

CIMIT: A Prototype Structure for Accelerating the Clinical Impact of Research on Novel Technologies

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Introduction

CIMIT is a center with a unique structure designed to connect technologists with clinicians in a proactive, deliberate, methodical manner. The goal at its founding was to accelerate the development of cost-effective technological solutions to pressing clinical problems. The premises were straightforward:

- 1) There have been huge advances in the technologies serving consumer markets, manufacturing industries, and national-defense needs. Yet the migration of those technologies toward the service of healthcare needs is slow – stymied by the difficulties of collaboration between those who know the clinical issues well and those who know available technologies well.
- 2) The most beneficial impact is derived when biomedical applications of modern technology are driven by clinical needs, not by “technology push” – and thus fit into the context of clinical practice and meet the demands of patients’ and clinician’s daily lives.
- 3) A given clinician or technologist with a potential paradigm-changing concept typically does not possess the skills or the resources to surmount all the obstacles of moving from bench to bedside, ultimate dissemination, and commercialization. Thus too many promising concepts wither from lack of experience with the requisite tasks of the full translational-research process

The basic conviction, in its founding, was that progress could be greatly accelerated by design and implementation of an organized, staffed, Facilitative structure. That structure was intended to provide support, mentoring, convening and problem-solving consultative service to innovative clinicians and technologists, as well as to serve as a virtual incubator for the most promising of their projects. No central laboratories would be created. Work would be done in the laboratories of chosen project leaders. A related belief was that close collaborations across disciplinary boundaries would be the key to success.

With this philosophy, CIMIT was developed and launched in 1997, with a consortium of major Boston institutions as founding members³. The mission was and remains simply to impact healthcare in a positive and cost-effective manner, drawing on the astounding developments in technology in the worlds of consumer products, industrial laboratories, and defense industries.

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³ Massachusetts General Hospital (MGH), Brigham and Women’s Hospital (BWH), Massachusetts Institute of Technology (MIT), Partners Healthcare System, and Draper National Laboratory were the founding institutions. Current membership includes additional Boston-based institutions as formal affiliates: BIDMC, Children’s Hospital, Boston University Medical Center, Boston University, Newton-Wellesley Hospital, and Harvard Medical School. Substantial financial investment was required and has been sustained for this ten-year period. MGH made the initial investment, with subsequent support from them as well as Partners Healthcare System. In addition all member institutions committed to cost sharing on all subcontracted awards from the outset, and, in recent years, have each contributed substantial annual support to the central operations expenses of CIMIT. Primary sustained Federal Support for CIMIT’s science and technology projects has come from the DoD via peer reviewed funding from TATRC (DAMD17-99-2-9001, DAMD17-02-2-0006, and W81XWH-07-2-0011). Individual philanthropy has met CIMIT’s remaining needs.

At the ten-year point, it is appropriate to report on CIMIT's progress and to describe its methodology in some detail. We have reached the point where its basic methodology is, in fact, being emulated in a major way by other institutions in the form of an international affiliate, MIMIT (Manchester: Integrating Medicine and Innovative Technology).⁴ Thus we have an existence proof that its methodology is both attractive and reproducible.

From this decade of experience we have reached three specific conclusions:

- 1) We believe and submit that CIMIT's structure has unique core elements that are worthy of adoption, for incorporation into existing translational-research centers elsewhere or for new structures such as MIMIT. For evidence we will offer CIMIT website citations which represent success stories – biomedical technology accomplishments by investigators who are firmly convinced that CIMIT's Facilitation was essential to their bench-to-bedside progress.
- 2) We do not believe that the CIMIT structure can or should be duplicated elsewhere in its exact form. Context is everything – local resources, institutional cultures, and the most workable collaborative governance model.
- 3) It is not possible to conduct some sort of controlled sociologic experiment to prove that the CIMIT structure is better than others with similar aims. There are simply too many variables in context, history and local strengths and weaknesses to permit a plausible quantitative comparison.

Readers can draw their own conclusions as to which elements of the CIMIT story are compelling and deserve emulation. It took the management judgment of MIMIT's leadership to embark on their launch, commit major resources, and adopt elements of CIMIT's methodology, without quantitative proof of efficacy. There is a paucity of self-analysis and reporting in this area, despite the mantra of translational research. If this report can, at a minimum, stimulate other translational or facilitative groups to do the same, it will have served a useful purpose. Together we can perhaps stretch the boundaries of the national conversation about enhancing translational research.

⁴ See <http://www.mimit.org.uk>.

Challenges to be Addressed:

Based on long and frustrating personal experience in bringing technologies from concept to ultimate clinical application, the members of an MGH Strategic Planning Taskforce, co-chaired by the authors of this report, had reached a conclusion in the early 1990's that inherent persistent obstacles should be bluntly articulated, and then an appropriate activist structure should be created to address these obstacles and thus increase the probability of success for innovative investigators. Specifically seven major challenges to collaborative multi-disciplinary engineering-biomedical collaboration and, by implication, to translational research, were articulated:

