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PI/PD Name: Allen Holder

Gender: ☒ Male ☐ Female

Ethnicity: (Choose one response) ☐ Hispanic or Latino ☒ Not Hispanic or Latino

Race:
(Select one or more)
- ☐ American Indian or Alaska Native
- ☐ Asian
- ☐ Black or African American
- ☐ Native Hawaiian or Other Pacific Islander
- ☒ White

Disability Status:
(Select one or more)
- ☐ Hearing Impairment
- ☐ Visual Impairment
- ☐ Mobility/Orthopedic Impairment
- ☐ Other
- ☒ None

Citizenship: (Choose one) ☒ U.S. Citizen ☐ Permanent Resident ☐ Other non-U.S. Citizen

Check here if you do not wish to provide any or all of the above information (excluding PI/PD name): ☐

REQUIRED: Check here if you are currently serving (or have previously served) as a PI, co-PI or PD on any federally funded project ☒

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PI/PD Name: Arthur D Hanna

Gender: ☒ Male ☐ Female

Ethnicity: (Choose one response) ☐ Hispanic or Latino ☒ Not Hispanic or Latino

Race:
(Select one or more)
- ☐ American Indian or Alaska Native
- ☐ Asian
- ☐ Black or African American
- ☐ Native Hawaiian or Other Pacific Islander
- ☒ White

Disability Status:
(Select one or more)
- ☐ Hearing Impairment
- ☐ Visual Impairment
- ☐ Mobility/Orthopedic Impairment
- ☐ Other
- ☒ None

Citizenship: (Choose one) ☒ U.S. Citizen ☐ Permanent Resident ☐ Other non-U.S. Citizen

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PI/PD Name: Bill Salter Jr.

Gender: ☐ Male ☐ Female

Ethnicity: (Choose one response) ☐ Hispanic or Latino ☐ Not Hispanic or Latino

Race:
(Select one or more)
- ☐ American Indian or Alaska Native
- ☐ Asian
- ☐ Black or African American
- ☐ Native Hawaiian or Other Pacific Islander
- ☐ White

Disability Status:
(Select one or more)
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- ☐ Visual Impairment
- ☐ Mobility/Orthopedic Impairment
- ☐ Other
- ☐ None

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PI/PD Name: Paul X Uhlig

Gender: ☒ Male ☐ Female

Ethnicity: (Choose one response) ☐ Hispanic or Latino ☒ Not Hispanic or Latino

Race:
(Select one or more)
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List of Suggested Reviewers or Reviewers Not To Include (optional)

SUGGESTED REVIEWERS:
Not Listed

REVIEWERS NOT TO INCLUDE:
Not Listed

COVER SHEET FOR PROPOSAL TO THE NATIONAL SCIENCE FOUNDATION

PROGRAM ANNOUNCEMENT/SOLICITATION NO./CLOSING DATE/if not in response to a program announcement/solicitation enter NSF 04-23	FOR NSF USE ONLY
NSF 06-559 10/17/06	NSF PROPOSAL NUMBER
FOR CONSIDERATION BY NSF ORGANIZATION UNIT(S) (Indicate the most specific unit known, i.e. program, division, etc.) DMS - WORKFORCE IN THE MATHEMAT SCI	

DATE RECEIVED	NUMBER OF COPIES	DIVISION ASSIGNED	FUND CODE	DUNS# (Data Universal Numbering System)	FILE LOCATION
				008133456	

EMPLOYER IDENTIFICATION NUMBER (EIN) OR TAXPAYER IDENTIFICATION NUMBER (TIN)	SHOW PREVIOUS AWARD NO. IF THIS IS	IS THIS PROPOSAL BEING SUBMITTED TO ANOTHER FEDERAL AGENCY?
741109633	☐ A RENEWAL ☐ AN ACCOMPLISHMENT-BASED RENEWAL	YES ☐ NO ☒ IF YES, LIST ACRONYM(S)

NAME OF ORGANIZATION TO WHICH AWARD SHOULD BE MADE	ADDRESS OF AWARDEE ORGANIZATION, INCLUDING 9 DIGIT ZIP CODE
Trinity University	Trinity University One Trinity Place San Antonio, TX. 782127200
AWARDEE ORGANIZATION CODE (IF KNOWN) 0036475000	
NAME OF PERFORMING ORGANIZATION, IF DIFFERENT FROM ABOVE	ADDRESS OF PERFORMING ORGANIZATION, IF DIFFERENT, INCLUDING 9 DIGIT ZIP CODE
PERFORMING ORGANIZATION CODE (IF KNOWN)	

IS AWARDEE ORGANIZATION (Check All That Apply) (See GPG II.C For Definitions)
☐ SMALL BUSINESS ☐ MINORITY BUSINESS
☐ FOR-PROFIT ORGANIZATION ☐ WOMAN-OWNED BUSINESS
☐ IF THIS IS A PRELIMINARY PROPOSAL THEN CHECK HERE

TITLE OF PROPOSED PROJECT **Mathematical Computation with Applications in Medical Physics**

REQUESTED AMOUNT	PROPOSED DURATION (1-60 MONTHS)	REQUESTED STARTING DATE	SHOW RELATED PRELIMINARY PROPOSAL NO. IF APPLICABLE
$ 295,888	45 months	08/15/07	

CHECK APPROPRIATE BOX(ES) IF THIS PROPOSAL INCLUDES ANY OF THE ITEMS LISTED BELOW

- ☐ BEGINNING INVESTIGATOR (GPG I.A)
- ☐ DISCLOSURE OF LOBBYING ACTIVITIES (GPG II.C)
- ☐ PROPRIETARY & PRIVILEGED INFORMATION (GPG I.B, II.C.1.d)
- ☐ HISTORIC PLACES (GPG II.C.2.j)
- ☐ SMALL GRANT FOR EXPLOR. RESEARCH (SGER) (GPG II.D.1)
- ☐ VERTEBRATE ANIMALS (GPG II.D.5) IACUC App. Date ____
- ☒ HUMAN SUBJECTS (GPG II.D.6) Exemption Subsection ____ or IRB App. Date 11/11/06
- ☐ INTERNATIONAL COOPERATIVE ACTIVITIES: COUNTRY/COUNTRIES INVOLVED (GPG II.C.2.j) ____
- ☐ HIGH RESOLUTION GRAPHICS/OTHER GRAPHICS WHERE EXACT COLOR REPRESENTATION IS REQUIRED FOR PROPER INTERPRETATION (GPG I.G.1)

PI/PD DEPARTMENT	PI/PD POSTAL ADDRESS
Mathematics	One Trinity Place San Antonio, TX 782123104 United States
PI/PD FAX NUMBER 210-999-8264	

NAMES (TYPED)	High Degree	Yr of Degree	Telephone Number	Electronic Mail Address
PI/PD NAME Allen Holder	PhD	1999	201-999-8241	aholder@trinity.edu
CO-PI/PD Arthur D Hanna	PhD	1996	210-431-2021	ahanna@stmarytx.edu
CO-PI/PD Bill Salter Jr.	DSc	2000	801-581-6903	bill.salter@hci.utah.edu
CO-PI/PD Paul X Uhlig	PhD	1997	210-436-3243	puhlig@stmarytx.edu
CO-PI/PD				

CERTIFICATION PAGE

Certification for Authorized Organizational Representative or Individual Applicant:

By signing and submitting this proposal, the individual applicant or the authorized official of the applicant institution is: (1) certifying that statements made herein are true and complete to the best of his/her knowledge; and (2) agreeing to accept the obligation to comply with NSF award terms and conditions if an award is made as a result of this application. Further, the applicant is hereby providing certifications regarding debarment and suspension, drug-free workplace, and lobbying activities (see below), as set forth in Grant Proposal Guide (GPG), NSF 04-23. Willful provision of false information in this application and its supporting documents or in reports required under an ensuing award is a criminal offense (U. S. Code, Title 18, Section 1001).

In addition, if the applicant institution employs more than fifty persons, the authorized official of the applicant institution is certifying that the institution has implemented a written and enforced conflict of interest policy that is consistent with the provisions of Grant Policy Manual Section 510; that to the best of his/her knowledge, all financial disclosures required by that conflict of interest policy have been made; and that all identified conflicts of interest will have been satisfactorily managed, reduced or eliminated prior to the institution's expenditure of any funds under the award, in accordance with the institution's conflict of interest policy. Conflicts which cannot be satisfactorily managed, reduced or eliminated must be disclosed to NSF.

Drug Free Work Place Certification

By electronically signing the NSF Proposal Cover Sheet, the Authorized Organizational Representative or Individual Applicant is providing the Drug Free Work Place Certification contained in Appendix C of the Grant Proposal Guide.

Debarment and Suspension Certification

(If answer "yes", please provide explanation.)

Is the organization or its principals presently debarred, suspended, proposed for debarment, declared ineligible, or voluntarily excluded from covered transactions by any Federal department or agency? Yes ☐ No ☒

By electronically signing the NSF Proposal Cover Sheet, the Authorized Organizational Representative or Individual Applicant is providing the Debarment and Suspension Certification contained in Appendix D of the Grant Proposal Guide.

Certification Regarding Lobbying

This certification is required for an award of a Federal contract, grant, or cooperative agreement exceeding $100,000 and for an award of a Federal loan or a commitment providing for the United States to insure or guarantee a loan exceeding $150,000.

Certification for Contracts, Grants, Loans and Cooperative Agreements

The undersigned certifies, to the best of his or her knowledge and belief, that:

(1) No federal appropriated funds have been paid or will be paid, by or on behalf of the undersigned, to any person for influencing or attempting to influence an officer or employee of any agency, a Member of Congress, an officer or employee of Congress, or an employee of a Member of Congress in connection with the awarding of any federal contract, the making of any Federal grant, the making of any Federal loan, the entering into of any cooperative agreement, and the extension, continuation, renewal, amendment, or modification of any Federal contract, grant, loan, or cooperative agreement.

(2) If any funds other than Federal appropriated funds have been paid or will be paid to any person for influencing or attempting to influence an officer or employee of any agency, a Member of Congress, an officer or employee of Congress, or an employee of a Member of Congress in connection with this Federal contract, grant, loan, or cooperative agreement, the undersigned shall complete and submit Standard Form-LLL, ''Disclosure of Lobbying Activities,'' in accordance with its instructions.

(3) The undersigned shall require that the language of this certification be included in the award documents for all subawards at all tiers including subcontracts, subgrants, and contracts under grants, loans, and cooperative agreements and that all subrecipients shall certify and disclose accordingly.

This certification is a material representation of fact upon which reliance was placed when this transaction was made or entered into. Submission of this certification is a prerequisite for making or entering into this transaction imposed by section 1352, Title 31, U.S. Code. Any person who fails to file the required certification shall be subject to a civil penalty of not less than $10,000 and not more than $100,000 for each such failure.

