBIR/STTR awards to companies for small animal imaging research and technology development, but few other awards to academic

medical institutions.[4] The Internet site reviews identified one SAIR (City of Hope/Beckman Research Institute) with small animal imaging capabilities and infrastructure, but the differing Internet site designs of academic medical centers suggested that this was not a methdologically valid approach to identifying the infrastructural capabilities of these organizations.

Is a SAIR Outcome Evaluation warranted?

It was found that a SAIR Outcome Evaluation is warranted for the following reasons:

- **The SAIR program is ripe for an outcome evaluation.** Periodic evaluation is critical to informing program management and strategic priority-setting. The SAIR program has proceeded through three funding cycles over eight years; a current RFA and solicitation of applications is underway for the fourth cycle. There is sufficient record from the awardees of the first and second cycles to observe outcomes.

- **SAIR activities, outcomes and impacts are sufficiently varied and complex that in-depth analysis beyond Feasibility Study is worthwhile.** In constructing a preliminary logic model for the program, the primary goal was to accurately represent the SAIR program with respect to inputs, activities, outputs, outcomes, impacts and external influences. The Feasibility Study, however, revealed that the outputs and outcomes of individual SAIRs appear to be sufficiently heterogenous that in-depth evaluation beyond the data collation-based efforts of a Feasibility Study would be required to understand and assess the outcomes of the program to date.

- **Evaluation of the program is timely**. The fourth RFA envisions a substantial management transition within the program; new awardees would change from the current R24 mechanism where individual awardees developed their own institutions' programs to a U24-based network setting joint goals and interacting more strongly with other NCI-funded research networks (e.g., Mouse Models of

[4] R21CA110181 (MD Anderson Cancer Center, "Array Detectors for Accelerated Small Animal MRI"); F32CA110422 (Washington University, St. Louis, "Small Animal Imaging of Prostate Cancer Therapies"); R01CA072895 (Medical Diagnostic Research Foundation, "2 & 3D Imaging of Contrast Agents in Animal Models") being the only three non-SBIR/STTR awards that matched both "imaging" and "animals" from the CRP downloads.

Human Cancers Consortium). While the Feasibility Study identified particular indicators to guide this management shift (e.g., there are few SAIR publications that cite multiple SAIR awards or that cite both Mouse Models and SAIR awards), further exploration of the activities and managerial strategies of SAIR awardees and their influence on program outcomes will provide vital insights to program staff as the transition occurs.

As demonstrated in the preliminary logic model (Figure 1 above), a number of components of the SAIR program proved irreducibly complex. This indicates that there are likely a variety of questions that could productively be answered by an Outcome Evaluation.

Is a SAIR Outcome Evaluation feasible?

It was concluded that a SAIR Outcome Evaluation is feasible, but there are significant challenges that must be considered in any successful evaluation design. Findings that support feasibility include the following:

- **Investigator Progress Reports can be used as a primary data source for several critical metrics.** As part of the Feasibility Study, the feasibility of using internal program documents was explored, with particular emphasis on the investigator progress reports. In general, it was concluded that the progress reports can be used as a systematic source of data on participants, core facilities, and resources generated by the program. The reports also contain a wealth of descriptive and anecdotal data in a variety of other areas that may prove useful in providing context for the evaluation.
- **Additional NIH databases can be used as complementary data sources.** Extensive use can also be made of NIH databases, particularly for program inputs and outputs. The two explored in depth as part of the Feasibility Study were the CRP database (used to identify other imaging-related awards funded by NCI) and MEDLINE.

Major challenges include the following:

- **SAIR institutions are not homogenous.** There is significant variation among SAIR institutions with respect to the integration of SAIR resources into the larger

institutional context (e.g., Cancer Center Support Grant use for SAI facilities) as well as the goals, activities, outputs, and outcomes of SAIR awards within institutions. This heterogeneity poses a particular challenge for quasi-experimental approaches to evaluation design; this challenge is further heightened by the heterogenity of small animal imaging research activities of non-SAIR institutions.

- **Much of the information contained in the progress reports is not suitable as a stand-alone data source for the evaluation.** As described above, the progress reports do contain information that can be used as part of an Outcome Evaluation, but many of the tables and narratives are not currently structured in a manner conducive to systematic reporting. Training activities, for example, are reported in highly variable fashion ranging from detailed descriptions of activities and names of participants to the near-absence of training information.

