Outcome Evaluation of the Small Animal Imaging Resource (SAIR) Program

Final Report: Public Version

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Executive Summary

Rationale for the Evaluation and Approach

Over the past several years, targeted molecular imaging has gained recognition as an indispensible tool for the detection and diagnosis of cancer as well as for research into the origins of carcinogenesis and metastasis. During the mid-1990s, however, the promise of molecular imaging had not yet been universally recognized, and the necessary tools and approaches for imaging at the molecular level were still in the early stages of development. In 1997, the National Cancer Institute (NCI) convened an Imaging Sciences Working Group (ISWG) in order to discuss investment needs and opportunities. In early 1998, a subgroup of the ISWG recommended that NCI should support dedicated small animal imaging facilities focusing on the study of genetically engineered mouse models.[1]

The Small Animal Imaging Resource (SAIR) program was created by NCI in 1999 as one programmatic response to this recommendation. The overall goal of SAIR is to develop and integrate small animal imaging research as a tool for advancing cancer research and improving clinical outcomes for cancer patients. Between 1999 and 2007, a total of fifteen institutions received SAIR funding in four separate rounds of competition; a total of twenty-three awards have been made to date. The R24 mechanism was used for the first three rounds of competitions. In the fourth competition, the program shifted to a consortium, with each award made using the U24 Resource-Related Research Related Cooperative Agreement mechanism. The total funding awarded for all four rounds of the SAIR RFA from FY 1999 to FY 2008 is $63.7 million, including $44.4 million in direct costs.

Following the recommendations of a Feasibility Study conducted between August 2006 and March 2007, NCI contracted with the Science and Technology Policy Institute (STPI) to conduct an Outcome Evaluation for the SAIR program in order to assess the extent to which the SAIR program has resulted in outcomes related to its program goals.

The overall approach to the SAIR outcome evaluation was cross-sectional. Because the Feasibility Study identified significant heterogeneity among the various SAIR awards, the main unit of analysis for the outcome evaluation was the individual award (or awardee institution as appropriate). The evaluation included the 12 institutions that received SAIR R24 awards in response to one or more of the first three SAIR Funding Opportunity Announcements (RFA-CA-98-023; RFA-CA-01-012; RFA-CA-04-011). Limited information was also collected on three additional institutions that received their first awards in the fourth round of competition (RFA-CA-07-004), but these institutions were not formally included in the evaluation effort.

[1] NCI Cancer Imaging Program, "In Vivo Molecular/Genetic Imaging Development" (Elias Zerhouni, MD, Chair), February 18-19, http://imaging.cancer.gov/reportsandpublications/ReportsandPresentations/ImagingSciencesWorkingGroup

The evaluation relied on three main sources for data on the SAIR program:

- Administrative data (e.g. SAIR applications and progress reports, Funding Opportunity Announcements, other program documentation)
- NIH and other US Government databases (e.g. NIH Query/View/Report system, MEDLINE)
- Informational interviews with stakeholders, including NIGMS staff members and the SAIR Principal Investigators (PIs)

The study was supported by a panel of three extramural experts (Dr. Panos Fatorous, Virginia Commonwealth University; Dr. Thomas Ruth, University of British Columbia; Dr. Juan Rogers, Georgia Institute of Technology). Two NCI staff members (Dr. Anne Menkens, NCI/Cancer Imaging Program; Dr. Lawrence Solomon, NCI/Office of Science Planning and Assessment) served as observers to the panel, providing factual clarification as needed. The expert panel advised study design and reviewed draft analyses to ensure the quality of the interpretation of study findings.

Attainment of Program Goals

The feasibility study identified four specific programmatic goals, three of which have been present throughout the program and a fourth goal added beginning with the 2000 Request for Applications. The evaluation's findings with respect to each goal are summarized below:

> *Program Goal 1: Build sustainable infrastructure for research involving small animal imaging at grantee institutions by providing necessary equipment (support for equipment dropped in 2006 RFA), supplies, and support/technical personnel.*

The goal of building infrastructure has been met, but it is not yet clear whether the infrastructure developed will be sustainable.

As described in Chapter 5, the SAIR program contributed to the purchase and/or construction of new small animal imaging equipment at all SAIR institutions, and all SAIR institutions have added imaging modalities using SAIR funding. Optical and microCT are the modalities that have been added most frequently by SAIR institutions. At many SAIR institutions, however, SAIR funds themselves represented a minority of the total funds devoted to purchase or construction of imaging equipment. The combined funding from sources to other than SAIR to SAIR institutions for imaging equipment was at least $22.6 million between 1999 and 2007, which is approximately triple the $7.5 million of SAIR program funds spent on equipment. In interviews, SAIR PIs tended to credit the SAIR program with helping to attract additional funding for infrastructure, particularly from institutional sources and the National Center for Research Resources (NCRR).

Sufficient time has not yet passed to assess the sustainability of the infrastructure that has been built with SAIR funds. At the three SAIR institutions that either no longer receive SAIR funding or had a gap in funding (University of Arizona, Stanford, and the University of Pennsylvania before its SAIR renewal), many of the small animal imaging capabilities added through the SAIR continue to function. PIs reported that these

capabilities are supported through user fees, institutional funding, and NCRR support for instrumentation purchase and upgrade. The University of Pennsylvania is notable for the formation of a School of Medicine-wide small animal imaging facility that houses imaging equipment and supports investigators from across the institution after the failure of its first renewal application; the re-funded SAIR now is one of the funding streams supporting this facility. At institutions funded in the second round and competitively renewed in 2006, however, several of the SAIR PIs stated that a decrease in the allowable direct costs (to $300,000) has constrained their operations and poses concerns for the future.

Program Goal 2: Increase the quantity and quality of small animal imaging in cancer research by facilitating access to and use of resources by investigators in a variety of cancer-related fields

This goal has been met, although the degree of integration of the small animal facility into cancer research at SAIR institutions has varied.

As described in Chapter 6, SAIR awardees engaged in a variety of activities designed to expand the community of small animal imaging researchers at their institutions, including training and support for pilot projects and/or pilot data collection. Other strategies described by PIs to increase the use of small animal imaging included outreach through the Cancer Center (e.g., Grand Rounds) and retreats; Internet sites; and outreach by the PI to make direct contact with potential users or to invite potential users to SAIR group meetings or seminars.

The SAIR RFA required that awardees support a minimum of six (raised to eight in the 2006 RFA) base grants. Records maintained by the SAIR PIs of actual users indicate that the 12 facilities funded during the first three award cohorts have supported 421 distinct awards – an average of thirty-five awards per institution. Although it was not feasible to identify which awards made use of SAIR resources in any given year (especially during the initial years of SAIR awards) comparing the number of awards supported with the number of awards listed in the SAIR initial applications indicated that most of the SAIR PIs reported at least twice as many awards making use of the facility as had been initially projected.

The evaluation considered the degree to which the SAIR facilities were integrated into their local Cancer Centers and other NCI translational research programs (e.g., ICMIC, SPORE, Mouse Models). Interviews with Cancer Center basic science directors as well as statements in application materials indicated that the SAIR award was a factor in the Cancer Centers' decision to include small animal imaging as one of their designated Core facilities at nine of the 12 SAIR institutions. Eight SAIR PIs reported that at least one project funded through the Cancer Center Support Grant (CCSG) made use of the SAIR-supported facility. Integration into local ICMICs was also strong, although somewhat variable by institution. SAIR facility use by SPORE, CCNE, Mouse Models, or NTROI awards has varied across institutions.

The evaluation also considered the degree to which cancer researchers across the SAIR institution made use of the SAIR facility using two measures of the breadth of SAIR influence: (1) the ratio of the total number of NCI awards acknowledged on SAIR

publications to the number of NCI-funded awards at the institution during the years the SAIR was operational; and (2) the number and percentage of acknowledgements in SAIR publications that went to the most-frequently acknowledged PI for each institution. SAIRs at Case Western, UC Davis, University of Pennsylvania, and Washington University fared relatively well on both measures of integration, while Duke, MGH, UCLA, and the University of Michigan appeared to be less well-integrated. Finally, at several institutions, investigators funded by NIH Institutes and Centers other than NCI or other organizations made active use of the SAIR-supported facility.

As described in Chapter 4, 951 SAIR publications were identified. The steady-state ratio of dollars per publication in a given year was approximately $50,000, disregarding the first year of SAIR program operations.

Program Goal 3: Support research focused on developing and improving technologies related to small animal imaging

This goal has been met at SAIR institutions, although both SAIR and non-SAIR funds contributed to its realization.

As described in Chapter 7, SAIR awards supported a range of research and technology development activities spanning hardware construction (32 projects), software/image registration activities (47 projects), and improved imaging methods and tools (53 projects). SAIR-supported investigators described key discoveries in each of these three categories. SAIR-developed equipment was identified as having been commercialized for two modalities: PET (two systems: one developed by University of Pennsylvania, commercialized by Philips and one developed by UCLA, commercialized by Concorde); and optical (developed by MGH, commercialized by Siemens, Kodak, and Olympus). Four SAIR awardees described collaborations with small businesses funded through the SBIR programs at NIH and DOE.

The SAIR program was not the sole source of support for any category of research and technology development. Other sources included NCI-funded translational research programs (e.g., ICMIC, CCNE, NTROI, particularly for imaging agents, methods, and reporters); NIBIB and NCRR P41s; and a NIBIB small animal imaging RFA and NCI/CIP program announcements that funded research targeting equipment development. In total, between 2001 and 2008 more than $30 million in R01/R21 funding for small animal imaging hardware- or software-related awards to principal investigators at SAIR institutions was identified by the evaluation, as well as three hardware-oriented P41 awards. A comparison of NIBIB and NCI imaging-related funding at SAIR and non-SAIR institutions suggests there may be substantial funding for small animal imaging hardware and software-related university research at non-SAIR institutions as well.

Another line of evidence supporting the conclusion that SAIR was not the sole source of funding for development of imaging technologies at SAIR institutions came from analysis of the acknowledgements on "technology development" SAIR publications. More than 90% of such SAIR publications at the nine SAIR institutions whose investigators were most diligent about acknowledging the SAIR award acknowledged at least one other award in addition to the SAIR. Only at Johns Hopkins (23%) and the

University of Arizona (46%) did a substantial percentage of "technology development" publications acknowledge only the SAIR award.

Program Goal 4: Provide training in cancer-related small animal imaging techniques and methodologies to investigators and support personnel from a variety of disciplines related to cancer

This goal appears to have been met, although available outcome data are limited and often anecdotal.

As described in Chapter 8, the SAIR institutions engaged in a wide variety of training activities, including seminar series, workshops, and support for students, junior faculty, technicians, and visiting faculty. PIs identified the SAIR program as relatively unique in providing funds for training activities related to small animal imaging. While training outcome data were not collected in uniform fashion across the SAIR institutions, outcomes included:

- At least 1000 individuals have participated in a SAIR-supported multi-day workshop.
- Two SAIR awardees described initiating new courses in small animal imaging.
- Five SAIR-supported postdoctoral fellows have received faculty positions at other institutions and three have received instructorships at their SAIR institutions.
- Four SAIR-supported postdoctoral fellows have received non-faculty research staff positions.
- One SAIR award has provided mid-career transition funding for two faculty members, one of whom has subsequently received NIH funding.
- Four SAIR awardees described using their visiting fellowship programs to help other institutions create small animal imaging programs.

Overall Findings

The evaluation and the program goal-specific findings lead to three overall findings:

Overall finding 1: SAIR is not the sole source of support for small animal imaging infrastructure (equipment and personnel) or technology development at any of the awarded institutions, and at several it may not even be among the most important sources of support for these activities.

As described in Chapter 3, receipt of the SAIR award at funded institutions generally preceded other sources of large-scale NCI support for small animal imaging, either within the Cancer Center structure or through other large programs. Currently, however, every SAIR institution (with the possible exception of Duke University) has a substantial organizational structure and infrastructure base for small animal imaging beyond the SAIR award, and in most cases the small animal imaging facility is also funded by the institution and/or through designation as a Cancer Center Shared Resource. The SAIR program can perhaps now best be characterized as providing an additional funding stream for imaging infrastructure, technology development, and training.

Table ES.1 summarizes the findings above and identifies complementarities between activities funded by the SAIR awards and other funding streams.

Table ES.1: Complementarities between SAIR and Other Funding Sources

Function	Non-SAIR Sources of Funding	Comments
Build/purchase new equipment	Institutional support, NCRR	
Maintain equipment	Institutional support, CCSG	
Support staff (technicians, faculty)	Institutional support, CCSG	
Operate facility (technical consulting, perform experiments)	Charge-backs, Institutional support, CCSG	
Pilot project funding or "*pro bono*" imaging support	CCSG pilot projects, Institutional support, P50/U54 developmental funds	Other sources of pilot funding not necessarily dedicated to small animal imaging
Hardware/software development	R01/R21, P41	
Imaging methods/ markers development	R01/R21, P41, P50/U54	
Degree training/ postdoctoral fellow support	T32/R25T, P50 Career Development	Other sources not specifically dedicated to small animal imaging
Junior faculty support	K-series, P50 Career Development	Other sources not specifically dedicated to small animal imaging
Hands-on training/ workshops	None identified	

Overall finding 2: There appears to be robust unmet demand for small animal imaging resource support at non-SAIR institutions.

As described in Chapter 3, in the most recent round of awards, NCI received 33 distinct applications and funded eight awards (24%). Of the 26 applications by institutions that had not previously received a SAIR award, three received awards (12%) whereas of the seven applications by institutions that had previously received a SAIR award, five received awards (70%). The difference in success rates between new and renewing applicants raises the concern that the SAIR program, as currently constituted, is difficult for new institutions to enter. A related concern described in Chapter 3 is the difference between SAIR and non-SAIR institutions regarding Cancer Center support for small animal imaging. As of 2007, all but one of the SAIR institutions, but only 14 of 51 non-SAIR Cancer Centers had a small animal imaging core resource. Moreover, as of 2007, 10 of the 12 Cancer Centers with SAIR awards had created or were in the process of creating an imaging-related research theme as opposed to six of 51 non-SAIR Cancer Centers.

Overall finding 3: There has been a recent shift in the NCI approach to funding core services and research resources.

As described in Chapter 3, the report of the NCI Translational Research Working Group, released in June 2007, includes an initiative related to the consolidation of core services and research infrastructure. The report recommends a shift in the approach by which NCI funds core services, stressing the role of the Cancer Center Support Grant as the primary source of funding for such infrastructure.[2] While the report does not recommend that NCI eliminate all separate resource-related R24 and U24 programs, it does imply that separate resource-supporting programs such as SAIR require a strong rationale for their continuation.

[2] The Report of the Translational Research Working Group of the National Cancer Advisory Board (June 2007), "Transforming Translation – Harnessing Discovery for Patient and Public Benefit", page 60.

Chapter 1: Introduction

1.1 Overview of SAIR

The Small Animal Imaging Resource (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 purpose of the SAIR program is to increase efficiency, synergy, and innovation of such research and to foster research interactions that cross disciplines, approaches and levels of analysis. [3]

The long-term goal of the SAIR program is to develop and integrate small animal imaging research as a tool for advancing cancer research and ultimately improving clinical outcomes for cancer patients. Intermediate goals of the program are to:

1. Build sustainable infrastructure for research involving small animal imaging at grantee institutions by providing necessary equipment, supplies, and support/technical personnel;
2. Increase the quantity and quality of small animal imaging in cancer research by facilitating access to and use of resources by investigators in a variety of cancer-related fields;
3. Support research focused on developing and improving technologies related to small animal imaging;
4. Provide training in cancer-related small animal imaging techniques and methodologies to investigators and support personnel from a variety of disciplines related to cancer.

NCI used the R24 mechanism for the first three rounds of SAIR competitions. In the fourth competition there was a change in mechanism from individual awards using the R24 to the formation of a consortium, with each award made using the U24 Resource-Related Research Related Cooperative Agreement mechanism. Between 1999 and 2007, a total of fifteen institutions received SAIR funding in four separate rounds; a total of twenty-three awards have been made to date. The total funding awarded for all four rounds of the SAIR RFA from FY 1999 to FY 2008 is $63.7 million, including $44.4 million in direct costs.

[3] This and subsequent paragraphs draw upon National Institutes of Health, "Small Animal Imaging Resource Program", Request for Applications RFA-CA-07-004, Release Date February 10th 2006, "Research Objectives" section.

1.2 Purpose of Outcome Evaluation

A feasibility study for the SAIR outcome evaluation was conducted between August 2006 and March 2007.[4] The feasibility study concluded that an outcome evaluation would be both feasible and warranted for the following reasons:

- SAIR-funded activities, outcomes and impacts are sufficiently varied and complex that in-depth analysis is required to document and understand them.
- The SAIR program is mature enough that it is reasonable to expect evidence for most intermediate-term outcomes to be available.
- Evaluation of the program is timely because the RFA cannot be brought to the NCI Executive Committee for renewal until an evaluation has been completed.

Following the recommendations of the feasibility study, NCI contracted with the Science and Technology Policy Institute (STPI) to conduct an outcome evaluation for the SAIR Program in August 2007. The primary purpose of the SAIR outcome evaluation has been to assess the extent to which the SAIR program has contributed to outcomes related to the four program goals. Evidence from the assessment will help to determine whether continued investment in SAIR is justified, and, if so, how the program might be improved to maximize success.

1.3 Structure of this Report

The balance of the report is organized into nine chapters. In Chapter 2, the evaluation design is described in detail, including a description of methods for data collection. Chapter 3 describes attributes of the various SAIR institutions in the context of program history and evolution, including funding and budget allocation, and leadership. Chapter 4 describes publications attributable to the SAIR award. Chapters 5-8 report on evaluation findings in outcome areas related to each of the four program goals:

- Infrastructure for Small Animal Imaging (Chapter 5)
- Use of Small Animal Imaging Infrastructure (Chapter 6)
- New Technology Development (Chapter 7)
- Training (Chapter 8)

Chapter 9 summarizes evaluative findings and recommendations.

Six Appendices include supplemental information collected as part of the Outcome Evaluation.

1. Appendix A: SAIR Logic Model
2. Appendix B: Thumbnail Sketches of the SAIR Awards
3. Appendix C: List of Awards Using the SAIR

[4] Science and Technology Policy Institute, "Feasibility Study for an Evaluation of the Small Animal Imaging Resource Program", March 2007

4. Appendix D: List of NCRR Small Animal Imaging S10 Awards to Cohort 1-3 Institutions
5. Appendix E: List of Identified non-SAIR Small Animal Imaging Equipment Development Awards at SAIR Institutions
6. Appendix F: Interview Guides

Chapter 2: Evaluation Methods

2.1 Evaluative Approach

The overall approach to the SAIR outcome evaluation was cross-sectional. Because the Feasibility Study identified significant heterogeneity among the various SAIR awards, the main unit of analysis for the outcome evaluation was the individual award (or awardee institution as appropriate). For outcome variables where data could meaningfully be aggregated across institutions (e.g., publications, number of awards making use of SAIR facilities), the SAIR program as a whole served as an alternate unit of analysis.

The evaluation included the 12 institutions that received SAIR R24 awards in response to one or more of the first three SAIR RFAs (RFA-CA-98-023; RFA-CA-01-012; RFA-CA-04-011).[5] Three additional institutions (MD Anderson, Vanderbilt, and University of Texas-Southwestern) first entered the program during the fourth cohort (RFA-CA-07-004); as they had just received funding at the start of the Outcome Evaluation, they were not formally included in the main part of the evaluation effort. However, these three institutions were considered to be of particular interest precisely because they independently arrived at a point where they could successfully compete for SAIR funds without previous support from the program. For this reason, limited information on small animal imaging-related infrastructure and outcomes was collected for these institutions during the time period when other institutions were receiving SAIR funding.

2.2 Study Questions

As described in Section 1.1, the feasibility study identified four specific program goals. The extent to which the SAIR program goals have been realized, how they were realized, and to what effect, are all relevant to the proposed outcome evaluation. These goals were used in combination with the program logic model (Appendix A) to develop the following evaluation study questions:

1. Has the SAIR program enhanced or built **sustainable infrastructure** for cancer-related small animal imaging research at the institutional level? (Corresponds to program goal 1)
    - What infrastructure has been purchased/built by the SAIR award or leveraged as a result of the receipt of SAIR funds?
    - Do small animal imaging infrastructure needs appear to be met at SAIR institutions?
    - Is there evidence that infrastructure built by SAIR is sustainable past the life of the grant?

[5] "SAIR institution" was defined as the university (or in the case of MGH and M.D. Anderson, research hospital) where the SAIR was located. At several institutions SAIR funding supported investigators from multiple institutions, either because of subawards to other institutions or through use of the SAIR facility by investigators outside the SAIR institution.

2. Has the SAIR program stimulated **new directions for cancer research** by providing access to equipment, services, and other resources for small animal imaging? (Corresponds to program goal 2)
    - Are SAIR resources widely used (and acknowledged) by investigators, including NCI-supported cancer researchers?
3. Has the SAIR program stimulated development or improvement of **technologies for small animal imaging**? (Corresponds to program goal 3)
    1. Has SAIR funded-research contributed, directly or indirectly, to the development of technologies for small animal imaging (e.g., imaging agents, new devices, device improvements, algorithms, protocols)?
    2. How is development of such technologies funded at SAIR institutions?
4. Has the SAIR program **expanded the community** of small animal imaging researchers? (Corresponds to program goal 4)
    - Do the training programs supported by SAIR funds expand the pool of small animal imagers at their institutions, in terms of both numbers and diversity?
    - Does training in small animal imaging techniques provided through SAIR facilities influence the research careers of the trained investigators and technicians?

2.3 Role of Expert Panel

The evaluation was supported by a panel of three extramural experts plus two NCI staff members who served as observers. The expert panel approved the study design, commented upon interview guides, and reviewed draft analyses to ensure the quality of the interpretation of study findings. The expert panel met twice by teleconference, on January 15th, 2008 and April 8th, 2008, and reviewed materials electronically between teleconferences. Panel members were:

- Dr. Panos Fatorous, Virginia Commonwealth University
- Dr. Thomas Ruth, University of British Columbia
- Dr. Juan Rogers, Georgia Institute of Technology
- Dr. Anne Menkens, NCI/Cancer Imaging Program (observer)
- Dr. Lawrence Solomon, NCI/Office of Science Planning and Assessment (observer)

2.4 Data Collection and Analysis

2.4.1 Data from Administrative Sources and Public Records

Information regarding SAIR awards and outputs was collected from a variety of sources at NCI including NIH databases, SAIR applications and investigator progress reports, and other administrative documents. Where relevant, data were also extracted from public sources including MEDLINE. The following information was extracted for the awards made to SAIR Cohort 1-3 institutions:

Funding provided to SAIR institutions by NCI. SAIR funding data from fiscal years 2001-2008 are available from NIH through its Query/View/Report (QVR) datasystem. QVR data were supplemented by programmatic data for fiscal year 1999 and 2000 provided by program staff. In this version of the report, only program-level data are shown.

SAIR administrative structure, budgets, key personnel, and training activities. Information was extracted from SAIR applications and progress reports.

SAIR publications. A database of SAIR publications was compiled from progress reports, renewal applications, and a MEDLINE search. All MEDLINE-indexed publications reported by the grantees were included in the database, as were MEDLINE-indexed publications that listed a SAIR award number in the acknowledgements field.[6] PIs were also invited to review the publications lists and add any publications they thought should be included; four SAIR PIs provided updates to the lists of publications initially identified. The SAIR publications database covers the period from program inception in 1999 to the end of fiscal year 2007. STPI characterized SAIR publications to identify those that described new uses of imaging technologies, the development of new imaging equipment or new algorithms for interpreting data, or new imaging agents, with the aim of distinguishing those publications from those where the SAIR facility was used by investigators to support the research (cancer-related or otherwise) they were conducting.

Other NIH awards reported to have received support from SAIR facilities. SAIR applications and progress reports were reviewed to identify lists of awards that made use of the resource.

Small animal imaging equipment at SAIR institutions. A list of equipment used for small animal imaging (that does not include ancillary equipment such as computing capabilities or animal handling facilities) present at each institution was created based upon SAIR applications and progress reports. The initial list was supplemented by searches of SAIR Internet sites and the NIH Computer Retrieval of Information on Scientific Projects (CRISP) datasystem to identify small animal imaging equipment-related National Center for Research Resources (NCRR) instrumentation awards made at SAIR institutions. PIs were also invited to review the draft equipment lists for completeness, though no changes were made based upon PI suggestions.

Research projects supported by SAIR funds. A list of individual research projects supported by the SAIR awards was created from renewal applications and progress reports. Supported projects were categorized along two dimensions: (1) whether the projects aimed to develop new equipment/hardware; software/image registration approaches; or new imaging methods, reporters, or agents and (2) the modality or

[6] In addition to the 951 MEDLINE-indexed publications, eighteen non-MEDLINE-indexed journal articles (from five SAIR awardees) were collected; because SAIR awardees differed in their reporting of non-MEDLINE-indexed articles (some including conference presentations and theses, others not providing any) they were not included in the discussion of publications in Chapter 4. Of the 951 MEDLINE-indexed publications, 814 (86%) included acknowledgements to NIH awards.

modalities to which the research corresponded. In this public version, only program-level data are shown.

Other NCI-administered and imaging-related awards to SAIR institutions. The report sections on SAIR usage (Chapter 6) and SAIR research (Chapter 7) include comparative information regarding other awards made to SAIR institutions. Three sets of CRISP and QVR searches were performed to identify this comparative information:

1. CRISP searches were performed to identify the list of all competing (new or renewed) NCI awards made to SAIR institutions during years that SAIR awards were funded.
2. CRISP and QVR searches were performed for each SAIR institution to identify small animal imaging-related awards whose PIs were named as SAIR key participants and whose biographies were included in SAIR applications in the relevant time period.
3. QVR searches were performed to identify awards made under imaging-related program announcements and RFAs of the NCI Cancer Imaging Program.

Applications for new funding making use of SAIR data or facilities. A list of applications (both NCI and non-NCI) described in SAIR renewal applications as having made use of the SAIR to provide pilot data or other supporting information was created. PIs were invited to review the draft database for completeness, although no feedback was received. It was possible to identify such grant applications for seven of the SAIR institutions.

Small animal imaging facilities at Cancer Centers. For SAIR institutions that are also Comprehensive Cancer Centers (11 of the 12 SAIR institutions; Stanford received its designation after the SAR award period concluded), Cancer Center Support Grant progress reports from FY 2007, and the most recent renewal applications (from FY 2004-2008) were analyzed to identify whether they supported small animal imaging core facilities, the funding level (if any) for a small animal imaging core, and the PI of that core. In this public version, only program-level data are shown.

2.4.2 Interviews with SAIR Program Participants

A series of interviews were conducted with SAIR program participants and investigators:

- The nine continuing SAIR PIs[7] from the first three cohorts were interviewed at length to understand SAIR outcomes at their institutions.
- The three SAIR PIs whose awards had not been renewed (Arizona, Stanford, University of Pennsylvania) to identify SAIR outcomes during the award period and the sustainability of the small animal imaging facility post-award.
- The three SAIR PIs whose institutions were first funded in the most recent cohort (M.D. Anderson, University of Texas Southwest Medical Center, Vanderbilt) participated in somewhat shorter discussions to describe the development of imaging strengths at their institutions.

[7] In one case (MGH), the co-PI was interviewed in place of the actual PI; in one case (UCLA), the co-PI and PI were interviewed separately.

- Five Cancer Center Associate Directors for Basic (or Translational) Research were interviewed to identify the role played by the SAIR and small animal imaging in the cancer research performed at their institutions and the relationship between SAIR and Cancer Center Support Grant. The five Associate Directors represent a convenience sample.

A separate interview discussion guide was developed for each of the groups described above. Each interview protocol was designed to facilitate "semi-structured" discussions comprised of open-ended questions and responses. Interviews occurred between February and September 2008, each lasting from 30 to 90 minutes. The interviews were conducted over the telephone with an audio recording service. Transcripts were coded to facilitate analysis of responses by theme.

2.5 Methodological Complications and Data Limitations

After assembling the lists of awards making use of the SAIR facility and the SAIR list of publications, these databases were cross-referenced to assess their degree of overlap. An initial analysis was performed to identify authors' acknowledging of the SAIR award number on SAIR publications. The analysis showed that the extent to which "SAIR publications" acknowledge the SAIR facility award number varies substantially across SAIR institutions – ranging from less than 10% to above 90% of the publications of individual SAIRs.

A second limitation is that there are substantial differences in the lists of awards making use of the SAIR facility and the lists of awards acknowledged on SAIR publications. It was not expected that all NIH awards reported to have used SAIR facilities would necessarily be acknowledged on a SAIR publication, nor was it expected that all publications acknowledging SAIR would acknowledge a SAIR award, but some degree of overlap between the two data sets was anticipated. Cross-referencing the two lists identified that the degree of overlap was generally low and also highly variable across SAIR institutions, ranging from 4% to 32% from individual SAIRs.

One potential explanation for the lack of overlap is that awards making use of the SAIR facility had not generated any publications through the end of fiscal year 2007; variations across institutions in the percentage of awards making use of the SAIR might affect the overlap calculation results. A test of this hypothesis showed that there was some variation in the percentage of awards making use of the SAIR facility that had not published by the end of FY 2007. After adjusting for unpublished awards, however, the finding does not appreciably change.

Chapter 3: SAIR Awards and Context

This chapter begins with a discussion of SAIR program origin and changes over time. The second section describes the awards and application success rates. The third section describes the institutional context for the SAIR facilities with respect to other funding for small animal imaging infrastructure. The fourth section describes program funding as well as allocation of budget dollars across various activities using SAIR funding.

3.1 Program Origin and Evolution

Over the past several years, targeted molecular imaging has become firmly established as an indispensible tool for the detection and diagnosis of cancer as well as for research into the origins of carcinogenesis and metastasis. During the mid-1990s, however, the promise of molecular imaging had not yet been universally recognized, and the necessary tools and approaches for imaging at the molecular level were still in the early stages of development. In 1997, the National Cancer Institute (NCI) convened an Imaging Sciences Working Group in order to engage in discussions of the issues and needs related to high priority investment opportunities. The Working Group formed seven task forces to provide recommendations to NCI.

One of the recommendations made by the *In Vivo* Molecular/Genetic Imaging Development task force in early 1998 was that NIH/NCI should support dedicated small animal imaging facilities focusing on the study of genetically engineered mouse models. The task force identified that the cancer research community had invested heavily in producing genetically-engineered mouse models as a means to understand the biology of cancer and to assess potential interventions. Imaging was identified as a technology having powerful potential, but at the time few imaging modalities optimized for small animal use were available. The task force's detailed recommendations, therefore, focused both on the creation of centers of excellence where imaging could occur and on new research that would develop the required technologies.[8]

Documents describing NCI's creation of the Small Animal Imaging Resource (SAIR) program, including the initial concept submission document to the NCI Board of Scientific Advisors and the initial RFA, identify the SAIR program as a direct

[8] NCI Cancer Imaging Program, "In Vivo Molecular/Genetic Imaging Development" (Elias Zerhouni, MD, Chair), February 18-19, 1998, Recommendation #4. http://imaging.cancer.gov/reportsandpublications/ReportsandPresentations/ImagingSciencesWorkingGroup page 4; last accessed May 15th, 2008.

programmatic response to this recommendation.[9] The first SAIR Request for Applications (RFA) was released in 1998. Using the R24 Resource-Related Research Projects, mechanism RFA-98-023 solicited applications for the support of shared resources for imaging small animals. The first year of the program was intended to fund three or four SAIR awards, at a total cost of $4.5 million, including the purchase of equipment to add imaging capabilities at SAIR institutions. Years 2-5 were intended to be funded at $2.1 million.

According to the 1998 RFA, SAIR funds were to be used to support the following activities:

- 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.

Subsequent SAIR RFAs were issued in 2000 (RFA-01-012); 2003 (RFA 04-011); and 2006 (RFA-07-004). Three major[10] changes were made to the program in subsequent RFAs.