AUTHORIZED ORGANIZATIONAL REPRESENTATIVE	SIGNATURE	DATE
NAME		

TELEPHONE NUMBER	ELECTRONIC MAIL ADDRESS	FAX NUMBER

*SUBMISSION OF SOCIAL SECURITY NUMBERS IS VOLUNTARY AND WILL NOT AFFECT THE ORGANIZATION'S ELIGIBILITY FOR AN AWARD. HOWEVER, THEY ARE AN INTEGRAL PART OF THE INFORMATION SYSTEM AND ASSIST IN PROCESSING THE PROPOSAL. SSN SOLICITED UNDER NSF ACT OF 1950, AS AMENDED.

Project Summary
Title: Mathematical Computation with Applications in Medical Physics
Program: Computational Science Training for Undergraduates in the Mathematical Sciences

---

The increased need for advanced computing in mathematics and the related disciplines of biology, engineering, physics and medicine is driving the need to improve the pedagogy of computer science within mathematics. The proposed program focuses on this need at the undergraduate level by offering hands-on education to the diverse and talented student populations at Trinity and St. Mary's Universities. This proposal builds on an established and successful program of undergraduate research that lives at the intersection of applied mathematics, computer science and medical physics. The primary research goal is to improve the design of radiotherapy treatments by investigating new models and algorithms. This goal is especially well suited to undergraduate research because of its intrinsic appeal and because the problem naturally supports a myriad of projects that are appropriate for undergraduate students.

The objectives of this proposal are twofold: 1) To advance the research of optimally designing radiotherapy treatments, and 2) To educate undergraduate students in mathematical computing so that they may support and even direct the goals of the first objective. Within the field of medical applications in mathematics and computer science, the problem of improving radiotherapy designs is one of the most important, as evidenced by the burgeoning literature on the subject. Moreover, approximately 1.2 million new cases of cancer are anticipated in 2006, with approximately half receiving treatments directly related to this proposal. Due to the inherent cognitive and computational complexity of the design process, the totality of treatment design is divided into three phases. Even if each phase is optimized, which is not current practice, there is no reason to believe that the resulting treatment would be optimal with regard to the overriding goal of removing the threat of cancer. The investigators propose to develop global models that will include all three phases of treatment design together with algorithms that optimally design treatments from these models.

The ongoing success of the investigators demonstrates that significant advances are possible in collaboration with undergraduates. A recent example deals with the first phase of treatment design, which is to select the pathways along which radiation will pass through the anatomy. An undergraduate being directed by one of the investigators noticed that this selection process was related to the question of optimally designing a vector quantizer, and this connection led to heuristics that were an improvement both theoretically and computationally.

The investigators will work closely with The Huntsman Cancer Institute (HCI) to ensure that the research is clinically grounded. The HCI will provide the computing resources to successfully fulfill the grant's objectives. In particular, participants will use distributed computing on a Beowulf cluster to significantly reduce the computation time of a radiobiological model that estimates how radiation travels through the anatomy.

This is a collaborative proposal among Trinity University, St. Mary's University and the HCI. There is already a strong research collaboration between the three institutions with regard to the objectives of this proposal. The four investigators have Ph.Ds in mathematics, applied mathematics, computer science and medical physics, and when combined they have 44 years of educational experience; 16 years of clinical experience; 40 publications (either appeared or in press) spread over mathematics, computer science, operations research and medical physics; directed 8 graduate students and 29 undergraduate research projects; and published with 19 undergraduates (two additional publications are sole-authored by undergraduates). Trinity and St. Mary's Universities have a combined student population that is 81% minority and female, with 83% of the current mathematics majors falling into this category (52 of 63). The research of this proposal will advance the education of a diverse student population in mathematical computing. These students will continue in graduate school and other careers empowered with the ability to perform advanced scientific computing.

TABLE OF CONTENTS

For font size and page formatting specifications, see GPG section II.C.

*Proposers may select any numbering mechanism for the proposal. The entire proposal however, must be paginated. Complete both columns only if the proposal is numbered consecutively.

Title: Mathematical Computation with Applications in Medical Physics
Program: Computational Science Training for Undergraduates in the Mathematical Sciences
Institutions: Trinity University, St. Mary's University - Texas, and
The Huntsman Cancer Institute
Principal Investigators: Allen Holder (Trinity University), Paul Uhlig (St. Mary's University),
Art Hanna (St. Mary's University) and Bill Salter (Huntsman Cancer Institute)

Overview:

Mathematical computation is becoming an invaluable tool in disciplines such as biology, engineering, medicine, and physics, and this proposal addresses the growing need for improved mathematical computation in the field of medical physics. Our particular goal is to detail how the interplay between mathematics and medical physics is particularly well suited for undergraduate research. Medical physics is a technical arm of modern medicine and is responsible for patient imaging and treatment procedures that use radiation. One of the most demanding tasks in medical physics lies with the design of radiotherapy and radiosurgery treatments, which is the primary focus of this proposal. About 1.2 million new cases of cancer are anticipated in 2006, of which about half will receive radiotherapy treatments. Such treatments fall into two general categories, brachytherapy and external beam radiotherapy, with the majority of treatments being external beam radiotherapy. Such treatments focus high-energy beams of ionizing radiation on a patient from an external source that is 1 meter from the center of the target.

Radiotherapy works because cancerous cells are slightly more susceptible to DNA damage than are healthy cells, a property referred to as a *therapeutic advantage*. Flooding a cancerous region with ionizing radiation creates a backlog of electrons in the mitochondrial membranes. The electrons bond with oxygen to create free radicals, which in turn damage DNA. This oxidative stress accounts for about 99% of the total tissue damage, with the remaining 1% being accounted for by direct interactions between the electrons and the DNA. The therapeutic advantage means that it is possible to irradiate a region so that normal tissues survive and cancerous tissues do not.

External beam radiotherapy is delivered in numerous modalities, and a detailed discussion of each is beyond the confines of this proposal. Instead, we introduce the fundamentals of Intensity Modulated Radiotherapy (IMRT), which is rapidly becoming the dominant treatment paradigm. In IMRT, a patient is immobilized and then treated by focusing numerous beams of radiation on the target from different positions on a sphere around the patient. The beam is modulated by a multileaf collimator that can shape the beam and hence shield sensitive portions of the anatomy. Although shaping the beam to conform to the boundary of the target was the collimator's initial use, medical physicists quickly realized that it could be used to modulate dose. This is accomplished by alternately shaping the beam and treating the patient. This tactic allows the high dose region of radiation to conform more accurately to the shape of the tumor, and the improved conformity subsequently results in improved sparing of healthy tissues of the patient. The discrete representation of this modulation subdivides the beam into a grid of sub-beams. For the numerical discussions below, we assume that there are 2522 positions on the sphere from which the beam can be focused on the patient (72 great circles through the north and south poles that are equally spaced at 5 degrees on the equator, with each great circle having positions equally spaced at 5 degrees). We further assume that each beam is subdivided into a 25×25 grid of sub-beams, making the total number of sub-beams approximately 1.6×10^6.

The overriding objective of treatment design is to decide how to deliver high levels of radiation to the target while sparing surrounding tissues. The design process falls into three steps. First, the angles of treatment are manually selected with sophisticated 3D imaging software that permits the designer to view a beam's pathway through the anatomy. Second, the amount of dose to deliver along each of the sub-beams in the selected angles is decided so as to optimize a function that scores a treatment. These sub-beam values form a *fluence pattern* over the grid of sub-beams, and each sub-beam's value is referred to as its fluence (this is a physical measure of the amount of energy delivered along the sub-beam). The resulting treatment is judged by determining if there is an appropriate lethal dose in the target and a correspondingly non-lethal dose in the important healthy tissues, and if the treatment is deemed adequate, it is accepted. Initial treatments are typically inadequate, and the process continues by modifying the collection of angles until the designer is satisfied. The third and final step is to find a sequence of collimator shapes that efficiently delivers the treatment. Efficiency is important since the longer a patient is treated the more likely he or she is to shift due to normal anatomical processes like breathing. Patient movement means that we are not treating the anatomy as planned and are increasing the risk of treatment.

Each of the three design phases has been addressed as an optimization process in the literature, and the middle phase that decides fluence values is automated in all commercial packages. Instead of citing the large literature on the subject, we point to the review articles [15, 18, 26, 28] and their respective bibliographies. The first phase that selects beams is handled manually by the designer and depends on his or her individual experience. The third phase is automated in commercial systems but is not necessarily optimized to find the most efficient treatment. A natural question to an initial investigator is why aren't all three phases linked and optimized to best treat the patient? Such a proposal has two fundamental answers:

- Linking the first two phases is trivial mathematically, but the problems are far too large to solve with standard algorithms on modern computers.
- In addition to the computational difficulties, we are faced with the fact that medical physicists are unable to give us a unique, real-valued function that captures all of the patient specific concerns.

We discuss both of these issues and their research aspects below.

The design process depends on a radiobiological model that estimates the rate at which dose is deposited in the anatomy. There are three models of varied sophistication, each of which renders a coefficient that we denote by $d_{(p,a,i)}$. This is the rate, in Grays per unit fluence, that position p in the anatomy accumulates dose from sub-beam i in angle a. The investigators of this proposal have worked with undergraduates in mathematics and computer science over the last 3 summers to develop a deterministic model that is based on [23, 24] and that is currently being validated by Dr. Salter at the Huntsman Cancer Institute. This research was supported by the NSF-SURF program at The Cancer Therapy and Research Center in San Antonio and by the department of Radiation Oncology at The Huntsman Cancer Institute in Salt Lake. A significant advantage of this proposal is that this tedious and time consuming development is complete, which means that we are immediately able to address subsequent research questions.

The end result of the radiobiological model is a dose matrix D, whose rows are indexed by p and whose columns are indexed by (a, i). Allowing $x_{(a,i)}$ to be the fluence value for sub-beam i in angle a, we have that the linear map $x \mapsto Dx$ transforms fluence values into anatomical dose. The linearity is not a modeling assumption but verified by clinical trials. So, while the coefficients of the linear map are derived from a nonlinear radiobiological model, the map that delivers radiation to the anatomy is linear.

Several modeling/treatment decisions need to be made before the dose matrix is constructed. One of these questions is how to discretize the continuous 3D anatomical dose. Others have recognized the importance of this decision including the first article in 1968 [5]. Clinical consensus is that the treatment should be judged on a discretization that places the positions indexed by p on a 3D grid with a spacing no greater than 2mm. On a $20 \times 20 \times 20\,\mathrm{cm}^3$ region, this leads to a matrix with approximately 1.6×10^{12} entries.

A second question deals with the fact that the patient lies horizontally on a table (commonly referred to as a treatment couch) that allows the patient to be repositioned so that the central point of focus, called the *isocenter*, can be adjusted. All commercial systems require that the location(s) of the isocenter(s) be decided manually. Recent work [27] shows that small adjustments in isocenter placement can dramatically improve or degrade treatment quality. There is currently no literature on optimizing this aspect of the design process, and it is one of the questions that we will focus on. The point to understand about the computational difficulty is that each isocenter location requires its own dose matrix, so if several isocenters are considered, a requisite number of dose matrices are needed. A third question follows from the fact that a linear accelerator is capable of generating different energies, and each energy requires its own dose matrix. Patient specific concerns can easily lead to 10 or more dose matrices for different isocenters and energies, requiring 1.6×10^{13} calculations with a 2mm resolution. Even with the most efficient radiobiological models, calculating this information can take days and over 600 Gigabytes of memory [7].