V. Recommendations for Design and Execution of SAIR Outcome Evaluation

Recommended Approach to Evaluation Design

There are three generic families of evaluation design that would ordinarily be considered for evaluation of a program such as SAIR:

- **Longitudinal** designs focus on changes in a program and its outcomes over time;
- **Cross-Sectional** designs aim to produce a current "snapshot" of a program and its outcomes;
- **Quasi-Experimental** approaches use comparison groups to draw conclusions about effects of the program.

In order to determine which option was best-suited for the SAIR Outcome Evaluation, four assessment criteria were developed:

1. Potential relevance of results to program and strategic planning;
2. Feasibility of collecting required data;

3. Potential payoff in terms of providing evidence for SAIR effect that will be compelling to stakeholders;
4. Risk of failure to detect differences and/or produce results that can be interpreted with confidence.

The longitudinal category was eliminated from consideration rather easily based on the first criterion; questions about evolution of the program over time would be academically interesting but, because of historical shifts in cancer imaging research and the state of knowledge/clinical practice, it is not clear that the program's past is relevant in moving forward. The advantages and disadvantages of the remaining two approaches for the SAIR evaluation were then considered more carefully. These are summarized below:

Advantages of Cross-Sectional Approach

- Well-suited to address a broad range of evaluation questions including process and outcome;
- Units of analysis can include the program, institution, and SAIR award as relevant;
- Current state of the program is likely most relevant moving forward.

Disadvantages of a Cross-Sectional Approach

- Evidence linking SAIR awards to outcomes would be more qualitative than quantitative;
- Design not well-adapted for rigorous comparisons.

Advantages of a Quasi-Experimental Approach

- When sample size is adequate and appropriate confounders are included in the analysis, provides strong quantitative evidence.

Disadvantages of a Quasi-Experimental Approach

- Since there are 10 current SAIR awards (12 total institutions) and a large number of relevant input variables, statistical power to detect differences will be low;

- Would require extensive new data collection about inputs and outputs at institution level, and much of this information may be unknown to the institutions themselves;
- Identification of appropriate comparison groups not necessarily straightforward, and small animal imaging activities and outputs of comparators are likely highly heterogenous as well;
- External comparison institutions may have little incentive to cooperate.

Applying the criteria discussed above, the following matrix was developed (Table 8):

Table 8: Generic Evaluation Planning and Decision Criteria

Criterion	Cross-Sectional	Quasi-Experimental
1. Relevance of results to program planning	High	High
2. Feasibility of collecting required data	High	Low
3. Potential payoff in terms of providing evidence for SAIR effect that will be compelling to stakeholders	Medium	High
4. Risk of failure to detect differences and/or produce results that can be interpreted with confidence	Low	High

Based on this evidence, a cross-sectional approach to the SAIR Outcome Evaluation Design was recommended. Such an approach is likely to provide information that will help the Cancer Imaging Program in moving forward. It will also allow evaluators to address a broad range of evaluation questions encompassing the entire logic model, and make the best use of existing data, and be most feasible for collecting the additional data needed. Most importantly, although the evidence it provides may be less compelling than a quasi-experimental approach, such an approach is most likely to demonstrate actual effects of the SAIR program with least risk of failure.

Details of Recommended Design for SAIR Outcome Evaluation

The details of the recommended evaluation design are discussed at length in the Proposal for Set-Aside Funds, to which this Feasibility Study Report is attached. What follows, therefore, is a brief overview of the design parameters. Please consult the full proposal for additional details.

Unit of Analysis

The main unit of analysis for the SAIR evaluation will be the grantee or comparator institution. The evaluation will focus on the 8 current SAIR institutions that were awarded in the first and second cohorts of awards, as well as the 2 institutions awarded in the first and second cohorts that did not receive renewals (Table 9, Groups A and B). Two current SAIR awardees (Case Western, UC Davis) first funded in the third cohort (FY 2004 RFA) will not be included because there has not yet been sufficient time for measurable outcomes to develop. It remains to be seen whether outcomes at SAIRs are sufficiently homogenous that the aggregated SAIR program outcomes could serve as an alternate unit of analysis; for variables where data can meaningfully be aggregated across institutions, this will also be attempted.