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[9] REQUEST FOR BSA CONCEPT APPROVAL REQUEST FOR APPLICATIONS (RFAs), Small Animal Imaging Resource Programs, April 1998, page 2. Also, note the near-citation of the imaging sciences working group report, "A major limitation to studying tumors with current imaging techniques is their limited applicability to contemporary tumor models. Key understanding of neoplastic behavior is being derived from molecular biological techniques which are often related to small animal models, particularly genetically engineered mice. Most biomedical imaging devices have been optimized for human studies and have inadequate spatial resolution for small animals and their tumors. However, most imaging techniques can be scaled down to yield very high resolution and signal sensitive in vivo images of mouse sized samples. Furthermore, there are some imaging techniques which could provide valuable information in small animal models, but are not applicable to human subjects. Therefore, in order to take advantage of the small animal tumor models being developed, it is recommended that dedicated small animal imaging laboratories be developed" with the language in the Background section of RFA-98-023, "A major limitation to studying tumors in model systems with current imaging techniques is the limited availability of small animal imaging systems. Most biomedical imaging devices have been optimized for human studies and have suboptimal spatial resolution for small animals and their tumors. However, imaging techniques can be scaled down to yield very high resolution and signal sensitivity for in vivo images of mouse-sized organs. Furthermore, there are some applications of imaging techniques which could provide valuable knowledge from small animal models, but are not feasible for human subjects. Therefore, in order to take full advantage of the small animal tumor models being developed, it has been recommended that dedicated small animal imaging laboratories be developed."

[10] Other more minor changes included increasing the requirement of base grants to eight and requiring the inclusion of a business plan in the application for funding.

The first, introduced in the 2000 RFA, was the addition of language introducing, "training for both professional and technical personnel in the techniques and methodologies of small animal imaging" as a new program objective.

The second, introduced in the 2006 RFA, was a reduction in funding levels (capping direct costs at $300,000) concomitant with the elimination of the requirement for SAIR institutions to add new small animal imaging modalities; previously there had not been a restriction on the maximum size of SAIR awards.

The third, also introduced in the 2006 RFA, was a change from individual awards using the R24 mechanism to the formation of a consortium, with each award made using the U24 Resource-Related Research Related Cooperative Agreement mechanism. One practical effect of the change in mechanism is that awards are now cooperative agreements rather than grants; another change that accompanied the shift to the U24 mechanism was the expectation that the SAIR awardees as a whole would pursue multi-institutional activities as part of a consortium approach. Examples of such consortium activities encouraged by the 2006 RFA included collaboration with the Mouse Models of Human Cancer Consortium (Mouse Models) in developing new imaging methods and approaches; creation of common data storage and image processing techniques; and participation in consortium-wide workshops or symposia.

One activity that followed from the shift to a consortium was the SAIR investigators' annual meeting, held annually beginning in 2007. The meeting represents an opportunity for PIs and investigators to present findings and discuss research directions. Most SAIR PIs interviewed had not seen many differences in the management and operations of their awards as the result of the shift to cooperative agreements. Those SAIR PIs who did recognize influences on their operations were split regarding the likely utility of the consortium approach in the future. For example, one PI commented, "I think that the U24 mechanism has started to bring the centers together into a more unified whole then was the case before." Another stated that, "The U24 cooperative agreement won't work… it's hard to pay attention to consortium because everyone has to always come up with new ideas, write papers, write grants, etc."

Recent developments regarding NCI's funding for translational research across the Institute may also influence the future of the SAIR program. The National Cancer Advisory Board convened a Translational Research Working Group (TRWG) between 2005 and 2007 to recommend NCI-wide changes to the structure and funding of "early translational" research.[11] The TRWG report, released in June 2007, includes an initiative related to the consolidation of core services and research infrastructure. The report recommends a shift in the approach by which NCI funds core services, stressing the role of the Cancer Center Support Grant as the primary source of funding for such

[11] More information on the TRWG can be found at http://www.cancer.gov/trwg

infrastructure.[12] While the report does not recommend that NCI eliminate all separate resource-related R24 and U24 programs, it does imply that separate resource-supporting programs such as SAIR require a strong rationale for their continuation.

3.2 SAIR Awards and Application Success Rates

Between 1999 and 2007, a total of fifteen institutions received SAIR funding in at least one of four rounds of competition following each of the four RFAs. Five institutions competed successfully for their first award in the first round, and five additional institutions were funded in the second round. In the third round, three of the institutions from Cohort 1 competed successfully for renewal and two new institutions received funding. In the fourth round, four of the awards from Cohort 2 were competitively renewed. In addition, one of the Cohort 1 institutions re-competed successfully, and awards were made to three new institutions (Table 3.1a).

[12] As described in the Report of the Translational Research Working Group of the National Cancer Advisory Board (June 2007), "Transforming Translation – Harnessing Discovery for Patient and Public Benefit", page 60, "For institutions with cancer centers, consolidation will be achieved by strengthening the role of cancer centers as the primary providers of core services... Guidelines for Cancer Center and P50, U-series, and RFA-directed P01 awards will be revised as necessary to incorporate the following principles for core services resource sharing.
1. Cancer centers will provide the core services infrastructure for key translational research resources at institutions with cancer centers.
2. Individual P50, U-series, P01, and other relevant awards will request funds either to access cancer center or other institutional core services or for materials/salary support for project staff to use those services.
3. New translational research Requests for Applications and Program Announcements will specify use of cancer center or other institutional core services.
4. If applicants consider required core services nonexistent or unavailable at their cancer center or institution, they must present a list of the relevant core services that do exist and a specific rationale for creation of the proposed new cores.
5. If a service is not available at an investigator's home institution, a preferred option will be to provide funds to use the services of a neighboring institution.
6. No award will mandate the creation of a separate core service if an appropriate core service is locally available at cancer centers, the home institution, or the NCI intramural program.

Table 3.1a: Institutions Receiving SAIR Funding, by Fiscal Year

SAIR Institution	99	00	01	02	03	04	05	06	07	08
University of Arizona	I	I	I	I	I	-	-	-	-	-
University of Michigan	I	I	I	I	I	R	R	R	R	R
University of Pennsylvania	I	I	I	I	I	-	-	-	R	R
Memorial Sloan Kettering Cancer Center	I	I	I	I	I	R	R	R	R	R
Washington University	I	I	I	I	I	R	R	R	R	R
Duke University	-	-	-	I	I	I	I	I	R	R
Johns Hopkins University	-	-	-	I	I	I	I	I	R	R
University of California – Los Angeles	-	-	-	I	I	I	I	I	R	R
Massachusetts General Hospital	-	-	-	I	I	I	I	I	R	R
Stanford University	-	-	-	I	I	I	I	I	-	-
University of California- Davis	-	-	-	-	-	I	I	I	I	I
Case Western Reserve University	-	-	-	-	-	I	I	I	I	I
M.D. Anderson Cancer Center	-	-	-	-	-	-	-	-	I	I
University of Texas – Southwestern Medical Center	-	-	-	-	-	-	-	-	I	I
Vanderbilt University	-	-	-	-	-	-	-	-	I	I

Source: STPI analysis of NIH Administrative Data
Note: "I" indicates the initial iteration of a funded SAIR; "R" indicates the renewal phase; "-" indicates no funding was received.

Table 3.1b: SAIR Applications and Success Rates, by Cohort

Measure	Cohort 1	Cohort 2	Cohort 3	Cohort 4
Total Number of SAIR Awards Made	5	5	5	8
Number of Applications	29	23	37	33
Percentage Funded	17%	22%	14%	24%
Number of Awards Made to Institutions Never Having Previously Received a SAIR Award	5	5	2	3
Number of Applications from Institutions Never Having Previously Received a SAIR Award	29	23	32	26
Success Rate for Institutions Never Having Previously Received a SAIR Award	17%	22%	6%	12%

Source: STPI analysis of NIH Administrative Data

Five new institutions were added in the latter two rounds (Table 3.1b), and the success rate for institutions that did not receive funding in the first two cohorts was less than 10% (five awards made from 58 applications by prospective SAIR institutions). This compares with the 60% success rate (three of five) for renewing institutions in Cohort 3 and the 70% rate for renewing institutions in Cohort 4 (five of seven).

3.3 Institutional Context for SAIR Awards

3.3.1 Institutional Location of the SAIR Facilities

The SAIR facilities are located in a variety of organizational structures:

- ***Part of interdisciplinary molecular imaging center/program in distinct center or institute (5 SAIR facilities):*** Case Western (Case Research Institute); MGH (Center for Molecular Imaging Research); UCLA (Crump Institute); UC Davis (Center for Molecular and Genomic Imaging) and Stanford (Clark Center/Stanford Center for Innovation in In-vivo Imaging)
- ***Service center, under aegis of Department of Radiology or School of Medicine (3 SAIR facilities):*** Johns Hopkins University; Washington University; University of Pennsylvania (renewal iteration)
- ***Uniting small animal imaging capabilities across multiple departments (3 SAIR facilities):*** University of Arizona; MSKCC; University of Pennsylvania (initial iteration)
- ***Under aegis of Comprehensive Cancer Center:*** University of Michigan
- ***Under aegis of other award:*** Duke University (where the SAIR award provides funding to the NCRR P41-funded Center for In Vivo Microscopy)

The University of Pennsylvania SAIR facility's organizational structure[13] was the only one to undergo a substantial shift – while the SAIR originally united capabilities held in multiple locations and departments, the School of Medicine and Department of Radiology acted to form a single, university-wide, small animal imaging facility that currently houses the University of Pennsylvania SAIR award after the conclusion of the initial SAIR award period.

3.3.2 Other Resources at SAIR Institutions

Before considering SAIR outcomes, it is important to recognize that the SAIR awards did not operate in isolation at any of the awarded institutions. Each institution had a variety of resources and funding streams supporting activities related to small animal imaging that overlapped with the SAIR. Resources considered potentially of interest for evaluation purposes included the following:

- Cancer Center Support Grants (CCSG)
- ICMICs
- Centers of Cancer Nanotechnology Excellence (CCNEs)
- Network for Translational Research: Optical Imaging (NTROI)
- Mouse Model consortium sites
- NCRR-funded Shared Instrumentation Grants

[13] One SAIR (UCLA) has seen a change in PIship; at UCLA Dr. Gambhir (the original PI) departed for Stanford University; Dr. Phelps assumed the PI role in the middle of UCLA's initial funding as part of Cohort 2.

Cancer Center Small Animal Imaging Shared Resources

CCSG progress reports and renewal applications were searched to identify whether the institutions had an active small animal imaging core. Of the 12 Cohort 1-3 SAIR awardees, 11 were affiliated with a CCSG that funded a core related to small animal imaging in 2007.[14] At six of those 11 SAIR institutions there is a CCSG small animal imaging core that is comparable to the SAIR in description and often overlapping in leadership, with the SAIR PI or co-PI serving as the Cancer Center Shared Resource PI or co-PI for all but UCLA. Only at one SAIR, however, was there an explicit identification of the Cancer Center shared resource as being equivalent to the SAIR; at the other institutions the CCSG animal imaging core had a different name. At three SAIR institutions the Cancer Center imaging shared resource included both clinical and pre-clinical imaging, with the SAIR mentioned as being one of the contributors to the resource; at one SAIR institution, the SAIR and the CCSG are both contributors to a School of Medicine-wide small animal imaging facility. At a single SAIR, however, there was no formal relationship between the Cancer Center Shared Resource and the SAIR facility; the animal imaging resource was more limited (optical imaging only) than the SAIR facility's capabilities.

At 10 of the SAIR institutions, the SAIR award preceded establishment of the CCSG shared resource for imaging, including two SAIR institutions where the SAIR award preceded the designation of the institution as a Cancer Center. Only at one SAIR did the inclusion of small animal imaging as a Cancer Center shared resource precede the award of SAIR funding.

Additionally, six of the 12 institutions had created a "molecular imaging" research theme at the Cancer Center as of 2007, and four more were in the process of doing so. At the institutions with existing programs, all of them are led by the SAIR PI or co-PI. In contrast, in 2007 14 of 51 (27%) Cancer Center institutions without a SAIR award supported small animal imaging CCSG Core facilities, and six (12%) had molecular imaging-related research themes.[15]

Other P-series and U-series Awards Related to Small Animal Imaging

In addition to the Cancer Center Support Grants, all of the SAIR institutions funded in the first three cohorts except one (Case Western Reserve University) also had at least one other large award for molecular or small animal imaging, and several had more than one (Table 3.2). Seven of the 12 SAIR institutions funded in the first three cohorts had ICMIC awards. Two SAIR institutions had CCNE awards, two were partners on CCNEs, and two institutions had an NTROI award. Four SAIR institutions have NCRR-funded P41 Centers listed on SAIR applications as providing support to small animal imaging technology development: Arizona, Duke, Stanford, and University of Pennsylvania. Three SAIR institutions also have Mouse Model consortium sites.

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[14] In general, Cancer Center applications did not include SAIR funding in their estimates of the "operating costs" of the small animal imaging facility. The UCLA application represented a singular example, including SAIR funding as part of the operating costs of the combined small animal imaging facility.

[15] Source: searches of 2007 Cancer Center Support Grant applications and progress reports. Five other Cancer Centers funded Animal or Mouse Models cores that include some imaging services.

Table 3.2: Other Programs Related to Small Animal Imaging at SAIR Institutions

SAIR Institution	ICMIC, CCNE, or NTROI	NCRR or NIBIB P41 related to small animal technology development	Mouse Models
Case Western	Pre-ICMIC		
Duke	Pre-ICMIC	Yes (Center for In Vivo Microscopy)	
Johns Hopkins	ICMIC		
MGH	ICMIC, Partner on MIT CCNE		
MSKCC	ICMIC		Yes
Stanford	ICMIC, CCNE, NTROI	Yes (Center for Advanced MR Technology)	
UC Davis			NCRR-funded U42 Mutant Mouse Regional Resource Center[16]
UCLA	ICMIC, Partner on Caltech, Stanford CCNEs		Yes
University of Arizona		Yes (Center for Gamma-Ray Imaging)	
University of Michigan	ICMIC		
University of Pennsylvania	Pre-ICMIC, NTROI	Yes (Resource for MR and Optical Research)	Yes
Washington University	ICMIC		

Source: STPI analysis of NIH Administrative Data
Note: NCRR and NIBIB P41s were identified through CRISP searches, and then cross-referenced against application materials to identify whether those facilities were named as providing support to the SAIR award. Two other NCRR P41s, at Johns Hopkins (Resource for Quantitative Functional MRI; P41RR015241) and Washington University (A Resource for Biomedical Mass Spectrometry, P41RR000954) are acknowledged by one or more SAIR publications, but were not identified as being specifically linked to the SAIR

Not only are multiple other imaging-related awards present at SAIR institutions, but also the leaderships of these awards are integrated into each other and to the SAIR. With the exception of Duke University, the SAIR PI is integrated into at least one other NCI-funded imaging-related activity at each institution; somewhat notable is the more disaggregated structure of imaging leadership at Washington University, where, as described in detail in the ICMIC Outcome Evaluation report, multiple PIs play differing leadership roles across the university.[17]

[16] U42RR014905, 1999-2009, KC Kent Lloyd Principal Investigator
[17] ICMIC Outcome Evaluation report *op. cit.*, Section 6.4.

3.4 SAIR Funding and Budget Allocations

The total funding awarded for all four cohorts of the SAIR RFA from FY 1999 to FY 2008 was $63.7 million, including $44.4 million in direct costs. The three institutions that have been continuously funded since the first round of competition (MSKCC, University of Michigan, and Washington University) have each received more than $4 million over ten years.

The evaluation analyzed the allocation of budget dollars by the most prevalent categories – salary support, equipment, and supplies – with the caveat that the budgets of institutions that list research projects separately such as the University of Pennsylvania are incompletely represented in this process. One common theme is that funding for personnel was approximately half of the budgets of the SAIR awards in the first two funding rounds, with a substantial percentage (20-30% for many of the SAIR awards) devoted to equipment purchase. During Cohorts 3 and 4, the percentage of funding devoted to salary support is higher and that devoted to equipment lower; one SAIR devoted the majority of funding to research projects, another devotes much of its funding to supporting time on SAIR equipment for researchers pursuing pilot projects or collecting initial data to support future grant applications.

In Cohorts 1 through 3, institutions were awarded approximately $500,000 per year in direct costs, but the average dropped to around $300,000 per institution per year in the fourth round as would be expected due to changes in the 2006 RFA discussed above (Table 3.3).

Table 3.3: Direct Costs by SAIR Cohort to Through FY2008

SAIR Cohort	Total Direct Costs to Date	Average Direct Cost per Year	First Year Direct Costs	Average of Other Years' Direct Costs	Average Direct Cost per Institution to Date
Cohort 1 (1999-2003)	$12.2M	$488K	$877K	$391K	$2.4M
Cohort 2 (2001-2006)	$15.3M	$509K	$741K	$463K	$3.1M
Cohort 3 (2004-2008)	$11.8M	$474K	$639K	$433K	$2.4M
Cohort 4 (2007-2008)	$5.1M	$316K	$289K	$344K	$0.6M

Source: STPI analysis of NIH Administrative Data
Note: Cohort 2 institutions received six years of funding. Cohort 4 data reflect only the first two years of funding, in fiscal years 2007 and 2008.

For the five SAIR awardees with previous funding renewed in Cohort 4, average annual funding – even excluding equipment – decreased by more than 40% relative to Cohort 2 funding, with non-equipment funding to each SAIR award decreasing by at least one-third. Similarly, funding for personnel decreased by approximately thirty percent. Interviews with Cohort 4 renewing PIs identified two specific concerns associated with the decrease in funding levels in the fourth cohort. One commonly-stated concern was that the change in funding levels not only made it impossible to purchase new imaging equipment, but also difficult to upgrade and fund support contracts for existing equipment. A related concern expressed was that the SAIR awardees needed to continue

heavy support for personnel in order to retain the personnel who had been attracted and trained during the initial funding period. Personnel funding for the Cohort 4 SAIRs fell by 30% relative to funding for personnel provided by their initial awards.

Chapter 4: SAIR Publications

As described in Chapter 2, a database of SAIR publications was assembled from programmatic records (e.g., applications, progress reports) and MEDLINE searches for peer reviewed journal articles in which authors acknowledged SAIR funding. SAIR PIs were also asked to review and verify the publications lists for their awards. The purpose of this chapter is to characterize these SAIR publications.

4.1 Number of Publications Attributed to SAIR

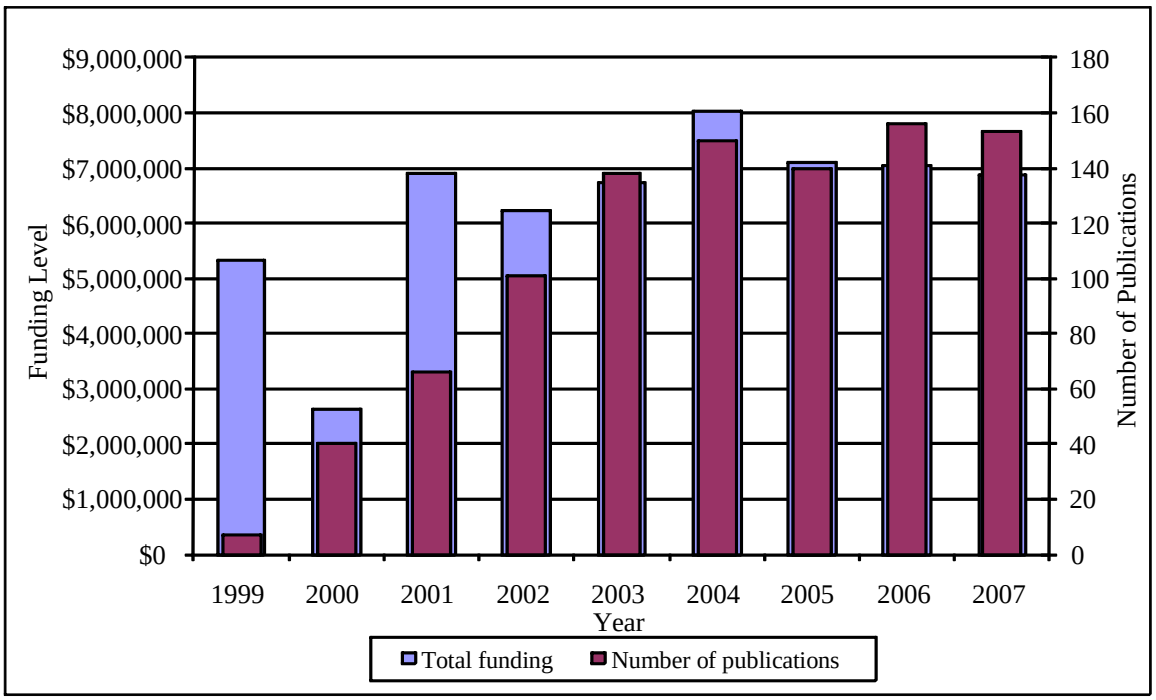
Using these methods, a total of 951 SAIR MEDLINE-indexed publications were identified (Table 4.1), of which four were associated with more than one SAIR award.

Table 4.1: SAIR Publications by Year of Publication

SAIR	1999	2000	2001	2002	2003	2004	2005	2006	2007 to 9/30	Total Publications	Average per Year of SAIR Funding
Case Western						0	3	7	20	30	7.5
Duke			0	1	3	13	13	13	13	56	8
Johns Hopkins			1	4	3	5	13	4	5	35	5
MGH				7	17	28	17	53	31	153	21.86
MSKCC	0	2	10	6	19	10	12	10	11	80	8.89
Stanford			7	13	11	13	13	6		63	10.5
UC Davis						3	5	14	19	41	10.25
UCLA			2	15	14	13	8	8	8	68	9.71
University of Arizona	0	3	5	8	12	15 (NF)	8 (NF)	2 (NF)		53	10.6
University of Michigan	3	6	2	6	4	8	12	18	16	75	8.33
University of Pennsylvania	3	26	31	27	34	25 (NF)	12 (NF)		1	159	26.5
Washington University	1	3	8	15	21	17	26	21	30	142	15.78
Program total	7	40	66	101	138	150	140	156	153	951	

Source: STPI analysis of SAIR publications database. Cells where numbers are entered denote years where the SAIR award was active, and the number of publications associated with the SAIR in that year. For the University of Arizona and the University of Pennsylvania, there are years in which the SAIR was not funded where publications associated with the award; those cells are denoted by "(NF)"
Note: Four SAIR publications – one jointly acknowledging the Duke and MGH SAIR awards; one jointly acknowledging Stanford and University of Michigan; one jointly acknowledging UCLA and Stanford; and one jointly acknowledging Washington University and UCLA – are double-counted.

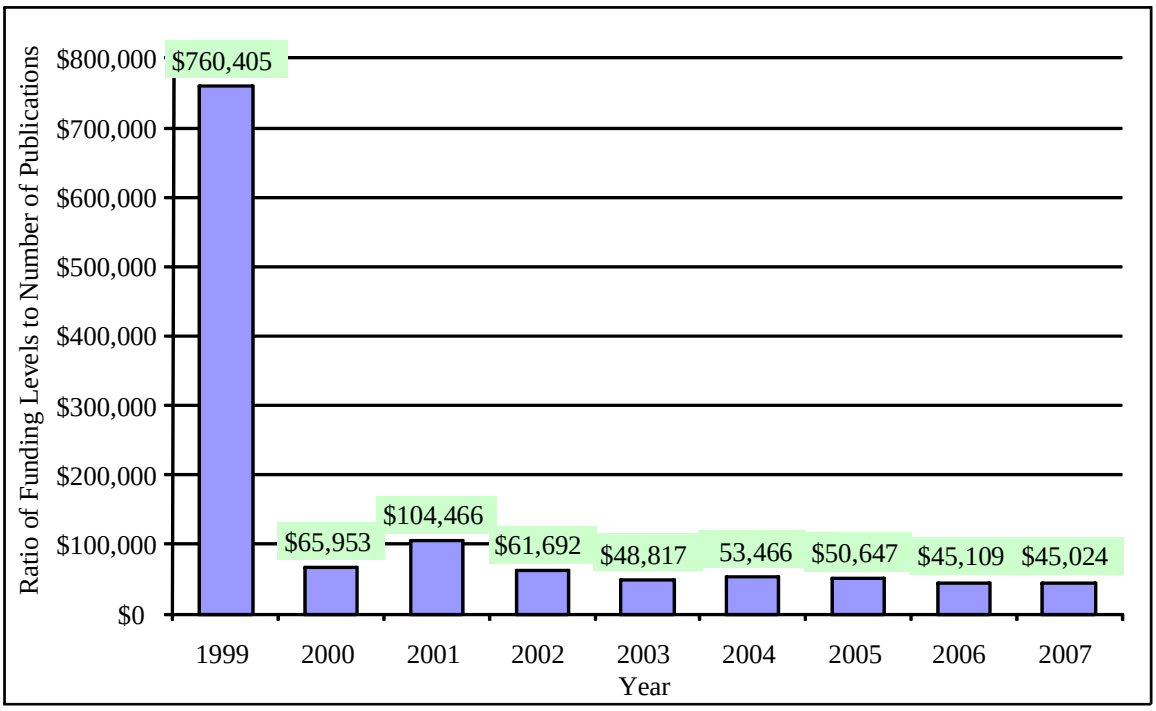
The University of Pennsylvania and MGH each supported more than 20 publications per year and Washington University approximately 15 per year. Most other SAIR awards produced between eight and 11 publications per year, with the exception of the five publications per year at Johns Hopkins. Taken together, the total number of publications per year associated with the SAIR program has increased over time, reaching approximate steady-state beginning in 2004 (Figure 4.1).



Source: STPI analysis of SAIR publications database, administrative records.
Note: Publications are shown for full calendar years (except for 2007)

Figure 4.1: SAIR Funding and Publications, 1999-2007

The steady-state ratio of dollars per publication in a given year was approximately $50,000, discounting the first year of SAIR program operations (Figure 4.2). The ratio in the program's initial year of 1999 was high, more than $750,000 in expenditures per publication, decreased to $60,000-$100,000 from 2000-2002, and then reached the steady-state level by 2003.



Source: STPI analysis of SAIR publications database, administrative records.
Note: Publications are shown for full calendar years (except for 2007)

Figure 4.2: Ratio of Programmatic Funding to Number of Publications, 1999-2007

4.2 Journals and Impact Factors for SAIR Publications

SAIR papers were published in 246 distinct journals spanning a range of fields, including fundamental biology, chemistry, cancer biology, clinical oncology, molecular imaging, and nuclear medicine. A total of eleven journals (4% of the 246 total) accounted for 39% of the total papers (372 of 951 papers); impact factors of those journals ranged between 2.121 and 9.643 (Table 4.2). The journals in which the largest number of articles appears include dedicated molecular imaging and nuclear medicine journals (*Magnetic Resonance in Medicine, Molecular Imaging, Journal of Nuclear Medicine, Nuclear Medicine and Biology*), journals devoted to cancer biology (*Cancer Research, Clinical Cancer Research, Neoplasia*), biomedical engineering and medical physics journals (*Journal of Biomedical Optics, Physics in Medicine and Biology*), a chemistry journal (*Bioconjugate Chemistry*), and a general journal (*Proceedings of the National Academy of Sciences*).

Table 4.2: Journals with Largest Number of SAIR Publications

Journal	Number of papers	Journal impact factor[18]
Magnetic Resonance in Medicine	63	3.427
Cancer Research	50	7.656
Molecular Imaging	44	N/A
Proceedings of the National Academy of Sciences of the United States of America	43	9.643
Journal of Nuclear Medicine	42	4.986
Physics in Medicine and Biology	23	2.873
Neoplasia	23	4.913
Journal of Biomedical Optics	22	3.823
Nuclear Medicine and Biology	21	2.87
Bioconjugate Chemistry	21	2.121
Clinical Cancer Research	20	6.177

Source: STPI analysis SAIR publications database and NIH library (for impact factors)

Thirty-two SAIR publications (3%) were in journals with impact factors of twenty or higher, including four papers in Science, four in Nature, and one in the New England Journal of Medicine (Table 4.3). Looking across all of the SAIR publications, the average impact factor was 5.516,[19] and the median was 4.041. Impact factor was not available for 78 publications.

Table 4.3: SAIR Publications in Very High-Impact-Factor Journals

Journal	Impact factor	Number of Publications
New England Journal of Medicine	51.296	1
Nature Reviews. Cancer	31.583	1
Science	30.028	4
Nature Medicine	28.588	8
Nature Immunology	27.596	2
Nature	26.681	4
Cancer Cell	24.077	6
Nature Biotechnology	22.672	5
Nature Reviews. Drug discovery	20.970	1

Source: STPI analysis of SAIR publications database and NIH library (for impact factors)

[18] Journal impact factors obtained via the NIH Library subscription to Thomson/Reuters Journal Citation Reports 2006.

[19] While there is not a commonly accepted definition of "high-impact-factor journal" or publications of "average" impact factors across biomedical research, the average impact factor of the ICMIC program's publications was 7.08 and median impact was 4.986. Forty-one ICMIC papers (6% of the total) were in journals with impact factors of twenty or above.

One potential explanation for the relatively low impact factors of SAIR research overall is that much research receiving direct support from the SAIR award focused on technology development, which tends to be published in specialized journals with lower impact factors. Variations in the intensity of technology development work may also account, at least in part, for the observed variation of impact factors among the SAIR awards. Figure 4.3 compares the impact factors of the journals for SAIR publications classified as "technology development" to the rest of the SAIR publications. As would be expected, the "technology development" publications clustered in journals with impact factors between 2 and 4 (48% of all technology development publications versus 31% of non-technology development publications). Few publications coded as "technology development" appeared in the highest-impact journals.

The median impact factor of the journals in which "technology development" publications appeared is 3.571 (corresponding to *Medical Physics*), and the mean 4.55. In contrast, the median impact factor of other publications is 4.514 (corresponding to *Human Gene Therapy*) and the mean 6.14. Although the non-technology-development publications are in journals with higher impact factors than the "technology development" publications (two-tailed t-test, $p < .001$) – the median, mean, and percentage of non-"technology development" publications in very high impact journals is still substantially lower than that of the ICMIC publications.

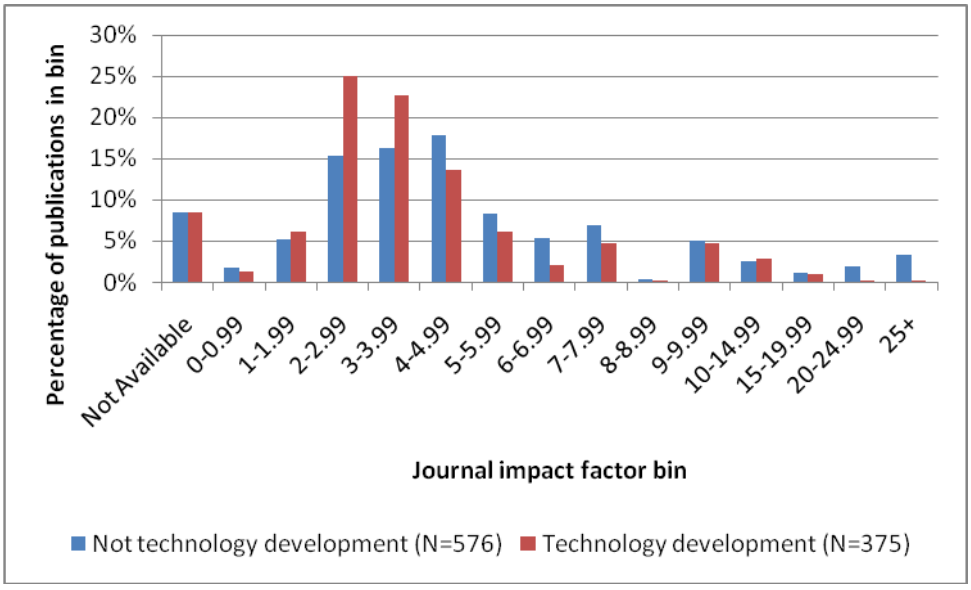


Figure 4.3: Impact Factors of SAIR Publications, Grouped by "Technology Development" Publications and Other SAIR Publications

Chapter 5: Infrastructure for Small Animal Imaging

This chapter describes outcomes related to the following SAIR program goal:

> *Build sustainable infrastructure for research involving small animal imaging at grantee institutions by providing necessary equipment (support for equipment dropped in 2006 RFA), supplies, and support/technical personnel.*

The first part of the chapter describes the SAIR role in building two types of infrastructure at SAIR institutions: equipment, and personnel.[20] The next section considers the experience of the new Cohort 4 SAIR institutions, each of which built sufficient infrastructure to compete successfully without a previous SAIR award. The final section considers whether small animal imaging infrastructure has proved to be sustainable at the three former SAIR institutions that did not receive renewals.