Physicians prescribe their treatment aspirations by limiting deviations from a goal dose. For example, the target's goal could be 50Gy with an absolute minimum of 45Gy. The physician is also likely to specify the percentage of the target that is allowed to violate the goal, say 10%. A surrounding structure might have a goal of no more than 35Gy, where 20% is allowed to violate this goal as long as the dose does not surpass 45Gy. It is customary to restrict the remaining normal tissue similarly, and we assume in this example that no part of the anatomy should receive more than 110% of the target's goal and that 50% of the normal tissue should be below 20Gy. Modeling the volumetric limitations is difficult because we do not have any spatial information indicating how the violations should be distributed over the structure. This means we have to consider all possible sub-volumes whose percentage of the entire structure is below the prescribed volume. This is handled by introducing a binary value v_p that indicates whether or not position p is above or below the corresponding bound. Allowing $T_p(x)$ to be the linear operator that delivers dose to the positions that are targeted, we are looking for a nonnegative fluence vector x that satisfies

$$T_p(x) \geq 45,\ T_p(x) \geq (1 - v_p)50,\ \sum_p v_p \leq 0.1 m_T, \tag{1}$$

where only targeted positions p are considered and m_T is the total number of targeted positions. If we let $C_p(x)$ and $N_p(x)$ be the operators that deliver dose to the positions within the critical structure and the normal tissue, then for this example we further require that

$$C_p(x) \leq 35 + 10 v_p,\ \sum_p v_p \leq 0.2 m_C \tag{2}$$

and

$$N_p(x) \leq 20 + 35 v_p,\ \sum_p v_p \leq 0.5 m_N, \tag{3}$$

where p is indexed appropriately and m_C and m_N are the natural analogs of m_T.

Notice that there is a binary variable for each of the 10^6 points in the anatomy where dose is calculated. This leads to a linear system of inequalities with 10^6 constraints, 1.6×10^6 nonnegative variables, and 10^6 binary variables on the $20 \times 20 \times 20\,\mathrm{cm}^3$ example above. Determining whether or not such a system is even feasible is problematic since the tree that describes the binary part of the problem has 2^{10^6} terminal leaves (possible solutions). Examining each of these is beyond our computational ability.

One of the research directions of this proposal is to investigate ways to reduce the number of binary variables. Others have dealt heuristically with the entire collection of binary variables [20, 21, 22], but our goal is to use the experience of the treatment designer to limit the number of binary variables. The treatment designer typically has an idea of where deviations from the treatment goals would be acceptable and where deviations should not be allowed. Some regions are inherently at high risk for recurrence, and under-irradiating these regions should not be allowed. Areas where the designer is asking for dose to go from a high level to a low level are typically understood to be places where violations are likely to occur, and thus, must often be tolerated. If the treatment designer could state the exact volume where violation is possible, then we could remove the binary variables all together. Working with Dr. Salter, we will develop automated structure segmentation that is based on his 16 years of experience to reduce the size of the regions where violations are possible. We anticipate that this will reduce the number of binary variables to below 10^3. Such research is relevant, important and novel.

While reducing the number of binary variables would be significant, this would only be a piece of the overall goal of linking the three design steps into a single cohesive model. This is because reducing the number of binary variables only reduces the size of the middle step of the design process. So, if this model is used as a foundation to include the first and/or the third steps, then the resulting model will be smaller due to the reductions in the middle step. However, other reductions are likely possible. For example, consider linking the first and second steps of the design process. Even with a reduction to 10^3 binary variables, there are still 1.6×10^6 nonnegative, continuous variables if each of the 2522 beams are to be considered. If we were instead trying to find fluence values for 10 specific beams, the number of nonnegative variables would be $6,250$. Notice the trial-and-error approach used in the clinic today asks the designer for a collection of angles, which significantly reduces the problem size and makes the problem more manageable. So, the current process is to ask the user to guide the search through the N element subsets of the angles under consideration. If each of N element subsets had to be considered individually to find a best collection, we would have to search through $\binom{2522}{10} \approx 2.8 \times 10^{27}$ subsets. Modeling this search is accomplished by introducing a new collection of binary variables, and we let u_a be 1 if angle a is selected and 0 otherwise. Then, in addition to (1) - (3), we need to add the constraints:

$$\sum_i x_{(a,i)} \leq u_a M \text{ (for each angle } a\text{), and } \sum_a u_a = N, \tag{4}$$

where M is an arbitrarily large value and N is the number of beams to be selected. This adds 2522 binary variables and 2523 constraints to the system. If the dose-volume constraints and the beam selection variables are both considered without reductions, this means we have a total of $1,002,522$ binary variables, 1.6×10^6 nonnegative variables, and $1,002,523$ constraints.

The system of equations describing the treatment goals can be infeasible, a topic that has been addressed by Dr. Holder [14]. In this case the goal is to return a solution that is as close as possible to satisfying the prescription. However, typically the feasible region is nonempty, and the problem is to find a best treatment. Deciding what 'optimal' means is a clinical issue that varies from clinic to clinic and from patient to patient. Treatments are judged with the aid of numerous graphical tools that do not readily map into $\mathbb{R}$. This increases the difficulty of modeling the design process as an optimization problem, but several suggestions exist in the literature. Objective functions that measure treatment quality fall into two broad categories, those that penalize deviation from the prescribed goals and those that are biological in nature. Let X be the collection of nonnegative (x, v, u) that satisfy (1)-(4), where both v and u are binary vectors with components v_p and u_a. A typical deviation model for the above example is

$$\min\{\omega_1 \|T(x) - 50\|_{p_T} + \omega_2 \|C(x)\|_{p_C} + \omega_3 \|N(x)\|_{p_N} : (x, v, u) \in X\}, \tag{5}$$

where the components of T, C and N are T_p, C_p and N_p over their appropriate indices. The type of optimization problem can be adjusted by altering the norms, and the importance of each structure is expressed through the weights ω_i, $i = 1, 2, 3$. The model is linear if p_T, p_C and p_N are one of 1 or ∞. The most common nonlinear model is to have $p_T = p_C = p_N = 2$. Alternatively, there are biological models that estimate the likelihood of an adverse or favorable condition, like the probability of a complication free treatment or the probability of tumor control. Allowing $F(T(x), C(x), N(x))$ to be one of these probabilities, we have that the requisite biologically based problem is

$$\max\{F(T(x), C(x), N(x)) : (x, v, u) \in X\}. \tag{6}$$

These are nonlinear, smooth models that are traditionally more difficult to solve than their deviation counterparts.

Models (5) and (6) perform two of the three steps of treatment design: they select angles and fluences for these angles. These models require the user to bound the number of angles; however, this is a surrogate to the real goal of reducing the treatment time. The underlying assumption is that the number of angles correlates with the time it takes to deliver the treatment, which is not true since it is more efficient to deliver angles that lie on the same great circle. This is because treating a patient with angles from a single great circle does not require an adjustment of the patient's position, but moving from one great circle to another does. In general, it more efficient to have many angles from a few great circles than to have a few angles distributed over multiple great circles. While the objective functions in (5) and (6) have different interpretations, they both define optimality exclusively in terms of how dose is distributed in the anatomy and ignore the competing goal of reducing treatment time. Instead, these models attempt to compensate by restricting the number of angles. The historical segregation of treatment design has lead to this misconception because the second phase of the design process was addressed in a way that asked the user to guide the beam selection. The easiest and most naive way to include beam selection into fluence optimization was to add the binary variables u_a as stated above, but this method does not accurately capture the essence of how beams are selected by an experienced user.

The third phase of treatment design has only recently been investigated in research initiated by Hamacher and colleagues [2, 3, 4, 6]. Since this phase is concerned with delivering a treatment as efficiently as possible, the objectives are naturally expressed in terms of time. Some models lead to polynomial time problems whereas others are known to be NP-hard. Similar to the beam selection problem, some researchers have suggested that we instead minimize the number of collimator shapes as a surrogate to reducing treatment time. Although this has merit when studied as an independent problem, it is a fallacious assumption from the perspective of optimizing the totality of the treatment since it may be more efficient to use several collimator shapes if the time to move from one to another is short. As with beam selection, the real issue is time.

When all three phases of treatment design are considered together we see that there are two overarching and competing objectives. The objective that has received the most attention is to deliver the radiation so that it is distributed in the anatomy to best achieve the goal of removing the threat of cancer with as few side affects as possible. This objective encourages complicated treatments that use numerous beams, great circles, and beam shapes. From this perspective a patient is considered to be static, and the concern of whether or not the treatment can actually be delivered as intended is ignored. The other objective is to design a treatment that can be delivered efficiently so that there is as little error as possible when delivered. This objective discourages complicated treatments that increase treatment time. What is needed to glue the entire process into a single model is an objective that simultaneously measures these two essential desires. The objective could be a mapping into $\mathbb{R}^n$ instead of $\mathbb{R}$ to capture the inherent multiple objective nature of the problem, see [9, 13] for established multiple objective results.

Having a unified objective would remove the hidden assumptions that have historically developed due to the division of the design process. Indeed, it appears obvious that the computational difficulty of a holistic approach should be less than the sum the individual steps. For example, if we redirect our focus to shortening treatment time instead of limiting the number of beams, then the somewhat unreasonable assertion that we need to consider all N element subsets of a larger collection is removed since the goal of delivering the treatment efficiently will guide which beams are selected. Our goal is to work with the Huntsman Cancer Institute to remove such assumptions so that we can decrease the computational burden and more adequately address the clinical meaning of an optimal treatment. The ultimate goals of this proposal are to

- Use this problem as a vehicle to educate undergraduates in computational mathematics and related computer science topics.
- Work closely with the medical physics community to capture the goals of treatment design in a single model that removes the historical assumptions that have lead to an overly burdensome problem, and
- Disseminate our findings to the mathematical and medical physics communities.

The first goal is not only possible but has already been demonstrated. Dr. Holder has been one of the leading researchers in optimizing radiotherapy treatments, with his first paper on the topic receiving the 2000 Pierskalla award as the best paper in Operations Research and Health Applications. Since then he has completed 7 research papers/chapters with 4 undergraduates on this topic (another preprint has an additional 3 undergraduate co-authors), and in total he has co-authored research articles that are either published or submitted with 19 different undergraduates.