Since presence of other awards that support imaging infrastructure is expected to influence outcomes, the grantee institutions will be divided into sub-groups for analysis based on presence or absence of such funding. Table 9 identifies two sub-groups based on presence or absence of a Cancer Center Small Animal Imaging Core; if other significant differences in availability of funding are discovered during the study, further sub-divisions may be necessary.

Table 9: Potential SAIR Comparison Institutions

Institution Type	*Group A: Current SAIR Institutions*[a]	*Group B: Former SAIR Institutions*	*Group C: Unsuccessful Applicants*	*Group D: Other Institutions of Interest*
Large Academic Medical Centers **without** Cancer Center Small Animal Imaging Cores	• University of Michigan • Duke • MGH • Stanford • Johns Hopkins	• University of Pennsylvania/ Fox Chase Cancer Research Center • University of Arizona	• UCSF • Fred Hutchinson Cancer Research Center/UW • University of North Carolina • University of Pittsburgh • Mayo Clinic • UAB	• City of Hope/Beckman Research Institute
Large Academic Medical Centers **with** Cancer Center Small Animal Imaging Cores	• MSKCC • Washington University • UCLA		• Vanderbilt • MD Anderson	

Feasibility Study findings suggest that a formal comparative design is likely to fail because SAIR activities and outcomes vary widely from institution to institution. However, in order to provide context for the cross-sectional outcome data from the SAIR institutions, supplementary data will be collected from several comparator institutions. The purpose of this data collection will be to understand the comparability of infrastructure capabilities at SAIR and non-SAIR institutions; how small animal imaging research is supported at non-SAIR institutions that have applied unsuccessfully for a SAIR award; and whether/how SAIR activities (e.g., training) and outcomes (e.g., multi-disciplinary small animal imaging research) occur at comparator institutions will also be evaluated.

As part of the Feasibility Study, nine potential comparators (defined operationally as non-SAIR institutions with substantial small animal imaging research activities) were identified. As shown in Table 9 (Groups C and D), all but one of these institutions have applied for a SAIR award without success.

Evaluation Design

The overall approach to the design of the proposed SAIR Outcome Evaluation will be cross-sectional, aiming to produce a broad "snapshot" of the program and its outcomes from inception through 2006. Such an approach is best suited to meet the objectives of the evaluation for the following reasons:

- Information about the most recent years is most likely to provide information that will help NCI in moving forward with the program;
- A cross-sectional design provides flexibility to address a broad range of evaluation questions;
- Such an approach would make the best use of existing data and be most feasible for collecting the additional data needed;
- A cross-sectional design is most likely to demonstrate actual effects of the SAIR program with least risk of failure to detect outcomes and impacts.
    - The potential heterogeneity of SAIR outcomes suggests that formal intervention-comparison designs may fail because with the exception of very broad outcome measures (e.g., publications) comparison across SAIR institutions – let alone between SAIR institutions and comparators – may not be meaningful.

The cross-sectional design for this study will emphasize documenting a broad range of program activities and outcomes and will attempt to link activities to outcomes through qualitative data collection.

Data Sources

- *Archival Data Organized:*
    - Publications from SAIR institutions and potential comparators (from MEDLINE, SAIR program staff)
    - Lists of SAIR key personnel (from SAIR progress reports)
    - Lists of SAIR training (from SAIR progress reports)
    - Lists of resources generated from SAIR awards (from SAIR progress reports)
    - Lists of SAIR infrastructure (from progress reports)
    - Patents by SAIR key personnel (patent search)

- Imaging-related clinical trials from SAIRs and potential comparators (from clinicaltrials.gov)
- NIH database searches for small animal imaging infrastructure

- *New Data to Be Collected:*
  - Bibliometric data for the MEDLINE –indexed publications collected from SAIR awards and any comparator institutions (assessment of research quality, multidisciplinary research).
  - Interviews with SAIR PIs and up to nine conparator PIs to address issues of infrastructure development and maintenance, including how small animal imaging resources have received support at the institutional level, as well as to identify unique features of the research funded by SAIR awards.
  - Interviews with nine cancer research investigators at SAIR and at comparator institutions to gain insight into use of small animal imaging infrastructure and capabilities and the influence of training, if any, on their research and careers.
  - Interviews with nine SAIR investigators and up to nine small animal imaging investigators at comparator institutions (likely but not necessarily the PIs) to identify translational products/resources/tools produced, their influence to date on clinical research/patient care, and use of core facilities.
  - Interviews with nine non-NCI funded research investigators who use the SAIR-supported infrastructure– as identified from citation analysis of SAIR publications – to gain insight into how the SAIR has influenced their research.
  - Curriculum vitae of cancer imaging investigators at SAIR institutions (for multi-disciplinarity assessment)

Appendix C (attached) relates the evaluation's high-level study questions to specific study questions/measures and data sources.