5.1 SAIR Role in Building Infrastructure

5.1.1 Equipment

In order to be competitive for an award, SAIR institutions needed to possess initial imaging capabilities. As described in application materials, nearly all of the SAIR facilities possessed MRI/MRS equipment; approximately half had access to PET, SPECT, and optical imaging equipment, and several SAIR institutions operated other modalities. SAIR awardees in Cohort 1 varied substantially in the number of modalities available. SAIR awardees in Cohort 2 had either two or three of the primary imaging modalities available. Cohort 3 SAIR awardees (either new to the program or renewing), however, had at least four imaging modalities at the time of award.

As already discussed, each of the first three SAIR RFAs required that funded institutions purchase or construct equipment in the first year of the award that would add an imaging modality to the capabilities offered to investigators. Total spending on equipment as described in application materials and progress reports was $7.5 million. More than half of the SAIR institutions used program funding to purchase optical and CT equipment, with four SAIR facilities adding PET and MRI, three adding autoradiography, and two adding SPECT (Table 5.1). One SAIR chose not to purchase any major modalities after the award was made, instead constructing optical and PET equipment. Funding for equipment varied by nearly one order of magnitude across the SAIR institutions. Those institutions purchasing/upgrading MR and PET equipment tended to use more of their budgets on equipment than those purchasing optical or CT equipment. SAIR awardees

[20] The SAIR awards were not intended to support construction and renovation of facilities, and SAIR funds were not used for this purpose. All of the SAIR institutions were required to have facilities and space available for the SAIR as a precondition for participation in the program. Nine of the 12 SAIR institutions, in application materials, described specific investments that had been made or were to be made for the purpose of supporting small animal imaging facilities. Several SAIR applications placed a dollar value (in excess of $47 million) on the extent of those investments. Generally, funding for construction and renovation came from institutional sources. Three of the SAIR awardees did not describe institutional funding for construction or renovation of small animal imaging facilities in their applications.

heavily engaged in custom construction of new equipment tended to use fewer funds for equipment purchase overall.

Table 5.1: Equipment Purchased with SAIR Funding

SAIR	MRI/ MRS	micro PET	Optical	micro CT	SPECT	Autoradiography	Equipment constructed rather than purchased
Case Western			X				
Duke		X					
Johns Hopkins		X				X	Integrated digital radiography/ gamma scintigraphy scanner
MGH	X	X	X	X	X		
MSKCC	X					X	
Stanford			X	X			
UC Davis			X	X			
UCLA			X	X			
University of Arizona			X	X	X		SPECT, SPECT/CT
University of Michigan	X			X	X	X	
University of Pennsylvania	X	X	X				Optical, PET/NMR
Washington University		X	X				Optical, PET
Total	4	4	8	6	2	3	

Source: STPI analysis of progress reports, applications, and interviews with SAIR PIs
Note: MGH SAIR provided supplementary information in October 2009 stating that funding was used to purchase optical (intravital fluorescent microscope), micro SPECT-CT, MRI/MRS (coils), and a portion of a micro PET-CT

> "[T]he key point is that having the Small Animal Imaging Resource, and having the connections that brings to a host of collaborators allows us to then write and justify successful shared instrumentation grant proposals. It's a huge leveraging opportunity, because you know those shared instrumentation grants, all have extensive sections of base grants that are you know, supported and impacted. And, many of those are themselves projects which are or were funded at least partially by the SAIR. So, because of a funneling type of effect, where those projects gets in seed money or some early money from the

The SAIR program was not the only source of funding for small animal imaging equipment at SAIR institutions. For example, six of the 12 SAIR institutions in the first three cohorts received at least one small animal imaging-related NCRR Shared Instrumentation Grant during the SAIR award; the University of Arizona received an award for MRI equipment in 2005, subsequent to the completion of

the SAIR award (Table 5.2). MRI was the most common modality purchased or upgraded, with eleven awards. Funding for these awards (not including the University of Pennsylvania 2000 MRI award, for which funding was not available from QVR) totaled $9.8 million – 30% more than the total funding for equipment provided by the SAIR program itself.

Table 5.2: Small Animal Imaging-Related Shared Instrumentation Grant Awards to Cohort 1-3 SAIR Institutions during or Subsequent to their First SAIR Awards

SAIR	MRI	CT	SPECT	PET	Auto-radiography	Number of awards
Case Western						0
Duke						0
Johns Hopkins						0
MGH						0
MSKCC	2002, 7		2003	2005		4
Stanford	2004					1
UC Davis			2007			1
UCLA						0
University of Arizona	2005					1
University of Michigan	2005					1
University of Pennsylvania	2000, 8	2003				3
Washington University	2001, 2, 5, 7	2003			2005	6
Number of awards for purchase/ upgrading	11	2	2	1	1	17

Source: STPI analysis of CRISP searches.
Note: Search performed on NCRR S10 awards, by institution, from 1998 onward; STPI identified relevant awards based upon award abstracts.
Note: Funding for University of Pennsylvania MRI award in 2000 not available.

A range of other funding sources – including institutional and departmental funds, private funding sources, other U.S. government support (e.g., NASA, DOE, NSF, DARPA), and other NIH funded awards (e.g., the Center for In Vivo Microscopy at Duke) were also used by SAIR institutions to purchase or construct equipment during the same time period as the SAIR award. Ten of the SAIR applications described specific items of equipment purchased through funding from sources other than the SAIR award itself or an NCRR Shared Instrumentation Grant, including:

- Eight purchasing MRI equipment
- Five purchasing optical equipment
- Three purchasing each of microPET and microCT, and
- Two purchasing each of SPECT and ultrasound

While cost was not listed for all pieces of equipment identified in applications as being institutionally-funded, $12.8 million in funding was identified as having been used for that purpose – nearly twice the $7.5 million listed as supporting equipment purchase in

the SAIR applications. Of that amount, $9.5 million (76%) was used to purchase MRI equipment.

As shown in Table 5.3, by the time of their most recent applications almost all of SAIR institutions had access to MRI, PET, optical, and CT capabilities; most had access to SPECT imaging; and many had ultrasound and autoradiography equipment.

Table 5.3: Capabilities Available at SAIR Institutions

SAIR	MRI/MRS	microPET	Optical	microCT	SPECT	Ultrasound	Autoradiography
Case Western	X	X	X	X	X		
Duke	X	X	X	X	X	X	
Johns Hopkins	X	X	X	X	X	X	X
MGH	X	X	X	X	X	X	
MSKCC	X	X	X	X	X		X
Stanford	X	X	X	X	X	X	X
UC Davis	X	X	X	X	X	X	
UCLA		X	X	X			X
University of Arizona	X		X	X	X		
University of Michigan	X	X	X	X	X		X
University of Pennsylvania	X	X	X	X	X	X	
Washington University	X	X	X	X			X
Total	11	11	12	12	10	6	6

Source: STPI analysis of progress reports, applications, and interviews with SAIR PIs

During interviews, SAIR PIs were divided in terms of their perceptions of the role that SAIR funding plays in supporting the infrastructure at their institutions. One group of PIs described the SAIR award as being the primary funder of small animal imaging infrastructure – either as the sole funder or the plurality funder of the infrastructure – while another group spoke of the catalytic role played by the SAIR award in catalyzing the receipt of other funds from the NIH and from their institutions.

> "It's basically 100 percent SAIR driven....This is kind of opening up our lab in a way--our own private research lab to the greater community" – SAIR PI

> "There was a strong activation energy barrier to building a small animal imaging facility. SAIR funding helped to overcome that energy barrier" – Cancer Center basic science director

PIs who spoke of the catalytic role played by the SAIR program mentioned a range of potential routes and influences. Interviewees at institutions that had received NCRR Shared Instrumentation Grants spoke of the role that SAIR played in building a community of dedicated users of the modality, which allowed them to demonstrate in their instrumentation grant applications that there was a substantial need for the

equipment and a large base of grantees who would be making use of it.

> "the SAIRP put imaging on the map at XXX. Prior to that, we had done small animal imaging for other labs, but could not get a mechanism established for doing this with some kind of reimbursement or cost sharing and it was difficult to expand its applications. The administrative environment was almost hostile" – SAIR PI

Another catalytic role described by principal investigators regarded institutional support for small animal imaging facilities. Several SAIR PIs described how the awarding of a SAIR grant, and its initial successes, led university administrators (at the department or dean level) to make additional large-scale investments in facilities and equipment. At five of the SAIR institutions, more funding was specifically identified as having been invested in small animal imaging from outside sources than the total value of the SAIR award itself, and at these institutions the PIs interviewed tended to attribute the investment to the initial SAIR award.

5.1.2 Personnel

The total number of people receiving salary support on SAIR awards in the most recent year of support varied widely. The most recent progress reports from each of the SAIRs reported that the number of personnel receiving salary support ranged from five to 30 individuals (Table 5.4):

Table 5.4: Number of Personnel Supported by the SAIRs in their Most Recent Year of Funding

SAIR	Total people supported
SAIR A	17
SAIR B	13
SAIR C	7
SAIR D	6
SAIR E	25
SAIR F	5
SAIR G	19
SAIR H	10
SAIR I	30
SAIR J	8
SAIR K	28
SAIR L	25

Source: STPI analysis SAIR applications and progress reports

SAIR institutions also varied with respect to the amount of time supported and the categories of personnel supported (Table 5.5). There was a threefold difference between the SAIR supporting the fewest person-months (39 person-months supported) and the most (more than 100 person-months supported).

Table 5.5: Percentage of Time Supported by Personnel Category and SAIR

SAIR Iteration	Total person-months supported	Faculty (includes PI/co-PI)	Research staff	Postdocs	Graduate students	Undergrads	Technical/ Admin. staff
SAIR A	72.6	17%	0%	83%	0%	0%	0%
SAIR B	78.2	16%	18%	21%	15%	0%	31%
SAIR C	39.0	8%	62%	0%	0%	0%	31%
SAIR D	28.1	7%	0%	93%	0%	0%	0%
SAIR E	75.4	28%	38%	0%	0%	0%	33%
SAIR F	16.8	14%	7%	0%	71%	0%	7%
SAIR G	33.5	19%	16%	13%	18%	0%	34%
SAIR H	44.4	41%	0%	0%	0%	0%	59%
SAIR I	110.0	20%	20%	29%	5%	0%	26%
SAIR J	41.4	12%	9%	22%	29%	0%	29%
SAIR K	119.2	14%	13%	0%	10%	20%	43%
SAIR L	78.8	9%	18%	0%	46%	0%	27%

Source: STPI analysis SAIR applications and progress reports

There were also differences in the type of personnel supported using SAIR funds:

- At four SAIRs, the majority of funded time was for staff – a combination of PhD-level research staff and technical staff
- At two SAIRs, the large majority of funded time was for postdoctoral researchers
- At two SAIRs, the majority of funded time was for graduate students
- Only at one SAIR did faculty time represent 40% or more of funded time
- At four SAIRs, support was balanced across multiple personnel categories

Small animal imaging facilities require a mix of technical expertise for successful operation, including technical direction, equipment operation, ancillary services (e.g., biostatistics, bioinformatics) and animal handing. At all of the SAIR facilities, faculty played a technical direction role, with one or more faculty members responsible for each modality. Generally, dedicated technicians carried out the actual experiments. Many SAIR PIs interviewed reported that their optical equipment was "turn-key" and so individual investigators were trained to use them without technician assistance. In contrast, SAIR PIs interviewed reported that PET, CT, and SPECT equipment required dedicated staff to perform the experiments because of radioactivity considerations. Regarding the MRI equipment, however, experience varied across SAIR awardees, where in some SAIR facilities investigators were encouraged to perform experiments themselves using the MRI equipment after training.

> "So, really what we do, unless we now at our SAIR is actually, we are preserving the know-how, and even preserving the, you know the people, the staff who actually can make this work in long term" – SAIR PI

Four of the SAIR PIs described institutional support for the hiring of new imaging-related faculty as part of their applications packages provided to the NCI.

At most SAIR facilities, technicians were only partially supported by the SAIR award itself. At some institutions fractions of several technicians' salaries were supported, while at others some technicians were fully supported by the SAIR award itself while other technicians were fully supported by other sources. There was only one SAIR where all of the technicians identified were fully supported by SAIR funds. The SAIR PIs identified the training and retention of skilled personnel as a critical service provided by the SAIR award – PIs who had been funded in both Cohorts 2 and 4 were especially concerned regarding the size of the Cohort 4 awards and their ability to retain sufficient technical staff after the decrease in the size of award in their renewals.

5.2 Infrastructure at Cohort 4 SAIR Institutions

The experience of the three recently-awarded SAIR institutions – MD Anderson, University of Texas Southwest Medical Center, and Vanderbilt – represents a different route to the development of small animal imaging capabilities. All three institutions built sufficient infrastructure to compete successfully without previous SAIR funding. With the exception of one SAIR's lacking optical imaging capabilities, all three SAIR facilities had either installed or were in the process of purchasing and installing equipment in each of the major imaging modalities in advance of receiving their awards.

All three institutions' applications mentioned the role played by institutional support for small animal imaging. Each institution had supported a small animal imaging core resource prior to the submission of the application; MD Anderson and Vanderbilt – the NCI-designated Cancer Centers among the new group of Cohort 4 SAIR awardees – had designated their facilities as Cancer Center Shared Resources prior to the SAIR application. Similarly, all three applications described the role of institutional funding in purchasing equipment and creating faculty positions related to small animal imaging.

> "One of the limitations has been--the way the Core Grant is set up, we get money from the Core Grant to support ongoing NIH-funded research or. So, had--when new investigators came that either didn't have NIH funding or had--didn't have funding in their NIH grant for paying the user fees for the facility, we had a real challenge on how to get them started. And that's really what we're using the SAIR grant for" – SAIR Cohort 4 PI.

There were some differences, however, in the paths to capability-building at the SAIR institutions. Both Vanderbilt and UT-Southwest had received pre-ICMIC P20 awards; UT-Southwest, in both application materials and SAIR Internet site, credited the pre-ICMIC as providing a foundation for the small animal imaging program.[21] Another difference lay in the support received for the purchase of imaging equipment from NCRR. Vanderbilt received support for one MRI console, the PET scanner, and one Xenogen optical scanner in advance of receiving SAIR support, and support for a SPECT system in June 2007. UT-Southwest received support for one optical scanner in September 2007, subsequent to the receipt of SAIR funding, and for a digital planar x-ray system in 2008. MD Anderson received partial support for the purchase of an MRI system from an NCRR S10.

[21] SW-SAIR Internet site, http://www.utsouthwestern.edu/utsw/cda/dept105665/files/318109.html, last accessed December 22nd, 2008.

5.3 Post-Award Sustainability: Non-Renewed SAIR Institutions

The three SAIR institutions whose awards were not renewed (Stanford, the University of Arizona, and, initially, the University of Pennsylvania) all maintained small animal imaging capabilities. The University of Pennsylvania was refunded as part of the SAIR Cohort 4, but beforehand the School of Medicine (under the aegis of the Department of Radiology) formed a school-wide Small Animal Imaging Facility and provided continuing funds for technology development and equipment purchase. The Small Animal Imaging Facility supports all medical school users; Centers awards (such as the University of Pennsylvania Cancer Center Support Grant and the SAIR post-renewal) provide additional funding to the facility as well. At Stanford and the University of Arizona, the capabilities created through the SAIR continue to be supported by a variety of sources. Support from the Cancer Center, user fees from grants that use the facility, and institutional funds are used to cover operating costs (including personnel), while NCRR Shared Instrumentation Grants and institutional funds are used to purchase and upgrade equipment.

None of the interviewees described the loss of the SAIR award as being catastrophic for small animal imaging at their institutions, although they tended to consider it damaging; one PI interviewed described the failure to be renewed as, "the loss of the SAIR was definitely felt on our end. I mean it hurt our program not to be supported on the SAIR." All of the PIs stated that having the SAIR award was vital to the degree of institutionalization that allowed the continuation of the capabilities; having the SAIR award helped to build the user base and catalyzed institutional support for the facility.

Chapter 6: Use of Small Animal Imaging Infrastructure

This chapter describes outcomes related to the second program goal:

> *Increase the quantity and quality of small animal imaging in cancer research by facilitating access to and use of resources by investigators in a variety of cancer-related fields*

The chapter begins with an analysis of the base grants listed on initial SAIR applications. The next section considers activities intended to spur use of the SAIR facility. A third section analyzes NIH awards and publications reported to have made use of SAIR facilities or otherwise be associated with SAIR awards. The fourth section considers degree to which the SAIR facilities were integrated with other NCI-supported research efforts at the SAIR institutions. The final section considers the integration of the SAIR facilities with NIH research supported by other ICs.

6.1 Initial Use of Small Animal Imaging: Base Grants Listed on Initial Applications

It was not feasible to identify the set of awards that were making use of small animal imaging at the time institutions submitted their initial applications for SAIR funding to NCI. As a proxy, Table 6.1 shows the number of awards (and the distribution of funding sources) listed as potential base grants and initial users of the SAIR in initially-funded applications. While each SAIR was required to identify six base grants in initial applications, several SAIR applications identified at least twice that number of awards, while others did not. Several SAIR applications initially identified five or fewer NCI-supported awards.

Table 6.1: Base Grants Initially Identified on Funded SAIR Applications

Institution	Total awards	Number NCI-Supported	Number Other NIH-Supported
SAIR A	19	12	0
SAIR B	19	14	4
SAIR C	8	4	3
SAIR D	13	10	3
SAIR E	9	4	2
SAIR F	10	6	2
SAIR G	12	9	3
SAIR H	9	8	0
SAIR I	12	6	5
SAIR J	7	5	0
SAIR K	12	8	1
SAIR L	7	5	1
Total	137	91	24

Source: STPI analysis of funded SAIR applications, anonymized.

The 22 non-NIH awards listed included eight DOD-funded awards, seven DOE-funded awards, and seven funded by scientific societies (e.g., American Cancer Society, Leukemia and Lymphoma Society) or foundations (e.g., Whitaker Foundation)

6.2 Activities Intended to Spur Use of the SAIR Facility

The SAIR institutions employed a variety of strategies to build the community of small animal imagers and cancer researchers using small animal imaging. Training efforts (described in Chapter 8) are used by all of the SAIR awardees to expand their communities of participants; in one of the interviews, training was described as a primary mechanism for long-term community expansion. Another often-used strategy for community building is for the SAIR to provide support to investigators for pilot projects or initial data that could support future investigations or grant proposals. Table 6.2 shows SAIR awardees' use of pilot project support.[22] All of the SAIR institutions but two described a program for pilot projects; six of the SAIR awardees provide funding from the award itself. One SAIR described providing pilot support for the first year of a new instrument's operation, to build a user base for the equipment. At one SAIR, although there was no evidence that the SAIR funds supported a specific, formal pilot program, the SAIR PI and co-PI lead three P50 and U54 awards that can be used as a source of funds for pilot imaging studies.

> "What you need to do is, have a constant aggressive approach to the cancer community making sure that they are aware that you can look at perfusion, that you can look at apoptosis, that you can look at the development of necrosis... I attend a lot of the cancer center's seminars, I pigeonhole people. I say, 'Look, I see you are looking at a glioma model. You know that we could use measurements of permeability in the blood brain barrier'" – SAIR PI

> "We think that the long term solution [to expanding the use of small animal imaging] is to actually train a cadre of students and post-docs in their laboratories that have the expertise in these various areas to do this research" – SAIR PI

Review of SAIR application materials and interviews with Cancer Center basic science directors were used to identify other sources of funding for pilot projects. The five basic science directors interviewed reported that Cancer Center pilot projects were devoted to imaging, with the process for funding those projects varying:

- Imaging projects funded from a general call for proposals
- Imaging projects funded from a general call, with imaging identified as a particular focus area within the call
- A specific call for imaging-related pilot projects

Application review identified three additional institutions where either the Department of Radiology or the Cancer Center provides funding for imaging-related pilot projects.

[22] An attempt was made to collect lists of grant applications or awards making use of pilot data from SAIR applications; as described in Chapter 2, only seven SAIR awardees tracked such information, an insufficient number to allow for analysis.

Table 6.2: Pilot Project Funding by SAIR Institutions

SAIR Institution	Pilot Funding Available	Comment
SAIR A	From SAIR	
SAIR B	From SAIR	
SAIR C	From SAIR, CCSG	SAIR pilot funding for first year of new equipment only
SAIR D	From other sources	Department of Radiology
SAIR E	From CCSG	
SAIR F	From SAIR, CCSG	
SAIR G	From SAIR	
SAIR H	From other sources	Department of Radiology
SAIR I	None identified	
SAIR J	None identified	
SAIR K	From SAIR, CCSG	
SAIR L	From SAIR, CCSG	

Source: STPI analysis of SAIR applications and progress reports; interviews with SAIR investigators

STPI analysis of application materials and interviews with SAIR PIs and Cancer Center basic science directors identified a range of additional strategies that were highlighted as important for their outreach efforts.[23] Six SAIR PIs or Cancer Center basic science directors at SAIR institutions identified the Cancer Center as critical to SAIR outreach efforts, either through the visibility associated with being a core facility or through outreach at Cancer Center symposia (e.g., Grand Rounds) and retreats. Three SAIR PIs highlighted the role of their Internet sites, and three described outreach by the PI to make direct contact with potential users or to invite potential users to SAIR group meetings or seminars. One SAIR PI credited departmental emails and newsletters, and one included outreach in the portfolio of an administrative staff member supported by the SAIR award.

6.3 NIH Awards and Publications Reported to Have Used SAIR Facilities and Data

6.3.1 Awards Supported by SAIR Facilities

The first and most direct indicator of use of SAIR infrastructure considered in the outcome evaluation was reported use of SAIR facilities. According to records kept by the SAIR PIs, 421 distinct awards made use of SAIR facilities, of which 336 were NIH-supported; of those 336 awards, 219 were NCI-supported (Table 6.3). At most institutions, NCI-funded awards represented between 40% and 60% of all awards making use of SAIR facilities.

[23] The information in this paragraph does not imply that only these strategies are used, just that they were considered sufficiently important to highlight.

Table 6.3: NIH Awards Identified as Having Used SAIR Facilities

Institution	Total awards	NCI-supported awards	Percentage of total awards NCI-supported	Other NIH-supported awards
SAIR A	25	20	80%	2
SAIR B	39	14	36%	12
SAIR C	36	18	50%	18
SAIR D	41	23	56%	8
SAIR E	61	28	46%	17
SAIR F	38	19	50%	12
SAIR G	21	14	67%	3
SAIR H	61	28	46%	16
SAIR I	23	12	52%	5
SAIR J	21	10	48%	9
SAIR K	28	14	50%	7
SAIR L	27	16	59%	8
Total	421	219	52%	117

Source: STPI analysis of SAIR administrative data

Table 6.4 compares the number of "user" awards identified in SAIR records with the number listed in the original SAIR applications (data from Tables 6.1 and 6.3). Most of the SAIR PIs reported at least twice as many awards making use of the facility as the number of awards listed on applications. At the same time, comparing the list of grants identified as making use of the SAIR with the lists of grants in the initial applications suggests that few SAIR PIs were able to predict with precision the awards that would make use of small animal imaging; only at two SAIRs were more than half of the initially-listed awards identified as having made use of the SAIR. A variant on this comparison is shown as the rightmost column, which identifies whether grants listed on each institution's applications either were reported to have made use of the SAIR facility or were acknowledged on SAIR publications.[24] If the base grants identified in the applications to the SAIR program is taken as a proxy for the "true" demand for imaging at the point of application, then demand for imaging has expanded dramatically at the majority of the SAIR institutions.

[24] See definition of "SAIR publications" Section 4.

Table 6.4: Comparison of Awards in Applications with Awards Using the SAIR Facility

Institution	Awards listed in Application	Awards Reported to Have Used SAIR Facility	Ratio of Column 2 to Column 1	Number of Awards in Applications that Used the SAIR Facility	Column 4 as Percentage of Column 1	Number of Awards in Applications that Used the SAIR Facility or Acknowledged in SAIR Publications
SAIR A	19	25	1.32	3	16%	9
SAIR B	19	39	2.05	1	5%	3
SAIR C	8	36	4.50	1	13%	3
SAIR D	13	41	3.15	1	8%	5
SAIR E	9	61	6.78	1	11%	2
SAIR F	10	38	3.80	2	20%	3
SAIR G	12	21	1.75	2	17%	3
SAIR H	9	61	6.78	5	56%	6
SAIR I	12	23	1.92	5	42%	7
SAIR J	7	21	3.00	3	43%	4
SAIR K	12	28	2.33	12	100%	12
SAIR L	7	27	3.86	2	29%	2
Total	137	421	3.07	38	28%	59

Source: STPI analysis of SAIR administrative data

6.3.2 Modalities Used at SAIR Facilities

Table 6.5 shows the imaging modality used by awards making use of SAIR facilities. Awards using MRI were used by more than half the SAIR-using awards where information was available at six SAIRs; SPECT/PET/CT were used by half or more awards at six SAIRs; and optical techniques were used often seven SAIRs. Many awards making use of the facility used multiple modality groups – at five SAIRs the average award used the SAIR for two or more modality groups.

Table 6.5: Grants Using the SAIR Facility, by Modality

Institution	Number of awards	MRI	SPECT/ CT/PET	Optical/ Biolum/ Fluro	Ultra-sound	Other	None Specified	Multi-modality ratio
SAIR A	25	16	14	10	0	2	7	2.22
SAIR B	39	22	10	19	0	0	1	1.34
SAIR C	36	16	6	24	0	0	0	1.28
SAIR D	41	17	11	16	2	0	18	2.00
SAIR E	61	21	29	13	0	0	15	1.31
SAIR F	38	21	11	6	5	0	3	1.23
SAIR G	21	12	16	6	2	1	5	2.25
SAIR H	61	29	16	29	0	8	7	1.37
SAIR I	23	1	7	7	0	0	11	1.25
SAIR J	21	0	13	5	0	0	7	1.29
SAIR K	28	15	8	6	0	0	10	1.61
SAIR L	27	4	20	3	3	0	5	1.36
Grand Total	421	174	161	144	12	11	89	1.48

Source: STPI analysis of SAIR administrative data
Note: Sum across rows should sum to more than the number of awards, as it is expected that awards use multiple modalities.
Note: Awards that use multiple modalities within a group (e.g., SPECT and CT) counted once.
Note: "Other" includes in vivo microscopy and autoradiography
Note: Indeterminate responses (e.g., used "All" modalities) coded as "None specified"

6.3.3 Publications Involving Use of SAIR Facility Funding

A second indicator of use of SAIR facilities (and other resources) was publications acknowledging support from SAIR awards. As described in Chapter 4, 951 SAIR publications were identified based on a combination of progress reports and MEDLINE searches. In total, 623 non-SAIR NIH awards were acknowledged in at least one publication that also acknowledged a SAIR award.[25] Table 6.6 summarizes the non-SAIR awards acknowledged in SAIR publications.

[25] In addition to the 1,676 non-SAIR acknowledgements for which complete information was available, there were an additional 60 acknowledgements that were not identifiable.

Table 6.6: Non-SAIR Awards Acknowledged on SAIR Publications

Type of Award	Number of acknowledgements	Number of publications	Number of distinct awards
All NCI-funded awards:	1,001	537	266
R01s	338	264	128
P01s	111	105	24
ICMIC or pre-ICMIC	229	223	14
SPORE	21	20	9
CCNE	5	5	2
Cancer Center	76	76	12
Mouse Models	3	3	3
Non NCI-funded awards	675	413	357
Total	1,676	814	623

Source: STPI analysis of SAIR publications and administrative data
Note: 28 awards are acknowledged by multiple SAIR awards; 26 by two SAIR awards, 1 (R01NS040801) by 3 SAIR awards, and 1 (R24CA086307 – the Washington University Radionuclide Resource) by 5 SAIR awards.

Sixty percent of the acknowledgements to non-SAIR awards on SAIR publications were NCI-administered (1,001 of 1,676), even though more individual awards acknowledged were not NCI-administered (357 non-NCI to 266 NCI). Of the acknowledgements to NCI-administered awards, one-third were to R01s (338 of 1,001 or 34%), and an additional one-quarter (229 of 1,001 or 23%) were to ICMIC or pre-ICMIC awards. A substantial number of SAIR publications acknowledged P01s (105 publications, 111 acknowledgements) and Cancer Centers (76 publications and acknowledgements), while fewer acknowledgements were to SPOREs, Mouse Model sites, or CCNEs.

6.4 Use of SAIR Facilities by Researchers with Other Funding from NCI

6.4.1 Integration with Cancer Center Support Grants (CCSG)

At the institutions where they exist, NCI-Designated Cancer Centers form the unifying and coordinating structures for cancer research. Degree of integration with the CCSG was therefore considered an important (but not necessarily deterministic) variable with respect to use of SAIR facilities.

All of the SAIR facilities but one are located at Cancer Centers that have designated a small animal imaging facility as a core service provided by the CCSG. Interviews with Cancer Center basic science directors as well as statements in application materials indicated that the presence of the SAIR award at nine of the 12 SAIR institutions had contributed to their Cancer Centers' subsequent decision to include small animal imaging as one of the designated CCSG Core facilities by increasing the user base for small animal imaging technology.

> "After funding of the SAIRP, the ICMIC followed and we became part of the Core Grant with very high visibility shortly thereafter. The Imaging Core is recognized for having a very high recoupment rate of expenses and being used by many laboratories and is highly regarded and I think the SAIR started the cascade. We did very well when the Core grant was renewed" – SAIR PI

Conversely, several SAIR PIs identified the CCSG at their institutions as critical to SAIR outreach efforts. Some described conducting outreach at Cancer Center symposia (e.g., Grand Rounds) and retreats. Others mentioned that the status of small animal imaging as a core facility of the Cancer Center helped to increase visibility for these technologies throughout the institution.

As shown in Table 6.7, records of SAIR facility use included the a project funded by the Cancer Center for eight SAIR institutions (with the MIT, rather than the Dana-Farber/Harvard Cancer Center, making use of the MGH SAIR).[26] Seventy-five SAIR publications acknowledging support from the local Cancer Centers were identified, of which two-thirds were either Washington University or MSKCC publications.

Table 6.7: Use of the SAIR Facility by Projects Supported through the Local Cancer Center Support Grant

SAIR	Does the List of Awards Supported include the Local Cancer Center?
Case Western	Yes
Duke	Yes
Johns Hopkins	No
MGH	MIT CC
MSKCC	Yes
Stanford	Not applicable
UC Davis	Yes
UCLA	Yes
University of Arizona	No
University of Michigan	Yes
University of Pennsylvania	No
Washington University	Yes

Source: STPI analysis of SAIR publications and administrative data

6.4.2 Integration with NCI-Sponsored Imaging-Related Translational Research Programs

> "The SAIR was critical for seed money for large multi-investigator grants." -- SAIR PI

The SAIR program predated the other NCI imaging-related, translational research programs (e.g., ICMIC, NTROI, CCNE), which allows for the assessment of whether and how awards funded by these programs have been making use of the SAIR facility. The section begins with a discussion of integration with ICMICs and pre-ICMICs; proceeds to assess integration with NTROI and CCNE; and concludes by identifying use of the SAIR facility by SPORE and Mouse Models awards.

[26] The Stanford Cancer Center (P30CA124435) was first designated in fiscal year 2007, after the SAIR funding had concluded, although the SAIR award was extended until 12/31/2007.