Through the gracious funding of the Huntsman Cancer Institute during the summer of 2006, Drs. Hanna and Uhlig worked with Drs. Holder and Salter to advance the computational tools needed by this project. They both have long and successful careers in undergraduate education and are now enthralled about the goals of this project. Dr. Uhlig is an associate professor of mathematics at St. Mary's University, and his robust background in pure and applied mathematics, combined with his recent education in computer science and last summer's research on this project, make him uniquely qualified to fulfill the goals of this grant at St. Mary's University. Dr. Hanna is an associate professor of computer science at St. Mary's University, and he adds a needed programming expertise. He has 27 years of programming and educational experience. He will be an invaluable resource to both the students and the investigators. Under this grant, these two investigators will advance the state of undergraduate research at St. Mary's and will be instrumental in achieving the first goal in the combined student population.

With respect to the second goal, we will work closely with Dr. Salter, who is the Chief of the Division of Medical Physics in the School of Medicine at the University of Utah's Huntsman Cancer Institute. Dr. Salter is especially well positioned to mediate the transition of knowledge between the mathematics and medical physics communities. He has a robust knowledge of clinical practice with over 15 years of experience. Additionally, his Ph.D. work implemented stochastic algorithms that formed the basis of the optimization routines in NOMOS' commercial system, and he has directed several Ph.D students in medical physics who have published in the area. His keen understanding of the computational challenges makes him especially aware of the importance of developing novel mathematical techniques. We are fortunate to have him as an investigator.

The goal of dissemination will be fulfilled by publishing articles in peer reviewed journals in mathematics, operations research, computer science, medical physics, and related educational venues. In particular, we emphasize the importance of publishing computational results in the medical physics literature. Publishing in the literature of the application is crucial if the mathematical advances are to transcend the barrier between academia and the clinic. Again, Dr. Salter will play a significant role in directing the clinical experiments.

We are asking for 3 years of funding to accomplish our goals. In the spring of 2007 we will begin recruiting rising juniors from both Trinity and St. Mary's Universities. These students will enter a research forum comprised of students in mathematics, computer science, physics, biology and other related disciplines. Students in the forum will participate in a Readings and Research course, which is described in the following section. The mathematics departments at Trinity and St. Mary's Universities support the dedication required by the investigators to complete the goals of this proposal and have agreed to include the Readings and Research course as part of their regularly scheduled teaching responsibilities for 8 consecutive semesters beginning the Fall of 2007. This guarantees that the educational goals of this proposal will constitute at least 25% of the educational responsibilities of each investigator at Trinity and St. Mary's Universities during the academic year. A succinct timetable for this proposal is found in Table 1.

	AY 07-08	Sum. 08	AY 08-09	Sum. 09	AY 09-10	Sum. 10	AY 10-11
Jr's	6 - 10	0	6 - 10	0	6 - 10	0	6 - 10
Sr's ($)	0	6 (6)	6 - 10 (6)	6 (6)	6 - 10 (6)	6 (6)	6 - 10 (6)
Total	6 - 8	6	12 - 20	6	12 - 20	6	12 - 20

Table 1: A time line for the proposed program. The tally for seniors includes rising seniors not students who have graduated. The value in parentheses represents the number of students receiving direct assistance from the grant. We anticipate that this program will continue beyond that of the grant and have indicated this by accepting juniors in the academic year of 2010-2011.

The students will be selected from two of the Southwest's most prestigious universities. Both Trinity University and St. Mary's University are categorized as Masters granting institutions by US News & World Report, but other than a few select graduate programs, the preponderance of both universities' focus is on undergraduate education within a liberal arts setting. Trinity has achieved a ranking of #1 in its category for 15 straight years, and St. Mary's has had an average ranking of 15 over the same period (there are 61 universities in this category). The entering SAT scores have averaged 1280 and 1064 at Trinity and St. Mary's Universities over the last 3 years. Both schools are ethnically diverse. Over the last 3 years, Trinity's student composition has been about 30% minorities (10% hispanic) and 55% female. St. Mary's student population is about 81% minority (70% hispanic) and 60% female. Moreover, the mathematics population at Trinity has averaged 50% females for many years, with 13 of the current 18 mathematics students being female. St. Mary's has a similar percentage of female mathematics majors, with 29 of current 45 majors being female. Combined, the two student populations majoring in mathematics is 83% female and minority. These facts support our participation goal.

Participation Goal We expect that at least 66% of the participants in this program will be minorities or female. In particular, we expect to draw from the sizable Hispanic population of the combined schools.

In the last 3 years graduates of the mathematics departments at Trinity and St. Mary's have continued graduate studies at Stanford University (computational mathematics), the University of California, Berkley (economics with an emphasis in computation and dynamic programming), Duke University (statistics), the University of Texas (operations research), Rice University (both applied mathematics and statistics), the University of Toronto (computer science), the University of Utah (mathematical biology), MD Anderson (medical physics), Texas A&M (industrial engineering and statistics), and the University of Houston (industrial engineering). This wide ranging success indicates that we have an established history of educating students in the theory and application of mathematics. Funding this proposal will strengthen two impressive programs and promises future success.

Nature of Student Activities:

The primary educational outlet during the academic year is a Reading and Research course that will be offered to juniors and seniors at both institutions (MATH 3-90 at Trinity and MT 5-60 at St. Mary's). Students will need the consent of the instructor (one of the investigators) to register for the course. First time participants will register for 1 academic hour each of their first two semesters in the course, and seniors who have previously completed both of the 1 hour courses will register for 3 academic hours. Students taking the course for 1 hour will focus on expanding their education in computational mathematics and on the particulars of using optimization to design radiotherapy treatments. This will include becoming proficient with the programming aspects of the project. Seniors who have completed the associated summer experience are expected to take two semesters of the course for 3 credit hours per semester. These students will also fulfill the important role of mentoring others in the class as peer tutors. Even with enthusiastic and bright students, learning complex mathematics and sophisticated programming techniques can be daunting. These peer tutors will hold regular office hours in the evening to assist their classmates. These student-to-student interactions are beneficial for several reasons: 1) younger students will gain from the experience of their more senior classmates, 2) seniors will reinforce their understanding of topics as they teach them, and 3) it will aid in continuation of knowledge from year-to-year. A similar design was implemented as part of an HHMI grant in the biology department, and this project has met with huge success. The educational experience we expect to deliver is significant, and participants will have a sizable time commitment. Being able to meet several evenings a week will foster an educational environment that supports this commitment.

The anticipation is that students will self organize into small teams that will work on individual problems. Entering participants will work with several groups to learn as much about the individual problems as possible. Needed background will be provided by the peer tutors and by the investigators. We will encourage the members of each team to be multi-faceted and include students from mixed disciplines and from both universities. The social and economic backgrounds of a typical student from each university is different, and one of the gems of this collaborative proposal is that it will welcome talented students into the field of computational mathematics from a community that is larger than either of the university's cultural experiences. The pursuit of science is one of humankind, and learning to respect this fact is important.

We cannot foresee all the different projects that might possibly be appropriate under the auspices of this grant, but several have already emerged as part of previous undergraduate research. A discussion of a few of these will provide examples of what we expect. Much of applied/computational mathematics is based in the realm of modeling, for it is the abstraction of a phenomena into mathematical language that allows us to consider the situation mathematically. Modeling is as much an art as it is a science, and it is often the case that a complicated real-world entity can lead to several models. Different models typically have different strengths, some may lead to better computational methods while others may be easier to work with theoretically. Since we hope to glue all three phases of treatment design into a single model, modeling is one of our most important goals. We expect that one of the teams will focus on developing new models. This team should be interdisciplinary because it requires an understanding of mathematics, computer science, physics and biology.

As an example of how modeling can affect the computational concerns of this proposal, we return to the problem of selecting beams (phase one of treatment design). A few years ago a Trinity undergraduate, Josh Reese, suggested that there was a connection between selecting beams and data compression. In the subsequent years, Dr. Holder and Mr. Reese proceeded to model beam selection as a problem in data compressions that is concerned with the optimal design of a Vector Quantization (VQ), a topic first introduced by Shannon (see [11] for more details). This new modeling approach has had several impacts, a succinct description of these events is listed below:

- The design of an optimal VQ is based on minimizing distortion, which is the expected value of a probability density. This new approach required that we model the probability of an angle being selected. This fact lead us to the realization that there was an algorithmic dependence on the type of solution returned by the fluence optimization (second phase of treatment design).

- We developed a new computational technique in an attempt to remove the algorithmic dependence and improve the interpretation of the probability. Dr. Holder in conversation with Dr. Ehrgott from the University of New Zealand discovered that this procedure had already been investigated in the area of multiple objective optimization and that the resulting probability was equivalent to calculating what was called a *balanced solution*. This probability has the favorable property that a beam is guaranteed to have a high probability if it is necessary for it to have a correspondingly high fluence value to treat the patient optimally. Unfortunately, the zero probabilities do not have the same interpretation, However, we proved that errors are made only in the final iteration of the algorithm.

- This new way of looking at beam selection lead Dr. Ehrgott, Dr. Holder, and Mr. Reese to rigorously define a beam selector as a mapping between collections of angles. They accumulated the sizable medical physics literature on the topic and analyzed each of these techniques as a mathematical entity. This analysis described why some methods performed better than others. Large scale computational testing was undertaken to validate the findings. Although the VQ method was not the fastest, it was the fastest that consistently gave clinically meaningful solutions.

- As the research continued, Dr. Holder began to realize that the optimal design of a VQ was related to the now classic problem in graph theory called the P-Median problem. Hakimi [12, 19] was the first to study this problem and is credited for showing that it is NP-Hard, but we now know that it is actually fixed parameter tractable, which means that it is generally NP-hard but becomes polynomial when some parameters are fixed. Hakimi's original result was that a continuous problem on a graph can be solved discretely, and the discrete version of the problem was called the P-Median problem. Hakimi required the edge weights to form a metric, an assumption that is often overlooked. Today the P-Median problem is often stated as being NP-Hard when the context of its application actually means that it is polynomial, and it is also stated as a problem on general networks independent of whether or not the edge weights form a metric. Dr. Holder proceeded to extend Hakimi's original result to the case where a metric is no longer needed, and he further showed that this extended P-Median problem was equivalent to the optimal design of a VQ. The equivalence is strong in the sense that there is a bijection between the feasible regions that maintains the objective value, so in essence the problems are identical except for terminology. This bridge between the two disciplines is important computationally since the heuristics developed for VQ are provably more efficient than those for the P-Median problem. Just in the last few months, Dr. Holder, Mr. Reese, and Dr. Lim used this bridge to prove that two of the most prominent heuristics in their respective disciplines are identical in many instances. This has lead to efficient and robust computational methods [16].

The idea that beam selection and data compression are related continues to have far reaching promise. The P-Median problem is one of the important transportation problems in Operations Research, and the fact that we can model beam selection as a P-Median problem hints at the possibility of modeling beam selection as other transportation problems. Moreover, the relationship between the two problems further suggests that the efficient VQ heuristics may apply to other binary problems in optimization. If this is true, then this research may affect the entire mathematical programming community.