Sampling strategies are necessary for several interview groups, especially:

- Comparator PIs (potentially the PI of unsuccessful SAIR applications from comparator institutions)

- Cancer imaging investigators using small animal imaging at SAIRs and comparators[5]
- Non-NCI funded investigators using SAIR infrastructure

As only nine investigators from each group will be interviewed, random samples will be drawn from the list of SAIR users already inventoried; from a list of researchers who were unsuccesful SAIR PIs; and at comparator institutions who are lead authors on small animal imaging publications. Given the small sample sizes and the lack of OMB clearance, interviews will be used to provide qualitative insights rather than for statistical purposes.

[5] All PIs and small animal imaging infrastructure coordinators/leaders at SAIR institutions will be interviewed; interview groups are sufficiently small as to not require OMB clearance.

Appendix A: Schema of SAIR/ICMIC Publications Database

Column	Field	Comments
A	Search	MEDLINE Search (ICMIC/SAIR or both) or electronic list (and which)
B	SAIR Publication (STPI Coded)?	Is this a SAIR publication (TRUE/FALSE)?
C	ICMIC Publication (STPI Coded)?	Is this an ICMIC publication (TRUE/FALSE)?
D	Home Institution (STPI Coded)?	Is the institution of the corresponding author a SAIR/ICMIC awardee (TRUE/FALSE)?
E	Institution of Corresponding Author(STPI coded)	Institution of Corresponding author (coded from column T)
F	PMID	PubMed ID
G	PubModel	Electronic or paper publication
H	ISSN	of journal
I	Volume	
J	Issue	
K	Year	
L	Month	
M	Day	
N	Journal Title	
O	ISO Journal	
P	Medline Journal	
Q	Title	of publication
R	Pages	
S	Abstract	
T	Affiliation	of corresponding author
U	Publication Type	
V	Review (STPI Coded)?	Is publication a review, comment, or meeting report(TRUE/FALSE)?
W	Language	
X	Journal Country	
Y	Keywords	
Z	(Keyword-)Associated Words	
AA	Grant Agency-Grant Number	
AB	Number of References cited	
AC-	Is the author list complete?	
AD	Author information	Three columns per publication (last name, first name and initial, first initials)

Appendix B: Schema of Citations in SAIR/ICMIC Publications Database

Column	Field	Comments
A	Search	MEDLINE Search (from database A)
B	SAIR/ICMIC home institution (STPI Coded)?	Is the institution of the corresponding author a SAIR/ICMIC awardee (from database A, TRUE/FALSE)?
C	Institution of Corresponding Author(STPI coded)	Institution of Corresponding author (from database A)
D	Is NCI?	NCI award (TRUE/FALSE)?
E	Is SAIRP?	SAIR (TRUE/FALSE)?
F	Is ICMIC?	ICMIC (TRUE/FALSE)?
G	Is Mouse Models?	MMHCC (TRUE/FALSE)?
H	Is EDRN?	EDRN (TRUE/FALSE)?
I	Is CCNE?	Nanotechonology center (TRUE/FALSE)?
J	PMID	PubMed ID (from database A)
K	As cited grant number	From database A
L	Cleaned grant number	STPI Coded: Standardized as possible
M	IC	NIH IC