ICMIC and pre-ICMIC Awards

Three separate measures of the "integration" of the ICMIC and pre-ICMIC awards with the SAIR facilities were calculated. A first measure is whether ICMIC awards were included in SAIR applications as base grants to be used by the facility. As the SAIR program pre-dates ICMIC, it is not feasible to compare the proposed base grants of Cohort 1 SAIR institutions with the ICMIC program. Comparison of the base grants for Cohort 2 SAIR institutions with the list of ICMICs and pre-ICMICs funded in 2000 (the only relevant cohort) shows that four of the five Cohort 2 institutions (all but Duke) listed the appropriate ICMIC or pre-ICMIC in their applications as an award likely to be supported by the SAIR facility.

The second measure of integration is whether the list of awards that made use of the SAIR facility includes the ICMIC or pre-ICMIC award. Of the seven ICMIC awards made to SAIR institutions (at Johns Hopkins, MGH, MSKCC, Stanford, UCLA, University of Michigan, and Washington University) all were on the list of awards making use of the SAIR facilities at their respective institutions; the two SAIR institutions with pre-ICMICs active at the time of SAIR application (Duke and University of Pennsylvania) did not report that the pre-ICMICs used the SAIR facility.

The third measure of integration is whether SAIR publications include acknowledgements to ICMIC or pre-ICMIC awards. As shown in Table 6.8, all seven of the institutions that had both SAIR and ICMIC awards had SAIR publications that acknowledged the ICMIC award, although the percentage of SAIR publications acknowledging the ICMIC varied from more than 70% at MGH to only 7% at Washington University. For five SAIR institutions (MGH, MSKCC, Stanford, UCLA, and the University of Michigan) the ICMIC award was acknowledged on one-third or more of SAIR publications, and was the most-acknowledged award. In addition, two SAIR facilities (MGH and Washington University) supported the University of Missouri-Columbia ICMIC. Of the three institutions with pre-ICMIC awards only (Case Western, Duke, and the University of Pennsylvania), acknowledgements of the pre-ICMIC on SAIR publications were frequent at Pennsylvania but more limited at Case Western and nonexistent at Duke.

The analysis, therefore, suggests that the ICMIC awardees made use of the SAIR facility (though usage varied). Of the three pre-ICMIC awardees, the pre-ICMIC at the University of Pennsylvania made use of the SAIR facility, while the Duke pre-ICMIC did not.

Table 6.8: Use of SAIR Facility by ICMIC and pre-ICMIC Awards

SAIR	Number and Percentage of SAIR publications acknowledging ICMIC or pre-ICMIC
Case Western	1 (5%)
Duke	0%
Johns Hopkins	5 (23%)
MGH	92 (75%)
MSKCC	24 (39%)
Stanford	15 (31%)
UCLA	30 (48%)
University of Michigan	30 (45%)
University of Pennsylvania	12 (10%)
Washington University	9 (7%)

Source: STPI analysis of SAIR publications and administrative data
Note: UC Davis and University of Arizona did not participate in the ICMIC program (although the University of California, Davis SAIR has one paper acknowledging USC pre-ICMIC), and the Case Western SAIR was funded after the pre-ICMIC award had been completed
Note: MGH SAIR has one paper acknowledging University of Missouri ICMIC; Washington University SAIR has three papers acknowledging University of Missouri ICMIC.

NTROI and CCNE Awards

Four SAIR institutions have had either an NTROI or CCNE award – with Stanford having one of each (UCLA, although not a CCNE institution, is a partner on both the Stanford and California Institute of Technology CCNEs). There has been some integration of the SAIR facility with those awards. Four of the six awards are listed as making use of the SAIR (all but the UCLA and Washington University SAIR facilities by their respective CCNEs), and SAIR publications acknowledge the University of Pennsylvania NTROI and the MGH and Washington University CCNEs.

SPORE and Mouse Models

STPI also analyzed the use by SAIR facilities of other NCI-funded translational research programs – SPORE and Mouse Models. Two SAIR applications identified a SPORE award as an initial base grant, and two Mouse Models awards were listed on SAIR applications. Of the seven SAIR institutions possessing one or more SPORE awards, (including the other Harvard hospitals for MGH) five SAIR institutions had publications that acknowledged SPORE funding, but only Johns Hopkins had a substantial number of acknowledgements. While four SAIR PIs reported that Mouse Models sites at their institutions made use of the facility, acknowledgements of Mouse Models awards were relatively rare on SAIR publications.

6.4.3 Integration with Other NCI-Funded Cancer Research at SAIR Institutions

While the previous sections discuss the use of the SAIR facility itself, this section places SAIR facility use in the context of all NCI awards made to the institution. Table 6.9 shows the percentage of all competing NCI awards made to SAIR institutions during the fiscal years where the SAIR award was active (ending with fiscal year 2007) reported as users of SAIR facilities and the percentage of those awards acknowledged on SAIR publications. As would be expected, the percentage of all NCI awards to the institution making use of SAIR facilities appears to have been low across all institutions, but it was somewhat higher at the SAIR institutions with the smallest number of NCI awards (e.g., Case Western, Arizona, UC Davis).

Table 6.9: Percentage of all NCI Awards to SAIR Institutions through 2007 Acknowledged on SAIR Publications

SAIR	Number of competing NCI-funded awards to SAIR institutions	Number of NCI awards to investigators at institution acknowledged on SAIR publications	Percent of NCI awards acknowledged on SAIR publications
Case Western	62	11	18%
Duke	209	6	3%
Johns Hopkins	253	11	4%
MGH	150	16	11%
MSKCC	250	33	13%
Stanford	143	10	7%
UC Davis	47	12	26%
UCLA	150	9	6%
University of Arizona	78	15	19%
University of Michigan	234	14	6%
University of Pennsylvania	217	31	14%
Washington University	166	21	13%

Source: STPI analysis of SAIR publications and administrative data; CRISP searches by institution
Note: The first column was generated by conducting CRISP searches by SAIR institution, including only competing awards, which competed during the years the SAIR award was active at the institution. Awards that competed successfully more than once during the study period were counted once for the purpose of this analysis; awards that did not compete (e.g., awards made before the start of the SAIR funding that continued during the funding period) were not included in the analysis.

Finally, the evaluation also considered the extent to which the awards acknowledged on SAIR publications represent of a small number of individual PIs. Table 6.10 shows the number and percentage of acknowledgements that went to the most-frequently

acknowledged PI for each institution. The SAIR institutions fell into three groups with respect to concentration of acknowledgements:

- At four institutions (Case Western, Johns Hopkins, University of Pennsylvania, Washington University), less than 20% of acknowledgements on SAIR publications were to the awards of a single PI
- At three institutions (MSKCC, Stanford, University of Arizona), 20%-30% of acknowledgements were to the awards of a single PI
- At five institutions (Duke, MGH, UCLA, UC Davis, University of Michigan), more than 40% of acknowledgements were to the awards of a single PI

Non-SAIR awards of the SAIR PI himself were most frequently acknowledged in publications at six of the SAIR institutions (Duke, MGH, Stanford, UCLA, University of Arizona, University of Michigan); at four SAIR institutions an R01-funded or P01-funded researcher was the most-acknowledged PI (Case Western, Johns Hopkins, UC Davis, University of Pennsylvania); at MSKCC the ICMIC PI was the most-acknowledged; at Washington University the Cancer Center Support Grant was the most acknowledged.

Table 6.10: Measures of Integration into SAIR Institutions: Acknowledgements of Non-SAIR Awards on SAIR Publications

SAIR	Number/percentage of Acknowledgements to Most-Acknowledged Individual PI	Who
Case Western	5 (12%)	R01 PI (Lee)
Duke	48 (56%)	SAIR PI (Johnson)
Johns Hopkins	6 (11%)	R01 Researcher (Wagner)
MGH	149 (47%)	SAIR PI (Weissleder)
MSKCC	34 (24%)	ICMIC PI (Blasberg)
Stanford	36 (29%)	SAIR PI (Contag)
UC Davis	22 (40%)	R01 Researcher (Ferrara)
UCLA	50 (42%)	SAIR PI (Gambhir)
University of Arizona	16 (24%)	SAIR PI (Gillies)
University of Michigan	68 (44%)	SAIR PI (Ross)
University of Pennsylvania	33 (13%)	R01 Researcher (Wehrli)
Washington University	41 (16%)	PI of Cancer Center (Eberlein)

Source: STPI analysis of SAIR publications and administrative data
Note: For the purpose of Table 6.10, both Michael Phelps and Sam Gambhir are considered the "SAIR PI"

Table 6.11 summarizes differences among the SAIR institutions with respect to acknowledgements to other NCI awards on SAIR publications. By the measures considered in this table (focusing on acknowledgements to publications), the SAIR awardees are broadly distributed, with SAIR institutions occupying six of the nine cells

of the table. SAIR institutions at the bottom-left corner of the table (e.g., Duke, MGH, UCLA, University of Michigan) are by these measures less broadly integrated into their home institutions than are the SAIR institutions near the upper-right corner (e.g., Case Western, UC Davis, University of Pennsylvania, and Washington University), which had a relatively high percentage of NCI awards acknowledged on publications as well as a relatively low concentration. Johns Hopkins appears to have been an outlier in that acknowledgements were not concentrated among a small group of PIs but the percentage of PIs acknowledged on SAIR publications remained relatively low.

Table 6.11: Summary of Measures of Integration

Measure	Percentage of NCI Awards to Institution Appearing on List of Acknowledged NCI Awards on SAIR Publications < 10%	Percentage 10-20%	Percentage > 20%
Percentage of Acknowledgements to Most-Acknowledged PI < 20%	Johns Hopkins	Case Western, University of Pennsylvania, Washington University	
Percentage 20-40%	Stanford	MSKCC, University of Arizona	UC Davis
Percentage > 40%	Duke, MGH, UCLA, University of Michigan		

6.5 Use of the SAIR Facilities and Data by Researchers with Funding from Sources Other than NCI

Of the 421 awards identified as having used the SAIR facilities, 117 (28%) were administered by other NIH Institutes and Centers (ICs) and 85 (20%) were from sources outside of NIH (Table 6.12). The largest number of non-NCI NIH awards were administered by the National Heart, Lung, and Blood Institute (NHLBI, 25 awards); the National Institute of Biomedical Imaging and Bioengineering (NIBIB, 25 awards); the National Institute of Neurological Disorders and Stroke (NINDS, 17 awards); and the National Institute of Diabetes and Digestive and Kidney Disease (NIDDK, 13 awards). Other sources of funding included associations/foundations/scientific societies (26 awards, including four from the Radiological Society of North America); other U.S. government agencies (including 10 DOD and nine DOE awards); institutional funding; state government; and industry sources.

Table 6.12: Number of Other Awards Using SAIR by Source

NIH IC Source	Number of awards	Percentage of non-NCI-funded awards
NHLBI	25	12%
NIBIB	25	12%
NINDS	17	8%
NIDDK	13	6%
NIAID	9	4%
NIGMS	7	3%
NCRR	4	2%
NIDCR	4	2%
8 other ICs	13	6%
Associations, Foundations, Scientific Societies	26	13%
Other USG (DOE, DOD, NASA, NSF)	26	13%
Institutional Funds	11	5%
Industry	8	4%
State Gov't	7	3%
Other/Unknown	7	3%

Source: STPI analysis of SAIR administrative data

Table 6.13 shows the number of awards reported to have used SAIR facilities by SAIR institution and source of the award. At most of the SAIR institutions between 20%-40% of awards reportedly using the facility were administered by other NIH Institutes and Centers. At four SAIR institutions, approximately 90% or more of all awards using the SAIR facility were NIH-funded, while at the other eight SAIR institutions 18-33% of awards were non-NIH.

Table 6.13: Awards Reported as Using SAIR Facilities, by Source

Institution	Total awards Using SAIR	NCI-supported awards	Percentage of total awards NCI-supported	Other NIH-supported awards	Other NIH-supported awards as a percentage of total awards	Non-NIH Supported Awards as Percentage of Total
SAIR A	25	20	80%	2	8%	12%
SAIR B	39	14	36%	12	31%	33%
SAIR C	36	18	50%	18	50%	0%
SAIR D	41	23	56%	8	20%	24%
SAIR E	61	28	46%	17	28%	26%
SAIR F	38	19	50%	12	32%	18%
SAIR G	21	14	67%	3	14%	19%
SAIR H	61	28	46%	16	26%	28%
SAIR I	23	12	52%	5	22%	26%
SAIR J	21	10	48%	9	43%	9%
SAIR K	28	14	50%	7	25%	25%
SAIR L	27	16	59%	8	30%	11%
Total	421	219	52%	117	28%	20%

Source: STPI analysis of SAIR administrative data

As shown in Table 6.3 above, approximately 40% of all of the NIH awards acknowledged on SAIR publications were funded by ICs other than NCI. Awards administered by 18 of the other 26 Institutes or Centers, as well as NIOSH (one of the Centers for Disease Control and Prevention) were acknowledged on SAIR publications; of these, however, 65% were to awards administered by four ICs: NHLBI, NIBIB, NCRR, and NINDS (data not shown).

Institutions differed in their patterns of acknowledgements to non-NCI awards on SAIR publications. The percentage of acknowledgements to NCI-administered awards ranged from 20% 90%. There was also substantial variation with respect to which non-NCI ICs' awards were acknowledged.

Chapter 7: New Technology Development

This chapter describes outcomes related to the third program goal:

> *Support research focused on developing and improving technologies related to small animal imaging*

The first section of this chapter describes technology development projects funded directly by the SAIR. The second discusses SAIR publications related to technology development. The third section reports on key discoveries as identified by the PIs and commercialization of SAIR technologies. The final section addresses other sources of support for technology development at SAIR institutions.

7.1 SAIR-Funded Technology Development Projects

7.1.1 SAIR-Funded Technology Development Projects Overview

All the SAIR institutions reported through applications and progress reports that they provided direct (monetary) support for research projects/activities that developed and improved technologies relating to small animal imaging. The degree to which "research projects" were discrete and well-defined entities varied across SAIR awardees, as did the quality of available descriptions, making them difficult to count and describe. Using best judgment, STPI distinguished 132 SAIR-funded technology development projects, although size, level of effort, and relative importance of each effort is unknown and may not be comparable.

Research projects were further categorized by the type of technology being developed: hardware/equipment, software and imaging markers/methods. Ten of the SAIR applications reported at least one equipment/hardware research activity, with 32 distinct activities described. Forty-seven software/image registration efforts were listed (all but two SAIRs reporting at least one such project), as were 53 projects related to imaging methods, markers, and reporters (all but one SAIR describing at least one).

Each research project reported in the SAIR applications was further categorized by imaging modality.[27]

Research projects in small animal imaging technology occurred mostly in MRI/MRS (33%), multimodality systems (21%) and optical systems (19%).

[27] STPI's characterization of the modalities of the research projects included "multimodality" and "multiple systems." The "multimodality" categorization refers to those modalities that are combined, either through hardware or software, to provide a greater understanding into the relationships between anatomical, biochemical, physiologic and/or pharmacologic information. An example of this is the fusion of anatomic (e.g., MR) and functional/molecular imaging (e.g., PET, NIRF). In contrast, the "multiple systems" categorization generally refers to research activities in software or imaging methods/markers, and is used when a development can be applied to multiple modalities. Example of this categorization included the development of image registration software and phantoms; also placed in this category were SAIR applications that described research into "contrast agents" but did not specify a modality or modalities.

7.1.2 Funded Projects Focused on Equipment/Hardware Development

Table 7.1 summarizes research projects focused on development or improvement of imaging equipment. Seven SAIRs were conducting projects focused on optical imaging hardware technology development. Three SAIRs were conducting research to develop multimodality hardware. Some examples include:

- Development of PET/MR scanner
- Combining optical and MR imaging technology for molecular detection, characterization and therapy assessment for cancer.

Table 7.1: Hardware/Equipment Projects of the SAIR Awardees

Institution	MRI/MRS	Optical	CT	PET	SPECT	Multimodality	Multiple Systems
SAIR B		X			X		
SAIR D	X	X		X		X	
SAIR E		X		X			
SAIR F				X		X	X
SAIR G		X					
SAIR H		X				X	
SAIR I	X	X			X		
SAIR J						X	X
SAIR K		X					
SAIR L			X	X			
Number of SAIRs with hardware projects involving modality	2	7	1	4	2	4	2

Source: STPI analysis of SAIR application materials
Note: SAIR A and SAIR C had no hardware/equipment projects

It was not feasible to systematically describe progress on individual SAIR software development or imaging methods research projects, as SAIR applications did not take a standard approach to describing progress in their research efforts.

7.2 SAIR Publications Related to Technology Development

From the list of SAIR publications described in Chapter 4, STPI distinguished those that could be classified as "technology development" as compared with those that primarily supported cancer research that made use of the facility itself. Table 7.2 shows that the percentage of publications coded by STPI as "technology development" varied substantially across the SAIR institutions – ranging from seven of MSKCC's 80 publications (9%) to more than half of the Case Western (79%).Western, Duke, UCLA, UC Davis, and University of Pennsylvania publications.

Table 7.2: Publications Coded as "Technology Development", by SAIR

Institution	Total Publications	Coded "Technology Development"	Percentage Coded "Technology Development"
Case Western	30	17	57%
Duke	56	30	54%
Johns Hopkins	35	14	40%
MGH	153	60	39%
MSKCC	80	7	9%
Stanford	63	17	27%
UC Davis	41	24	59%
UCLA	68	39	57%
University of Arizona	53	13	25%
University of Michigan	75	20	27%
University of Pennsylvania	159	89	56%
Washington University	142	47	33%
Total	955	377	39%

Source: STPI analysis of SAIR Publications database
Note: Four publications are double-counted

It was not the case that all of the technology development SAIR publications resulted entirely from SAIR support. One approach to assessing degree of attributability of technology development was to consider acknowledgements to awards other than the SAIR. More than 90% of technology development SAIR publications that acknowledged any support acknowledged support from other awards in addition to the SAIR (Table 7.3). For SAIR publications at five institutions, at least some percentage of the technology development publications acknowledged only the SAIR – with the SAIR award appearing to play a singular role in technology development in publications associated with the Johns Hopkins (23% of technology development publications cite only the SAIR) and University of Arizona (46%) SAIR awards. At four other SAIR institutions, there were no technology development SAIR publications that acknowledged only the SAIR award.

Table 7.3: Awards Acknowledged by SAIR Technology Development Publications

SAIR	Number of Technology Development publications that with one or more acknowledgements	Number of Technology Development publications that acknowledge only the SAIR	Percentage of Technology Development publications that acknowledge only the SAIR
Duke	29	0	0%
Johns Hopkins	13	3	23%
MGH	56	0	0%
MSKCC	7	0	0%
Stanford	17	0	0%
UCLA	39	3	8%
University of Arizona	13	6	46%
University of Michigan	19	1	5%
Washington University	46	5	11%
Total	239	18	8%

Source: STPI analysis of SAIR publications database
Note: As described in Chapter 2, Case Western, UC Davis, and the University of Pennsylvania are excluded from the analysis because of the low percentage of SAIR publications that acknowledge the SAIR award.

SAIR institutions varied widely in the extent to which acknowledged awards on technology development publications were NCI-funded (Table 7.4). At Duke, for example, fewer than 30% of the acknowledgements were to NCI-administered awards. At the other extreme, virtually all technology development publications at MSKCC and the University of Michigan solely acknowledged NCI support.

Table 7.4: Acknowledgement of non-SAIR NCI and non-NCI Awards, by SAIR

SAIR	Number of Technology Development publications with acknowledgements	Number of NIH awards to institution acknowledged on those publications	% of awards NCI	Number of acknowledgements of all NIH awards on those publications	% acknowledgements to NCI grants
Case Western	13	12	42%	15	40%
Duke	29	8	63%	37	24%
Johns Hopkins	13	14	43%	17	47%
MGH	56	20	50%	120	73%
MSKCC	7	9	89%	14	93%
Stanford	17	17	29%	39	36%
UC Davis	21	17	41%	31	52%
UCLA	39	10	50%	55	85%
University of Arizona	13	8	63%	10	60%
University of Michigan	19	8	88%	31	97%
University of Pennsylvania	70	49	47%	124	60%
Washington University	46	31	42%	72	57%
Total	343	203	49%	565	62%

Source: STPI analysis of SAIR publications database
Note: Because of the institution-by-institution variation in citation to the SAIR award, acknowledgement of the SAIR awards themselves are excluded from this analysis.

7.3 Key Discoveries

SAIR PIs were asked during interviews to identify the most significant discoveries made using SAIR funds and/or the SAIR facility. In most cases the SAIR PIs described a result that was sufficiently well-developed to have been reported in one or more peer-reviewed journal articles, although some of the technologies described had been disseminated only as conference papers or remained sufficiently under development to have been described only in progress reports. Each of the SAIR PIs specified[28] between two and four key discoveries, which are summarized below.

[28] Note: Rather than describing key discoveries in the interview, the Case Western PI wrote a longer document, from which two discoveries were extracted by STPI. The MGH SAIR provided an updated list of key discoveries in October 2009, which replaced the list described in the interview with the PI. The MGH SAIR list also mentioned that the SAIR had been involved in several important basic cancer research discoveries, and mentioned specifically the recent discovery of a splenic monocyte reservoir (Science 2009;325:612).

Discoveries related to small animal imaging equipment/hardware:

- Ultrahigh-speed optical coherence tomography (Case Western)
- Micro-CT with respiratory and cardiac gating (Duke)
- Fluorescence Mediated Tomography (MGH)
- FMT-CT (MGH)
- Worked closely with Gamma Medica to develop small animal SPECT (Stanford)
- Low cost, high sensitivity PET detectors (UC Davis)
- Laser induced fluorescent detection by Optical Coherence Tomography (University of Arizona)
- A-PET: a small animal PET camera (University of Pennsylvania)
- Handheld optical scanner for breast cancer detection (University of Pennsylvania)
- High resolution microPET (Washington University)
- Quantitative diffuse optical tomography for small animals (Washington University)

Discoveries related to small animal imaging software/image registration technologies:

- Multimodality registration without a dedicated multimodality scanner (MSKCC)
- Animal-specific positioning molds for registration of repeat imaging studies (MSKCC)
- Method of image registration for small animal, multi-modality imaging (UCLA)
- MIPortal, MGH's image archiving and retrieval system providing secure access to multi-modality imaging data (MGH)
- CMIR Image, an image processing software package (MGH)
- Plug-ins for OSIRIX open-source imaging software for MRI analysis and multi-modality image analysis (MGH)

Discoveries relating to new imaging methods, imaging agents, or reporters:

- Paramagnetic chemical exchange saturation transfer (PARACEST) MRI contrast agents for protease detection (Case Western)
- High-resolution vascular imaging of the rat spine using liposomal blood pool MR agent (Duke)
- Localized, image-guided blood brain barrier disruption (Duke)
- Imaging bacteriolytic cancer therapy (Johns Hopkins)
- Bortezomib-induced enzyme-targeted radiation therapy in herpesvirus-associated tumors (Johns Hopkins)
- ABCG2/BCRP expression modulates D-Luciferin based bioluminescence imaging (Johns Hopkins)
- Radiolabeled anti-claudin 4 and anti-prostate stem cell antigen imaging in experimental models of pancreatic cancer (Johns Hopkins)

- Multiple new imaging agents: ^{111}In-FXIII, ^{64}Cu-CLIO, ^{18}F-CLIO, MPO-Gd, AMTA (CLIOgly), VLIN-28, ^{18}F-4V, telomerase sensor, MMPsense, Cathepsin K sensor (MGH)
- In vivo tumor lactate relaxation measurements by selective multiple-quantum-coherence (MSKCC)
- Monitoring protein-protein interactions using split synthetic renilla luciferase protein-fragment-assisted complementation (Stanford)
- Use of quantum dots as in vivo reagents (Stanford)
- Stimulus-responsive contrast agent for ultrasound molecular imaging (UC Davis)
- Optical bioluminescence and positron emission tomography imaging of a novel fusion reporter gene in tumor xenografts of living mice (UCLA)
- Early response of prostate carcinoma xenografts to docetaxel chemotherapy monitored with diffusion MRI (University of Arizona)
- Unique molecular reporters for c-MET (University of Michigan)
- Molecular imaging of Akt kinase activity (University of Michigan)
- Noninvasive imaging of apoptosis and its application in cancer therapeutics (University of Michigan)
- Three dimensional MR diffusion image of the prostate (Washington University)
- Diagnosing tumor hypoxia non-invasively (Washington University)

Of the 46 key discoveries described, more than half (28) fell into the category of "imaging agents, reporters, or methods", while the bulk of the remainder (18) were the development of new small animal imaging equipment. New equipment development covered several primary imaging modalities, including optical (MGH, Washington University, University of Arizona, University of Pennsylvania); PET (University of Pennsylvania, UC Davis, and Washington University); CT (Duke); and SPECT (Stanford, University of Arizona). Table 7.5 summarizes the key discoveries by SAIR.

Table 7.5: Key Discoveries by SAIR

Institution	Equipment	Software	Imaging agents, reporters, or methods: SAIR supported	Imaging agents, reporters, or methods: Base Grant Supported	Total
Case Western	1	0	1	0	2
Duke	1	0	0	2	3
Johns Hopkins	0	0	1	3	4
MGH	2	3	0	10+	15+
MSKCC	0	2	1	0	3
Stanford	1	0	2	0	3
UC Davis	1	0	0	1	2
UCLA	0	1	1	0	2
University Arizona	2	0	0	1	3
University of Michigan	0	0	0	3	3
University of Pennsylvania	2	0	0	0	2
Washington University	2	0	0	2	4
Total	12	6	6	22+	46

Source: STPI analysis of SAIR PI interviews

Most of the SAIR PIs (all but the Johns Hopkins and University of Michigan PIs) described key discoveries in more than one category; eight of the SAIR PIs described at least one key discovery related to equipment development and ten of the PIs described at least one key discovery related to new methods, agents, or reporters.

Comparing the PI-reported key discoveries related to imaging methods, reporters, or agents with the applications and progress reports for the corresponding institution, showed that the majority (22 of 28) of those "key discoveries" noted by the PIs in the interviews were supported by base grants and not directly using SAIR research funds. While SAIR facilities were used, the actual research appears to have been supported by another award.

7.4 Commercialization of Imaging Technologies from SAIR Institutions

A number of the SAIR-funded research and development efforts on small animal imaging tools have resulted in investment and commercialization by medical equipment manufacturers. The commercialization of new small animal imaging prototypes that were once supported by the SAIR reflects the potential for innovation in small animal imaging research.

Examples of successful commercialization of equipment built based upon SAIR research and prototyping include:

- A-PET: μPET imager developed by University of Pennsylvania and commercialized by Philips
- First dedicated animal microPET system developed by UCLA and commercialized by Concorde Microsystems
- MGH development of optical systems for Fluorescence Mediated Tomography (FMT) commercialized by Kodak, VisEn Medical, Olympus, and Siemens

SAIR personnel also serve as collaborators on small animal imaging device-related SBIRs:

- MGH investigators collaborating with Genex Technologies on three-dimension DOT scanners (NIH SBIR award R44ES012360, 2003-2007)
- UC Davis investigators collaborating with Radiation Monitoring Devices on the design of low-cost PET scanners (NIH SBIR award R44RR015992, 2001-5; DOE SBIR award DE-FG02-05ER84298; DE-FG02-06ER84432, 2005-6)
- UC Davis investigators collaborating with Radiation Monitoring Devices on the design of small animal PET/CT scanners (NIH SBIR award R44CA101243, 2005-8)
- UC Davis investigators collaborating with Radiation Monitoring Devices on the design of small animal PET/MR scanners (NIH SBIR award R44NS055377, 2006-9; DOE SBIR award DE-FG02-06ER84432)
- University of Pennsylvania investigators collaborating with Optical Devices, Inc. on the development of detectors for molecular beacons (NIH SBIR award R44CA096016, 2002-6)
- Washington University investigators collaborating with OptoSonics to develop a Thermoacoustic Computed Tomography hybrid ultrasound/optical scanner (NIH SBIR award R44CA102891, 2004-7)
- Washington University investigators collaborating with Doty Scientific to develop improved RF coils for small animal MRI equipment (NIH SBIR award R44EB000445, 2001-2005)
- Washington University investigators collaborating with Luna Innovations on nanomaterials for MR imaging (NIH SBIR award R43CA110313, 2004-7)

7.5 Need for Imaging Technology Development Funds

Although it is not directly related to SAIR outcomes, an additional question considered by the evaluation is the extent to which SAIR funding for imaging technology development is occupying a singular niche at these institutions. As described in Chapter 6, NCI has a number of other investments in imaging-related programs at SAIR institutions, especially through translational research programs (e.g., ICMIC, NTROI,

CCNE). In general, the translational research programs have focused more on developing imaging methods, reporters, and agents rather than equipment and software.[29]

However, equipment and software development has been supported at SAIR institutions through several programs and initiatives at NCI and elsewhere. Examples of awards that overlapped with SAIR include:

NIBIB- or NCRR-funded P41 Centers

- Center for In Vivo Microscopy (P41NCRR005909, Duke University. CIVM is the organizational structure in which the SAIR is housed, same PI as SAIR, CIVM acknowledged on 35 SAIR publications)
- Center for Gamma-Ray Imaging (P41EB002305, University of Arizona, at least five projects focused on small animal imaging[30])
- Resource for Magnetic Resonance and Optical Research (P41RR002305, University of Pennsylvania, award acknowledged on 10 SAIR publications)

R01 and R21 awards funded by NIBIB under RFA 03-002, "Systems and methods for small animal imaging"[31]

- Pinhole SPECT (R01EB001910, Duke, transitioned to the University of Pennsylvania mid-award)
- Pinhole SPECT (R01EB001809 , University of Pennsylvania, transitioned to Thomas Jefferson University mid-award)

[29] RFA 03-002, "SYSTEMS AND METHODS FOR SMALL ANIMAL IMAGING", released November 2002. The RFA made 20 awards (11 R01, 9 R01) totaling $12 million in direct costs. Of those 20 awards, six were made to SAIR institutions (and one to a PI who switched midproject from a non-SAIR to a SAIR institution). Ten of the projects ($6.5 million in direct costs) were coded by STPI as "equipment" rather than "imaging methods." Of those ten, two were to SAIR institutions; other institutions funded included Baylor, Columbia University, Dartmouth, Texas A&M, the University of Arkansas, and the University of Virginia.

[30] Based of CRISP searches and abstract review of the 17 P41 projects.

[31] "Novel Technologies for In Vivo Imaging" (e.g., PAR 01-101, PAR 03-124, PA 04-095, PA 06-398" and "Industry-Academic Partnerships for Development of Biomedical Imaging Systems and Methods that Are Cancer Specific" (PAR 03-157, PAR 07-214). These program announcements, unlike the NIBIB RFA, are not specific to small animal imaging. These program announcements have funded 128 individual awards, representing more than $70 million in direct costs between 2002-2008. Of those 128 awards, 23 (total direct costs of $12.9 million) were identified from STPI review of abstracts as being specifically for small animal imaging. Ten awards were made to investigators at SAIR institutions (and one to a PI who switched midproject from a SAIR to a non-SAIR institution), totaling $4.8 million. Other institutions receiving funding for small animal imaging equipment from these solicitations included Columbia, Dartmouth, UC Irvine, University of Illinois Urbana-Champaign, University of Washington, and Virginia Tech.

R01/R21 Awards from NCI Cancer Imaging Program RFAs and PAs[32]

- Prepolarized MRI prototype (R33EB000777, Stanford)
- Low-cost PET imaging (R01CA134632, UC Davis)[33]
- COMKAT software development (R33CA10107, Case Western)
- Optical/ultrasound hybrid system (R21CA110167, MGH)
- Development of a confocal theta fluorescence microscope (R21CA109988, Stanford)
- Fluorescence endoscopy (R21CA113964, University of Arizona)
- Multidimensional nonuniform fast Fourier transform (NUFFT) algorithms (R21CA114680, Duke)
- Fiber-based NIR multiphoton microscope (R21CA123537, Washington University)
- Small animal SPECT/CT (R21EB004940, University of Michigan)

Twenty-seven additional investigator-initiated R01 and R21 awards to investigators named as key personnel on applications at ten SAIR institutions related to the development of small animal imaging-related hardware, software, or animal handling procedures.