A current undergraduate at Trinity, Evan O'Dea, is working on analyzing the issue of incorrectly assigning zero probabilities to beams. He was supported by an HHMI grant over the summer of 2006 to conduct this research under the tutelage of Dr. Holder. Although we were initially concerned with the mathematical and computational issues of treatment design, we quickly understood that we were undertaking a new approach to the long standing problem of identifying the collection of implied equalities in a linear system of inequalities. The larger problem is paramount in many computational problems because it allows us to reduce the dimension of the problem. What we recognized is that calculating the balanced solution typically, but not always, identifies the implied equalities. In fact, it always identifies the implied equalities but may identify inequalities that are not implied. Our research to this point has proven that the balanced solution is a vertex of a related polyhedron, which means that we can calculate the balanced solution in polynomial time. We additionally have partial results that support the (hopefully true) conjecture that the balanced solution exactly identifies the implied equalities over a dense subset of right-hand sides. If this is true, then we will have established that we can identify in polynomial time the implied equalities of a perturbed linear system, where the amount of perturbation is arbitrarily small. We are in the process of computationally testing this conjecture.

Mathematics and theoretical computer science are only part of mathematical computing, and at some point a researcher needs to implement and test their ideas. There is often a void between theory and implementation, and this is an important lesson to learn. We have fortunately received funding the past three summers to implement a radiobiological mode that is known to be 97% accurate in water based tests [23, 24]. Although this model is considered efficient, computation can still take days. One of the teams will address the problem of distributing the calculations over a Beowulf cluster of 30 linux machines that is maintained at the Huntsman Cancer Institute. Although generating a dose matrix is embarrassingly parallel, distribution of the computing is complicated by our software design. The radiobiological model is written in C++ but is used as an extension to the scripting language php. This design is especially useful since it allows us to interact with patient data stored in a MySQL database as well as with other software packages like AMPL and CPLEX. It further allows us to use an Internet browser as a graphical interface. The downside to this design is that it does not naturally fit into the standard philosophy of MPI, which complicates distribution.

We further hope to take advantage of the cluster by writing global algorithms that are tailored to the design of radiotherapy treatments. Global algorithms are intended to be used on nonlinear, nonconvex problems that may or may not have integer variables. Example algorithms include simulated annealing, tabu search, and genetic algorithms. Our current numerical work uses the AMPL modeling software, which in turn links to a suite of solvers that actually preforms the optimization. This has the advantage that we are harnessing the power of some the best optimization routines, but has the disadvantage that it limits which models can be solved. Much of the medical physics literature is based on simulated annealing, which is often massaged to address the needs of the problem. We do not have access to similar routines through AMPL but consider it important for two reasons. First, we need to be able to make head-to-head comparisons with previously reported results, which is only possible if we can implement their solution methodologies. Second, a global solver would give us free reign over the form of the optimization model, which we believe will be necessary in an attempt to link all three phases of treatment design. It is likely that an interplay between a global algorithm, like simulated annealing, and traditional algorithm, like Newton's method, will work well on the large problems we face. Distributing and analyzing these procedures promises to be fruitful.

The computer science training of this project is necessarily broad, which supports the very nature of mathematical computation. Indeed, to say that one is educated in mathematical computation requires a working knowledge of more than the traditional programming languages like C/C++ and FORTRAN. The interaction of different disciplines depends on the transfer and manipulation of data and the interaction of various software packages. Our computer science curriculum will include the following skills:

- Proficiency with C/C++, including how to use makefiles and compile libraries/shared objects for use with other software.
- Software design issues that address how to collaboratively work in small teams to successfully achieve larger goals.
- An ability to use scripting languages such as Perl and php to interact with other programs. We will also make sure that students know how to write extensions to these languages that are tailored to specific needs.
- A working knowledge of databases.
- Experience with standard mathematical packages such as Matlab, Maple, and R.
- Document preparation in LaTeX.

With these skills in hand, students will be prepared to work in any mathematical environment requiring computation.

From the above discussion it is obvious that the question of optimally designing radiotherapy treatments can lead to cutting edge mathematics and computation that advances the academic disciplines and the application in medical physics. These problems are not only approachable by undergraduates but have at times been spearheaded by undergraduates. The research that has already been accomplished in conjunction with, indeed is due to, undergraduate efforts is presented in [1, 10, 17, 25]. These articles have either appeared or are submitted to peer-reviewed journals, and we point out that [25] is a sole authored undergraduate publication. There are three ways in which support of this grant will directly advance the state of current research:

- The mathematical analysis and computational results will be published in peer-reviewed journals.
- As a byproduct of the need to have head-to-head comparisons between different models and solution techniques, we will develop a library of problems so that the community can make appropriate numerical comparisons.
- The end result with regards to software will be an academic treatment system available to other researchers.

The need for the last two items has been expressed in [8]. The continued research of this project will enhance the already well established efforts in undergraduate research and will help continue our stream of research contributions. In this light, we view support of this grant as increasing undergraduate participation in an already established research program. The focus is to advance science, and in doing so, we will introduce students to the realm of research through mathematical computing.

Connection to Regular Academic Studies:

The Reading and Research course will be open to all students up to a typical class size of 20 at each institution. The investigators suspect that the CSUMS initiative was started due to the lack of computing experience evidenced by many mathematics students. The alumni surveys conducted by Trinity's mathematics department almost unanimously state that the biggest hole in our mathematics curriculum was a lack of computer science. This was addressed 5 years ago by mandating that all mathematics majors take Principals of Algorithm Design I. This rule has not been in effect long enough to know if it has fulfilled its objective, but many in the department believe that we need to do more.

Much of that first course will be on how to use computer resources, including document preparation with LaTeX, how to use scripting languages to link different software packages, MATLAB© programming, and object oriented programming with C++. All of these tools are needed by the project, and students taking the course for 1 hour will be expected to gain proficiency with each. These how-to topics in scientific computing are different than the pedagogical needs of a first course in computer science, and the investigators have often been told by previous computer science and mathematics students that working on early parts of this project gave them valuable skills that they were not otherwise exposed to. As such, this course will provide valuable tools in scientific computing to a wide range of students. All of these students will have access to the peer tutoring sessions sponsored by the grant.

The mathematics departments at both Trinity and St. Mary's Universities have made curricular attempts in the past to emphasize computational mathematics. Trinity introduced a minor in Scientific Computing in the Fall of 2006 and St. Mary's recently introduced a degree in the Mathematical Sciences that requires a minor in biomathematics, computer science, engineering, chemistry, operations research, or physics. Both of these curricular projects are timely and demonstrate that both universities have already expressed an interest in supporting the goals of the CSUMS initiative. Students participating in this grant are natural candidates for these programs, and the investigators will encourage Trinity students to complete a minor in Scientific Computing and St. Mary's students to complete the degree in Mathematical Sciences. This will help bolster participation in computational avenues through the mathematical degrees. The success of these students will provide a draw for future students and will help solidify computation as a mainstream topic. In particular, we will work to include elements of this project into the associated curricula at Trinity and St. Mary's.

To ensure that the mathematics populations of both institutions are aware of the advances made by this program, participants will make presentations annually in a majors' seminar (Trinity University) and at a math club meeting (St. Mary's University). These presentations will bring awareness to the the junior courses and will aid in recruiting students.

Research Environment and Mentoring Activities:

During the academic year students will meet twice per week with the investigators of this project, once at their home institution and once as a collective group at one of the institutions. The weekly meetings at the home institutions will be hands-on education, where the investigator(s) will act as a resource to the smaller group. These meetings could be small lectures used to augment a topic of interest that is not part of the traditional undergraduate curriculum or it could be assistance with pertinent computer resources. The purpose of this meeting is to tailor the educational opportunities to the individual students and to the varying student teams. We anticipate this meeting will last at least 2 hours, and if possible, it will be scheduled to allow the flexibility to meet as long as needed. We do not want to be bound by a pre-specified schedule if we are making progress. Many mathematical concepts require a sustained development to gain understanding, and we aim to accommodate such focus as needed.

On Friday afternoons the entire student cohort from both universities will meet in a colloquial environment. These meetings will alternate between Trinity and St. Mary's from semester to semester. Most weeks one of the student groups will be asked to present their progress and to identify the next set of problems. This presentation is expected to last about 30 minutes, after which the entire group will be asked to provide assistance and suggestions. We feel that this colloquium atmosphere is crucial for the bigger project to succeed, for without such a venue we would have several small projects working in isolation. This is a recipe for disaster if the smaller pieces of the theory, computation, and analysis are to coalesce into something meaningful. About a third of these meetings will be reserved for formal colloquiums by outside speakers. We anticipate drawing speakers from computational mathematics, medical physics, and mathematical biology. The investigator(s) at the home institution will be responsible for organizing these colloquiums. Money is requested to support the travel and expenses for these speakers.

Six mathematics students between their junior and senior years will be selected competitively to participate in a summer research program. The students who participate in this experience are expected to dedicate themselves to their selected problem for 10 weeks of the summer. The investigators will guide this research with daily meetings. To successfully complete this experience, students must 1) complete a written description of their research and 2) either speak or present a poster at the Trinity Undergraduate Research Gala at the end of the summer, which will include presentations from all the undergraduate groups on campus. Drafts of the written report will be due at the end of weeks 3 and 7, and the investigators will return comments within one week. Learning to express oneself technically is challenging, and the goal of this schedule is to assist young researchers as they discover the importance of clear and concise exposition. To prepare students for their final presentation, we will guide students through two intermediate colloquiums in which they will present their current work to the rest of the group. These colloquiums will take place at the end weeks 4 and 6.

Trinity's support of undergraduate research in mathematics and the sciences is unparalleled and growing. Undergraduate research is currently supported by the National Science Foundation (REU and SURF), the Howard Hughes Medical Institute, the KECK foundation, as well as many other individual grants. In the last two summers, there were 69 and 97 students on campus participating in undergraduate research on topics from Biology, Chemistry, Computer Science, Engineering, Geosciences, Mathematics, Neuroscience, Physics, Political Science, and Psychology. The six students selected annually to participate in the summer program of this proposal will become part of Trinity's summer research culture. Trinity will provide housing and will open its infrastructure to those participating. Summer research students may additionally receive 1 hour of research credit at no cost. Drs. Uhlig and Hanna will be given office space at Trinity so that they can more easily participate as research mentors. Each of the summer students will be granted full student privileges during the summer, which includes access to all computer labs, library access, and athletic facilities. Additionally, each of these students will have a study space in one of the computer labs.

The mathematics department maintains a server that has research licenses for several common mathematical software packages, such as Maple, Matlab, CPLEX, AMPL, and R. The current development of the software has been accomplished on this machine, and we expect that it will continue to support prototype development. However, our most recent developments have shown that this machine will not be sufficient as we begin to address clinical cases. The problem is that the computation and storage of the dose matrices far exceeds the memory limitations of a 32-bit processor. We are fortunate that Dr. Salter has a Beowulf cluster of 30 linux machines, and as discussed above, one of the initial goals of the proposal is to distribute the computation of the dose matrices over this cluster. Although this will decrease the time needed to generate the dose matrices, it will not solve the problem that these matrices need to be collected onto a single machine for use with AMPL and CPLEX. To proceed, we need a 64-bit processor with substantial memory so that we can use the dose matrices to form the requisite optimization problems. To support this need, we have requested funding for a single 64-bit server that will be added to the Beowulf cluster.