- 1) Peer-review funding processes had devolved to low-risk profiles, leaving early-stage ideas starving for support for proof-of-concept. Thus the first challenge was to develop new locally informed mechanisms for funding promising early-stage work and talented neophyte innovators.
- 2) Even when early-stage, higher-risk funding was available, new concepts often ended at the publication stage, satisfying the academic imperative. Yet publications are not an adequate means to assure adoption, dissemination and implementation of effective new paradigm-shifting technologies and practices. The consequent challenge was to develop effective follow-up mechanisms beyond pilot grants, to increase the probability of ultimate impact.
- 3) Multi-disciplinary and interdisciplinary collaborative work was not, and still is not, adequately rewarded by traditional granting mechanisms and academic promotion processes. Review mechanisms are not well matched to the nature of such work. Efforts to overcome or bypass that inherent bias were needed.
- 4) Industry was too often regarded as simply a commercial outlet for licensed technologies. To the contrary, industry should be regarded as a strong potential contributing collaborator to technology development from the earliest possible moment in the innovative process, if effective technology transfer is to be expected, and if the latest of proprietary technologies are to be exploited in clever ways. Assistance was seen as necessary for investigators to find productive collaborations with appropriate industry colleagues.
- 5) Implementation, in the form of prototypes or even of full clinical-service paradigms, required skills disjoint from those of typical clinicians, technologists, or biomedical researchers. Here again, collaboration amongst innovative clinicians and creative technologists, brokered by skilled Facilitative multi-disciplinary professionals, was seen as the need and the opportunity.
- 6) Navigating regulatory-approval and reimbursement pathways required collaboration of yet another set of professionals, and a structured approach was needed to connect innovators with the needed help.
- 7) Lastly, a more subtle but critically important challenge was identified: if a clinician or clinically involved technologist demonstrated a truly innovative personal character and developed a strikingly innovative concept, the most effective pathway to further development typically required that individual to literally leave their stimulating clinical environment and move in whole or in part to industry. Usually, when that happened, the institution and society were not well served in the larger sense. In effect such an individual was uprooted, and further innovation was stifled. Thus the challenge was to make it easier for such a person to become a "serial innovator", still grounded in their clinical environment, but appropriately connected with relevant competent technologic and entrepreneurial collaborators to effect the successful transfer of technology.
- 8) A related challenge, constantly cited locally and nationally, was that of remedying the tensions of perceived or real conflict of interest, versus the understandable desire of inventive personalities to share in economic value generated.

CIMIT's Structural Response:

A key element of CIMIT's designed methodology was to fund very early high-risk high-payoff ideas, without even requiring pilot data from applicant teams. However, beyond that simple basis, CIMIT invested heavily in building a powerful, dedicated Facilitative infrastructure. The fundamental concept was to staff such a structure with highly experienced individuals from multiple disciplines and multiple backgrounds, each of whom had decades of experience in bringing technological ideas of clinical importance to full fruition. These would be individuals who, in their own work, had proven the ability to overcome all obstacles to success and to transcend the legendary "valley of death"⁵. Staff with these characteristics and track record were successfully recruited over the first few years of CIMIT's existence, and many have stayed with the Center throughout, sharing a passion for its role.⁶ Those who left did so for outstanding opportunities in industry and academe, and credit their experience with CIMIT as factors in their own career success stories in managing multidisciplinary research and development programs.⁷

In providing pilot funding, CIMIT's intention was to use the wisdom of these central staff members to allocate all awards. External reviewers could be used for assessment of scientific and technical issues, but the fundamental decisions of whether there was an opportunity in a proposed idea would be made by the staff, functioning in a "management" mode and as a team, rather than in a conventional risk-averse, peer-review mode. Most importantly, all awards would involve intense follow-up, to assure that appropriate expectations were set and met, and that the central staff offered Facilitation at key moments of need. It was recognized from the outset that investing in the right people might be more important than the merits of a specific project proposal put forth

A key decision, alluded to above, was to focus on biomedical devices and technology – not only because of the shortage of NIH funding in that domain, but also because the timeline from raw idea to first-in-human use could be astoundingly short, allowing CIMIT to make dramatic impact in a few years, thus demonstrating its utility and offering the hope of justifying sustaining funding from various sources – and even potentially from royalty income or equity redemptions.

The reader may recognize that these elements are not dissimilar from activist early-stage venture-capital funding in the for-profit world. Yet, beyond these basic elements, there were many other structural competencies built into CIMIT that were intended to fit the context of the academic non-profit research world. In a sense, CIMIT is an adaptation of proven business investment techniques to the more subtle and complex world of academic researchers and clinicians. Those additional features will become clear in the description of CIMIT's core staff functions.

Some tactics were driven more by practical constraints than by philosophy. For example, CIMIT is resource-limited to granting only modest seed funding to promising projects. In addition, the nature and year-to-year uncertainty of CIMIT's external grant and philanthropic funding limits it to committing funding to projects for only one year at a time. In addition, CIMIT would not support, with its funds or intellectual resources, those ideas or projects, which could be funded or supported elsewhere. However, the central staff members continue to "Facilitate" the most promising of these projects for many years after seed funding. ("Facilitate" is a verb used constantly within CIMIT, and thus we shall capitalize it, for emphasis, in this report.) Facilitation includes helping investigators find follow-on funding from other sources if there is

⁵ D. Butler, Translational Research: Crossing the Valley of Death. *Nature*, 2008; 453, p 840-842.

⁶ The work described here as well as the individual innovations represent the talent and dedication of dozens of members of the growing CIMIT community. Without attempting a comprehensive list of individuals deserving acknowledgement, the authors wish to especially highlight the veteran senior staff involved in most or all of this ten-year effort and who remain with us today: Thomas Brady, Janice Crosby, Steve Dawson, Keith Isaacson, Colleen Kigin, David Rattner, and Kirby Vosburgh.

⁷ Donald Baim, Scott Gazelle, Jim Muller, Steven Oesterle, Jonathan Rosen, and John Smith

a clear outcome in view. In some cases, Facilitation alone, without any seed funding, has proven sufficient to enable success. Data on the yield in catalyzing follow-on funding are offered in Table A, entitled “Enabled Funding”.

At this point, CIMIT has provided seed funding for over 450 projects over its ten years, an average of 50 new ones each year, and is Facilitating an average of 150 at any given time, either prior to, during, or after the one year of seed funding. See [Funded Projects](#) on cimit.org for a representative sample from the full historical list.