While it is not feasible to precisely identify the use of SAIR funds for equipment/hardware/software research, estimates can be made for the purpose of comparability with other programs and efforts. Assuming that 40% of SAIR funds were directed to research (midrange of the 33%-50% directive in the RFA) and that the funding for each individual SAIR research project identified (the list of 132) was identical at each SAIR, this suggests that approximately 60% of that research funding was intended for equipment (79 of the 132 projects were hardware or software); therefore, 25% of SAIR costs (across the program) are potentially allocable to such research. Applying this estimating procedure to the direct costs of SAIR awards first funded in Cohorts 1-3 ($42.6 million between 1999-2008) suggests that approximately $10.9 million was available for such research.

[32] The outcome evaluation of the ICMIC program, for example, identified forty-nine Research Components, all of which aimed to develop new reagents, imaging agents, or markers – two-thirds of them (34 of 49) intended for potential future human use (ICMIC Outcome Evaluation, pages 18-19. Similarly, only one of the ICMIC key discoveries (and one corresponding highly cited paper) was for imaging hardware – MGH discoveries related to fluorescence molecular imaging (ICMIC Outcome Evaluation, pages 31-34. Similarly, the CCNE RFA (RFA-CA-05-24) identifies new imaging agents and therapeutics, rather than small animal imaging hardware or software, as a program goal in the Background section; applying CCNEs were required to demonstrate small animal imaging capabilities as a precondition for award. The NTROI RFA was intended to support the development of optical imaging technologies for both human and pre-clinical/small animal applications, including both imaging agents/probes and new equipment and technology development (RFA-CA-03-002).

[33] The SSPM technologies developed under this award are also supported under a variety of DOE SBIR awards to Radiation Monitoring Devices (e.g., DE-FG02-07ER84752; DE-FG02-06ER84589), but linkage to the SAIR could not be confirmed.

Table 7.6 summarizes the results of the above non-SAIR research searches for awards related to small animal imaging hardware or software. The right hand column of the table is an estimate of the total SAIR funding allocated to hardware or software research. For all three cohorts, funding for R01/R21 equipment- or software-based research at the SAIR likely exceeded SAIR funding for such research by a factor of two or more; this finding was true for the SAIR institutions as a whole as well. At three SAIR institutions funding for research likely was comparable (within a factor of two) to non-SAIR funding, while only at two SAIRs was SAIR funding likely the larger source of funding for research efforts related to small animal imaging hardware and software.

Table 7.6: Comparison of Identified Small Animal Imaging Hardware or Software-Related R01/R21 Funding at SAIR Institutions with Estimated SAIR Allocation of Funds to Hardware and Software Research

SAIR Funding Cohort	Total Funding for Identified Small Animal Imaging Technology Development Funding 2001-2008 (M$)	Number of Distinct Awards Included in Total	Estimated SAIR Funding Allocated to Hardware/Software Research Through 2008	Ratio of Column 1 to Column 3
Cohort 1	$10.80	18	$5.10	2.12
Cohort 2	$9.20	15	$4.10	2.24
Cohort 3	$7.90	9	$1.60	4.94
Total	$30.70	42	$10.90	2.82

Source: STPI analysis of SAIR administrative data and results of CRISP/QVR searches
Note: Estimate of SAIR allocation based upon uniform estimate 40% of SAIR funds allocated to research, multiplied by the percentage of projects per SAIR for hardware- or software-based research

Chapter 8: Training

This chapter describes outcomes related to the final program goal:

> *Provide training in cancer-related small animal imaging techniques and methodologies to investigators and support personnel from a variety of disciplines related to cancer*

The first part of this chapter describes the types of training activities supported through the SAIR awards. Three sets of outcomes are then described: hands-on training through workshops, coursework, and integration into training programs; career development for postdoctoral fellows and junior faculty; and the results of visiting fellowships.

> "[I]s there anybody else here at XXX doing small animal imaging training and I think the answer is no, I think we are it." – SAIR PI

8.1 SAIR Training Activities

As noted in Section 3.1, training was introduced as an objective beginning with the 2000 RFA. In 2002, the Cancer Imaging Program ran a competition for training-related supplements for the Cohort 1 SAIR awardees; four of the five SAIR institutions (all but the University of Pennsylvania) received supplemental funding to carry out training activities.

SAIR awardees conducted a wide variety of training activities. These activities are summarized in Table 8.1 and described in more detail below.

Table 8.1: Training Activities of the SAIR Awardees

Training Type	SAIR A	SAIR B	SAIR C	SAIR D	SAIR E	SAIR F	SAIR G	SAIR H	SAIR I	SAIR J	SAIR K	SAIR L
Multi-day workshop		Yes	Yes		Yes	Yes	Yes	Yes	Yes			Yes
SAIR seminars/speaker series	Yes	Yes	Yes	Yes		Yes	Yes	Yes	Yes	Yes	Yes	
Undergraduate training			Yes			Yes	Yes		Yes		Yes	
Support for graduate students/ postdoctoral fellows	Yes (PD)	Yes (GS)		Yes (PD)		Yes (Both)	Yes (Both)		Yes (Both)	Yes (Both)	Yes (GS)	Yes (Both)
Lectures/courses/ labs as part of courses in SA imaging		Yes					Yes		Yes	Yes	Yes	Yes
Integration into T32s/K12s/ R25Ts	Yes	Yes						Yes	Yes	Yes	Yes	Yes
Other program of hands-on training to graduate students/ postdoctoral fellows			Yes		Yes	Yes	Yes	Yes		Yes		
Junior faculty support/ training			Yes				Yes		Yes			
Visiting faculty		Yes	Yes		Yes						Yes	Yes
Visiting students							Yes					
Animal care/techniques training for technicians	Yes	Yes					Yes	Yes				
Technologist training and career development	Yes							Yes		Yes		
Web-based materials									Yes	Yes		Yes
Textbook writing			Yes									
Instrumentation development training		Yes										
K-12 activities						Yes						

Source: STPI analysis of SAIR applications, progress reports, and interviews with SAIR investigators

8.1.1 Multi-day Workshops and Seminar Series

Ten SAIR awardees reported sponsoring seminars or speaker series, and eight of the 12 SAIR awardees have conducted multi-day workshops for training in small animal imaging techniques.[34] Five of the SAIR awardees run periodic workshops on multiple aspects of small-animal imaging, while two SAIRs have run more narrowly focused seminars aimed at specific aspects of small animal imaging.

- SAIR A: Two-day workshop on use of IVIS optical imaging equipment (26 attend lecture, 21 attend hands-on training sessions)
- SAIR A: One-plus day workshop on use of Vevo ultrasound scanner (40 attend lecture, 12 attend hands-on training session)
- SAIR B: 2004 workshop on animal monitoring
- SAIR E: SAIR has held three Advanced Symposia. Approximately 100 scientists attended each symposium
- SAIR F: Annual workshops on small animal imaging with approximately 100 participants per year
- SAIR G: Five workshops on small animal imaging, attracting an average of approximately 100 participants per symposium
- SAIR H: Annual three-day workshops on small animal imaging attracting approximately 20-40 participants from the local area
- SAIR L: Annual two-day workshops with approximately twenty participants per workshop

8.1.2 Hands-On Training for Undergraduate and Graduate Students

Four of the SAIR awardees provided research support for undergraduates. One SAIR's funds were used to provide research opportunities to students at community colleges. At one SAIR, the microinjector used for digital subtraction autoradiography was constructed by an undergraduate engineering student as a senior honors project.

In addition, all of the SAIR awards provided some form of training to graduate students and postdoctoral fellows, though approaches differed. Seven of the SAIR institutions provided direct funding for graduate students – in some cases full time (four SAIRs) and part-time in others (three SAIRs). Seven of the SAIR awards provided support for postdoctoral fellows.

Six of the SAIR applications described involvement in graduate courses on small animal imaging-related topics, either through use of SAIR facilities or lectures given by SAIR personnel.

[34] NCI also sponsors a Cancer Imaging Camp, which was held at Duke University in 2007 and 2008.

All of the SAIR awardees at institutions possessing T32 or R25T programs in molecular imaging training described a role played by the SAIR in the program.[35] In addition, one SAIR described the addition of small animal imaging into a T32 as a consequence of SAIR funding, and two SAIRs described the integration of the SAIR into NIBIB-funded T32s in biomedical imaging.

8.1.3 Support for Junior Faculty

Three SAIR applications described support for junior faculty. One SAIR runs a competition each year for pilot projects submitted by junior faculty or faculty from underrepresented groups; one SAIR charges lower fees for the use of imaging equipment to junior faculty; and one SAIR preferentially chose awards whose PIs were junior faculty in their listed set of base grants to support; four K-series awards were SAIR-supported.

8.1.4 Support for Visiting Faculty and Students

Six SAIR applications identified training to visiting faculty (and one SAIR to visiting students) as an activity undertaken using SAIR funding. In another example, one SAIR has held training sessions for faculty at other regional institutions.

8.1.5 Technical Training and Certification[36]

Five of the SAIR applications specifically highlighted training for technicians/technologists, including both animal care and handling training as well technician participation in graduate student courses. Examples include:

- At SAIR K, all four full-time SAIR staff members have completed ARC/IACUC approved basic animal handling training. These technicians are subsequently providing training to imaging faculty and staff at the institution.
- SAIR L developed an internal training program for certification of cyclotron operators, and the program was used to certify a radiochemistry staff member as a cyclotron operator.

8.1.6 Other Training Activities

Other training strategies described include:[37]

- Development of web-based curricula as introductions to imaging modalities
- Writing a textbook on small animal imaging
- Training of investigators in the development of small animal imaging instrumentation
- Creating a "Digital Dissection of the Mouse" module for middle school and high school science classes, and SAIR participants lecture in K-12 settings.

[35] See the ICMIC Outcome Evaluation, Section 7.1 for additional information regarding molecular imaging-related T32s and ICMIC (and SAIR) institutions.
[36] Examples are partial quotations drawn from applications and progress reports.
[37] Examples are partial quotations drawn from applications and progress reports.

8.1.7 Other Support for Training in Small Animal Imaging at SAIR Institutions

In interviews, PIs frequently identified the SAIR award as the primary (or sole) designated funding sources for cancer-related small animal imaging training at their institutions. A notable exception was the NCI Cancer Imaging Camp, an intensive six-day imaging training program funded by the Cancer Imaging Program in June 2007, with a second iteration held in 2008. Both workshops were held at Duke, and they attracted faculty from across multiple SAIR institutions as lecturers. The camp focuses on training postdoctoral researchers and junior faculty, with 16 trainees participating in 2007 and 20 participants in 2008. The program includes both lectures and hands-on training sessions to expose participants to the use of MRI, CT, SPECT, optical imaging, PET, and ultrasound.

An evaluation process for the first imaging camp was conducted. Participants were asked to rate the quality of the lectures and the laboratory sessions. Respondents were also asked about whether participation in the camp increased their knowledge of the modalities and made them more likely to use small animal imaging in their own research. Virtually all of the respondents agreed (or strongly agreed) that their participation in the camp had increased their knowledge of all six modalities. Participants were more divided in assessing their readiness to begin using the modalities in their own research, with most participants expressing readiness to use the more turn-key optical and ultrasound equipment, and fewer stating that they were confident in the use of MR, CT, SPECT, and PET. No follow-up with participants was available that identified whether they were in fact beginning to use or more likely to use small animal imaging modalities in their own research. Few other sources of small animal imaging training funds at SAIR institutions were identified.

8.2 Career Development Outcomes

8.2.1 Outcomes of Support for Postdoctoral Fellows

As described above, nine of the SAIR awards funded (or planned to provide)[38] support for graduate students or postdoctoral researchers. Seven SAIR awards provided support for graduate students, but no information on the training outcomes of those students was available through progress reports and application materials. The evaluation, therefore, focused upon the postdoctoral researchers supported at seven of the SAIR institutions.

STPI assembled the list of named postdoctoral researchers supported using SAIR funds. Twenty-two named postdoctoral fellows from six SAIR institutions were identified. Of those 22 postdoctoral researchers:

- Five SAIR-supported postdoctoral fellows were identified as having received faculty positions at other institutions.
- Three SAIR-supported postdoctoral fellows became instructors at SAIR institutions.

[38] The University of Arizona SAIR Year 5 progress report stated that it had not been successful in attracting graduate students to date.

- Three SAIR-supported postdoctoral fellows have been hired as Research Associates at their SAIR institution (two at Stanford and one at Johns Hopkins). One SAIR postdoc is a researcher at the California Institute of Technology, serving as the Associate Director for Small Animal Imaging at the Caltech Brain Imaging Center.
- One SAIR postdoc is working in industry, at General Electric.
- Nine SAIR postdoctoral fellows appear to still be completing their postdoctoral training at their SAIR institutions.
- Follow-on information could not be identified for one postdoc.

8.2.2 Recruitment/Mentorship of Junior Faculty

> "Because of the SAIR program, I think, and the infrastructure that we had, we were able to recruit, in collaboration with Internal Medicine, an MD/PhD, a new assistant professor" – SAIR PI

As described above, one SAIR supported the research of junior faculty. K-series awards of four faculty members (two NHLBI, two NIDDK) were included among the grants supported by the SAIR. SAIR PIs were also asked whether the presence of the SAIR helped to attract junior faculty to their institutions. Several PIs gave generic "yes" answers, while two interviewees named specific faculty members for whom the SAIR was a strong recruiting point.

8.3 Outcomes of Visiting Fellows Programs

Five of the SAIR awards funded visiting fellowship or technology transfer opportunities for faculty, including both substantial awards for visiting faculty andsmaller visiting fellowship awards for technology transfer and to foster learning/collaboration opportunities.

Chapter 9: Findings

The SAIR program has funded fifteen institutions through four competitions since fiscal year 1999, at a total program cost through FY 2008 of $63.7 million. Before presenting findings and recommendations regarding this program, however, it is important to note a number of sources of heterogeneity make it very difficult to draw valid conclusions about the program as a whole. The first major source of heterogeneity comes from differences in how SAIR funds were allocated among equipment purchase/development, personnel support, and development research to meet perceived infrastructure needs at the various institutions. Second, SAIR institutions varied widely with respect to three other parameters: background and research interests of faculty; instrumentation available for small animal imaging at the start of the program; and non-SAIR sources of support for small animal imaging activities. At no SAIR institution was the SAIR award the only major source of support for small animal imaging infrastructure and development research during the period of SAIR funding, and at several it was one of many. Third, there was variability in quantity, quality, and types of administrative and management information collected by each SAIR. As described in the previous chapters, the operational definition of seemingly-common concepts such as a "SAIR publication" or "SAIR-supported research" appears to have varied across SAIR institutions.

One additional concern in evaluating the SAIR program is the potential for traditional measures of programmatic success (such as publications in high-impact journals) to bring programmatic goals into conflict or to obscure them. If publications in high-impact journals is seen as a measure of programmatic "success", that may discriminate against those SAIR awardees that are more heavily focused on hardware development or the identification of new image registration techniques, which are more likely to be published in specialist journals with lower impact factors than are discoveries with more direct potential therapeutic benefit or basic scientific interest. Longer-term measures of the value of SAIR research, such as the relationships between SAIR-supported investigators and the imaging device manufacturers or the adoption and commercialization of SAIR-developed approaches, may be more appropriate indicators of the success of the SAIR program than journal publication. Similarly, measures of training that track traditional career development outcomes likely understate the impact of skills development and hands-on training in the use of small animal imaging by researchers.

This chapter consists of one overall finding section and four findings sections corresponding to the individual program goals.

9.1. Overall Findings

Overall finding 1: SAIR is not the sole source of support for small animal imaging infrastructure (equipment and personnel) or technology development at any of the awarded institutions, and at several it may not even have been among the most important sources of support for these activities.

As described in Chapter 3, receipt of the SAIR award at funded institutions generally preceded other sources of large-scale NCI support for small animal imaging, either within

the Cancer Center structure or through other large programs. At the inception of the SAIR program, only one institution had established a Cancer Center shared resource for imaging. Of the eight SAIR institutions that had ICMIC, NTROI, or CCNE awards, the SAIR preceded the other awards at four institutions; ICMIC preceded SAIR at two institutions, and pre-ICMICs preceded SAIR at two others.

Currently, however, every SAIR institution has an organizational structure and infrastructure base for small animal imaging. Of the 12 Cohort 1-3 SAIR awardees, eleven were affiliated with a CCSG that funded a core related to small animal imaging in 2007. Six of the 12 institutions had created a "molecular imaging" research theme at the Cancer Center as of 2007, and four more were in the process of doing so. As described in Chapter 5, all SAIR institutions have supplemented NCI funds with their own to purchase equipment, hire faculty, and/or support technical personnel. While there were institutions where SAIR provided the sole or primary NCI support for small animal imaging infrastructure at the outset of the program, the SAIR award can perhaps now best be characterized as providing an additional funding stream for imaging infrastructure, technology development, and training.

Table 9.1 identifies complementarities between activities funded by the SAIR awards and other funding streams. Specific complementarities will be discussed below in sections devoted to each of the four program goals.

Table 9.1: Complementarities between SAIR and Other Funding Sources

Function	Non-SAIR Sources of Funding	Comments
Build/purchase new equipment	Institutional support, NCRR	
Maintain equipment	Institutional support, CCSG	
Support staff (technicians, faculty)	Institutional support, CCSG	
Operate facility (technical consulting, perform experiments)	Charge-backs, Institutional support, CCSG	
Pilot project funding or "*pro bono*" imaging support	CCSG pilot projects, Institutional support, P50/U54 developmental funds	Other sources of pilot funding not necessarily dedicated to small animal imaging
Hardware/software development	R01/R21, P41	
Imaging methods/ markers development	R01/R21, P41, P50/U54	
Degree training/ postdoctoral fellow support	T32/R25T, P50 Career Development	Other sources not specifically dedicated to small animal imaging
Junior faculty support	K-series, P50 Career Development	Other sources not specifically dedicated to small animal imaging
Hands-on training/ workshops	None identified	

Overall finding 2: There appears to be robust unmet demand for small animal imaging resource support.

As described in Chapter 3, in the most recent round of awards, NCI received 33 distinct applications and funded eight of them (24%); three of the 26 applications by institutions that had not previously received a SAIR award (12%) and five of the seven applications by institutions that had previously received a SAIR award (70%). The difference in success rates between new and renewing applicants raises the concern that the SAIR program, as currently constituted, is difficult for new institutions to enter. A related concern described in Chapter 3 is the difference between SAIR and non-SAIR institutions regarding Cancer Center support for a small animal imaging resource (all but one of the SAIR institutions as of 2007, but only 14 of 51 (27%) Cancer Center institutions without a SAIR award as of 2007) and the Cancer Center's creation of an imaging-related research theme (10 of the 12 SAIR institutions that had been funded as of 2007, as opposed to six of 51 non-SAIR institutions). For small animal imaging to become a standard technique for basic and translational cancer research, it will need to be disseminated to all of the leading cancer research institutions, such as those designated as

Cancer Centers by NCI. To date, small animal imaging resources appear to remain concentrated in a subset of those institutions.

Overall finding 3: There has been a recent shift in the NCI approach to funding core services and research resources.

As described in Chapter 3, the report of the NCI Translational Research Working Group, released in June 2007, includes an initiative related to the consolidation of core services and research infrastructure. The report recommends a shift in the approach by which NCI funds core services, stressing the role of the Cancer Center Support Grant as the primary source of funding for such infrastructure.[39] While the report does not recommend that NCI eliminate all separate resource-related R24 and U24 programs, it does imply that separate resource-supporting programs such as SAIR require a strong rationale for their continuation.

9.2 Findings Relative to Program Goals

9.1.2 Building sustainable infrastructure (Program Goal 1)[40]

1. *The SAIR program contributed to the purchase and construction of new small animal imaging equipment at all SAIR institutions. At many SAIR institutions, however, SAIR funds themselves represented a minority of the total funds devoted to this purpose.*

All SAIR institutions have added imaging modalities using SAIR funding either by buying/upgrading or building equipment, with optical and microCT being the most-added modalities. Most SAIR facilities have used program funding to add at least two modalities. While most equipment was purchased, some SAIRs invested in constructing their own customized equipment.

In addition to purchases made using SAIR funds, all of the SAIR institutions have used NCRR Shared Instrumentation Grants and/or institutional funding to purchase new equipment, and many had funding from other sources as well. These included other NCI programs (e.g., Cancer Center Support Grants); other NIH ICs (e.g., NCRR P41s); other government agencies (e.g., DOE, NASA, NSF); state sources; and private funding. The combined funding from these sources to SAIR institutions for imaging equipment was at least $22.6 million between 1999 and 2007, which is approximately triple the $7.5 million of SAIR program funds spent on equipment. In interviews, SAIR PIs tended to credit the SAIR program with helping to attract additional funding for infrastructure, particularly from institutional sources and NCRR.

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[39] As described in the Report of the Translational Research Working Group of the National Cancer Advisory Board (June 2007), "Transforming Translation – Harnessing Discovery for Patient and Public Benefit", page 60, "For institutions with cancer centers, consolidation will be achieved by strengthening the role of cancer centers as the primary providers of core services... Guidelines for Cancer Center and P50, U-series, and RFA-directed P01 awards will be revised as necessary to incorporate the following principles for core services resource sharing.

[40] "Infrastructure" for small animal imaging was defined to include both equipment and personnel. Discussions of "sustainability" focused on the Cohort 1-3 SAIR awardees whose awards were not renewed and on the new Cohort 4 SAIR awardees.

By 2007, using a combination of resources, all of the SAIR-supported small animal imaging facilities had at least three of MR, CT, PET, and optical equipment available, with all but two SAIRs having all four. Ten of the 12 SAIR facilities had SPECT capabilities, and six had ultrasound.

As described in Chapter 3, shifts in the RFA have reduced the role of infrastructure purchase relative to other program goals. With the decrease in funding to $300,000 and the relaxation of the requirement to use SAIR funds to purchase new equipment, SAIR institutions funded in the fourth cohort of awards have been unlikely to use program funding to purchase or construct new equipment. Of the five funded SAIRs in Cohort 4, only the one planned to use the award for equipment purchase.

2. *The SAIR program contributed to the support for technical personnel to operate the small animal imaging facilities, with the relative contribution of SAIR and other funding sources varying by institution.*

All of the SAIR awardees currently participating in the program except for one described hiring technicians, although the percentage of the technical staff funded through the SAIR award itself varied substantially. Some SAIR institutions relied heavily or solely on SAIR funds and others supported technicians through institutional funds. The need for technical support varied by modality; interviewees reported that optical equipment was more or less "turn-key" but PET, CT, and SPECT equipment required dedicated staff to perform the experiments because of radioactivity considerations. Opinions on the need for technical support for MRI were mixed.

3. *It is too early to assess the sustainability of the infrastructure built through the SAIR program.*

Sufficient time has not yet passed to assess the sustainability of the infrastructure that has been built with SAIR funds. At the three former SAIR institutions where funding was not renewed (University of Arizona, Stanford, and the University of Pennsylvania before its SAIR renewal), many of the small animal imaging capabilities added through the SAIR appear to still exist. PIs reported that these capabilities are supported through user fees, institutional funding, and NCRR support for instrumentation purchase and upgrade. The University of Pennsylvania is notable for the formation of a School of Medicine-wide small animal imaging facility that houses imaging equipment and supports investigators from across the institution after the failure of its first renewal application; the re-funded SAIR now is one of the funding streams supporting this facility.

Several of the SAIR PIs whose awards were funded in the second round and competitively renewed in 2006 reported that the decrease in the allowable direct costs (to $300,000) has constrained their operations and poses concerns for the future. If the allowable maximum remains at Cohort 4 levels, it is reasonable to expect that the SAIR institutions funded in Cohort 3 may face similar problems if and when they are competitively renewed.

9.1.3. Facilitate use of resources (Program goal 2)

1. *SAIR awardees engaged in a variety of activities designed to expand the community of small animal imaging researchers at their institutions, the most significant of which were training and support for pilot projects and/or pilot data collection.*

The SAIR awardees employed a variety of strategies to build the community of small animal imagers and cancer researchers using small animal imaging. One primary strategy was for the SAIR to fund investigators for pilot projects or provide "*pro bono*" imaging support. All of the SAIR institutions but two had a program for pilot projects and/or *"pro bono"* imaging support; six of the SAIR institutions provide funding from the SAIR award itself. It was not feasible to consistently track the results of pilot project funding across the SAIR awards. Lists of awards funded based upon SAIR-supported pilot data were available for only seven of the institutions, and it was not clear that even those seven SAIR awardees' lists were complete.

Other strategies described by PIs to increase the use of small animal imaging included outreach through the Cancer Center (e.g., Grand Rounds) and retreats (six SAIR institutions); Internet sites (three SAIR institutions); and outreach by the PI to make direct contact with potential users or to invite potential users to SAIR group meetings or seminars (three SAIR institutions).

2. *There is clear evidence that the use of small animal imaging by cancer researchers at SAIR institutions has increased.*

The SAIR RFA required that awardees support a minimum of six (raised to eight in the 2006 RFA) base grants. Some SAIR PIs listed close to twenty awards in their initially funded applications that they anticipated would be supported, although the average number was approximately 11. Records maintained by the SAIR PIs of actual users indicate that the facilities have supported 421 distinct awards, of which 219 (52%) were NCI-funded; 117 (28%) funded by other NIH Institutes and Centers, and the remaining 20% by others, including DOE, NSF, DOD, state government, industry, foundations, and institutional funding. At two SAIRs two-thirds or more of reported users were NCI-supported, while at other SAIR institutions the percentage ranged from 36%-59%.

Although it was not feasible to identify which awards made use of SAIR resources in any given year (especially during the initial years of SAIR awards) comparing the number of awards supported with the number of awards listed in the initial applications indicated that most of the SAIR PIs reported at least twice as many awards making use of the facility as initially projected. Moreover, comparing the awards making use of the SAIR-supported facility with the base grants in the initial applications suggests that few SAIR PIs were able to predict with precision the awards that would make use of small animal imaging. Only at two SAIRs were more than half of the initially-listed awards identified as having made use of the SAIR.

While it was not feasible to conduct institution-level surveys to identify the extent to which small animal imaging is being used by investigators at SAIR institutions, two proxy measures of the breadth of SAIR influence were constructed: (1) the ratio of the

number of awards acknowledged on SAIR publications to the number of NCI-funded awards at the institution during the years the SAIR was operational and (2) concentration of acknowledgements of awards other than the SAIR on SAIR publications in a single investigator. Case Western, UC Davis, University of Pennsylvania, and Washington University scored relatively well on both measures of integration, while Duke, MGH, UCLA, and the University of Michigan scored less well.

3. *Integration at the Cancer Center and into local ICMICs has been strong; SAIR use by SPORE, CCNE, Mouse Models, or NTROI awards has varied across institutions.*

Interviews with Cancer Center basic science directors as well as statements in application materials indicated that nine of the 12 SAIR institutions had contributed to their Cancer Centers' subsequent decision to include small animal imaging as one of their designated Core facilities by increasing the user base for small animal imaging technology. Eight SAIR PIs reported that at least one project funded through the CCSG made use of the SAIR-supported facility. The seven ICMIC awardees at SAIR institutions made use of the SAIR facility (though usage varied). Four SAIR institutions have had either an NTROI or CCNE award, and there is some integration of the SAIR facility with those awards. Of the seven SAIR institutions possessing one or more SPORE awards, five SAIR institutions had publications that acknowledged SPORE funding. While four SAIR PIs reported that Mouse Models sites at their institutions made use of the facility, acknowledgements of Mouse Models awards were relatively rare on SAIR publications.

4. *At several institutions, investigators funded by non-NCI ICs or other organizations made active use of the SAIR-supported facility.*

Of the 421 awards reported as making use of the SAIR-supported small animal imaging facility, 202 (48%) were not NCI-administered. Of the non-NCI NIH Institutes (117 awards), the largest number of awards were administered by NHLBI, NIBIB, NINDS, and NIDDK. Other sources of funding included associations/foundations/scientific societies (26 awards); other U.S. government agencies (including 10 DOD and nine DOE awards); institutional funding; state government; and industry sources. At most of the institutions between 20%-40% of awards using the SAIR-supported facility were administered by other NIH ICs. At four SAIR institutions approximately 90% or more of all awards using the SAIR facility were NIH-funded, while at the other eight SAIR institutions 18-33% of awards were non-NIH. Approximately 40% of all of the NIH awards acknowledged on SAIR publications were funded by ICs other than NCI.

5. *A total of 951 publications either acknowledged SAIR support or were identified in progress reports as SAIR-associated.*

Although the SAIR program does not have associated with it a desired outcome such as "high-quality research" that is directly measurable using publications-based evidence, publications were used as a measure of the use of the SAIR facility by investigators – recognizing that the ability of the awardees to identify "SAIR" publications varied across institutions. Nine hundred and fifty-one SAIR publications were identified (including four publications associated with two SAIR awards each). Three SAIR awardees each

supported 15 or more publications per year, and all other SAIR awardees except for one produced between eight and 11 publications per year.

The steady-state ratio of dollars per publication in a given year was approximately $50,000, disregarding the first year of SAIR program operations. To date, there is not an NCI-wide (or NIH-wide) benchmark for publications associated with infrastructure (whether NCRR S10 awards, the NCI Cancer Center P30 awards, or other NCI U24 programs) against which this result can be compared.

SAIR papers were published in 246 distinct journals spanning a range of fields. Thirty-two SAIR publications (3%) were in journals with impact factors of twenty or higher, including four papers in *Science*, four in *Nature*, and one in the *New England Journal of Medicine*.

9.1.4. Technology development (Program goal 3)

1. *SAIR awards supported a range of research and technology development activities spanning hardware construction, software/image registration activities, and improved imaging methods and tools.*

The evaluation identified 132 distinct SAIR-supported technology development projects, including hardware (32 projects), software/image registration (47 projects), and imaging agents/markers/reporters (53 projects). Research projects occurred mostly in MRI/MRS (33%), multimodality systems (21%) and optical systems (19%). The individual SAIR awards varied in the modalities upon which they concentrated technology development efforts. The size, level of effort, and relative importance of each individual research project is could be identified for only a few research projects, so they may not be comparable.

2. *Key discoveries by SAIR-supported investigators occurred in each of the three research and technology development categories and several SAIR-supported hardware projects have been commercialized.*

SAIR PIs were asked during interviews to identify the most significant new technology discoveries made using SAIR funds. Forty-six key discoveries were described, of which more than half (28) fell into the category of "imaging agents, reporters, or methods", and 12 involved new small animal imaging equipment. The research underlying 22 of the 28 key discoveries in imaging agents/reporters/methods were funded through non-SAIR base grants, while funding for the other six was traced to the SAIR award. New equipment development covered most of the primary imaging modalities, including optical, PET, CT, and SPECT.

SAIR-developed equipment was identified as having been commercialized for two modalities: PET (two systems: one developed by University of Pennsylvania, commercialized by Philips and one developed by UCLA, commercialized by Concorde); and optical (developed by MGH, commercialized by Siemens, Kodak, VisEn Medical, and Olympus). Four SAIR awardees described collaborations with small businesses funded through the SBIR programs at NIH and DOE.

3. *SAIR is one of several funding sources for small animal imaging technology research and technology development projects at SAIR institutions, and at most institutions is not the primary source of funding.*

The SAIR program was not the sole source of support for any category of research and technology development. The NCI-funded translational research programs already demonstrated to have overlapped with the SAIR program (e.g., ICMIC, CCNE, NTROI) provided funding for technology development, particularly in the area of imaging agents, methods, and reporters. Other programs, particularly NIBIB and NCRR P41s; a NIBIB small animal imaging RFA; and NCI/CIP program announcements supported research targeting equipment development. In total, between 2001 and 2008 more than $30 million in R01/R21 funding for small animal imaging hardware- or software-related awards to principal investigators at SAIR institutions was identified by the evaluation, as well as three hardware-oriented P41 awards. While a comprehensive search for small animal imaging related hardware and software research at NIH was not feasible, a comparison of NIBIB and NCI imaging-related RFA funding at SAIR and non-SAIR institutions suggests there may be substantial funding for small animal imaging hardware and software-related university research at non-SAIR institutions as well.