Student Recruitment and Selection:

The idea of using mathematics and its related computational insights to fight cancer has a special allure that draws students. Indeed, the project has an intrinsic and tangible value that appeals to many, including the investigators. A fundamental knowledge of the problem in its totality requires a foundation in cellular biology, optics, computer science, and of course, mathematics. We expect and encourage the participation of students outside mathematics, and we will distribute an announcement describing the Readings an Research course to the chairs of all related disciplines each spring. The chairs will be asked to arrange for an announcement in any appropriate student venue, such as a majors' seminar, a student forum like the physics club, or in a course such as genetics. The application will clearly state that anyone interested in an educational experience with mathematical computation is welcome, and additionally that those with mathematical tendencies can compete for future funding.

Each student will need the permission of the instructor to register for the Readings and Research course (this is easily accommodated by both registrars). It is important that we control the population because if it were open to general registration it might fill with students wanting a 1 hour experience without the possibility of continuation. Although we hope to accommodate as many of these students as possible, we need to guarantee that there is a core of entering students who expect to compete for summer support and continue with the 3 hour courses. The best way to do this is to interview students and make sure that those demonstrating the highest promise get to register first. Future promise is valued over previous achievement when entering the course, and while these topics are often correlated, this is not necessarily the case for many of the first generation college students we hope to attract. A student with aptitude, talent and enthusiasm who has not yet broadened his or her mathematical education still has 2 years to do so. Indeed, participation in this project will provide motivation and resources to achieve success.

We generally believe that students will need to have completed their first two years before having the educational maturity to enter the program. Students who want to compete for summer support are expected to have completed the Calculus sequence and linear algebra together with a collection of courses such as differential equations, statistics, real analysis, or numerical analysis. Additional coursework in computer science, physics and/or biology would be an added advantage. Juniors completing the second 1 hour course that have additionally declared a major in mathematics are eligible for the summer experience. The application will consist of an academic transcript, 2 letters of reference, and a 3 to 5 page proposal that identifies the problems to be addressed over the summer. The two 1 hour courses are designed to prepare students for this proposal. The advantage of such an application is that it identifies how well prepared a student is to address the proposed project, and unlike the criteria to enter the program, preparation is the most desired quality. Students who enter the program with weaker backgrounds but demonstrate substantial potential will have exposure to the problems for approximately 6 months before this proposal is due. Considering that this will include significant hands-on learning, this is certainly enough time for a bright, motivated student to compete for one of the summer positions.

Project Management:

Since this is a collaborative proposal among 3 institutions, managing student expectations and project development will require extra effort. The investigators at Trinity and St. Mary's University are responsible for the educational goals of this proposal, and they will meet twice per month to discuss the state of the program. Dr. Hanna will be in charge of outlining the computer science curriculum for the Reading and Research courses, and part of these meetings will be devoted to a discussion of this topic. The status of the individual teams will also be discussed, and in particular, we will consider the possible need to adjust the focus or constituency of the individual teams. One of the meetings near the beginning of each semester will be about organizing the Friday colloquiums. Speakers will be invited by consensus and will be selected on the current needs of the project. For example, if the students are learning about matrix factorizations, we will invite a numerical linear algebraist. Additionally, some of the colloquiums will focus on graduate opportunities in computational and applied mathematics. These colloquiums could be led by the investigators or they could be visits from faculty at other institutions who are interested in talking about their graduate program.

The importance of having Dr. Salter as an investigator can not be overstated. If we lose a tangible link to the clinic, then we are not doing applied mathematics. We will depend on Dr. Salter for guidance about what is and is not clinically relevant and to provide clinical data for numerical tests. He will also direct publications in the medical physics literature. We have worked closely with Dr. Salter in the past, and we see no hindrance with a remote collaboration as long as we regularly discuss the project. Dr. Salter has agreed to 3 week long visits in September, January and May so that he can provide hands-on guidance at the beginning of each semester and at the beginning of the summer research program. We have additionally asked for partial support of Dr. Salter's post-doctoral student in medical physics, who will be able to be onsite for a few weeks of the summer project. These visits guarantee a sustained link with the related discipline. We are further requesting funds for the three investigators in San Antonio to travel to the Huntsman Cancer Institute in Salt Lake, Utah. A similar trip was part of previous funding, and it was hugely successful to have all four investigators in the same location as the computer resources. We do not think that student travel to Utah is needed. In fact, our experience with undergraduate research has shown that time away from the students is important. Although the interplay between education and research is paramount to this proposal, it is equally important for the investigators to have a time when they can pursue the research goals of the proposal to advance the program and identify future problems.

During the summer the 3 investigators in San Antonio will meet daily with each other and with the 6 students. Managing the teams over the summer will vary from year to year depending on the research of that summer. Some years it may be appropriate to have fewer groups working on bigger problems and others it may be better to have more groups working on smaller problems. With 3 advisers and 6 students, one-on-one mentoring is assured.

Project Evaluation and Reporting:

Students will complete course evaluations after each academic semester as part of normal university procedure. However, we do not feel that the standard questionnaires are sufficient. In addition to the typical course evaluations, we will administer a second anonymous questionnaire that asks:

- How have the research goals of this course affected your education? In particular, address the topics that you have learned that you would have otherwise not.
- Has this course altered your post graduation goals? If so, please elaborate on what you plan to pursue after graduation.
- Have the interactions of the different institutions broadened your educational experience? If so, please elaborate.
- What would you alter about the program?
- What was your favorite experience?

Students completing both years of the program will complete this questionnaire 4 times, which will allow us to measure the influence this program is having on their future plans. The feedback about what they would change and what they enjoyed will be used to adjust the program as it continues.

At the end of each academic year we will interview students individually to more completely understand their experience. These discussions are not bound to a list of questions, and hence, we will be able to pursue details that are likely to be missed on a questionnaire. The students at Trinity University will be interviewed by Dr. Holder and the students at St. Mary's University by Dr. Uhlig. During a brief meeting before the interviews, these two investigators will discuss how to generally align the discussions, but again, we do not want to precompile a list of questions.

Any program, no matter how well it is designed, can benefit from an outside perspective, and at the beginning of 2009-2010 academic year we will invite an external reviewer to spend a few days with the program. This visit will correspond with Dr. Salter's visit, providing access to all the investigators. The reviewer will 1) meet with the students and the investigators, both individually and collectively, 2) meet with administrators at Trinity and St. Mary's Universities to measure their support and the influence this proposal is having on the larger academic community, and 3) will tour the campuses and facilities.

Once the visit concludes, the reviewer will detail his or her conclusions in a report. The finding of the report will be used to adjust the program as needed. The report will be forwarded to the program directors for review.

To measure student progress, we will give mid-term and final exams in the Reading and Research courses. After all, these are academic courses and grades need to be assigned. Since much of the education will be devoted to individuals and teams, we recognize that we may need to tailor exams for each student. This will take serious effort, but we believe it is necessary to measure student progress. The grades on these exams will be averaged to form a semester grade. Exams for the juniors will have a computing component so that we can measure their proficiency with the computing resources. Example tests will be forwarded to the program directors with the external review in 2009 and at the end of the grant.

To validate that we are achieving our goal of preparing students for a career in computational mathematics, we will annually contact each of our past participants to discuss how their participation in this project influenced them after graduation. These comments will be compiled and forwarded to the program director.

Our quantitative expectations are simple:

- We expect to author at least two research publications per year with undergraduate co-authors. These publications should appear in peer-reviewed journals.
- We expect 50% of the participants to pursue graduate studies in applied/computational/pure mathematics or a related discipline where mathematical computation is integral to the program.
- We expect to present our research annually at local, national, and international venues. Undergraduates should give at least 50% of these presentations.

Evaluation is crucial to the achievement of these expectations. The investigators take seriously the need to review and alter the program as needed to make the program a success.

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Ph.D. in Applied Mathematics, The University of Colorado at Denver, 1999.

M.S. in Mathematics, The University of Southern Mississippi, 1993.

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Positions Held:

Associate Professor, Trinity University, 2005-

Adjunct Professor of Radiation Oncology, University of Texas Health Science Center at San Antonio, 2003- .

Assistant Professor, Trinity University, 1999-2005 .

Visiting Research Professor, Hearin Center for Enterprise Science, 2002-2004.

Mathematics Instructor, University of Colorado at Denver, 1998-1999.

Synergistic Activities:

Co-authored research papers with 16 undergraduates.

The paper *Designing Radiotherapy Plans with Elastic Constraints and Interior Point Methods* was awarded the INFORMS William Pierskalla Award in Health Applications, 2000.

Editorial positions for *Algorithmic Operations Research*, *Topics in Operations Research*, and *Optimization and Engineering*.

President of the the Health Applications Section of the Institute of Operations Research and Management Science, 2005.

Received 8 teaching distinctions.

Publications Closely Related to the Project:
Note: Undergraduate student authors indicated with a *.

1. *Designing Radiotherapy Plans with Elastic Constraints and Interior Point Methods*, 2003, Health Care and Management Science, vol. 6, num. 1, pages 5 - 16.
2. *The Relationship Between the Number of Shots and the Quality of Gamma Knife Radiosurgeries*, 2005, co-authored with D. Cheek, M. Fuss and B. Salter, Optimization and Engineering, vol. 6, num. 4, pages 449-462.
3. *Partitioning Multiple Objective Optimal Solutions with Applications in Radiotherapy Design*, 2006, Optimization and Engineering, vol. 7, pages 501-526.
4. *Beam Selection in Radiotherapy Design*, 2005, co-authored with M. Ehrgott and J. Reese*, Trinity University, Mathematics Technical Report #95, San Antonio, TX, submitted to Linear Algebra and Its Applications.
5. *Comparing Beam Selection Strategies in Radiotherapy Treatment Design: The Influence of Dose Point Resolution*, 2005, co-authored with R. Acosta*, M. Ehrgott, D. Nevin*, J. Reese*, and B. Salter, submitted to the 2005 proceedings of the Coimbra Workshop on Optimization in Medicine.

Other Significant Publications

1. *The Relationship Between Discrete Vector Quantization and the P-Median Problem*, 2006, co-authored with G. Lim and J. Reese*, submitted to INFORMS J. on Computing.
2. *Simultaneous Data Perturbations and Analytic Center Convergence*, 2004, SIAM Journal on Optimization, vol. 14, num. 3, pages 841-868.
3. *An Extension of the Fundamental Theorem of Linear Programming*, 2002, co-authored with A. Brown*, A. Gedlaman*, and S. Martinez*, Operations Research Letters, vol. 30, num. 5,
4. *The Asymptotic Optimal Partition and Extensions of The Nonsubstitution Theorem*, 2002, co-authored with J. R. Hasfura-Buenaga and J. Stuart, Linear Algebra and Its Applications, vol. 394, pages 145-167.
5. *Asymptotic Sign Solvability and the Dynamic Nonsubstitution Theorem*, 2003, co-authored with L. Cayton*, R. Herring*, J. Holzer*, C. Nightingale*, and T. Stohs*, to appear in Mathematical Methods in Operations Research.