In summary, CIMIT was designed to be, in business terms, an “activist investor”, yet one that can function comfortably in an academic culture. It does this by being “both a catalyst and a fuel source”, in the words of one of its supporters. It finds projects of promise. It funds high-risk, high-payoff projects and individuals with promise. It then Facilitates the progress of those individuals and projects as far as is justified by results. All three functions require core competencies and processes within the central staff of CIMIT. These functions will be described in detail later in this report. In finding, funding and Facilitating, it connects creative people across the boundaries of traditional disciplines and established institutions.

Finding Innovative Concepts in need of Support:

CIMIT seeks multidisciplinary projects with collaborative teams behind them. Given the barriers between disciplines, it was clear from the outset that one of CIMIT’s activist activities would need to be convening and connecting individuals with complementary skills, who then would have a higher likelihood of epiphanies and would pursue them with a shared passion. This process of connecting individuals requires a major investment in a continuing program of convening events. Weekly forums are offered openly to all comers, with invitations disseminated through numerous email lists of our own and of our member institutions. The content of these two-hour seminars represent both clinical problems in need of technologic innovation as well as powerful technologies with potential yet undefined clinical application. These forums are also opportunities for presenting CIMIT success stories, highlighting role models, etc.

A major annual event pulling all stakeholders together is CIMIT’s Innovation Congress, open to all. A unique feature, in addition to the conventional format of poster and platform presentations, is a huge physical exhibit created afresh each year, with the help of CIMIT’s industry collaborators, which is organized entirely around the process of patient care. It can be thought of as a theme park in medical technology. The purpose is not to sell any company’s products, but to illustrate technologies’ future value in the actual context of patient-care areas, mocked up for the purpose of this Congress. It is designed to stimulate fresh thinking amongst attendees as to how and where they might contribute to more effective care in venues ranging from the home to the tertiary-care procedural suites.

The most personal form of searching for new players with new concepts involves individuals whom CIMIT dubs as “Site Miners”. These individuals, described in more detail in a later section, are respected individuals within the faculty of each member institution who seek out exciting opportunities and who offer easy access to information about CIMIT, what it can offer, and whether a nascent idea fits within its scope.

All of these outreach efforts, plus video downloads and news postings on the website (<http://www.cimit.org>), special-topic symposia, short courses, etc., are designed to attract potential applicants, connect them with each other and draw their attention to the specialized professional help that CIMIT can provide in a pathway to success. Ultimately funding is chemotactic, even in small amounts, so the RFA’s and funding formats described next are key to drawing innovators into the CIMIT community in an effective fashion.

Funding Mechanisms for Accelerating Innovation:

CIMIT is neither designed nor intended to sustain projects with funding through an extended period of years. It uses its limited funds by injecting them at key points of need where other sources are not available for an exciting concept and team, and when progress depends on a special and rapid injection of support. Several mechanisms have been developed with experience over these ten years. They are designed to capture the interest of innovators with ideas that do not fit conventional project-funding mechanisms of federal agencies. All are announced by CIMIT on its web site and by emailed and printed announcement of RFA's with periodic deadlines. The categories of awards at the present stage of CIMIT's evolution are shown in Table A.

It is important to note that prior to any of its formal review processes, CIMIT's staff invests great effort in seeking out innovative nascent concepts as well as potential contributors and collaborators. In addition the staff pre-screens inquiries so as to help potential applicants determine the potential fit of their ideas with CIMIT's mission. The goal is to minimize wasted effort and disappointment in writing proposals destined for rejection, while also encouraging applications from those who might not have realized their actual likelihood of success. (The scope of these interactions, both pre and post-award, will become clearer in later sections of this report.)

Facilitating Success of Projects:

Facilitation simply means providing a project or project leader with the right help at the right time in the right place. That makes it a highly personal process. It requires, to use a medical analogy, a customized care plan. That may mean:

- Connecting project leaders with individuals or teams that need complementary skills. These may be people who never would have met under normal circumstances. Good applications for funding arise from these connections.
- Bringing in appropriate industrial resources, technologies, or prototyping skills at whatever stage they are needed.
- Funding prototype development to prove a concept or to allow animal or human studies. Such prototypes clearly add value and plausibility to any ultimate licensing efforts.
- Guiding and supporting project leaders through the challenges of obtaining needed regulatory approvals and protection of any IP for subsequent licensing.
- Helping with obtaining needed follow-on funding for needed work beyond the pilot stage, including potential philanthropy.
- Assisting with any needed business planning, reimbursement analysis, connections with licensees or investors, and other issues of actual launch of a given technology in healthcare.
- Assisting in solving administrative problems with IP management, contract negotiation, grants administration, regulatory compliance, etc.

After ten years of experience, CIMIT's leadership has come to a firm conviction that a major budget commitment is needed to provide effective Facilitative help. Thus approximately 30% of CIMIT's expenditures goes toward support of CIMIT's permanent Facilitative staff and their functions. After allocating 10% for administrative staff, CIMIT spends the remaining 60% on its seed-award and program funding to project investigators, on its other awards, and on its scientific-program leaders.

It can be a difficult task to explain and defend the substantial central-staff portion of this allocation when describing CIMIT's methodology to donors and funding sponsors. Facilitation of CIMIT's intense sort is not a familiar concept. It is too easy to misconstrue this expense as some sort of overhead for CIMIT's project-sponsorship, rather than as the skilled R&D management that it comprises. It can also be misunderstood as a substitute for conventional single-discipline mentoring. CIMIT's leadership makes no apologies for the expenditure. But they struggle to overcome these misconceptions, occasionally even within CIMIT's parent institutions. In contrast with this, CIMIT's expert external reviewers – who are scientific, medical and industrial leaders familiar with the challenges of multidisciplinary work -- have applauded this budget tactic as the signal characteristic most important to CIMIT's success with advancing projects and careers.