More than 90% of SAIR publications classified as "technology development" at the nine SAIR institutions whose investigators were most diligent about acknowledging the SAIR award acknowledged awards in addition to the SAIR. Only at Johns Hopkins (23%) and the University of Arizona (46%) did a substantial percentage of "technology development" publications acknowledge only the SAIR award.

9.1.5 Training (Program goal 4)

1. *SAIR funding supported a broad range of training activities at different institutions, based upon institutional needs and circumstances.*

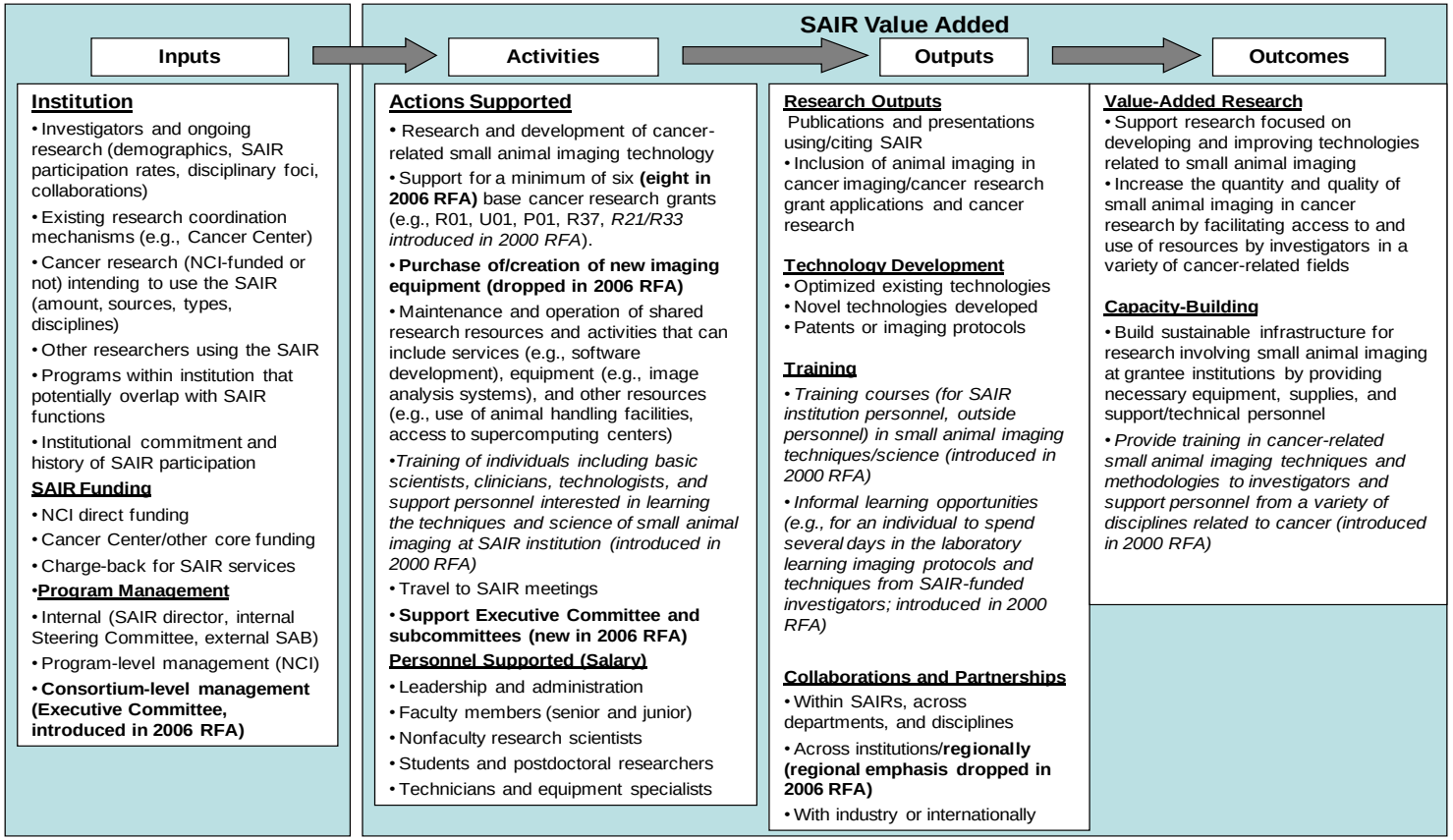
The SAIR awardees conducted a wide variety of training activities. Ten SAIR awardees reported sponsoring seminars or speaker series, and eight of the 12 SAIR institutions conducted multi-day workshops for training in small animal imaging techniques. All of the SAIR awardees provided some form of training to undergraduates, graduate students, or postdoctoral fellows, though approaches differed. Five SAIR institutions identified training to visiting faculty (and one provided training to visiting students) as an activity undertaken by the SAIR, including support for visiting professorships at one SAIR. Five of the SAIR awardees specifically highlighted training for technicians/technologists, including both animal care and handling as well technician participation in graduate student courses. Three SAIR awardees described support for junior faculty. Other training-related activities included development of textbooks and online training materials for use outside the SAIR.

Outcomes included:

- At least 1000 individuals have participated in a SAIR-supported multi-day workshop.
- Two SAIR awardees described initiating new courses in small animal imaging.
- Five SAIR-supported postdoctoral fellows have received faculty positions at other institutions and three have received instructorships at their SAIR institutions.

- Four SAIR-supported postdoctoral fellows have received non-faculty research staff positions.
- One SAIR award has provided mid-career transition funding for two faculty members, one of whom has subsequently received NIH funding.
- Four SAIR awardees described using their visiting fellowship programs to help other institutions create small animal imaging programs.

Appendix A: SAIR Logic Model



Small Animal Imaging Resource Program Final Logic Model

The SAIR logic model describes program inputs, program activities, program outputs, and outcomes, as well as external factors impinging upon the program.

Program inputs are:

- Institution
    - Investigators and ongoing research (demographics, SAIR participation rates, disciplinary foci, collaborations)
    - Existing research coordination mechanisms (e.g., Cancer Center)
    - Cancer research (NCI-funded or not) intending to use the SAIR (amount, sources, types, disciplines)
    - Other researchers using the SAIR
    - Programs within institution that potentially overlap with SAIR functions
    - Institutional commitment and history of SAIR participation
- SAIR Funding
    - NCI direct funding
    - Cancer Center/other core funding
    - Charge-back for SAIR services
- Program Management
    - Internal (SAIR director, internal Steering Committee, external SAB)
    - Program-level management (NCI)
    - Consortium-level management (Executive Committee, introduced in 2006 RFA)

Program activities are:

- Actions Supported
    - Research and development of cancer-related small animal imaging technology
    - Support for a minimum of six (eight in 2006 RFA) base cancer research grants (e.g., R01, U01, P01, R37, R21/R33 introduced in 2000 RFA).
    - Purchase of/creation of new imaging equipment (dropped in 2006 RFA)
    - Maintenance and operation of shared research resources and activities that can include services (e.g., software development), equipment (e.g., image analysis systems), and other resources (e.g., use of animal handling facilities, access to supercomputing centers)
    - Training of individuals including basic scientists, clinicians, technologists, and support personnel interested in learning the techniques and science of small animal imaging at SAIR institution (introduced in 2000 RFA)
    - Travel to SAIR meetings
    - Support Executive Committee and subcommittees (new in 2006 RFA)
- Personnel Supported (Salary)
    - Leadership and administration
    - Faculty members (senior and junior)
    - Nonfaculty research scientists
    - Students and postdoctoral researchers
    - Technicians and equipment specialists

Program outputs are:

- Publications and presentations using/citing SAIR
    - Inclusion of animal imaging in cancer imaging/cancer research grant applications and cancer research
- Technology Development
    - Optimized existing technologies
    - Novel technologies developed
    - Patents or imaging protocols
- Training
    - Training courses (for SAIR institution personnel, outside personnel) in small animal imaging techniques/science (introduced in 2000 RFA)
    - Informal learning opportunities (e.g., for an individual to spend several days in the laboratory learning imaging protocols and techniques from SAIR-funded investigators; introduced in 2000 RFA)
- Collaborations and Partnerships
    - Within SAIRs, across departments, and disciplines
    - Across institutions/regionally (regional emphasis dropped in 2006 RFA)
    - With industry or internationally

Program outcomes are:

- Value-Added Research
    - Support research focused on developing and improving technologies related to small animal imaging
    - Increase the quantity and quality of small animal imaging in cancer research by facilitating access to and use of resources by investigators in a variety of cancer-related fields
- Capacity-Building
    - Build sustainable infrastructure for research involving small animal imaging at grantee institutions by providing necessary equipment, supplies, and support/technical personnel
    - Provide training in cancer-related small animal imaging techniques and methodologies to investigators and support personnel from a variety of disciplines related to cancer (introduced in 2000 RFA)

External factors include:

- Advances in animal models and cancer imaging technologies
- Changes in biomedical research funding
- NCI/NIH priorities, mission and resources

Appendix B: Thumbnail Sketches of the SAIR Awards

Title	Northeastern Ohio Animal Imaging Resource Center (NOAIRC)
PI Name	Jeffery L. Duerk
PI Institution	Case Western Reserve University
Is ICMIC Institution	Pre-ICMIC
Grant Number	U24CA110943
Start Year/End Year	2004/2009
Structure	Part of interdisciplinary molecular imaging center/program in distinct center or institute
Award Abstract (CRISP)	We propose to form the Northeastern Ohio Animal Imaging Resource Center (NOAIRC) to provide the many regional cancer researchers with state-of-the-art small animal, molecular and cellular imaging facilities and expertise. Systems will include a combined micro- x-ray computed tomography/SPECT system, a clinical SPECT system with pin-hole collimators, a high resolution micro-PET system, and 7T and g.4T small animal MR imaging and spectroscopy systems. All are already on-site or ordered from recent grant awards and institutional sources. With an SAIRP award, we will acquire a bioluminescence/fluorescence imaging system to facilitate reporter gene methods and new opportunities in novel agents (e.g., quantum dots). We will also create small animal optical coherence tomography with color Doppler and microscopic OCT to promote in vivo spectroscopic methods and high spatial and temporal analysis of structure and function (e.g., perfusion). Interdisciplinary backing for this project is unprecedented with financial and other commitments from three schools of Case Western Reserve University (Medicine, Engineering, Arts & Sciences), the University Hospitals of Cleveland, the Case Comprehensive Cancer Center, and the State of Ohio. In addition to core resources via nuclear imaging, MR imaging and spectroscopy, bioluminescence/fluorescence, and OCT, the NOAIRC will also provide an integrated environment with core facilities in quantitative image analysis and visualization, animal welfare/experiment preparation and novel imaging agents like functionalized liposomes or CEST agents. This latter core integrates with our radionuclide imaging capabilities, our ongoing biomolecular and nanoscale engineering for targeted therapeutics initiative, ongoing research in reporter genes, and a P20 In-vivo and molecular Imaging Center planning grant to add strategic strength in molecular imaging. All of these will be within a single facility to promote cross-collaboration and interdisciplinary research, This proposal brings together researchers in imaging with the many regional scientists who are studying cancer biology via small animal models and rapidly gaining an appreciation of the power of in vivo imaging. We aim to advance small animal imaging technology by developing new image acquisition and analysis methods, new methods in reporter genes and functionalized agents, and pharmacokinetic modeling. We will apply developments to experiments in cancer biology and therapy. Animal welfare/preparation research will focus on analysis of physiologic effects of anesthesia and developing new formulations that maintain the physiology to be measured, while providing state-of-the-art methods for blood sampling and monitoring. The NOAIRC will include a strong educational focus to create a long-range impact. It will invigorate strong Ph.D. programs in imaging already at Case. It will strengthen educational programs for basic and clinical scientists in cancer via integration with existing T32 and K12 grants and promote new horizons via K25 proposals. The result will be clinicians, scientists, and engineers trained for the next generation of conventional and molecular imaging techniques.

Key Discoveries (from interviews)	• Ultrahigh-speed optical coherence tomography • Paramagnetic chemical exchange saturation transfer (PARACEST) MRI contrast agents for protease detection
Total Publications	30

Title	Duke Molecular Imaging Center
PI Name	G. Allan Johnson, PhD
PI Institution	Duke University
Is ICMIC Institution	Pre-ICMIC
Grant Number	U24CA092656
Start Year/End Year	2001/2012
Structure	Under aegis of NCRR P41-funded Center for In Vivo Microscopy
Award Abstract (CRISP)	We propose the continuation and expansion of the Duke Molecular Imaging Center (DUMIC) as a central element of the Duke Center for In Vivo Microscopy's (CIVM) effort to expand the utility and access of small animal imaging methods for the widest range of cancer researchers. More specifically, we will do the following: 1. We will integrate all of the Center's activities into the broader imaging initiatives of the University and Medical Center to increase service access for cancer researchers to our existing four MRI, microPET, micro-DSA, micro-CT, micro-ultrasound, and Xenogen optical imaging systems. We will develop high-throughput protocols and deploy a network infrastructure to efficiently design, execute and analyze these small animal imaging protocols. 2. We will extend the capability of our 7.0 T MRI system through a novel slice-selective radial acquisition method to provide higher spatial and contrast resolution along with greater immunity to motion. 3. We will extend the capability of our micro-DSA system (under complementary support from other sources) to provide digital subtraction angiography at spatial resolution down to 20 microns and temporal resolution to 10 ms. 4. We will develop the Molecular Imaging Workbench, a novel, flexible multimodality imaging system that combines micro-CT, digital tomosynthesis for 4D perfusion imaging, and near infrared fluorescent imaging. The system will be constructed in a modular fashion allowing ready extension to other optical imaging methods (GFP, bioluminescence, and micro-SPECT). 5. We will expand our educational program to educate the existing generation of cancer researchers in the potential for small animal imaging. We will reach out across the spectrum.
Key Discoveries (from interviews)	• Micro-CT with respiratory and cardiac gating • High-resolution vascular imaging of the rat spine using liposomal blood pool MR agent • Localized, image-guided blood brain barrier disruption
Total Publications	56

Title	Small Animal Imaging Resource
PI Name	Martin G. Pomper
PI Institution	Johns Hopkins University
Is ICMIC Institution	Yes
Grant Number	U24CA092871
Start Year/End Year	2001/2012
Structure	Service center, under aegis of Department of Radiology
Award Abstract (CRISP)	Small animal imaging is increasingly recognized as an important facet of preclinical and translational cancer research. Perhaps most significant among the clear advantages of imaging experimental animals is that physiology, pathology and novel phenotypes can be understood in the most relevant milieu - in an intact, living system. Less obvious is the fact that often the most significant leap forward that an already important biological study takes is when its results can be extended to the in vivo case - a necessary and often sufficient precondition for success in the clinic. The Johns Hopkins Small Animal Imaging Resource Program (SAIRP) labors to provide that translational step, generating the confidence necessary to move new cancer therapies to patients. During the next funding period we will continue to complement the already strong magnetic resonance imaging program housed within the In Vivo Cellular and Molecular Imaging Center (ICMIC) with the development of new radiopharmaceutical and optical imaging probes and techniques. We will also expand our mission in several important ways, namely by broadening our educational program to include neighboring institutions, by incorporating elements of industry - focusing on small companies interested in molecular imaging research - and we will offer our expertise in synthetic chemistry and probe development to the SAIRP consortium members who may benefit from it. We will do that while supporting 15 base grants that derive from 3 institutions, but primarily emanate from our own Comprehensive Cancer Center. Although diverse, the base grants are loosely grouped into 3 themes: targets (reflecting the proliferation of high-throughput target identification methods), cells (due to the many and increasing gene and cell therapy protocols in the Cancer Center) and organs (taking advantage of the SPORE programs and other organ-based cancer research initiatives at Johns Hopkins). We will also continue to serve members of the Cancer Center and elsewhere in less formal ways, providing advice, education, training and pilot data that will further their own cancer research and concurrently enable the SAIRP to become a self-sustaining entity. Our ultimate goal is to move small animal imaging science forward - to the point where the incorporation of such imaging techniques becomes second nature in the daily practice of cancer researchers.
Key Discoveries (from interviews)	• Imaging bacteriolytic cancer therapy • Bortezomib-induced enzyme-targeted radiation therapy in herpesvirus-associated tumors • ABCG2/BCRP expression modulates D-Luciferin based bioluminescence imaging • Radiolabeled anti-claudin 4 and anti-prostate stem cell antigen imaging in experimental models of pancreatic cancer
Total Publications	35

Title	Small Animal Imaging Resource
PI Name	Ralph Weissleder, MD, PhD
PI Institution	Massachusetts General Hospital
Is ICMIC Institution	Yes
Grant Number	U24CA092782
Start Year/End Year	2001/2012
Structure	Part of interdisciplinary molecular imaging center/program (Center for Molecular Imaging Research)
Award Abstract (CRISP)	The overall goal of this U24 application is to continue supporting a team of investigators to develop new and provide established, state-of-the-art high resolution mouse imaging techniques to local cancer investigators. The Harvard Small Animal Imaging Resource (SAIR) has a proven track record for innovation in molecular imaging and clinical translation, has served over 70 regional cancer investigators and currently performs imaging studies for over 40 cancer related base grants. The Program is affiliated with two NCI designated Cancer Centers (the Dana Farber Harvard Cancer Center (DFHCC) and the MIT Center for Cancer Research) and several Mouse Model of Human Cancer Consortia (MMHCC). The specific goals of the SAIR are to: 1) increase the availability and expand types of high resolution mouse imaging systems, 2) develop new techniques and methods to image cellular and molecular information of specific cancers and organs, 3) assist with image acquisition, 4) maintain and ensure the proper use of imaging equipment, 5) assist in image analysis, processing, quantitation, interpretation and image fusion and 6) provide training to investigators and collaborators with regard to a) small animal handling and monitoring, b) small animal imaging and c) the specifics of utilizing the array of imaging equipment best to address the specific questions at hand. Ancillary cores of this Program include a Pathology, Chemistry, Cell and Bioinformatics Cores. Multidisciplinary training will involve participation in hands-on projects, seminars and didactic lecture series. The overall focus of this proposal is to provide a shared resource and tools, which allow cancer researchers to incorporate state-of-the-art imaging technologies into their individual research studies. The SAIR has become a dynamic and diverse resource wherein exchange of techniques and ideas occurs rapidly and fosters interdisciplinary collaborations in cancer research.
Key Discoveries (from interviews)	• Optical tomography devices for mice • Fluorescent imaging technologies
Total Publications	153

Title	Memorial Sloan Kettering Small Animal Imaging Research
PI Name	Jason Koutcher, MD, PhD
PI Institution	Sloan-Kettering Institute for Cancer Research
Is ICMIC Institution	Yes
Grant Number	R24CA083084
Start Year/End Year	1999/2009
Structure	United small imaging capabilities across multiple departments
Award Abstract (CRISP)	Research at Memorial Sloan Kettering Cancer Center is focused on cancer diagnosis and enhancing response to treatment. Because tumors are heterogeneous, both between individuals and within a single tumor, non-invasive imaging studies are necessary to provide information about variations in response. The main technologies we will focus on include nuclear magnetic resonance (NMR), positron emission tomography (PET), and optical imaging, although other instruments are part of the application. The 3 imaging techniques chosen were based on the fact that they will provide complementary information. NMR imaging provides high spatial resolution but modest functional data. PET and NMR spectroscopy have poorer spatial resolution but provide valuable chemical/metabolic information. Optical imaging can provide very sensitive imaging tools to detect very small numbers of cells and thus these modalities have different strengths. We focus on enhancing the ancillary/support services to maximize information available from the different studies. Image analysis/correlation is important since in most studies, multiple imaging studies are done and it is critical to spatially align different or longitudinal studies. The Synthetic Chemistry and Vector Cores are critical for developing novel tools for exploring signaling pathways, and molecular events related to oncogenesis, treatment, cell death and host toxicity. Enhancement of imaging techniques to maintain state of the art methodologies, improving current techniques, and converting imaging into a more quantitative science is vital. A wide range of oncologic issues will be studied to exploit these tools in developing newer and better targeted drugs, to minimize host toxicity, to develop standards of response criteria for cytostatic drugs and detect responses/failures earlier in the course of treatment. The range of projects studied include predicting tumor response to treatment, dosimetry for radioimmunotherapy, pharmacology, gene therapy and imaging, tumor metabolism, and evaluating responses to novel cytostatic agents. Research at MSKCC is translational and the goals of many of these projects are to be moved to the clinic in the shortest time feasible. Leadership will come from the imaging scientists (Drs. Koutcher, Blasberg and Larson) and also from the molecular pharmacology group who will meet monthly along with a Technology Committee, to decide which problems are important and appropriate to be addressed by imaging technology.
Key Discoveries (from interviews)	• Multimodality registration without a dedicated multimodality scanner • Animal-specific positioning molds for registration of repeat imaging studies • In vivo tumor lactate relaxation measurements by selective multiple-quantum-coherence
Total Publications	80

Title	Stanford University's Small Animal Imaging Resource
PI Name	Christopher H. Contag, PhD
PI Institution	Stanford University
Is ICMIC Institution	Yes
Grant Number	R24CA92862
Start Year/End Year	2001/2006
Structure	Part of interdisciplinary molecular imaging center/program in distinct center or institute
Award Abstract (CRISP)	In vivo imaging of neoplastic disease at early stages or as residual disease after therapy is difficult due to relatively low cell numbers, weak signals and previously insensitive detection methods. At late stages, functional changes are relevant to treatment but have been difficult to discern in vivo. In an interdisciplinary approach, the here assembled consortium of investigators will address these obstacles through the use of novel optical imaging strategies, and improvements to the more conventional imaging modalities of MRI, CT and SPECT. These will permit us to address questions pertaining to the genetics, physiology and therapy of neoplastic disease by monitoring both structural and functional changes in small animal models of cancer noninvasively and in real-time. The optical imaging system, developed by investigators in this core resource program, uses cells labeled with the genetic reporters, such as luciferase, which encode photoproteins that emit light which is detectable by highly-sensitive CCD-cameras from outside the animal's body. This enables us to observe as few as a thousand cells and perform in viva functional analyses. As such, examination of the cells' response to drugs and physiological stimuli can be assessed. State of the art MR imaging will be employed in conjunction with the optical methods, and in parallel, to complement and strengthen the analyses. To enhance detection sensitivity and resolution, engineering faculty will develop new adaptations to MRI, including a novel prepolarized system, to increase versatility. New micro-CT and micro-SPECT systems will be deployed for structural analyses and molecular detection, respectively, in animal models. We will modify reporter genes and contrast agents, assess gene expression in transgenic animals, determine the role of specific genes in the development and control of cancer, optimize optical detectors and apply state of the art MRI methods to small animal models. Furthermore, this multiple modality approach enables us to evaluate the efficacy of combination drug therapies and novel immune cell therapies in treating various types of tumor cells at different disease stages. The specific aims of this application are aimed at increasing the capabilities of investigators in the molecular and cellular in vivo study of cancer, develop improved imaging technologies that push the limits of current bioimaging methods, introduce young investigators to state of the art imaging, and accelerate the in vivo quantitative evaluation of novel antineoplastic therapeutics. These goals will be met by generating a shared imaging research resource at Stanford University with the ability of spatiotemporal analyses of both structure and function in neoplastic disease models.
Key Discoveries (from interviews)	• Worked closely with Gamma Medica to develop small animal SPECT • Monitoring protein-protein interactions using split synthetic renilla luciferase protein-fragment-assisted complementation • Use of quantum dots as in vivo reagents
Total Publications	63

Title	UC-Davis Mouse Cancer Imaging Resource
PI Name	Simon R. Cherry, PhD
PI Institution	University of California-Davis
Is ICMIC Institution	No
Grant Number	U24CA110804
Start Year/End Year	2004/2009
Structure	Part of interdisciplinary molecular imaging center/program in distinct center or institute
Award Abstract (CRISP)	We propose to establish the UC Davis Mouse Cancer Imaging Program (MCIP), in which we integrate our expertise and resources in small animal imaging and mouse biology, and work closely with our leading cancer researchers to create new opportunities and directions for studying the basic biology, treatment and prevention of cancer. The program will be housed in our new small animal imaging center with equipment and expertise for PET, optical imaging and ultrasound, with MRI capability being provided by the immediately adjacent NMR facility. We propose to add a microCT scanner to the center. Mouse pathology will also form an integral part of the MCIP and will be incorporated through the Mouse Biology Program. The MCIP will initially support seven diverse base grants. One unique feature of the MCIP is that it will establish a satellite site at UMDNJ-Robert Wood Johnson Medical School as part of a demonstration project for expanding the reach of major imaging programs. The MCIP will also support three technology development projects focused on dynamic CT imaging in the mouse, a simplified PET scanner for the biology lab, and the development of methodology for quantitative, multimodality phantoms. In addition, our extensive funding base in small animal technology research will be leveraged for the MCIP. The MCIP is enhanced by a range of important ancillary resources, including a biomedical cyclotron and radiochemistry program, expertise in mouse handling and physiologic monitoring, core laboratories and expertise for creating genetically-engineered mouse models, and support for networking, data handling, databases, and biostatistics. We also propose a training program, with a practical imaging course, internships, and web-based material. Finally, the MCIP describes a clear structure for governance and for providing imaging-related services to cancer researchers at UC Davis and beyond.
Key Discoveries (from interviews)	• Low cost, high sensitivity PET detectors • Stimulus-responsive contrast agent for ultrasound molecular imaging
Total Publications	41

Title	UCLA Imaging Resource for Mouse Cancer Models
PI Name	Michael E. Phelps, PhD
PI Institution	UCLA
Is ICMIC Institution	Yes
Grant Number	U24CA092865
Start Year/End Year	2001/2012
Structure	Part of interdisciplinary molecular imaging center/program in distinct center or institute
Award Abstract (CRISP)	UCLA has a mature small animal imaging program based on micro-positron emission tomography, x-ray micro computed tomography, in-vivo bioluminescence and digital whole body autoradiography imaging. Central to this program, is our small animal imaging resource (SAIR), which provides service and support through a state of the art facility to more than 24 independent Principal Investigators funded through the NIH and other agencies. Most of the research projects of these investigators are focused in cancer diagnosis and therapy. In addition to this service component, the roles of the SAIR within the UCLA and the US environments are to: (a) educate students, post-doctoral scholars, physicians and other biology researchers from within and outside UCLA in the tools, technologies and applications of imaging, and (b) foster collaborations and develop new technologies and methodologies that will improve the quantitative capabilities of non-invasive imaging. These goals will hopefully lead to better understanding of human disease and might lead to better methods for diagnosis and treatment of cancer. As part of this SAIR proposal, besides the research support and education, two developmental projects are included, that should improve the quality and quantitative accuracy of the acquired data, while they reduce the impact from radiation exposure on the studied subjects. The first project will seek to standardize the animal handling and care part of the imaging protocol prior to, during and after the procedure, such that the animal's response is as uniform as possible. The second project seeks to estimate at first, secondly optimize and thirdly track the radiation exposure to the animal subjects throughout sequences of multiple imaging experiments that can last several months. Both these projects will greatly benefit not only the research experiments carried through the UCLA SAIR, but all preclinical research in the US.
Key Discoveries (from interviews)	• Method of image registration for small animal, multi-modality imaging • Optical bioluminescence and PET imaging of a novel fusion reporter gene in tumor xenografts of living mice
Total Publications	68
Notes	Dr. Gambhir departed as the PI of the UCLA SAIR in 2004 to lead the Molecular Imaging Program at Stanford

Title	Southwest Small Animal Imaging Resource
PI Name	Robert J. Gillies
PI Institution	University of Arizona
Is ICMIC Institution	No
Grant Number	R24CA083148
Start Year/End Year	1999/2003
Total Amount Received	Round 1- $2.9M
Structure	Uniting small animal imaging capabilities across multiple departments
Award Abstract (CRISP)	The University of Arizona Health Sciences Center and the Arizona Comprehensive Cancer Center propose to establish the Southwest Animal Imaging Resource (SWAIR). The purpose of the SWAIR is to provide the cancer research community access to state-of-the-art in vivo imaging based on magnetic resonance (MR), single photon emission computed tomography (SPECT) and optical coherence tomography (OCT). The integrated program will also provide common access to essential cores for veterinary anesthesia and computing/electrical engineering. The major purpose of the SWAIR will be to provide state-of-the-art imaging access to the base grants. Eight cancer-related research programs form the original cohort of base grants. These represent diverse aspects of cancer research, from basic cellular and molecular mechanisms, to diagnosis, to monitoring and improving therapeutic response. The program will support continuing research to improve the application of the imaging modalities to cancer biology in vivo. MR research will continue to improve methods for spectral imaging (MRSI), high resolution morphometry, motion-insensitive diffusion imaging, pH imaging, and analyses of Gadolinium-enhanced dynamic contrast. These techniques will be applied and developed on newly upgraded 4.7 and 9.4 Tesla instruments. SPECT research will involve construction of a state-of-the-art high-resolution FASTSPECT system, which will be dedicated to animal imaging. Research will focus on improved detectors, readout electronics, and system characterization. The latter is essential for optimizing the spatial resolution of the SPECT system. In the OCT program, a dedicated instrument will be constructed and applied non-invasively to image skin lesions in experimental animals. Research will continue to improve the applicability of this relatively new technology to the diagnosis and serial monitoring of epidermal and epithelial lesions in vivo. Research will also be conducted in the veterinary anesthesia core to continue to improve anesthesia formulations that do not interfere with the physiology being measured. This is an important issue since these modern imaging techniques monitor functional properties of tumors, which can be perturbed in the anesthetized state. The electrical/computing core will help with the construction and maintenance of the imaging instruments. It will also provide support the general computing resources of the entire program.
Key Discoveries (from interviews)	• Laser induced fluorescent detection by Optical Coherence Tomography • Early response of prostate carcinoma xenografts to docetaxel chemotherapy monitored with diffusion MRI
Total Publications	53

Title	Michigan Small Animal Imaging Resource (MSAIR)
PI Name	Brian D. Ross, PhD, MS
PI Institution	University of Michigan
Is ICMIC Institution	Yes
Grant Number	U24CA083099
Start Year/End Year	1999/2009
Structure	Under aegis of Comprehensive Cancer Center
Award Abstract (CRISP)	The establishment of the Michigan Small Animal Imaging Resource (MSAIR) four years ago at the University of Michigan has proved extremely successful. During this time, the MSAIR facility has doubled in overall space and is scheduled to double in size again with a concurrent move to the new Biomedical Science Research Building which will be the focal point of the University of Michigan Medical School. This is part of an expanding Life Sciences Initiative within Michigan which emphasizes collaborative, intellectual innovation and multidisciplinary research. This facility will also house a state-of-the-art vivarium that has been planned to be integrated together with the MSAIR. Furthermore, the number and types of imaging modalities available for users has dramatically increased during the initial funding of the MSAIR. This includes the addition of a horizontal bore 9.4 tesla MRI system with microgradient coils, addition of two in vivo bioluminescent imaging systems, addition of two microPET systems available for imaging of rodents and monkeys, addition of a fluorescent imaging system and finally, inclusion of a MicroCT system. The number of cancer investigators who have utilized the MSAIR during the initial funding period has also seen remarkable growth (5-fold), thus making an important impact in cancer research. The objectives of this current proposal are to: 1) Acquire a combined SPECT/CT device capable of scanning both mice and rats. 2) Recruit a radiochemist to the MSAIR for synthesis of custom PET/SPECT probes. The addition of a radiochemist dedicated to assisting MSAIR users with labeled probes for both PET and SPECT will fulfill a need expressed by many investigators. 3) Provide Core services in molecular biology for the production of custom recombinant protein probes and recombinant cell lines. 4) Initiate a training laboratory and lecture workshop for training investigators in the use of imaging technologies for cancer research. The overall focus of this proposal is to provide a shared resource and the tools which allow cancer researchers to incorporate state-of-the-art imaging technologies into their individual research interests. Moreover, the MSAIR has become a central, diverse and dynamic resource facility wherein exchange of techniques and ideas can occur, which fosters productive interdisciplinary collaborations in cancer research.
Key Discoveries (from interviews)	• Unique molecular reporters for c-MET • Molecular imaging of Akt kinase activity • Noninvasive imaging of apoptosis and its application in cancer therapeutics
Total Publications	75