Appendix C: Relationship of Outcomes, Study Questions, and Data Sources

Key Questions (s) to be addressed	Information Required	Information Source(s)	Data Collection Methods	Data Analysis Methods	Limitations	Potential Conclusions from Analyses
Has the SAIR Program enhanced or built **sustainable infrastructure** for cancer-related small animal imaging research at the institutional level?	Amount and types of imaging **equipment** at SAIR institutions and comparators	Investigators; Progress Reports	Interviews; Document Review	Qualitative Analysis; Descriptive Statistics	Information for comparators may be anecdotal	Characterization of SAIR outcomes
	Amount and types of imaging **supplies** at SAIR institutions and comparators	Investigators; Progress Reports	Interviews; Document Review	Qualitative Analysis; Descriptive Statistics	Information for comparators may be anecdotal	Characterization of SAIR outcomes
	Number and type of imaging **technicians and support personnel** at SAIR institutions and comparators	Investigators; Progress Reports	Interviews; Document Review	Qualitative Analysis; Descriptive Statistics	Information for comparators may be anecdotal	Characterization of SAIR outcomes
	Funding sources for imaging infrastructure at SAIR and comparator institutions	Investigators; Progress Reports	Interviews; Document Review	Qualitative Analysis; Descriptive Statistics	Information for comparators may be anecdotal	Characterization of SAIR outcomes
	Areas of **unmet need** for infrastructure at SAIR and comparator institutions	Investigators	Interviews	Qualitative Analysis		Characterization of SAIR outcomes

Key Questions (s) to be addressed	Information Required	Information Source(s)	Data Collection Methods	Data Analysis Methods	Limitations	Potential Conclusions from Analyses
Has SAIR stimulated **new directions for cancer research** by providing access to equipment, services, and other resources for small animal imaging?	Number of imaging-related **publications** at SAIR and comparator institutions; Citations and journal impact of publications	MEDLINE	Download	Bibliometric Analysis	Will miss publications where SAIR or comparator authors are not corresponding author	Characterization of SAIR outcomes
	Number of imaging-related **clinical trials** and **technologies in pre-clinical development** at SAIR and comparator institutions	Clinicaltrials.gov; Progress Reports; Investigators	Document Review; Interviews	Descriptive Statistics; Qualitative Analysis	Information for comparators may be anecdotal	Characterization of SAIR outcomes
	Number of **NIH-supported investigators** or projects citing SAIR award	MEDLINE	Download	Descriptive Statistices	Some authors may fail to cite the award	Characterization of SAIR outcomes
	Number, character, and productivity of imaging **collaborations** at SAIR and comparator institutions	MEDLINE; Curriculum vitae; Researchers	Downloads; Interviews	Bibliometric Analysis; CV Analysis; Qualitative Analysis	May not have access to all curriculum vitae	Characterization of SAIR outcomes
Has SAIR stimulated development or improvement of **technologies for**	Number of **publications** resulting from SAIR-funded research on imaging technologies	Progress Reports	Document Review	Descriptive Statistics		Characterization of SAIR outcomes

Key Questions (s) to be addressed	Information Required	Information Source(s)	Data Collection Methods	Data Analysis Methods	Limitations	Potential Conclusions from Analyses
small animal imaging?	Number of new or improved **imaging technologies** associated with SAIR and comparator institutions	Progress Reports; Investigators	Document Review; Interviews	Descriptive Statistics; Qualitative Analysis	Information for comparators may be anecdotal	Characterization of SAIR outcomes
	Funding sources for research on imaging technologies at SAIR and comparator institutions	Investigators	Interviews	Qualitative Analysis	Information for comparators may be anecdotal	Characterization of SAIR outcomes
Has the SAIR Program **expanded the community** of small animal imaging researchers?	Number, subject, and goals of formal and informal **training programs** in imaging techniques and methods at SAIR and comparator institutions	Progress Reports; Investigators	Document Review; Interviews	Descriptive Statistics; Qualitative Analysis	Information for comparators may be anecdotal	Characterization of SAIR outcomes
	Number, seniority, and disciplines of **trainees** benefiting from SAIR-supported training	Progress Reports; Investigators; Curriculum Vitae	Document Review; Interviews	Descriptive Statistics; Qualitative Analysis		Characterization of SAIR outcomes
	Funding sources and mechanisms for training in small animal imaging at SAIR and comparator institutions	Investigators	Interviews	Qualitative Analysis	Information for comparators may be anecdotal	Characterization of SAIR outcomes

Key Questions (s) to be addressed	Information Required	Information Source(s)	Data Collection Methods	Data Analysis Methods	Limitations	Potential Conclusions from Analyses
	Number of former trainees **pursuing careers** (or intending to pursue careers) in imaging	Investigators	Interviews	Qualitative Analysis	May be too soon for outcomes in this area to be measurable	Characterization of SAIR outcomes
	Number of former trainees **authoring** at least one imaging paper	MEDLINE	Download	Descriptive Statistics		Characterization of SAIR outcomes