To illustrate the full meaning of "Facilitation", the figure at <http://www.cimit.org/services-facilitationdiagram.html> and the story at <http://www.cimit.org/about-stories-kneesurgery.html> depict the processes, events, timeline and interrelationships of CIMIT staff work with an investigator for one of our more intense, but not atypical, CIMIT-sponsored projects (physiologic ACL repair). The staffing described below evolved over time to meet the sorts of needs described here and specifically illustrated by the Figure.

This is obviously a complicated case-specific process. Yet it is essential to make access to the array of resources straightforward for the novice investigator. To lubricate that interface process, CIMIT tries to match a specific central staff member to each awardee or applicant deserving such attention, as a kind of personal account representative or case worker. The assigned contact person may be the staff member with an existing acquaintanceship from prior work, or a staff member with a particularly appropriate expertise. The workload per investigator is highly variable, depending on project, progress and obstacles envisioned or encountered. It may range from an email of introduction, with no follow-on effort needed, to a weekly investment of time and even further CIMIT funding to engage needed consultants or for prototype development. As specialized needs are identified, the representative makes the appropriate introductions. CIMIT has not yet found a reliable algorithm for predicting this effort level. The staff uses their judgment on a case-by-case basis, as the project evolves. Periodic reviews by central staff of the full portfolio of active projects are valuable in maintaining the key Facilitative relationships and identifying new opportunities for helpful intervention.

All of CIMIT's staff including its leadership are committed to spend a fraction of their time as CIMIT Contact Representatives. The percentage effort varies, of course, according to individual expertise and the match with the needs of the projects at hand. In general, however, this basic interface effort consumes at least 20% of every individual's time, applying their own skill and experience in one-on-one coaching, mentoring, and direct problem-solving, not only with project leaders or awardees, but also with potential applicants. In addition, of course, work is generated as other representatives call on each staff member as an expert for deeper assistance in filling a specific need. Indeed, the majority of each staff member's time is spent managing the core Facilitative service under their command. (These roles will be described in the next section.) In order to be effective at all of this, every CIMIT staff member not only needs to keep up in his or her own field of expertise, and to network in his or her own professional circle, but also to participate in team meetings and CIMIT convening events in order to spot the opportunities for useful intervention, as well as to be highly visible and accessible to potential applicants and current awardees.

There is a point in the life cycle of a project or relationship where CIMIT's help must wind down. It may come when a project hits a clear dead end. It may come when a competing technology obviates the idea. It may come because the investigator simply does not respond with alacrity to the challenges. The hope, however, is that it will come from successful hand-off to other champions. For example, CIMIT does not fund or manage wide clinical trials of a promising technology. If such trials are justified, the assumption is that clinical-trial funding can be obtained from an industry, foundation or federal sponsor. CIMIT's resources are too limited to fund work at that more expansive stage. The most dramatic of CIMIT's "launches" of this form is the OCT project, directed by Gary Terney, M.D., Ph.D. and Brett Bouma,

Ph.D., which has gone on to develop additional optical diagnostic technologies and attracted millions of dollars of direct external funding and even to license its technology to major industrial partners.⁸

In summary, Facilitation is very expensive, and that leads to a real challenge in defending CIMIT's balance of expenditures. It also requires judicious choices of the investment of time, since time is money. All of this leads next to the description of CIMIT's central staff.

CIMIT Staffing

CIMIT's central paid staff must have certain characteristics to be effective:

- Experience in working across boundaries, and the needed communication skill
- Successful track records of relevance to the tasks outlined here
- Readiness for the "give-back" self-less portion of their careers
- Generosity of spirit in fostering collaboration without requiring credit
- Passionate commitment to improving healthcare.

Specific primary roles for CIMIT staff have evolved and been refined in the course of these ten years, in order to best carry out the functions described in the opening paragraphs. Current staff, roles, and backgrounds are listed on the website at the link noted.⁹ Four of the more unconventional key roles will be described here in some detail:

Site Miners: The most unusual, inventive and productive of CIMIT's special roles has been that of "Site Miner".¹⁰ These individuals have proven to be the key to penetrating the multiple isolated member institutions, and connecting people and ideas across the cultural walls of these institutions and even across the boundaries separating departments within them. They literally "mine" the institutions for projects and people deserving CIMIT's attention and help. The characteristics of CIMIT site miners are as follows:

- Respected senior clinicians and/or scientists within the specific institution – well know to other faculty and well respected as mentors.
- Multi-disciplinary in their own training and work.
- Selected by a search group appointed by the CEO of the institution and the Director of CIMIT.
- Daring in their own career choices.
- Reporting to the CEO of the institution, and paid by that CEO.
- Knowledgeable in the politics and networks of their home institution.
- Still active in clinical or research work.
- Committed to at least 20% and preferably 40 to 50% effort as a funded site miner
- Willing participants in regular team meetings with all other site miners from all member institutions.
- Willing participants in periodic CIMIT leadership meetings.
- Attendees at other CIMIT convening events.

⁸ <http://www.cimit.org/programs-opticaldiagnostics.html>

⁹ <http://www.cimit.org/about-facilitationleaders.html>

¹⁰ <http://www.cimit.org/about-siteminers.html>

The core reason for the effectiveness of this site-miner role is perhaps not obvious. Involvement via a site miner avoids activating the natural institutional antibodies of an institution to the “invasion” of an external entity. Co-investment in the role creates a sense of shared ownership of success by the institution (and its CEO) together with CIMIT. Inherently, the site miners surface ideas and then advocate for them in the award process in a manner that assures more distributed CIMIT funding and Facilitation effort than would occur if driven only by an inbred central staff with a narrower network. They provide far greater visibility for the value of CIMIT within each member institution.