Collaborators over the Past 48 Months: R. Acosta (Stanford Univ.), L. Cayton (Univ. of California San Diego), C. Davis (Univ. of Utah), M. Ehrgott (Univ. of New Zealand), M. Fuss (Univ. of Texas Health Science Center in San Antonio) A. Gedlaman (Univ. of Texas), A. Hanna (St. Mary's University) R. Herring (Univ. of California Berkley), J. Holzer (Univ. of Wisconsin), D. LLagostera (Univ. of Houston), D. Nevin (Texas A&M Univ.), C. Nightingale (Oregon State Univ.), B. Salter (Univ. of Utah), T. Stohs (unknown), and P. Uhlig (St. Mary's University).

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Education:

Ph.D. in Computer Science Education, The University of Texas at Austin, 1996.

M.S. in Computer Science, The University of Texas at Dallas, 1977.

B.S. (with Honors) in Physics, St. Mary's University, 1975.

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Positions Held:

Associate Professor, St. Mary's University, 1996-present.

Assistant Professor, St. Mary's University, 1985-1996.

Instructor, St. Mary's University, 1982-1985.

Adjunct Professor, University of Texas at El Paso, 1981-1982.

Synergistic Activities:

Submitted paper for SIGCSE Conference 2007,*The Use of a Computer Simulation to Support the Teaching of Operating System Concepts* co-authored with P. Fink.

Holistic Scoring of Handwritten Computer Programs, Spring 2001, SIGCSE Bulletin, vol. 33, no. 1.

1994 Distinguished Faculty Award for being the outstanding faculty member in the St. Mary's University School of Science, Engineering and Technology.

Consult extensively with other departments to develop software simulation tools to support fellow faculty research.

Publications Closely Related to the Project:
Note: Undergraduate student authors indicated with a *.

1. *Radiotherapy optimAl Design: Academic Software for Benchmarking and Research*, co-authored with R. Acosta*, W. Brick*, A. Holder, D. Lara*, G. McQuilen*, D. Nevin*, B. Salter, and P. Uhlig.

Collaborators over the Past 48 Months: L. Holder (St. Mary's University), A. Holder (Trinity University), P. Uhlig (St. Mary's University), and B. Salter (Univiversity of Utah).

Thesis Adviser: L. Ray Carry (The University of Texas at Austin).

Bill Salter, Biographical Sketch
University of Utah, Dept. of Radiation Oncology
1950 Circle of Hope drive, Salt Lake City, Utah 84109
bill.salter@hci.utah.edu

Education:

Ph.D. in Medical Physics, The University of Texas Health Science Center, San Antonio, TX., 1996

B.S. Applied Mathematical Science- Engineering Track, The University of Houston Texas, 1990.

Positions Held:

Associate Professor - Department of Radiation Oncology, University of Utah, Dec. 2005-

Assistant Professor - Department of Radiation Oncology, University of Texas Health Science Center at San Antonio, 1996-2005 .

Director of Medical Physics, Cancer Therapy and Reserch Center, San Antonio, TX, Feb. 2005-Dec. 2005 .

Associate Director of Medical Physics, Cancer Therapy and Reserch Center, San Antonio, TX, 1998-Feb. 2005.

Synergistic Activities:

Supervising professor for 4 Ph.D. students.

Supervising professor for 2 M.S. students.

Committee member for 3 Ph.D. students.

Associate Editor *Journal of Applied Clinical Medical Physics*

Reviewer for *International Journal of Radiation Oncology Biology and Physics*, *Medical Physics Journal*, *Journal of Applied Clinical Medical Physics* and *Physics in Medicine and Biology.*

President - American Association of Physicists in Medicine - Southwest Chapter

Publications Closely Related to the Project:
Note: Undergraduate student authors indicated with a *.

1. *The Relationship Between the Number of Shots and the Quality of Gamma Knife Radiosurgeries*, 2005, co-authored with D. Cheek, M. Fuss and B. Salter, Optimization and Engineering, vol. 6, num. 4, pages 449-462.

2. *Comparing Beam Selection Strategies in Radiotherapy Treatment Design: The Influence of Dose Point Resolution*, 2005, co-authored with R. Acosta*, M. Ehrgott, D. Nevin*, J. Reese*, and B. Salter, submitted to the 2005 proceedings of the Coimbra Workshop on Optimization in Medicine.

3. *A Tutorial on Radiation Oncology and Optimization*, 2004, co-authored with B. Salter, Tutorials on Emerging Methodologies and Applications in Operations Research, H. Greenberg, ed., chap. 4, Kluwer Academic Publishers.

4. *Optimization of Isocenter Location for Intracranial Stereotactic Radiosurgery*, co-authored with V. Sarkar, working paper.

5. *Radiotherapy optimAl Design: Academic Software for Benchmarking and Research*, co-authored with R. Acosta*, W. Brick*, A. Holder, D. Lara*, G. McQuilen*, D. Nevin*, B. Salter and P. Uhlig.

Other Significant Publications

1. *An oblique arc capable patient positioning system for sequential tomotherapy*, Salter, et al, 2001, Med Phys 2001;28(12): 2475-88.

2. *NOMOS Peacock IMRT utilizing the Beak post collimation device*, Salter, et al, 2001, Med Dosim 2002;26(1): 37-45.

3. *Extracranial Stereotactic Radiotherapy and Radiosurgery*, with M. Fuss, to appear as a chapter in Tomotherapeutic Approaches, B. Slotman, T. Solberg, and R. Wurm, eds, Marcel Dekker, New York.

4. *Intensity-modulated Radiosurgery for childhood arteriovenous malformations*, with M. Fuss, J-L Caron, D. Vollmer, and T. Herman, Acta Neurochirurgica, 2005, in press.

5. *Daily ultrasound-based image-guided targeting for radiotherapy of upper abdominal malignancies*, with M. Fuss, S. Cavanaugh, C. Fuss, A. Sadeghi, C. Fuller, A. Ameduri, J. Hevezi, T. Herman, C. Thomas, Int J Radiat Oncol Biol Phys. 2004 Jul 15;59(4):1245-56.

Collaborators over the Past 48 Months:
R. Cheng (University of Oklahoma Health Science Center-HSC) D. Cheek (LSU/Mary Bird Perkins cancer center) P. Rassiah (University of Texas HSC at san Antonio) J. Tanyi (University of Arizona) R. Acosta (Stanford Univ.), M. Ehrgott (Univ. of New Zealand), M. Fuss (Univ. of Texas Health Science Center in San Antonio/Oregon Health and Sciences University) D. Nevin (Texas A&M Univ.),

Thesis Adviser: James Hevezi (The University of Texas Health Science Center at San Antonio).

Paul X. Uhlig, Biographical Sketch
St. Mary's University, Department of Mathematics
One Camino Santa Maria, San Antonio, Texas 78228
puhlig@stmarytx.edu, `http://ats.stmarytx.edu/~puhlig/`

Education:

Ph.D. in Mathematics, Rice University, Houston, TX, 1997.

M.A. in Mathematics, Rice University, Houston, TX, 1995.

B.S. in Mathematics, St. Mary's University, San Antonio, TX, 1990.

Positions Held:

Associate Professor, St. Mary's University, 2002-

Assistant Professor, St. Mary's University, 1997-2002.

Synergistic Activities:

Advisor, summer undergraduate research project, 2005, involving image processing and search algorithms. Results presented at TX Section MAA Meeting, Spring 2006, Wichita Falls, TX.

TX Section MAA, Level II Director, 2002-2004.

Advised three senior theses.

Ongoing collaboration with Dr. Hanna to integrate mathematics into the computer science curriculum through practical examinations based on challenging mathematics problems.

2000 Distinguished Faculty Award, St. Mary's University.

Publications Closely Related to the Project:
Note: Undergraduate student authors indicated with a *.

1. *Radiotherapy optimAl Design: Academic Software for Benchmarking and Research*, co-authored with R. Acosta*, W. Brick*, A. Hanna, A. Holder, D. Lara*, G. McQuilen*, D. Nevin*, and B. Salter, in preparation.

Other Significant Publications

1. *Where Best to Hold a Drum Fast*, 2003, co-authored with Steve Cox, SIAM SIREV Vol. 45 Issue 1, pp. 75-92, (2003).
2. *Minimal Compliance Fastening of Elastic Bodies*, co-authored with Steve Cox, Structural and Multidisciplinary Optimization, Vol. 22 No. 2, pp. 139-148 (2001).
3. *On The Optimal Insulation of Conductors*, co-authored with S. Cox and B. Kawohl, Journal of Optimization Theory and Applications, Vol. 100, No. 2, pp. 253-263, (1999).
4. *Where Best to Hold a Drum Fast*, co-authored with S. Cox, SIAM Journal on Optimization, Vol. 9 No. 4, pp. 948-964, (1999).

Collaborators over the Past 48 Months: A. Hanna (St. Mary's University) A. Holder (Trinity University) D. P. Phillips (University of Dallas), and B. Salter (Univ. of Utah).

Thesis Adviser: Steven J. Cox (Rice University).

SUMMARY PROPOSAL BUDGET

YEAR 1

FOR NSF USE ONLY		
PROPOSAL NO.	DURATION (months)	
	Proposed	Granted
AWARD NO.		