Title	Pennsylvania Small Animal Imaging Resource (Penn-SAIR)
PI Name	Jerry D. Glickson, PhD
PI Institution	University of Pennsylvania
Is ICMIC Institution	Pre-ICMIC
Grant Number	U24CA083105
Start Year/End Year	1999/2005 and 2007/2012
Structure	Initial iteration: Uniting small animal imaging capabilities across multiple departments Renewal iteration: Under Department of Radiology/School of Medicine
Award Abstract (CRISP). *Note: this appendix leaves out the list of eight base projects mentioned in the abstract.*	Small Animal Imaging Research program is proposed at U. Penn. (Penn-SAIR) supporting cancer research at Penn, the Wistar Institute, the Children's Hospital of Philadelphia (CHOP), the Lankenau Institute for Medical Research and Thomas Jefferson University; it will be available to other institutions within the Philadelphia region and world-wide. The program builds on a fully self-supported existing Small Animal Research Facility (SAIF). The SAIF, which came into existence with the termination of funding for the SAIRP and Pre-ICMIC programs, serves the needs of Penn as well as the cooperating institutions. It is supported by the Department of Radiology and the Comprehensive Cancer Center, of which it is a core. A complete administrative structure including an Oversight Committee, a Steering Committee, User Committee and an Animal Oversight Committee is already functioning. A Scientific Oversight Committee and Internal and External Advisory Boards would be added to supervise the base projects and imaging technology programs of the proposed SAIR....The SAIR will support core facilities for NMR (MRI, MRS, and perfused cells), Nuclear Medicine (mPET, mSPECT, mCT), Optical Imaging, Bioluminescence, and Ultrasound with ancillary facilities for Radiochemistry, Chemistry, Molecular Biology, Image Analysis and Animal Tumor Models. Imaging technology developmental programs are proposed in NMR (DCE MRI, lactate/choline imaging, hyperpolarized 13C probes), PET(combined ?PET/MR/Optical imager), Optical Imaging (tomographic NIR imaging of tumor hypoxia by phosphorescence lifetime measurement), Radiochemistry (development of [18F] ethanolamine as a phospholipid metabolism probe), Chemistry (lipoprotein based iron oxide delivery system, GLUT1 targeted Gd-chelates, NIR molecular beacons for detecting specific phospholipases), and Molecular Biology (peptide nucleic acid based molecular beacons targeting the BRAF V600D,E mutation). A training program for physicians, graduate students, postdoctoral fellows and technicians is proposed.
Key Discoveries (from interviews)	• A-PET: a small animal PET camera • Handheld optical scanner for breast cancer detection
Total Publications	159
Notes	University of Pennsylvania was a Cohort 1 SAIR (funding received 1999-2003; no cost extension to 2005). Its Cohort 3 renewal application was not approved for funding, while its Cohort 4 application was funded in 2007

Title	Washington University Small Animal Imaging Resource (WUSAIR)
PI Name	Joseph J.H. Ackerman
PI Institution	Washington University
Is ICMIC Institution	Yes
Grant Number	U24CA083060
Start Year/End Year	1999/2009
Structure	Service Center, under aegis of Department of Radiology
Award Abstract (CRISP)	The Washington University Small Animal Imaging Resource (WUSAIR), one of the five original Small Animal Imaging Resource Program (SAIRP) centers funded in 1999, provides state-of-the-art facilities and infrastructure for MRI, PET, CT and optical imaging of mice, rats and other small laboratory animals. Located in the heart of the Washington University Medical Center, WUSAIR combines instrumental and intellectual capabilities found at few other institutions. WUSAIR serves a broad community of cancer scientists, non-expert in MRI, CT, PET or optical technology, who have a pressing need for quantitative image analysis of small laboratory animal model systems. A particular focus is on mouse and rat models of cancer. WUSAIR also provides research and development at the frontier of imaging technology in an effort to make the most powerful new imaging strategies available to its community of users. The ancillary services and capabilities within WUSAIR include physics and engineering support for the development and design of new hardware and imaging methods; informatics support for local and remote data access, analysis, visualization and archival; new contrast agent development; biostatistics consultation for experiment planning and data analysis; and animal procedure assistance for surgical procedures, catheter placement and maintenance and monitoring of physiologic status during imaging experiments. In addition to providing access to and maintenance of MRI, PET, CT and optical small animal scanners and ancillary facilities, WUSAIR services include assistance and training of researchers in small animal imaging procedures and data analysis. Importantly, WUSAIR is intended to bring imaging expertise fully into the cancer research community by encouraging individuals in collaborating research groups to become competent in hands-on small animal imaging methods. Providing a training center for small animal cancer imaging science extends the impact of WUSAIR beyond that of simply providing imaging services. This training program includes support for a yearly advanced imaging symposium, introductory teaching sessions for local researchers, and technology transfer through multiple-day exchanges of imaging scientists between WUSAIR and other centers of imaging excellence.
Key Discoveries (from interviews)	• High Resolution microPET • Quantitative diffuse optical tomography for small animals • Three dimensional MR diffusion image of the prostate • Diagnosing tumor hypoxia non-invasively
Relationship Between SAIR and Cancer Center Small Animal Imaging Shared Resource	SAIR and Cancer Center small animal imaging resource are the same
Total Publications	142

Appendix C: List of Awards Using the SAIR

Case Western

- PI: Agata Exner; Awarding Organization: NIH(R01CA118399)
- PI: Anna van Heeckeren; Awarding Organization: NIH(R21HL076752)
- PI: Baowei Fei; Awarding Organization: NIH(R21CA120536)
- PI: Bingcheng Wang; Awarding Organization: NIH(R01CA092259)
- PI: Flask/Keri; Awarding Organization: American Cancer Society
- PI: Jinming Gao; Awarding Organization: NIH(R01CA090606)
- PI: Jinming Gao; Awarding Organization: NIH(R21CA093993)
- PI: Jinming Gao; Awarding Organization: Whitaker Foundation
- PI: Joseph Nadeau; Awarding Organization: NIH(R01CA075056)
- PI: Keith McCrae; Awarding Organization: NIH(R01HL076810)
- PI: Mahmood Ghannoum; Awarding Organization: NIH(R01AI035097)
- PI: Marco Cabrera; Awarding Organization: NIH(P50GM066309)
- PI: Mark Pagel; Awarding Organization: Ohio Biotechnology Research and Technology Transfer Fund
- PI: Nancy Oleinick; Awarding Organization: NIH(P01CA048735)
- PI: Nancy Oleinick; Awarding Organization: NIH(R01CA083917)
- PI: Nancy Oleinick; Awarding Organization: Ohio Biotechnology Research and Technology Transfer Fund
- PI: Ruth Keri; Awarding Organization: DoD(DAMD17-01-1-0195)
- PI: Ruth Keri; Awarding Organization: NIH(R01CA090398)
- PI: Sanjay Gupta; Awarding Organization: NIH(R01CA108512)
- PI: Scot Remick; Awarding Organization: NIH(U01CA062502)
- PI: Shenandoah Robinson; Awarding Organization: NIH(K08NS046486)
- PI: Stanton Gerson; Awarding Organization: NIH(P30CA043703)
- PI: Stanton Gerson; Awarding Organization: NIH(R01CA073062)
- PI: Sunjay Gupta; Awarding Organization: Cancer Research Foundation
- PI: Vinod Labhasetwar; Awarding Organization: NIH(R01EB005822)
- PI: Zhenghong Lee; Awarding Organization: DOE(DE-FG02-03ER63597)
- PI: Zhenghong Lee; Awarding Organization: NIH(R01CA095307)
- PI: Zhenghong Lee; Awarding Organization: NIH(R21EB001847)

Duke

- PI: Badea, Cristian; Awarding Organization: NIH(R21CA124584)
- PI: Berridge, Brian; Awarding Organization: GlaxoSmith Kline
- PI: Bigner, Darrell D; Awarding Organization: NIH(P50CA108786)
- PI: Bigner, Darrell D; Awarding Organization: NIH(R37CA011898)
- PI: Chikaraishi, Dona; Awarding Organization: NIH(P41RR005959)
- PI: Coffman, Thomas; Awarding Organization: NIH(R01DK069896)
- PI: Dewhirst, Mark W; Awarding Organization: NIH(P01CA042745)
- PI: Driehuys, Bastiaan; Awarding Organization: NIH(R21HL087094)

- PI: Edward P. Patz, Jr.; Awarding Organization: NIH(R01CA109384)
- PI: Hochgeschwender, Ute; Awarding Organization: private grant
- PI: Kirsch, David; Awarding Organization: NIH(K08CA114176)
- PI: Leergaard, Trygve; Awarding Organization: Res Council of Norway(178571/V40)
- PI: Liu, Qing H.; Awarding Organization: NIH(R21CA114680)
- PI: Lyerly, H. Kim; Awarding Organization: NIH(P30CA014236)
- PI: Lyerly, H. Kim; Awarding Organization: NIH(P50CA089496)
- PI: Nelson, Rendon; Awarding Organization: NIH(R01CA104392)
- PI: Nicchitta, Christopher V.; Awarding Organization: NIH
- PI: Nightingale, Kathryn R.; Awarding Organization: NIH(R01CA114075)
- PI: Norton, John; Awarding Organization: NIH(G20RR021330)
- PI: Palmer, Scott; Awarding Organization: NIH(P50HL084917)
- PI: Piantadosi, Claude A; Awarding Organization: NIH(R01HL090679)
- PI: Ramanujam, Nimmi; Awarding Organization: NIH(R01CA100559)
- PI: Ranamujam, Nimmi; Awarding Organization: NIH(R21CA108490)
- PI: Ranamujam, Nimmi; Awarding Organization: NIH(R21EB002742)
- PI: Ranamujam, Nimmi; Awarding Organization: Coulter Foundation
- PI: Ranamujam, Nimmi; Awarding Organization: DoD
- PI: Soderling, Scott; Awarding Organization: NIH(R01NS059957)
- PI: Staats, Herman; Awarding Organization: NIH(R01AI064879)
- PI: Stamler, Johnathan; Awarding Organization: NIH(F32HL094058)
- PI: Sulik, Kathleen; Awarding Organization: NIH(P50AA011605)
- PI: Trahey, Gregg; Awarding Organization: NIH(R01CA114093)
- PI: Vaidyanathan, Ganesan; Awarding Organization: NIH(R01CA093371)
- PI: Vujaskovic, Zeljko; Awarding Organization: NIH(R01CA098452)
- PI: Warren Warren; Awarding Organization: NIH(R01EB002122)
- PI: Warren Warren; Awarding Organization: GE
- PI: Wechsler-Reya, Robert; Awarding Organization: NIH(R01NS052323)
- PI: Wergin, Melanie; Awarding Organization: GlaxoSmith Kline
- PI: Zalutsky, Michael; Awarding Organization: NIH(R37CA042324)

Johns Hopkins

- PI: Akhilesh Pandey; Awarding Organization: NIH(R01CA106424)
- PI: Carolyn Bertozzi; Awarding Organization: NIH(R01GM058867)
- PI: Chi Dang; Awarding Organization: NIH(R01CA057341)
- PI: Elizabeth Jaffee; Awarding Organization: NIH(U19CA113341)
- PI: George Sgorous; Awarding Organization: NIH(R01CA113797)
- PI: John Laterra; Awarding Organization: NIH(R01NS032148)
- PI: John Laterra; Awarding Organization: Dana Foundation
- PI: John Wong; Awarding Organization: NIH(R01CA108449)
- PI: Kenneth Kinzler; Awarding Organization: NIH(R37CA057345)
- PI: Linzhao Cheng; Awarding Organization: NIH(R01HL073781)
- PI: Manuel Hidalgo; Awarding Organization: NIH(R01CA116554)

- PI: Martin Pomper; Awarding Organization: Thomas Jefferson National Laboratory
- PI: Martin Pomper; Awarding Organization: AstraZenica
- PI: Martin Pomper; Awarding Organization: AdMeTech
- PI: Paul Fisher (Columbia U); Awarding Organization: NIH(R01CA035675)
- PI: Richard Ambinder; Awarding Organization: NIH(P50CA096888)
- PI: T.C. Wu; Awarding Organization: NIH(P50CA098252)
- PI: T.C. Wu; Awarding Organization: NIH(R01CA114425)
- PI: William Nelson; Awarding Organization: NIH(P50CA058236)
- PI: Zaver Bhujwalla; Awarding Organization: NIH(P50CA103175)
- PI: Zaver Bhujwalla; Awarding Organization: NIH(R01CA082337)

MGH

- PI: Andrew Luster, MD, PhD; Awarding Organization: NIH(R01AI040618)
- PI: Anil Rustgi, MD, PhD; Awarding Organization: NIH(R01DK060694)
- PI: ChingHsuan Tung, PhD; Awarding Organization: NIH(R01CA099385)
- PI: Christophe Benoist, MD, PhD; Awarding Organization: NIH(R21AI055467)
- PI: David Kirsch, MD, PhD; Awarding Organization: RSNA, Am Soc Clin Oncol Young Investigator Award
- PI: David Scadden, MD; Awarding Organization: NIH(R01DK050234)
- PI: David Scadden, MD; Awarding Organization: NIH(R01HL065909)
- PI: David Sosnovik, MD; Awarding Organization: RSNA
- PI: Diane Mathis, PhD; Awarding Organization: NIH(P01AI054904)
- PI: Douglas Hanahan, PhD; Awarding Organization: NIH(R01CA045234)
- PI: Farouc Jaffer, MD, PhD; Awarding Organization: Unknown
- PI: Fred Hochberg; Awarding Organization: NIH(P01CA069246)
- PI: Gary J. Brenner; Awarding Organization: Children's Tumor Foundation
- PI: Gregory Verdine, PhD; Awarding Organization: NIH(R01CA100742)
- PI: Gregory Verdine, PhD; Awarding Organization: NIH(R01GM044853)
- PI: Helen Shih, MD; Awarding Organization: NIH(R33CA091807)
- PI: J. Manuel Perez, PhD; Awarding Organization: NIH(K01CA101781)
- PI: John Chen, MD; Awarding Organization: RSNA
- PI: Kash Khazaie, PhD; Awarding Organization: NIH(R01CA104547)
- PI: Kimberly Kelly, PhD; Awarding Organization: AACR Grant
- PI: Kimberly Kelly, PhD; Awarding Organization: Lustgarten Foundation
- PI: Kwok Wong, MD; Awarding Organization: Claudia Adams Barr Program in Cancer Research
- PI: Kwok Wong, MD; Awarding Organization: DFCI
- PI: Kwok Wong, MD; Awarding Organization: DFCI
- PI: Kwok Wong, MD; Awarding Organization: DFCI
- PI: Lee Josephson, PhD; Awarding Organization: NIH(R01EB000662)
- PI: Lee Josephson, PhD; Awarding Organization: NIH(R01EB004472)
- PI: Lew Cantley, MD, PhD; Awarding Organization: NIH(P01CA089021)
- PI: Lynda Chin, PhD; Awarding Organization: NIH(R01CA093947)

- PI: Maguire; Comer; Leroy; Awarding Organization: Unknown(1200-203958)
- PI: Mark Poznansky, MD, PhD; Awarding Organization: NIH(R01AI049757)
- PI: Michael Atkins; Awarding Organization: NIH(P50CA101942)
- PI: Michael Seiden, MD; Awarding Organization: NIH(R01CA089150)
- PI: Michael Seiden, MD; Awarding Organization: Dorris Duke Foundation
- PI: Mikael Pittet, PhD; Awarding Organization: NIH(R01CA096978)
- PI: Nabeel Bardeesy; Awarding Organization: Unknown(205025)
- PI: Peter Hauschka, PhD; Awarding Organization: NIH(R01AR048799)
- PI: Raju Kucherlapati (Einstein); Awarding Organization: NIH(U01CA084301)
- PI: Raju Kucherlapati, PhD; Awarding Organization: NIH(U01ES011010)
- PI: Ralph Weissleder, MD, PhD; Awarding Organization: NIH(P50CA086355)
- PI: Ralph Weissleder, MD, PhD; Awarding Organization: NIH(R01CA085240)
- PI: Ralph Weissleder, MD, PhD; Awarding Organization: NIH(R01CA086782)
- PI: Richard Hynes; Awarding Organization: NIH(U54CA126515)
- PI: Robert Bachoo, MD, PhD; Awarding Organization: NIH(K08NS042737)
- PI: Robert Langer, PhD (MIT); Awarding Organization: NIH(U54CA119349)
- PI: Ronald DePinho, MD; Awarding Organization: NIH(P01CA095616)
- PI: Ronald DePinho, MD; Awarding Organization: NIH(P01CA117969)
- PI: Ronald DePinho, MD; Awarding Organization: NIH(U01CA084313)
- PI: Samuel Rabkin and William Curry; Awarding Organization: MGHMAO PhysicianScientist
- PI: Sangeeta Bhatia; Awarding Organization: NIH(R01CA101830)
- PI: Sangeeta Bhatia; Awarding Organization: Bhatia Lab
- PI: Tyler Jacks, PhD (MIT); Awarding Organization: NIH(P30CA014051)
- PI: Tyler Jacks, PhD (MIT); Awarding Organization: NIH(U01CA084306)
- PI: Uli von Andrian, MD, PhD; Awarding Organization: NIH(R01AI061663)
- PI: Umar Mahmood, MD, PhD; Awarding Organization: NIH(R01EB001872)
- PI: Vasilis Ntziachristos, PhD; Awarding Organization: NIH(R01EB000750)
- PI: Vasilis Ntziachristos, PhD; Awarding Organization: NIH(R21CA110167)
- PI: William Kaelin, MD; Awarding Organization: NIH(R01CA068490)
- PI: William Kaelin, MD; Awarding Organization: NIH(R01CA076120)
- PI: William T. Curry; Awarding Organization: Rappaport Research Scholarship
- PI: Wynn Volkert (University of Missouri-Columbia); Awarding Organization: NIH(P50CA103130)

MSKCC

- PI: Alan Houghton; Awarding Organization: NIH(P01CA033049)
- PI: Clifton Ling; Awarding Organization: NIH(R01CA084596)
- PI: David Nanus (Weill); Awarding Organization: NIH(R01CA080240)
- PI: David Scheinberg; Awarding Organization: NIH(R01CA055349)
- PI: David Spriggs; Awarding Organization: NIH(R01CA084009)
- PI: Eric Holland; Awarding Organization: NIH(P20CA097011)
- PI: Eric Holland; Awarding Organization: NIH(R01CA094842)
- PI: Eric Holland; Awarding Organization: NIH(R01CA100688)

- PI: Filippo Giancotti; Awarding Organization: NIH(R37CA058976)
- PI: Harold Varmus; Awarding Organization: NIH(P30CA008748)
- PI: Juri Gelovani; Awarding Organization: DOE(DE-FG02-02ER6348)
- PI: Larry Norton; Awarding Organization: NIH(P01CA094060)
- PI: M. Beal (Weill); Awarding Organization: NIH(R01NS039258)
- PI: Marilyn Resh; Awarding Organization: NIH(R01CA096582)
- PI: Michel Sadelain; Awarding Organization: NIH(P01CA059350)
- PI: Neil Rosen; Awarding Organization: NIH(U01CA091178)
- PI: Nurit Kalderon; Awarding Organization: NIH(R01NS039375)
- PI: Peter Scardino; Awarding Organization: NIH(P50CA092629)
- PI: Pier Paolo Pandolfi; Awarding Organization: NIH(U01CA084292)
- PI: Richard O'Reilly; Awarding Organization: NIH(P01CA023766)
- PI: Ron Blasberg; Awarding Organization: NIH(P50CA086438)
- PI: Ron Blasberg; Awarding Organization: NIH(R01CA102673)
- PI: Steven Larson; Awarding Organization: DOE(DE-FG02- 86ER60407)
- PI: Steven Larson; Awarding Organization: DOE(DE-FG02-95ER62039)
- PI: Yuman Fong; Awarding Organization: NIH(R01CA075416)

Stanford

- PI: Amato Giaccia; Awarding Organization: NIH(P01CA067166)
- PI: Christopher Contag; Awarding Organization: NIH(P20CA086312)
- PI: Christopher Contag; Awarding Organization: NIH(R21CA109988)
- PI: Christopher Contag; Awarding Organization: NIH(U54CA105296)
- PI: Dean Felsher; Awarding Organization: NIH(R01CA089305)
- PI: Dennis Matthews; Awarding Organization: NSF(0120999)
- PI: Edgar Engleman; Awarding Organization: NIH(P01HL057443)
- PI: Edward E. Graves and Karyn A. Goodman; Awarding Organization: Lerner Family Foundation
- PI: Francis Blankenberg; Awarding Organization: NIH(R01EB000898)
- PI: Harry Greenberg; Awarding Organization: NIH(P30DK056339)
- PI: Irving Weissman; Awarding Organization: NIH(R01HL058770)
- PI: Nicholas Denko; Awarding Organization: NIH(R01CA100132)
- PI: Paul Wender; Awarding Organization: NIH(R37CA031845)
- PI: Robert Negrin; Awarding Organization: NIH(P01CA049605)
- PI: Robert Negrin; Awarding Organization: NIH(R01HL075462)
- PI: Samuel Gambhir; Awarding Organization: NIH(P50CA114747)
- PI: Samuel Gambhir; Awarding Organization: NIH(R01CA082214)
- PI: Samuel Gambhir; Awarding Organization: NIH(U54CA119367)
- PI: Xiaoyuan Chen; Awarding Organization: NIH(R21CA102123)
- PI: Unknown; Awarding Organization: DoD(F49620-00-1-0349)
- PI: Unknown; Awarding Organization: DOE
- PI: Unknown; Awarding Organization: Stanford Internal Support - Stanford Program in Biomedical Engineering and Child Health Initiative-Lucille Packard Foundation

- PI: Unknown; Awarding Organization: JDFR

UC Davis

- PI: Abate-Shen, Cory; Awarding Organization: NIH(U01CA084294)
- PI: Abbey, Craig; Awarding Organization: NIH(R21CA102733)
- PI: Boone, John; Awarding Organization: NIH(R21EB004643)
- PI: Borowsky, Alexander; Awarding Organization: California Breast Cancer Research Program(#11IB-0158)
- PI: Cardiff, Robert; Awarding Organization: NIH(R01CA089140)
- PI: Cherry, Simon; Awarding Organization: NIH(R01CA121783)
- PI: Cherry, Simon; Awarding Organization: NIH(R01EB000230)
- PI: Cherry, Simon; Awarding Organization: NIH(R01EB000561)
- PI: Dayton, Paul; Awarding Organization: NIH(R21CA098692)
- PI: De Vere White, Ralph; Awarding Organization: NIH(P30CA093373)
- PI: DeNardo, Gerald; Awarding Organization: NIH(P01CA047829)
- PI: Ferrara, Katherine; Awarding Organization: NIH(R01CA103828)
- PI: Ferrara, Katherine; Awarding Organization: NIH(R01CA112356)
- PI: Gregg, Jeffrey; Awarding Organization: NIH(R03CA117465)
- PI: Jacobs, Russell; Awarding Organization: NIH(R01EB000993)
- PI: Lam, Kit; Awarding Organization: NIH(R01CA115483)
- PI: Lam, Kit; Awarding Organization: NIH(R21CA102732)
- PI: Lam, Kit; Awarding Organization: NIH(U19CA113298)
- PI: Meares, Claude; Awarding Organization: NIH(R01CA016861)
- PI: Qi, Jinyi; Awarding Organization: NIH(R01EB000194)
- PI: Qi, Jinyi; Awarding Organization: NIH(R01EB005322)
- PI: Sutcliffe, Julie; Awarding Organization: DOE(Grant # not yet issued)
- PI: Sutcliffe, Julie; Awarding Organization: NIH(R21CA107792)
- PI: Sutcliffe, Julie; Awarding Organization: NIH(R33CA107792)
- PI: Tarantal, Alice; Awarding Organization: NIH(P50HL085036)
- PI: Tuscano, Joseph; Awarding Organization: Leukemia & Lymphoma Society
- PI: Zern, Mark; Awarding Organization: NIH(R21DK070038)

UCLA

- PI: Andrew Raubitchek (City of Hope); Awarding Organization: NIH(P01CA043904)
- PI: Andrew Saxon; Awarding Organization: NIH(P01AI050495)
- PI: ARION CHATZIIOANNOU; Awarding Organization: NIH(R01EB001458)
- PI: Charles Sawyers; Awarding Organization: NIH(U01CA084128)
- PI: Christine Wu; Awarding Organization: University of California/Discovery
- PI: Daniel Kaufman; Awarding Organization: NIH(R01DK068506)
- PI: Daniel Kaufman; Awarding Organization: NIH(R21DK069839)
- PI: Gary Small; Awarding Organization: NIH(P01AG025831)
- PI: Harvey Herschman; Awarding Organization: NIH(P50CA086306)
- PI: Harvey Herschman; Awarding Organization: NIH(R01CA084572)

- PI: Heinrich Schelbert; Awarding Organization: NIH(R01HL033177)
- PI: Hong Wu; Awarding Organization: NIH(R01CA107166)
- PI: Jay Lieberman; Awarding Organization: NIH(R01CA103039)
- PI: Jean DeKernion; Awarding Organization: NIH(P50CA092131)
- PI: Judith Gasson; Awarding Organization: NIH(P30CA016042)
- PI: Kang Ting; Awarding Organization: NIH(R01DE016107)
- PI: Lily Wu; Awarding Organization: NIH(R01CA101904)
- PI: Michael Phelps; Awarding Organization: DOE(DE-FC03-02ER63420)
- PI: Nori Kasahara; Awarding Organization: NIH(R01CA105171)
- PI: Sherie Morrison; Awarding Organization: NIH(R01GM074051)
- PI: Sung-Cheng (Henry) Huang; Awarding Organization: NIH(R01EB001943)

University of Arizona

- PI: Alberding; Awarding Organization: NIH(F31HL069735)
- PI: Barrett; Awarding Organization: NIH(P41EB002035)
- PI: Barton; Awarding Organization: NIH(K02EB000163)
- PI: Barton; Awarding Organization: NSF(NSF 9978820)
- PI: Barton; Awarding Organization: Unknown(Prop 301 small imaging grant)
- PI: Barton; Awarding Organization: Whitaker Foundation.
- PI: Bowden; Awarding Organization: NIH(R01CA040584)
- PI: Cherrington; Awarding Organization: NIH(K22ES011646)
- PI: Dorr; Awarding Organization: NIH(P01CA017094)
- PI: Dr. Ashley Welch (UT Austin); Awarding Organization: NSF(NSF 9986296)
- PI: Fregosi; Awarding Organization: NIH(R01HL068162)
- PI: Galons; Awarding Organization: NIH(R01CA088285)
- PI: Gatenby; Awarding Organization: NIH(R01CA093650)
- PI: Gemer; Awarding Organization: NIH(P01CA072008)
- PI: Gerner; Awarding Organization: NIH(P50CA095060)
- PI: Gillies; Awarding Organization: NIH(R01CA077975)
- PI: Gillies; Awarding Organization: NIH(R01CA095944)
- PI: Gillies; Awarding Organization: NIH(R01CA097360)
- PI: Gillies; Awarding Organization: Aventis
- PI: Gillies; Awarding Organization: Paraseghian Foundation
- PI: Gmitro; Awarding Organization: ADCRC(ADCRC 6-073)
- PI: Gmitro; Awarding Organization: NIH(R33CA094287)
- PI: Hoying; Awarding Organization: NIH(K02CA067067)
- PI: Hoying; Awarding Organization: NIH(R01HL063732)
- PI: Hoying; Awarding Organization: NIH(T32HL007249)
- PI: Hoying; Awarding Organization: NIH(T32HL007955)
- PI: Lutz; Awarding Organization: NIH(R01CA080130)
- PI: McGrath; Awarding Organization: MSU Foundation
- PI: Powis; Awarding Organization: NIH(U54CA090821)
- PI: Raghunand; Awarding Organization: NIH(R21DK063124)
- PI: Seeger; Awarding Organization: AHSC(AHSC UPERCC)

- PI: Stopeck; Awarding Organization: NIH(R21CA088288)
- PI: Trouard; Awarding Organization: NIH(R01CA082813)
- PI: Trouard; Awarding Organization: NIH(R21RR014274)
- PI: Witte; Awarding Organization: NIH(R01HL071206)
- PI: Witte; Awarding Organization: NIH(R21AT000495)
- PI: Witte; Awarding Organization: ADCRC
- PI: Zinn (UAB); Awarding Organization: NIH(P50CA083591)
- PI: Zinn (UAB); Awarding Organization: NIH(R01CA080104)

University of Michigan

- PI: Brian Ross; Awarding Organization: NIH(P01CA085878)
- PI: Brian Ross; Awarding Organization: NIH(P50CA093990)
- PI: Chung Owyang; Awarding Organization: NIH(P30DK034933)
- PI: David Pinsky; Awarding Organization: NIH(R01HL085149)
- PI: Diane Simeone; Awarding Organization: NIH(R01DK061507)
- PI: Edward Domino; Awarding Organization: NIH(R01DA018974)
- PI: Emina Haung; Awarding Organization: NIH(K08CA091975)
- PI: Evan Keller; Awarding Organization: NIH(P01CA093900)
- PI: Gary Luker; Awarding Organization: NIH(R21AI066192)
- PI: Gregory Wolf; Awarding Organization: NIH(P50CA097248)
- PI: Guohua Xi; Awarding Organization: NIH(R01NS039866)
- PI: Jacques Nor; Awarding Organization: NIH(R01DE015948)
- PI: James L. Baker Jr.; Awarding Organization: NIH(R01CA119409)
- PI: Jaques Nor; Awarding Organization: NIH(R01DE016586)
- PI: John Younger; Awarding Organization: NIH(R01GM069438)
- PI: Joseph Metzger; Awarding Organization: NIH(P01AG015434)
- PI: Keith Kirkwood; Awarding Organization: NIH(R01DE018290)
- PI: Kenneth Pienta; Awarding Organization: NIH(P50CA069568)
- PI: Kenneth Pienta; Awarding Organization: NIH(R01CA102872)
- PI: Kun-Liang Guan; Awarding Organization: NIH(R01GM051586)
- PI: Laurence Baker; Awarding Organization: NIH(U10CA027057)
- PI: Lois Weisman; Awarding Organization: NIH(R01GM050403)
- PI: Max Wicha; Awarding Organization: NIH(P30CA046592)
- PI: Max Wicha; Awarding Organization: NIH(R01CA101860)
- PI: Michael Berens; Awarding Organization: NIH(R21NS043446)
- PI: Pavan Reddy; Awarding Organization: NIH(R01HL090775)
- PI: Raoul Kopelman; Awarding Organization: NIH(R01EB007977)
- PI: Rolf Barth; Awarding Organization: NIH(R01CA098945)
- PI: Sally Camper; Awarding Organization: NIH(R37HD030428)
- PI: Scott Snyder; Awarding Organization: NIH(R01CA089448)
- PI: Theodore Lawrence; Awarding Organization: NIH(R01CA080145)
- PI: Victor Yang; Awarding Organization: NIH(R01CA114612)
- PI: William Ensminger; Awarding Organization: NIH(R01CA084117)
- PI: William Giannobile; Awarding Organization: NIH(R01DE013397)

- PI: Yang, Liu; Awarding Organization: NIH(R01CA120901)
- PI: Yi Sun; Awarding Organization: NIH(R01CA118762)