In addition, Site Miners serve as role models for interdisciplinary careers, and can advocate effectively within their own institutions for the career advancement (academic promotion) of interdisciplinary faculty who would otherwise fall into the cracks between departments and promotion committees. With experience, it has become clear that less than half-time involvement in CIMIT by site miners leads to rapidly diminishing effectiveness. It requires at least 20% effort to participate in the team meetings, weekly forum presentations, and other central activities. The remainder of funded time is invested within the site miner’s home institution interacting with potential and current project leaders and faculty.

Program Leaders¹¹: These eminent clinician scientists and technologists have distinction and expertise within a specific scientific domain, yet they do not function as managers of CIMIT-supported research. They serve a broader integrative role. Each is a scout assuring familiarity with the general flow of ideas and activities in a specific scientific or technical area in which a cluster of current projects fit. They either can judge viability and coach effectively, or they know the experts who can render third-party opinions as needed or who can be drawn into collaborations. The programs named by CIMIT thus evolve with time, as opportunities evolve and frontiers move. The current Programs within CIMIT are listed on the website¹², but these are reviewed annually and change. Each has a designated Program Leader.

It is important to note that CIMIT is open to proposed ideas that fall outside these Programs. In fact it is the emergence of a cluster of exciting unconventional proposals that can trigger the creation of a new Program and the search for an appropriately skilled new Program leader willing to commit time to CIMIT central. Conversely, it is the paucity of interesting new ideas that can lead CIMIT’s leadership to “sunset” a Program. An alternative reason for discontinuing a Program focus may be that the field has evolved to be so main-stream as to no longer justify investment of CIMIT’s limited resources and time. As an example, earlier CIMIT-supported work included major support of cardiovascular vulnerable-plaque detection technologies. That activity has a life of its own now, and independently acquired support. It no longer needs guidance from a CIMIT Program Leader. Concurrently, neurotechnology emerged to represent 20% of current effort, and a distinguished Program Leader was identified from one of the member institutions, and appointed to guide, integrate, and catalyze CIMIT-supported projects in that area.¹³

Clinical Systems Innovation Managers: CSI is a special fundable domain within CIMIT, as indicated earlier. CIMIT’s leadership appreciated early on that isolated technology innovations by themselves are not enough to trigger reform of a healthcare pathway or process. Multiple innovations, together with major administrative commitment and institutional operational resources are required to change care processes. The first such major effort of CIMIT’s was the “OR of the Future”, which has been described in great detail on the website.¹⁴ As exciting as the technology innovations within it are, and as inspiring as the process changes are to other facility designers and other institutions, the major advantage in CIMIT’s methodology has been the use of the ORF as a Learning Laboratory for the safe introduction and evaluation of new technologies from any source, before widespread adoption.

¹¹ <http://www.cimit.org/about-programleaders.html>

¹² <http://www.cimit.org/programs.html>

¹³ <http://www.cimit.org/programs-neurotechnology.html>

¹⁴ <http://www.cimit.org/programs-operatingroom.html>

Some promising commercial technologies have met a well-deserved demise in this highly instrumented test site by failing to meet expectations, while others have accumulated metrics of such promise as to support their launch as products of national interest. The host institution as well as the field at large reaps the value. Visitors to this site are constant, and CIMIT has found it necessary as well as valuable to organize formal short-courses in order to handle the demand without interfering excessively with ongoing daily clinical work. CIMIT has now gone on to use this concept of the Learning Laboratory for other inpatient and outpatient settings. CIMIT works with an Ambulatory Practice of the Future project, sponsored by MGH, an Emergency Department of the Future Project sponsored by Beth Israel Hospital, a Neonatal ICU of the Future sponsored by Children's Hospital, and others – all in the same spirit. Each of these projects obviously requires enormous administrative commitment, space, institutional capital funds, clinical leadership, and ongoing investment in metrics. Little of that would happen without the brokering efforts of CIMIT's senior CSI staff¹⁵, the seed funds of CIMIT for key individuals and fiducial projects, and the intense involvement of selected industrial collaborators from CIMIT's Industry Liaison Program (described below). Each is a story deserving separate telling elsewhere, but the general approach is highlighted via the ORF story as one of CIMIT's unique methodological accomplishments.

Projects and Grants Management: The administrative burdens of CIMIT's work go well beyond the frame of standard research administration. The volume of work required to manage the influx of pre-proposals and proposals, and to compulsively track awards and their compliance with sponsor and institutional policies, when dealing with a multiplicity of member institutions, is, in short, staggering. In a typical year there are 50 new awards with 50 fund set-ups and many of those are under sub-contract to our member institutions. And there are 150 active project funds at any given time that have not yet closed out. CIMIT's internal grants administration staff number just 3, and they work hand-in-hand with the central research administrations of the members in assuring compliance with both sponsors' requirements and institutions' policies. In addition, senior science leadership of CIMIT work with investigators on the countless questions and issues that arise of particular technical complexity, by nature of the translational effort. Even more importantly, the senior staff endeavor to make appropriate connections between and among applicants and experts, both pre and post-award.

Though this description is brief, the workload is unusual as well as intense, and requires unique breadth of skill in staffing. Relying on the academic institutions' research administrations would be insufficient Facilitation for these complicated relationships. All of this administrative work is supported by an internal CIMIT database, so that a full project record is maintained not only for current projects, but for the full 10-year history of CIMIT. This allows retrospective studies of success and failure, and derivation of lessons to guide future funding and Facilitation.

CIMIT Cores

Industry Liaison Program: CIMIT's successful functioning depends on respecting the expertise that industry and its technologists and scientists bring to the collaborative process. It does not simply look to industry for sponsored-research funding or for licensing intellectual property. That characteristic alone distinguishes CIMIT's methodology from that of most academic centers and laboratories. Given the range of projects that CIMIT sponsors and the corresponding breadth of needed technological input, CIMIT developed an Industry Liaison Program (ILP) of substantial size.¹⁶ At any given moment there are about 40 corporate members, ranging in size from start-ups to global corporations (see link for

¹⁵ <http://www.cimit.org/programs-clinicalsystems.html>

¹⁶ <http://www.cimit.org/services-industryliaison.html>

current list and their diversity ¹⁷). In addition, the database of former members and key industry contacts numbers in the hundreds.

Membership requires either payment of an annual fee to cover costs of maintaining liaison, or the in-kind contribution of technology, equipment, engineering time, etc., to support a CIMIT project or program. The elements of the ILP program involve a full-time staff of four, bridging the cultural and geographical barriers which normally inhibit collaboration, tracking developments in domains of interest to spot opportunities, helping with grant applications specific to industry collaborations such as those for SBIR or NIST support for small companies, generating newsletters, distributing invitations to events, coordinating meaningful participation in CIMIT's annual Innovation Congress (the dynamic hands-on meeting described earlier), and so on. The individuals in this group all have deep experience in industry prior to coming to CIMIT. The staff work as account executives, in effect, with each of the member companies, which range from two-person startups to major global-industry leaders. To be effective, the staff needs familiarity with the majority of CIMIT projects in active or past status, in order to spot opportunities for matchmaking. Actual licensing agreements are consummated by the technology licensing offices of the member institutions – but CIMIT's ILP staff support those efforts, keep them moving, and track down market opportunities.

This ILP activity is not designed to produce net income. It is seen as essential to maintaining communication and catalyzing needed collaborations. It is also a unique portal for small companies to enter the intimidating, even Byzantine, world of the academic medical centers at a neutral place which can form connections of validated merit. Larger companies have their own network of well chosen medical experts to accomplish that in their given product area, and their membership is thus valuable to CIMIT, but not amenable to a large fee. Smaller companies need CIMIT the most – they are frequently stymied or even misled by a given opinion leader they may encounter when approaching the academic world without wise unbiased guidance. Yet they are typically cash poor, and their most useful contributions to CIMIT are in-kind services.

One of the most striking and even surprising areas of success for CIMIT's ILP program has been its role as a conduit, even as a magnet, for much larger companies which have previously been operating totally outside the medical-device or healthcare domain, yet have technologies of great potential value to healthcare and wish to pursue applications. CIMIT has enjoyed brokering several success stories by engaging such companies in healthcare – companies that now have developed medical product lines that are cost-effective assets to the care process.¹⁸ These entrees represent huge new opportunities for those companies in a previously inaccessible major sector of the economy.

Eventually revenue can flow back to the member institutions from licensing arrangements with such companies from commercial success, but it is too early in CIMIT's lifetime for that to be a large revenue stream for its own renewal – given that all IP is owned by the member institutions (under Bayh-Dole assignment). Only in certain situations does CIMIT derive a portion of royalty income or equity-proceeds distributions through negotiated umbrella agreements with its member institutions, and CIMIT is moving away from even that small stake in order to eliminate any disincentive for institutions and their investigators to seek CIMIT help. The ILP staff work closely with the technology licensing offices of the member institutions, under the guidelines of the governance documents. CIMIT is actively seeking novel, more effective, yet conflict-free, mechanisms to share in economic value generated, with the purpose of diversifying its revenue sources.

Regulatory Affairs and Medical-Device Reimbursement Mechanisms: In its earlier days, CIMIT funded its own staff of technology-savvy regulatory experts and technology assessment and reimbursement experts. These individuals rapidly

¹⁷ <http://www.cimit.org/services-ilpcompanies.html>

¹⁸ E.g., <http://www.livedata.com>

gained in prominence and generated grant funded work of their own as well as filling an important consultative need for industry. Thus CIMIT restructured this function, and in effect outsourced it to those individuals in their evolving academic and private-practice roles.¹⁹ That suited the episodic and stochastic nature of the need in the most cost-effective manner for CIMIT. At this point several such individuals with science degrees, medical degrees, or law degrees, are on call for CIMIT on a contract basis.

Development Office: CIMIT quickly found the need to create (fund) its own development staff for several reasons.²⁰ To raise philanthropic support for CIMIT's central operations and award programs required a target audience which differed from that traditionally available to its stakeholder institutions. CIMIT's purposes are not disease specific and thus did not tent to appeal to grateful patients or to donors with disease-specific passion. Its funding needs are for a "process" – which is a subtle thing to explain and for which to solicit support. Special relationships with foundations and unique donors required special cultivation. Beyond that, CIMIT needed a development staff to be able to offer help to its project leaders for their efforts in seeking follow-on funding for projects after the initial modest seed support from CIMIT. And in this role, CIMIT has several notable success stories which justify the premise. It should be noted that other CIMIT staff are pulled into these efforts depending on their networks – particularly in seeking government support. Two such programs which now functions almost entirely with external support, garnered with CIMIT help, are its simulation programs and its "Plug and Play" interoperability initiative.²¹

Communications Staff: Given the many outreach efforts described in this report, it has also proven essential to have a full-time dedicated staff (three FTE's) for CIMIT's communication needs, for "marketing" its forums and symposia, and for assisting investigators and project leaders in getting appropriate press attention for their success.²²

Technology Implementation: A myriad of skills are required to launch a program into the commercial domain. To lead and coordinate those efforts and to work with the dozens of project leaders, CIMIT supports a staff of two FTE's solely for this purpose.²³ Their background is in business, consulting and science. They know the business world and how to analyze the commercial prospects of a promising project and present it to the appropriate audience with the correct terminology and analytic rigor. In addition, they work with the ILP staff to prepare or buttress SBIR applications for those small businesses that have interest in and passion for a CIMIT project approaching launch. The TI staff speak the language of senior executives in industry and understand how to align incentives and structure deals.