University of Pennsylvania

- PI: Britton Chance; Awarding Organization: NIH(N01CA097065)
- PI: Britton Chance; Awarding Organization: NIH(R01CA072895)
- PI: Britton Chance; Awarding Organization: NIH(R21DK058516)
- PI: Craig Thompson; Awarding Organization: NIH(P01CA104838)
- PI: Dennis Leeper (TJU); Awarding Organization: NIH(P01CA056690)
- PI: Gang Zheng; Awarding Organization: DoD(DAMD17-03-1-0373)
- PI: Gang Zheng; Awarding Organization: NIH(N01CA037119)
- PI: Gang Zheng; Awarding Organization: NIH(R21CA095330)
- PI: Gang Zheng; Awarding Organization: Oncologic Foundation of Buffalo
- PI: Gang Zheng; Awarding Organization: RSNA
- PI: Garrett Brodeur; Awarding Organization: NIH(P01CA097323)
- PI: Hank Kung; Awarding Organization: NIH(R01EB002171)
- PI: Harish Poptani; Awarding Organization: NIH(R21HD048582)
- PI: Harish Poptani; Awarding Organization: University Research Foundation
- PI: James Delikatny; Awarding Organization: NIH(R21CA079718)
- PI: James Delikatny; Awarding Organization: NIH(R21EB002537)
- PI: James Delikatny; Awarding Organization: University Research Foundation
- PI: Janet Sawicki (Lankenau); Awarding Organization: DoD(DOD OC050002)
- PI: Jerry Glickson; Awarding Organization: NIH(R01CA051935)
- PI: Jerry Glickson; Awarding Organization: NIH(R01CA051950)
- PI: Jerry Glickson; Awarding Organization: NIH(R01CA101700)
- PI: John Biaglow; Awarding Organization: NIH(R37CA044982)
- PI: John Wolfe (CHOP); Awarding Organization: NIH(R01DK063973)
- PI: Lewis Chodosh; Awarding Organization: NIH(R01CA093719)
- PI: Lewis Chodosh; Awarding Organization: NIH(R01CA098371)
- PI: Lewis Chodosh; Awarding Organization: NIH(U01CA105490)
- PI: Louis Soslowsky; Awarding Organization: NIH(P30AR050950)
- PI: Mark Greene; Awarding Organization: NIH(P01CA089480)
- PI: Meenhard Herlyn; Awarding Organization: NIH(P01CA025874)
- PI: Meenhard Herlyn; Awarding Organization: NIH(P50CA093372)
- PI: Meenhard Herlyn; Awarding Organization: NIH(R01CA047159)
- PI: Ramachandran Murali; Awarding Organization: Susan G. Komen Breast Cancer Foundation(IMG0201367)
- PI: Rong Zhou; Awarding Organization: NIH(R21EB002473)
- PI: Rong Zhou; Awarding Organization: American Heart Association
- PI: Rong Zhou; Awarding Organization: PA Dept. of Health
- PI: Rong Zhou; Awarding Organization: Glaxo-Smith Kline/Penn Internal Grant
- PI: Shoko Nioka (Optical Devices, Inc); Awarding Organization: NIH(R44CA096016)
- PI: Wafik El-Deiry; Awarding Organization: NIH(R01CA123258)

- PI: Wafik El-Deiry; Awarding Organization: NIH(U54CA105008)
- PI: Warren Warren; Awarding Organization: NIH(R21RR019770)
- PI: William Lee; Awarding Organization: NIH(R01CA099519)

Washington University

- PI: Achilefu; Awarding Organization: NSF(BES-01194889)
- PI: Achilefu; Awarding Organization: DOD(DAMD 17-0210613)
- PI: Achilefu; Awarding Organization: NIH(R01CA109754)
- PI: Achilefu; Awarding Organization: NIH(R01EB001430)
- PI: Achilefu; Awarding Organization: NIH(R21CA123537)
- PI: Achilefu; Awarding Organization: NIH(R33CA100972)
- PI: Ackerman; Awarding Organization: NIH(R43CA110313)
- PI: Anderson; Awarding Organization: NIH(R01CA064475)
- PI: Arbeit; Awarding Organization: NIH(N01CN43303)
- PI: Arbeit; Awarding Organization: NIH(R01CA090722)
- PI: Arbeit; Awarding Organization: NIH(R01CA101012)
- PI: Bayly; Awarding Organization: NIH(R21NS045237)
- PI: Conradi; Awarding Organization: GEMI(GEMI: Lung Imaging with C2F6 Gas by F-19 MR: Mapping Ventilation and Specific Surface Area)
- PI: Cross; Awarding Organization: NMSS (National Multiple Sclerosis Society)(CA1012-A-13)
- PI: Culver; Awarding Organization: NIH(K25NS044339)
- PI: Culver; Awarding Organization: NIH(R21EB007924)
- PI: Eberlein; Awarding Organization: NIH(P30CA091842)
- PI: Edwards; Awarding Organization: NIH(R21CA131660)
- PI: Gelb/Ackerman; Awarding Organization: NSF(CHE-0443511)
- PI: Gropler; Awarding Organization: NIH(P01HL013851)
- PI: Gutmann; Awarding Organization: DOD(DAMD 17-03-1-0215)
- PI: Gutmann; Awarding Organization: DOD(NF 050028)
- PI: Gutmann; Awarding Organization: NIH(R21NS054629)
- PI: Gutmann (UNC); Awarding Organization: NIH(U01CA084314)
- PI: Inder; Awarding Organization: NIH(R01HL007492)
- PI: Katzenellenbogen (UIUC); Awarding Organization: NIH(R01CA025836)
- PI: Katzenellenbogen (UIUC); Awarding Organization: NIH(R37DK015556)
- PI: Knight (Temple); Awarding Organization: NIH(R01CA096792)
- PI: Lewis; Awarding Organization: DOD(W23RYX-4206-N671)
- PI: Lewis; Awarding Organization: DOD(W81XWH-04-0906)
- PI: Linette; Awarding Organization: American Cancer Society(58-010-49)
- PI: Mach; Awarding Organization: NIH(R21CA121952)
- PI: Mach; Awarding Organization: NIH(R33CA102869)
- PI: McLeod; Awarding Organization: NIH(R21CA102461)
- PI: Neil; Awarding Organization: NIH(R01NS035912)
- PI: Neil; Awarding Organization: NIH(R01NS037357)
- PI: Nelson; Awarding Organization: NASA(NNJ04HC90G)

- PI: none; Awarding Organization: American Heart Association(Grant-in-Aid Award #0660057Z)
- PI: Piwnica-Worms; Awarding Organization: NIH(P50CA094056)
- PI: Rogers; Awarding Organization: NIH(R01EB004533)
- PI: Rogers; Awarding Organization: ACS(RPG-00-067-01-CCE)
- PI: Song; Awarding Organization: NIH(R01NS047592)
- PI: Song; Awarding Organization: NIH(R01NS054194)
- PI: Volkert (Missouri-Columbia); Awarding Organization: NIH(P50CA101330)
- PI: Weber; Awarding Organization: NIH(R01CA127008)
- PI: Weilbaecher; Awarding Organization: NIH(R01CA097250)
- PI: Welch; Awarding Organization: DOE(DE-FG02-84ER-60218)
- PI: Welch; Awarding Organization: DOE(DE-FG02-87ER-60512)
- PI: Welch; Awarding Organization: NIH(R24CA086307)
- PI: Wong (UNH); Awarding Organization: NIH(R01CA093375)
- PI: Wooley; Awarding Organization: NIH(U01HL080729)
- PI: Yablonskiy; Awarding Organization: NIH(R01HL070037)
- PI: Yablonskiy; Awarding Organization: NIH(R01NS041519)
- PI: You; Awarding Organization: NIH(N01CN43308)
- PI: You; Awarding Organization: NIH(R01AT003203)
- PI: You; Awarding Organization: NIH(R01CA058554)
- PI: You; Awarding Organization: NIH(R01CA093643)
- PI: You; Awarding Organization: NIH(R01CA096103)
- PI: You; Awarding Organization: NIH(R01CA099187)
- PI: You; Awarding Organization: NIH(R01CA113793)
- PI: Unknown; Awarding Organization: Varian NMR Systems(CG0048-03)

Appendix D: List of NCRR Small Animal Imaging S10 Awards to Cohort 1-3 Institutions

MSKCC

- PI: KOUTCHER, JASON A. Title: 500 MHz Wide Bore NMR System. Start Year of S10 Award: 2002. (STPI Coding of Type of Instrument: MRI)
- PI: STRAUSS, HARRY W. Title: MICROSPECT IN TUMOR IMAGING. Start Year of S10 Award: 2003. (STPI Coding of Type of Instrument: MicroSPECT)
- PI: LARSON, STEVEN. Title: Shared Instrument: Focus microPET. Start Year of S10 Award: 2005. (STPI Coding of Type of Instrument: PET)
- PI: KOUTCHER, JASON A. Title: 9.4T/20 cm MRI for Cancer Research. Start Year of S10 Award: 2007. (STPI Coding of Type of Instrument: MRI)

Stanford

- PI: MOSELEY, MICHAEL. Title: High Field GE Experimental MR Scanner. Start Year of S10 Award: 2004. (STPI Coding of Type of Instrument: MRI)

UC Davis

- PI: CHERRY, SIMON R. Title: A microSPECT scanner for Molecular Imaging. Start Year of S10 Award: 2007. (STPI Coding of Type of Instrument: MicroSPECT)

University of Arizona

- PI: GALONS, JEAN-PHILIPPE. Title: Magnex Model MRBR 7T/201 AS Shielded Magnet System. Start Year of S10 Award: 2005. (STPI Coding of Type of Instrument: MRI)

University of Michigan

- PI: ROSS, BRIAN D. Title: 7.0T/210 Imaging System. Start Year of S10 Award: 2005. (STPI Coding of Type of Instrument: MRI)

University of Pennsylvania

- PI: GLICKSON, JERRY D. Title: 9.4T NMR SPECTROMETER/IMAGER UPGRADE. Start Year of S10 Award: 2000. (STPI Coding of Type of Instrument: MRI)
- PI: ACTON, PAUL D. Title: MicroCT for Imaging Small Animals. Start Year of S10 Award: 2003. (STPI Coding of Type of Instrument: MicroCT)
- PI: PICKUP, STEPHEN. Title: Console for a 4.7 T small animal MRI system. Start Year of S10 Award: 2008. (STPI Coding of Type of Instrument: MRI)

Washington University

- PI: ACKERMAN, JOSEPH J. Title: REQUEST TO UPGRADE 600 MHZ NMR SYSTEM. Start Year of S10 Award: 2001. (STPI Coding of Type of Instrument: MRI)

- PI: ACKERMAN, JOSEPH J. Title: Small Animal 11.75 Tesla Magnetic Resonance Scanner. Start Year of S10 Award: 2002. (STPI Coding of Type of Instrument: MRI)
- PI: LAFOREST, RICHARD. Title: Acquisition of a Small Animal CT Scanner. Start Year of S10 Award: 2003. (STPI Coding of Type of Instrument: MicroCT)
- PI: ACKERMAN, JOSEPH J.. Title: 4.7 Tesla MRI Scanner Console and Gradient System. Start Year of S10 Award: 2005. (STPI Coding of Type of Instrument: MRI)
- PI: LEWIS, JASON S. Title: Beta Imager 2000Z Digital Imaging System. Start Year of S10 Award: 2005. (STPI Coding of Type of Instrument: Autoradiography)
- PI: ACKERMAN, JOSEPH J. Title: System Upgrade for Small-Animal MRI. Start Year of S10 Award: 2007. (STPI Coding of Type of Instrument: MRI)

Appendix E: List of Identified non-SAIR Small Animal Imaging Equipment Development Awards at SAIR Institutions

Case Western

1. PI: MUZIC, RAYMOND F. Title: COMKAT:Compartment Model Kinetic Analysis/Imaging (Award number: R33CA101073)
2. PI: WILSON, DAVID L. Title: TISSUE RESPONSE IN IMRI GUIDED CANCER THERAPY (Award number: R01CA084433)

Duke

1. PI: BADEA, CRISTIAN T. Title: Tumor perfusion in small animals with tomographic digital subtraction angiography (Award number: R21CA124584)
2. PI: LIU, QING H. Title: NUFFT for Multi-Modality In Vivo Imaging (Award number: R21CA114680)
3. PI: METZLER, SCOTT DEAN. Title: Accurate and Precise Calibrations for Pinhole SPECT (Award number: R01EB001910)
4. PI: NIGHTINGALE, KATHRYN R. Title: Quantifying Liver Fibrosis with Acoustic Radiation Force (Award number: R01EB002132)
5. PI: RAMANUJAM, NIMMI. Title: Fiber Probe designs for Epithelial Precancer Detection (Award number: R21CA108490)

Johns Hopkins

1. PI: TSUI, BENJAMIN M. Title: High-Resolution SPECT for Molecular Imaging (Award number: R01EB001558)
2. PI: WONG, JOHN W. Title: An Image Guided Small Animal Radiation Research Platform (Award number: R01CA108449)

MGH

1. PI: NTZIACHRISTOS, VASILIS. Title: 3D Time Domain Molecular Imaging (Award number: R01EB000750)
2. PI: NTZIACHRISTOS, VASILIS. Title: Hybrid Complete Protection Flourescence Molecular Tomography and X-ray CT (Award number: R01EB006432)
3. PI: NTZIACHRISTOS, VASILIS. Title: Hybrid optical-ultrasound scanner for cancer imaging (Award number: R21CA110167)
4. PI: WEISSLEDER, RALPH. Title: Hybrid Complete Protection Flourescence Molecular Tomography and X-ray CT (Award number: R01EB006432)
5. PI: WEISSLEDER, RALPH. Title: Diffuse optical tomography system for molecular imaging (Award number: R21CA091807)

MSKCC

1. PI: LING, CLIFTON C. Title: Multimodality Biological Imaging of Cancer/Tumor Hypoxia (Award number: R01CA084596)

Stanford

1. PI: CONTAG, CHRISTOPHER H. Title: Miniature Confocal Theta Flourescence Microscope (Award number: R21CA109988)
2. PI: LEVIN, CRAIG S. Title: New Scintillation Light Detection Concepts for PET (Award number: R21EB003283)
3. PI: MACOVSKI, ALBERT. Title: Low-Cost, High-Quality Prepolarized MRI Head Scanner (Award number: R33EB000777)
4. PI: WANG, THOMAS D. Title: Miniature Confocal Theta Flourescence Microscope (Award number: R33CA109988)

University of Arizona

1. PI: BARTON, JENNIFER K. Title: Dual-Modality System for Imaging Colon Cancer in Mice (Award number: R01CA109385)
2. PI: BARTON, JENNIFER K. Title: Optical Imaging of Ovarian Carcinogenesis in a Rat Menopause Model (Award number: R01CA119200)
3. PI: BARTON, JENNIFER K. Title: Parallel OCT System for Endoscopic Imaging (Award number: R01EB001032)
4. PI: GMITRO, ARTHUR F. Title: Ultra-Miniature Multi-Modal Endoscopes (Award number: R21CA113964)
5. PI: LUKASIK, VICTORIA M. Title: Tumor NMR Images are Affected by Anesthetic (Award number: R21CA102227)
6. PI: PETERSON, TODD E. Title: Sub-millimeter Nuclear Medicine Imaging at Low Energies (Award number: R21EB000776)
7. PI: RAGHUNAND, NATARAJAN. Title: Tumor NMR Images are Affected by Anesthetic (Award number: R21CA102227)

UC Davis

1. PI: ABBEY, CRAIG KENDALL. Title: Quantitative Assessment of Murine Tumors with MicroPET (Award number: R21CA102733)
2. PI: BOONE, JOHN M. Title: Hybrid Nuclear/X-ray Projection System for Mouse Imaging (Award number: R21EB004643)
3. PI: CHERRY, SIMON R. Title: Hyperspectral Optical Tomography for Molecular Imaging (Award number: R01CA121783)
4. PI: CHERRY, SIMON R. Title: A MICRO CT/PET SCANNER FOR IN VIVO SCREENING OF MICE (Award number: R01EB000230)
5. PI: CHERRY, SIMON R. Title: HIGH RESOLUTION PET IMAGING OF MOUSE MODELS OF CANCER (Award number: R01EB000561)
6. PI: CHERRY, SIMON R (contact); SHAH, KANAI S. Title: Development of a Small Animal PET Scanner Using Solid State Photomultipliers (Award number: R01CA134632)
7. PI: JACOBS, RUSSELL E. Title: Multimodal mPET & mMRI Imaging Instrumentation (Award number: R01EB000993)

UCLA

1. PI: CHATZIIOANNOU, ARION XENOFON. Title: A Novel Detector for Combined Optical and PET Imaging (Award number: R01EB001458)

University of Michigan

1. PI: MENG, LING-JIAN. Title: Very High Resolution SPECT/CT System (Award number: R21EB004940)
2. PI: WANG, THOMAS D. Title: Miniature Confocal Theta Flourescence Microscope (Award number: R33CA109988)

University of Pennsylvania

1. PI: ACTON, PAUL D./THAKUR, MATTHEW L. Title: Improved Molecular Imaging with SPECT (Award number: R01EB001809)
2. PI: CHANCE, BRITTON. Title: 2 & 3D Imaging of Contrast Agents in Animal Models (Award number: R01CA072895)
3. PI: CHANCE, BRITTON. Title: FUNCTIONAL OPTICAL IMAGING OF BRAIN INJURY (fNIRI) (Award number: R01NS036633)
4. PI: GLICKSON, JERRY D. Title: 1H NMR STUDIES OF NON-HODGKINS LYMPHOMA (Award number: R01CA101700)
5. PI: METZLER, SCOTT DEAN. Title: Accurate and Precise Calibrations for Pinhole SPECT (Award number: R01EB001910)
6. PI: WARREN, WARREN S. Title: Two-Photon Absorption Imaging by Laser Pulse Shaping (Award number: R21RR019770)

Washington University

1. PI: ACHILEFU, SAMUEL. Title: Optical Probes & Methods for Imaging Integrin Expression (Award number: R01CA109754)
2. PI: ACHILEFU, SAMUEL. Title: Multiphoton microscopy using near infrared Dyes (Award number: R21CA123537)
3. PI: TAI, YUAN-CHUAN. Title: A Novel Device to Allow Zoom-In Imaging for PET Scanners (Award number: R21CA110011)

Appendix F: SAIR PI Interview Guides

Cohort 1-3 PIs with Continuing Awards

Planning, Management, and Organization

1. What are the goals of your SAIR award?
    a. PROBE: Developing new research techniques in small animal imaging? Provide infrastructure support to the small animal imaging community?
    b. Have the goals changed or evolved over time? Have goals been added? Dropped?
2. Of the total usage of the SAIR, can you estimate approximately what fraction is general usage of the infrastructure by other PIs (i.e. support for standard R01 grants, etc.), and what fraction is being used to improve tools and techniques (i.e. improving throughput of equipment, better contrast agents, etc.)?
3. How do researchers at your institution come to use the SAIR facility?
    a. Is there outreach (historical or ongoing) to the balance of the cancer research community at your institution? To other departments/researchers?
    b. [IF ANY] Describe this outreach. What are the mechanisms? Are there formal public announcements or do you simply contact colleagues you know might be interested?
    c. Are there other locations at your institution where researchers can use the same equipment housed in your SAIR core (i.e. are there duplicate pieces of equipment on campus that are equivalent?). If so, what equipment is that?
4. Do researchers from other institutions use the SAIR facility? If so, how do they come to do so?

Physical Infrastructure

5. What is the name of the organizational entity where the SAIR is housed?
6. Please describe in general how SAIR funding has been used to **purchase** small animal imaging equipment.
    a. Which pieces of large-scale instrumentation were purchased (in whole or in part) using SAIR funds – and why those particular ones?
7. Please describe in general how SAIR funding has been used to **support** small animal imaging equipment.
    a. Which pieces of instrumentation are being staffed (part-time/full-time) using SAIR funds? Who is staffing them?
    b. Are any pieces of instrumentation open-access to researchers?
    c. Is there technical support staff available to researchers who use the facility to interpret their data?
8. Who uses the SAIR facility? How many researchers are:
    a. Faculty members/PIs
    b. Graduate students or postdocs
    c. Staff scientists
    d. Other users

9. For the past 6 months, what percent of the available facility time is the SAIR-supported equipment being used? Is this more or less than before the last 6 months?
10. What role does the SAIR play at your institution relative to other funding sources for small animal imaging research infrastructure?
    a. Are other major equipment grants being used to support the small animal imaging research facility (NCRR S10, NCRR P41)?
        i. If yes, is there a distinct role played by the SAIR funding? Do the funding streams support different people/activities/equipment/research, or are the funds largely commingled?
11. Do you think the small animal imaging-related physical infrastructure at your institution is adequate to meet the needs of the affiliated imaging researchers?
    a. If additional funds were available for physical infrastructure, what would you do with them?

Broader Community-Building

12. Approximately what percentage of the small animal imaging researchers at your institution have used the SAIR in the last year? Approximately what percentage of cancer researchers?
13. How many non-cancer researchers have used the SAIR in the last year?
14. Overall, has there been an increase in the use of small animal imaging in cancer research at your institution since the SAIR began?
    a. To what extent do you believe any increases are attributable to SAIR funding (as opposed to other funding sources or simply the evolution/diffusion of the technology)? Why or why not?
    b. Are there aspects of the SAIR program that you think have been particularly important in this regard?
    c. Can you list any new NIH grants that have been generated as a result of having the Small Animal Imaging facility at your institution?
        i. Can you indicate which of these grants are new, and which are extensions of already existing grants?
    d. In your opinion, did any extant funding or infrastructure that your institution had prior to SAIR help you to obtain SAIR funding?

Research and Collaboration

15. What important research discoveries related to technologies/techniques/approaches to small animal imaging have been made with SAIR support?
    a. Why do you think discoveries are important?
    b. PROBES:
        i. Were you on any of the projects you just mentioned? Which researchers/projects contributed to those results?
        ii. If collaborations were involved, had you/the collaborators worked together before the SAIR award? Do you think the SAIR enhanced the collaboration?
        iii. Did the research rely on physical infrastructure funded through the SAIR?

iv. Did the SAIR contribute in any other way?

16. What important cancer research discoveries have been made with SAIR support?
    a. PROBES:
        i. Which researchers/projects contributed to those results?
        ii. If collaborations were involved, had the collaborators worked together before the SAIR award? Do you think the SAIR enhanced the collaboration?
        iii. Did the research rely on physical infrastructure funded through the SAIR?
        iv. Did the SAIR contribute in any other way?
17. Have any SAIR research findings or outputs impacted translational research/clinical trials?
    a. If yes, please describe.
    b. Do you anticipate this happening in the future?

Training and Career Development

18. Does the SAIR offer formal training courses (for SAIR institution personnel, outside personnel) in small animal imaging techniques/science?
    a. If yes, please describe
19. Does the SAIR offer informal learning opportunities (e.g., for an individual to spend several days in the laboratory learning imaging protocols and techniques from SAIR-funded investigators)?
    a. If yes, please describe
20. Are there other training opportunities provided at your SAIR?
    a. To graduate students/postdocs?
    b. To investigators?
21. Are there any other sources of support for small animal imaging training at your institution?
    a. If yes, are the same students or fellows typically supported by multiple sources?
    b. Is SAIR training distinct from other types of training?
22. Do you believe that access to the infrastructure that SAIR provides has played a role in attracting faculty members to your institution? Do you feel that SAIR has been pivotal in attracting and hiring faculty?

Summary and Conclusion

23. What has been the influence of changing the program from awarding funds using an R24 grant mechanism to a U24 cooperative agreement approach?
    a. Has there been a change in your interactions with NCI staff?
    b. Has there been a change in your interactions with other SAIRs?
24. Are there any changes you would like to see made to the SAIR program? What are they?
25. Do you have any suggestions for NCI?
26. Is there anything else we haven't asked that you'd like to tell us about your SAIR or the SAIR program?
27. May we contact you later if we need clarification or further information?

Cohort 1-3 PIs Whose Awards Had Concluded

Planning, Management, and Organization

1. What were the goals of your SAIR award?
    a. PROBE: Developing new research techniques in small animal imaging? Provide infrastructure support to the small animal imaging community?
    b. Did the goals changed or evolved over time?
2. Of the total usage of the SAIR, can you estimate approximately what fraction was general usage of the infrastructure by other PIs (i.e. support for standard R01 grants, etc.), and what fraction is being used to improve tools and techniques (i.e. improving throughput of equipment, better contrast agents, etc.)?
    a. How did researchers at your institution come to use the SAIR facility?
3. Was there outreach (historical or ongoing) to the balance of the cancer research community at your institution? To other departments/researchers?
    a. [IF ANY] Describe this outreach. What are the mechanisms? Are there formal public announcements or do you simply contact colleagues you know might be interested?
4. Are there other locations at your institution where researchers can use the same equipment housed in your SAIR core (i.e. are there duplicate pieces of equipment on campus that are equivalent?). If so, what equipment is that?
5. Did researchers from other institutions use the SAIR facility? If so, how do they come to do so?

Physical Infrastructure

6. What is the name of the organizational entity where the SAIR is housed?
7. Please describe in general how SAIR funding was used to **purchase** small animal imaging equipment.
    a. Which pieces of large-scale instrumentation were purchased (in whole or in part) using SAIR funds – and why those particular ones?
8. Did your institution make investments in instrumentation during the period of the SAIR award and afterward?
9. Please describe in general how SAIR funding was used to **support** small animal imaging equipment.
    a. Which pieces of instrumentation were being staffed (part-time/full-time) using SAIR funds?
    b. Were any pieces of instrumentation open-access to researchers?
    c. Was there technical support staff available to researchers who use the facility to interpret their data?
10. Please describe how support for small animal imaging equipment is being supported currently.
    a. Are other major equipment grants being used to support the small animal imaging research facility (NCRR S10, NCRR P41)?
11. Who used the SAIR facility? How many researchers were:
    a. Faculty members/PIs
    b. Graduate students or postdocs

    c. Staff scientists
    d. Other users
12. Has the usage of small animal imaging equipment changed since SAIR funding for the facility ended?
13. Do you think the small animal imaging-related physical infrastructure at your institution is adequate to meet the needs of the affiliated imaging researchers? Has the conclusion of SAIR funding changed the facility's ability to meet users' needs?
14. If additional funds were available for physical infrastructure, what would you do with them?

Broader Community-Building

15. Approximately what percentage of the small animal imaging researchers at your institution have used the small animal imaging equipment in the last year? Approximately what percentage of cancer researchers?
    a. Has this percentage changed since the conclusion of SAIR funding?
16. Overall, was there an increase in the use of small animal imaging in cancer research at your institution since the SAIR began?
17. Can you list any new NIH grants that were generated as a result of having the Small Animal Imaging facility at your institution?
    a. Can you indicate which of these grants are new, and which are extensions of already existing grants?
18. In your opinion, did any extant funding or infrastructure that your institution had prior to SAIR help you to obtain SAIR funding?

Research and Collaboration

19. What important research discoveries related to technologies/techniques/approaches to small animal imaging have been made with SAIR support?
    a. Why do you think discoveries are important?
    b. PROBES:
        i. Were you on any of the projects you just mentioned? Which researchers/projects contributed to those results?
        ii. If collaborations were involved, had you/the collaborators worked together before the SAIR award? Do you think the SAIR enhanced the collaboration?
        iii. Did the research rely on physical infrastructure funded through the SAIR?
        iv. Did the SAIR contribute in any other way?
20. What important cancer research discoveries have been made with SAIR support?
    a. PROBES:
    b. Which researchers/projects contributed to those results?
    c. If collaborations were involved, had the collaborators worked together before the SAIR award? Do you think the SAIR enhanced the collaboration?
    d. Did the research rely on physical infrastructure funded through the SAIR?
    e. Did the SAIR contribute in any other way?

21. Have any SAIR research findings or outputs impacted translational research/clinical trials?
    a. If yes, please describe.
    b. Do you anticipate this happening in the future?

Training and Career Development

22. Did the SAIR offer formal training courses (for SAIR institution personnel, outside personnel) in small animal imaging techniques/science?
    a. If yes, please describe
23. Did the SAIR offer informal learning opportunities (e.g., for an individual to spend several days in the laboratory learning imaging protocols and techniques from SAIR-funded investigators)?
    a. If yes, please describe
24. Were there other training opportunities provided at your SAIR?
    a. To graduate students/postdocs?
    b. To investigators?
25. Are there any other sources of support for small animal imaging training at your institution that are currently being used to support small animal imaging training now that the SAIR award has concluded?
26. Do you believe that access to the infrastructure that SAIR provided played a role in attracting faculty members to your institution? Do you feel that SAIR was pivotal in attracting and hiring faculty?

Summary and Conclusion

27. Are there any changes you would like to see made to the SAIR program? What are they?
28. Do you have any suggestions for NCI?
29. Is there anything else we haven't asked that you'd like to tell us about your SAIR or the SAIR program?
30. May we contact you later if we need clarification or further information?

New Cohort 4 PIs

Context

1. To what extent is small animal imaging already commonly used by investigators?
    a. Where are there opportunities for expanding the use of imaging?
    b. If so, will SAIR help to exploit these opportunities?
2. Are you planning on outreach to researchers at your institution to use the SAIR facility?
    a. Are you planning on outreach (historical or ongoing) to the balance of the cancer research community at your institution? To other departments/researchers?
    b. Are there non-cancer researchers who are planning on using (or already using the SAIR)?

Physical Infrastructure

Now that you have received the SAIR award:

1. Are you planning to purchase any equipment using your SAIR award? If yes, please describe what equipment and why?
2. Who/what skills are you looking to hire?
3. What are your plans for small animal imaging research? In which modalities will you be concentrating and why?
4. Are there other major equipment grants at your institution being used to support small animal imaging equipment (NCRR S10, NCRR P41)? Where will the SAIR Core Facility be located?
5. If so, will there be a distinct role played by the SAIR funding? Will the SAIR funding stream support different people/activities/equipment/research, or will the funds be largely commingled?
6. Do you think the small animal imaging-related physical infrastructure at your institution is adequate to meet the needs of the affiliated imaging researchers?
7. If additional funds were available for physical infrastructure, what would you do with them?

Training and Career Development

8. Will the SAIR offer formal <u>training courses</u> (for SAIR institution personnel, outside personnel) in small animal imaging techniques/science?
9. If yes, please describe
10. Will the SAIR offer <u>informal learning opportunities</u> (e.g., for an individual to spend several days in the laboratory learning imaging protocols and techniques from SAIR-funded investigators)?
    a. If yes, please describe
11. Will there be other training opportunities provided at your SAIR, if so, what kind?
    a. To graduate students/postdocs?
    b. To investigators?
12. Are there any other sources of support for <u>small animal imaging training</u> at your institution?

a. If yes, are the same students or fellows typically supported by multiple sources?
b. Is SAIR training distinct from other types of training?

Summary and Conclusion

13. If an institution has a Mouse Models Consortium award: Do any pre-existing collaborations exist between the SAIR key personnel and participants in the Mouse Models Consortium award at your institution?
    a. Are you planning on forging new collaborations? If so, describe.
    b. Are you planning on working with other MMHCC sites?
14. Are there any changes you would like to see made to the SAIR program? Do you have any suggestions for NCI?
15. Is there anything else we haven't asked that you'd like to tell us about your SAIR or the SAIR program?

Cancer Center Leadership

Research themes

1. How was the set of CC research themes decided upon?
    a. If there is an imaging-related theme [we know which have them], when was it created?
2. How are pilot projects awarded?
    a. Is there a specific pool for pilot projects set aside for basic research?
    b. If yes, what kinds of projects have been recently funded? Any small animal imaging-related?

CCSG support for the small animal imaging facility:

3. When did the facility first become a CCSG core [true at all of the Cancer Centers at SAIR institutions except for MGH]?
    a. How was the decision made?
4. Is there any advertising of the existence of the facility that is done by the Cancer Center itself?

Use of animal imaging by basic researchers

5. Can you estimate approximately what fraction of CC investigators are using small animal imaging in their research?
6. Did the existence of the SAIR facility make investigators more likely to use imaging as a research tool – or was the technology naturally evolving in that direction?