Measuring Impact:

To achieve widespread adoption of the best ideas, evaluation of projects and proof of efficacy is needed, even though CIMIT cannot afford to fund clinical trials per se. CIMIT's staff can, however, help bring a business mind-set to such evaluations once projects approach human use or achieve first-in-human status, and can even involve payers in the process. If it can be compellingly predicted that care can be improved at lower cost, then there will be a case for wide adoption and CIMIT will have achieved its mission.

¹⁹ <http://www.cimit.org/services-regulatoryaffairs.html>

²⁰ <http://www.cimit.org/services-fundingfacilitation.html>

²¹ <http://www.cimit.org/programs-simulation.html> and <http://www.cimit.org/programs-mdplugandplay.html>

²² <http://www.cimit.org/services-marketing.html>

²³ <http://www.cimit.org/services-technologyimplementation.html>

CIMIT is embarking on yet a deeper retrospective analysis of impact, with the goal of better understanding the extent to which it might have invested its limited resources (seed funds and Facilitation time) even more frugally, with even greater impact. The results of that study will be published in due course, upon completion of the work. Given the enormous variety of cases, it will be more of an anthropological study than a statistical one, and the analysis methods will draw more on the techniques of business-school case-study methodology than on scientific analysis.

Reproducibility

CIMIT has been visited by more than two dozen institutions with interest in replicating its structure and methodology in different locales. As a result of the extensive discussions held with expert visiting delegations, and from our experience in working with the creation of MIMIT, the necessary ingredients for creating a similar Center are becoming clearer:

- Commitment by a major opinion-leading institution, with significant and sustained funding to allow recruitment of central staff, and support until some self-sustaining resources are developed.
- Leadership, in the form of locally, if not nationally, respected individuals, with deep interdisciplinary skills as well as strong administrative ability, and with the willingness to make a nearly full-time career commitment to such an endeavor.
- Critical mass of research activity in a variety of disciplines within a small geographic area, as a substrate, given that intense interdisciplinary collaboration is much more of a “contact sport” than is collaboration within a single well defined scientific discipline.
- Agreement by member institutions to share any proceeds from licensing of IP or from enabled commercialization, so as to begin to provide an ongoing form of support for the central structure.
- Institutional commitment to the longevity of the structure, so that philanthropy can be successfully cultivated and top-notch staff can be recruited and retained.

The experience of CIMIT as to the intensity of personal interaction required to Facilitate success strongly suggests that a single structure cannot serve multiple cities effectively. The proximity of member institutions within Boston is clearly one of the assets to CIMIT’s success, in that an enormous grant volume and a large variety of disciplinary expertise exist literally within a 10-minute radius from the offices of CIMIT’s central Facilitation staff.

If other CIMIT-like structures can be created in other cities, as was accomplished with MIMIT²⁴, one can foresee a national or international community developing, comprised of these. Best practices could be shared and connections could be forged that would bridge between disparate geographic areas, not just disparate disciplines.

Sustainability

The question of financial sustainability is central. Philanthropy is an appealing answer, glibly described, but frustratingly difficult to achieve. The challenge is to attract endowment funds for a catalytic process that does not have a specific single-disease focus. Funding for specific projects, once defined and established, is not so difficult, but funding for the seemingly abstract activities of Facilitation is extremely elusive. Fortunately the Department of Defense saw, early on, and has continued to see great value in CIMIT’s work because the results in this domain of medical technologies have clear dual-use value. This has led to continued DoD support for 10 years, without which CIMIT would not have reached

²⁴ <http://www.mimit.org.uk>

this stage. However that funding mechanism is neither generalizable, nor is it sustainable even for CIMIT for the indefinite future. Increasingly CIMIT's member institutions have supported their proportionate share of the central facilitation expense of CIMIT in recognition of its value to their individual and collective success

Long-term sustainability will depend on continued support from its member institutions, and perhaps on greater return on the value added by CIMIT's involvement in economically successful projects and even in spin-off companies. The relative neutrality of CIMIT, as not being a direct care-giver in the healthcare system, can defuse the conflict-of-interest perceptions that member institutions face when contemplating taking equity in companies developing new technologies.

Home institutions in a CIMIT-like structure should see investment in such a structure as part of the cost of doing business in biomedical research, of propagating effective technologies, and of providing leading-edge cost-effective clinical care, if their goal is more than just academic publication, per se. Indeed, CIMIT receives its critical core staff support, based on this investment logic, from all of its members. In contrast to CIMIT's unique success with DoD grants, this local funding mechanism is, indeed, generalizable. And it is just such a commitment that made the launch of MIMIT possible.

Ultimately, however, support in the form of meaningful unrestricted amounts for amplifying or duplicating the CIMIT mechanisms can only be envisioned from federal or major-foundation sources.

Applicability to other Research Domains

The question often comes up: can a CIMIT-like structure work outside of the domain of medical devices, e.g., drug development? The answer may be positive, yet it has not been possible to demonstrate that. Given the much longer timeline between concept and result in the drug-discovery process, doubt is justified. Furthermore, there is such a large, established and expensive pipeline process in drug discovery that the incremental effect of any academic center's Facilitative efforts would be greatly diluted and harder to measure. Certainly activist foundations such as Faster Cure²⁵ aim to accelerate progress in understanding the mechanisms of disease more quickly and to develop preventive or curative drugs more rapidly. Their methodologies share some of the same elements discussed in this article, such as convening experts from multiple disciplines and managing the actual R&D work. Other CIMIT methodologies are rarely if ever seen elsewhere, such as the coaching and mentoring of researchers at early-stage work by a core senior staff, the use of site miners, the tight collaborative integration with industry, and the ability to help analyze and overcome business and regulatory obstacles to introduction.

Given the enormous investment in basic "curiosity-driven" research for the advancement of basic biomedical understanding, it would seem that any activity with the potential for such acceleration is worth a comparatively minuscule investment, even if demonstration of optimal efficacy is difficult and slow. However, the leadership and stakeholders in CIMIT, after a decade of Sisyphean effort to diversify its funding sources, reluctantly accept the reality that CIMIT must stay focused on technology and devices, the domain with the shortest timeline, in order to achieve sustainability. Some sustained support can then come from revenue on licensed IP from new products and services, and from institutional, foundation and federal support based on a demonstrated track record within that comparatively short timeframe.

Conclusions:

²⁵ <http://www.fastercures.org>

The question of establishing more such catalytic and managerial structures ultimately becomes one for funding agencies and foundations. For a hypothetical, if the NIH or even a major foundation were, out of frustration with limited yield from its translational-research efforts, to invest ¼ of 1% of its total budget in supporting the continuance or establishment of CIMIT-like structures, that would be sufficient to fund a dozen such structures in appropriate locations around the country – geographic areas that have the necessary critical mass of academic and industrial activity. That would likely accelerate and Facilitate impact of those funded projects and programs seen as most relevant to the NIH Roadmap initiative²⁶, at least those with technological and/or device components to their work. It would seem that at least a modest experiment, bigger than a single CIMIT, is justified by the basic logic of the functions described here, as well as by the encouraging results of CIMIT's relatively brief history.

²⁶ <http://nihroadmap.nih.gov>

Table A: Funding Mechanisms

CIMIT's formal review and award mechanisms have evolved over the years into a simplified two-step process to allow easy submission of raw ideas and easy triage of those applications which are or are not a fit to CIMIT's mission. The first step is a two-page pre-proposal, sufficient to allow winnowing the volume of applicants by approximately half. With quick "turn-around" time, the authors of the most intriguing half of the applications are then asked for a fuller 10-page proposal, without elaborate accessory materials, and these are carefully reviewed in an intensive round-table process. Current categories are as follows (N.B.: not all of these grant mechanisms are currently utilized. A current list is given at the link in the footnote ²⁷):

- New-Concept Awards (NCA's): Most situations that come to CIMIT's attention have early-stage needs for support of proof-of-concept for an idea judged promising by CIMIT's internal review process. These awards are offered in three sizes, called, for simplicity, small, medium or large, i.e., \$25,000, \$50,000 or \$100,000 maximum. All are for one year's duration, but with no-cost extensions allowed. Indirect costs are provided to the applicants' institutions, on top of these direct-cost amounts, but at a reduced rate with the requirement of institutional cost sharing.
- Working Group Awards (WGA's): experience has shown that occasionally the most pressing need for funding is at an even earlier stage, i.e., to gather a multidisciplinary group together to focus on a vaguely defined clinical need and characterize that need with sufficient specificity and cleverness to allow clinicians and technologists to attack it most effectively. CIMIT addresses these emergent opportunities with so-called Working Group awards of up to \$25,000, to cover such expenses as travel to other sites, focus-group expense, staff support for meetings, etc., to catalyze a group's formation and support its work.
- Career Development Awards (CDA's): After several years of experience with the intimate and intense executive process used for review of new-concept applications, it became clear that some individual applicants had a perfect profile for an application-oriented multidisciplinary career, if only they had a bit of support and encouragement to step out of the traditional research-career path, however they did not yet have a well formed project articulated in their application. Thus CIMIT created CDA awards. These have been life changing for many recipients despite their modest size of \$50,000 maximum for one year of salary support, plus funds for fringe-benefit cost. Here again, indirect costs are awarded on top of that, but at CIMIT's reduced rate. Though it is too early to declare complete success in fostering future stars, the early results are exciting enough for CIMIT to strongly support this category going forward.
- Fast Forward Awards (FFA's): On occasion a demonstrated need is presented for funding for a clinician to visit another institution for a modest period of time to learn a new technique and to import that knowledge back to their CIMIT member institution, for further innovation and clinical application. The typical need for such a Fast-Forward grant is less than \$10,000.
- Clinical Systems Innovation Awards (CSI's): As CIMIT evolved and developed great pride in its earliest clinical innovation programs such as MGH's "OR of the Future", its leadership saw a critical need that could only be served by a special category of seed funding and associated Facilitation work. The issues in CSI work were not so much scientific as clinical, and the criteria for success were not those used in traditional grant review of scientific and engineering innovativeness. The CSI criteria were about systems feasibility, the very processes of patient care, and of the potential for rapid clinical propagation for greater efficiency and an improved patient experience. The best CSI projects were relatively simple technologically, yet were innovative in a striking manner, offering a potential transformative effect in the quality, cost or safety of care. A separate set of criteria was written, and a separate review group was constituted, comprised of those CIMIT staff with the greatest

²⁷ <http://www.cimit.org/grants-typesofgrants.html>

experience in the delivery of high-technology healthcare services. CSI projects usually involve intimate contact with patients during the care process. While information technologies are occasionally part of a project, CIMIT's CSI awards are rarely given to pure I.T. efforts. Ample other funding sources are usually available for I.T. work. A separate budget allocation for the CSI program was established for clarity. CSI funding levels vary, but are typically less than \$50,000.

- Graduate Student Awards (GSA's): As desirable as it seems to support students in the same spirit as CDA awards, the extended timeline of student-thesis work creates a logistic issue not yet overcome, given that CIMIT's primary funding is one year at a time. Only a few multi-year awards in this category have been possible – all funded by philanthropic sources. CIMIT's leadership recognizes the long-term benefit of offering graduate students the financial freedom to take the risk of departing from conventional single-discipline pathways, and the value of immersing them together with like-minded mentors. Thus the hope is for greater philanthropic support for this category going forward.