ORGANIZATION
Trinity University

PRINCIPAL INVESTIGATOR / PROJECT DIRECTOR
Allen Holder

A. SENIOR PERSONNEL: PI/PD, Co-PI's, Faculty and Other Senior Associates (List each separately with title, A.7. show number in brackets)	NSF Funded Person-months CAL	ACAD	SUMR	Funds Requested By proposer	Funds granted by NSF (if different)
1. Allen Holder - PI	0.00	0.00	1.00	$ 7,000	$
2. Arthur D Hanna - CO-PI	0.00	0.00	0.50	3,500	
3. Bill Salter Jr. - CO-PI	0.00	0.00	0.00	0	
4. Paul X Uhlig - CO-PI	0.00	0.00	0.50	3,500	
5.					
6. (0) OTHERS (LIST INDIVIDUALLY ON BUDGET JUSTIFICATION PAGE)	0.00	0.00	0.00	0	
7. (4) TOTAL SENIOR PERSONNEL (1 - 6)	0.00	0.00	2.00	14,000	
B. OTHER PERSONNEL (SHOW NUMBERS IN BRACKETS)					
1. (1) POST DOCTORAL ASSOCIATES	0.00	0.00	1.00	3,500	
2. (0) OTHER PROFESSIONALS (TECHNICIAN, PROGRAMMER, ETC.)	0.00	0.00	0.00	0	
3. (0) GRADUATE STUDENTS				0	
4. (6) UNDERGRADUATE STUDENTS				18,000	
5. (0) SECRETARIAL - CLERICAL (IF CHARGED DIRECTLY)				0	
6. (1) OTHER				2,000	
TOTAL SALARIES AND WAGES (A + B)				37,500	
C. FRINGE BENEFITS (IF CHARGED AS DIRECT COSTS)				4,896	
TOTAL SALARIES, WAGES AND FRINGE BENEFITS (A + B + C)				42,396	
D. EQUIPMENT (LIST ITEM AND DOLLAR AMOUNT FOR EACH ITEM EXCEEDING $5,000.) 64-Bit Server + Software $ 8,500					
TOTAL EQUIPMENT				8,500	
E. TRAVEL 1. DOMESTIC (INCL. CANADA, MEXICO AND U.S. POSSESSIONS)				8,800	
2. FOREIGN				0	
F. PARTICIPANT SUPPORT COSTS 1. STIPENDS $ 24,000 2. TRAVEL 3,600 3. SUBSISTENCE 0 4. OTHER 0					
TOTAL NUMBER OF PARTICIPANTS (6) TOTAL PARTICIPANT COSTS				27,600	
G. OTHER DIRECT COSTS					
1. MATERIALS AND SUPPLIES				0	
2. PUBLICATION COSTS/DOCUMENTATION/DISSEMINATION				0	
3. CONSULTANT SERVICES				0	
4. COMPUTER SERVICES				0	
5. SUBAWARDS				0	
6. OTHER				8,000	
TOTAL OTHER DIRECT COSTS				8,000	
H. TOTAL DIRECT COSTS (A THROUGH G)				95,296	
I. INDIRECT COSTS (F&A)(SPECIFY RATE AND BASE) 25% of Student Stipends (Rate: 25.0000, Base: 24000)					
TOTAL INDIRECT COSTS (F&A)				6,000	
J. TOTAL DIRECT AND INDIRECT COSTS (H + I)				101,296	
K. RESIDUAL FUNDS (IF FOR FURTHER SUPPORT OF CURRENT PROJECTS SEE GPG II.C.6.j.)				0	
L. AMOUNT OF THIS REQUEST (J) OR (J MINUS K)				$ 101,296	$

M. COST SHARING PROPOSED LEVEL $ 0 AGREED LEVEL IF DIFFERENT $

PI/PD NAME
Allen Holder

ORG. REP. NAME*

FOR NSF USE ONLY		
INDIRECT COST RATE VERIFICATION		
Date Checked	Date Of Rate Sheet	Initials - ORG

 *ELECTRONIC SIGNATURES REQUIRED FOR REVISED BUDGET

SUMMARY PROPOSAL BUDGET YEAR 2

ORGANIZATION: Trinity University	FOR NSF USE ONLY	PROPOSAL NO.	DURATION (months) Proposed	Granted
PRINCIPAL INVESTIGATOR / PROJECT DIRECTOR: Allen Holder		AWARD NO.		

A. SENIOR PERSONNEL: PI/PD, Co-PI's, Faculty and Other Senior Associates (List each separately with title, A.7. show number in brackets)	NSF Funded Person-months CAL	ACAD	SUMR	Funds Requested By proposer	Funds granted by NSF (if different)
1. Allen Holder - PI	0.00	0.00	1.00	$ 7,000	$
2. Arthur D Hanna - CO-PI	0.00	0.00	0.50	3,500	
3. Bill Salter Jr. - CO-PI	0.00	0.00	0.00	0	
4. Paul X Uhlig - CO-PI	0.00	0.00	0.50	3,500	
5.					
6. (0) OTHERS (LIST INDIVIDUALLY ON BUDGET JUSTIFICATION PAGE)	0.00	0.00	0.00	0	
7. (4) TOTAL SENIOR PERSONNEL (1 - 6)	0.00	0.00	2.00	14,000	
B. OTHER PERSONNEL (SHOW NUMBERS IN BRACKETS)					
1. (1) POST DOCTORAL ASSOCIATES	0.00	0.00	1.00	3,500	
2. (0) OTHER PROFESSIONALS (TECHNICIAN, PROGRAMMER, ETC.)	0.00	0.00	0.00	0	
3. (0) GRADUATE STUDENTS				0	
4. (6) UNDERGRADUATE STUDENTS				18,000	
5. (0) SECRETARIAL - CLERICAL (IF CHARGED DIRECTLY)				0	
6. (1) OTHER				2,000	
TOTAL SALARIES AND WAGES (A + B)				37,500	
C. FRINGE BENEFITS (IF CHARGED AS DIRECT COSTS)				4,896	
TOTAL SALARIES, WAGES AND FRINGE BENEFITS (A + B + C)				42,396	
D. EQUIPMENT (LIST ITEM AND DOLLAR AMOUNT FOR EACH ITEM EXCEEDING $5,000.)					
TOTAL EQUIPMENT				0	
E. TRAVEL 1. DOMESTIC (INCL. CANADA, MEXICO AND U.S. POSSESSIONS)				11,800	
2. FOREIGN				0	
F. PARTICIPANT SUPPORT COSTS 1. STIPENDS $ 24,000 2. TRAVEL 3,600 3. SUBSISTENCE 0 4. OTHER 0					
TOTAL NUMBER OF PARTICIPANTS (6) TOTAL PARTICIPANT COSTS				27,600	
G. OTHER DIRECT COSTS					
1. MATERIALS AND SUPPLIES				0	
2. PUBLICATION COSTS/DOCUMENTATION/DISSEMINATION				0	
3. CONSULTANT SERVICES				3,000	
4. COMPUTER SERVICES				0	
5. SUBAWARDS				0	
6. OTHER				8,000	
TOTAL OTHER DIRECT COSTS				11,000	
H. TOTAL DIRECT COSTS (A THROUGH G)				92,796	
I. INDIRECT COSTS (F&A)(SPECIFY RATE AND BASE) 25% of Student Stipends (Rate: 25.0000, Base: 24000)					
TOTAL INDIRECT COSTS (F&A)				6,000	
J. TOTAL DIRECT AND INDIRECT COSTS (H + I)				98,796	
K. RESIDUAL FUNDS (IF FOR FURTHER SUPPORT OF CURRENT PROJECTS SEE GPG II.C.6.j.)				0	
L. AMOUNT OF THIS REQUEST (J) OR (J MINUS K)				$ 98,796	$

M. COST SHARING PROPOSED LEVEL $ 0	AGREED LEVEL IF DIFFERENT $		
PI/PD NAME: Allen Holder	FOR NSF USE ONLY INDIRECT COST RATE VERIFICATION		
ORG. REP. NAME*	Date Checked	Date Of Rate Sheet	Initials - ORG

 *ELECTRONIC SIGNATURES REQUIRED FOR REVISED BUDGET

SUMMARY PROPOSAL BUDGET

YEAR 3

	FOR NSF USE ONLY		
ORGANIZATION Trinity University	PROPOSAL NO.	DURATION (months) Proposed	Granted
PRINCIPAL INVESTIGATOR / PROJECT DIRECTOR Allen Holder	AWARD NO.		

A. SENIOR PERSONNEL: PI/PD, Co-PI's, Faculty and Other Senior Associates (List each separately with title, A.7. show number in brackets)	NSF Funded Person-months CAL	ACAD	SUMR	Funds Requested By proposer	Funds granted by NSF (if different)
1. Allen Holder - PI	0.00	0.00	1.00	$ 7,000	$
2. Arthur D Hanna - CO-PI	0.00	0.00	0.50	3,500	
3. Bill Salter Jr. - CO-PI	0.00	0.00	0.00	0	
4. Paul X Uhlig - CO-PI	0.00	0.00	0.50	3,500	
5.					
6. (0) OTHERS (LIST INDIVIDUALLY ON BUDGET JUSTIFICATION PAGE)	0.00	0.00	0.00	0	
7. (4) TOTAL SENIOR PERSONNEL (1 - 6)	0.00	0.00	2.00	14,000	
B. OTHER PERSONNEL (SHOW NUMBERS IN BRACKETS)					
1. (1) POST DOCTORAL ASSOCIATES	0.00	0.00	1.00	3,500	
2. (0) OTHER PROFESSIONALS (TECHNICIAN, PROGRAMMER, ETC.)	0.00	0.00	0.00	0	
3. (0) GRADUATE STUDENTS				0	
4. (6) UNDERGRADUATE STUDENTS				18,000	
5. (0) SECRETARIAL - CLERICAL (IF CHARGED DIRECTLY)				0	
6. (1) OTHER				2,000	
TOTAL SALARIES AND WAGES (A + B)				37,500	
C. FRINGE BENEFITS (IF CHARGED AS DIRECT COSTS)				4,896	
TOTAL SALARIES, WAGES AND FRINGE BENEFITS (A + B + C)				42,396	
D. EQUIPMENT (LIST ITEM AND DOLLAR AMOUNT FOR EACH ITEM EXCEEDING $5,000.)					
TOTAL EQUIPMENT				0	
E. TRAVEL 1. DOMESTIC (INCL. CANADA, MEXICO AND U.S. POSSESSIONS)				11,800	
2. FOREIGN				0	
F. PARTICIPANT SUPPORT COSTS 1. STIPENDS $ 24,000 2. TRAVEL 3,600 3. SUBSISTENCE 0 4. OTHER 0					
TOTAL NUMBER OF PARTICIPANTS (6) TOTAL PARTICIPANT COSTS				27,600	
G. OTHER DIRECT COSTS					
1. MATERIALS AND SUPPLIES				0	
2. PUBLICATION COSTS/DOCUMENTATION/DISSEMINATION				0	
3. CONSULTANT SERVICES				0	
4. COMPUTER SERVICES				0	
5. SUBAWARDS				0	
6. OTHER				8,000	
TOTAL OTHER DIRECT COSTS				8,000	
H. TOTAL DIRECT COSTS (A THROUGH G)				89,796	
I. INDIRECT COSTS (F&A)(SPECIFY RATE AND BASE) 25% of Student Stipends (Rate: 25.0000, Base: 24000)					
TOTAL INDIRECT COSTS (F&A)				6,000	
J. TOTAL DIRECT AND INDIRECT COSTS (H + I)				95,796	
K. RESIDUAL FUNDS (IF FOR FURTHER SUPPORT OF CURRENT PROJECTS SEE GPG II.C.6.j.)				0	
L. AMOUNT OF THIS REQUEST (J) OR (J MINUS K)				$ 95,796	$

M. COST SHARING PROPOSED LEVEL $ 0 AGREED LEVEL IF DIFFERENT $

PI/PD NAME	FOR NSF USE ONLY		
Allen Holder	INDIRECT COST RATE VERIFICATION		
ORG. REP. NAME*	Date Checked	Date Of Rate Sheet	Initials - ORG

 *ELECTRONIC SIGNATURES REQUIRED FOR REVISED BUDGET

SUMMARY PROPOSAL BUDGET

Cumulative

ORGANIZATION **Trinity University**				**FOR NSF USE ONLY** PROPOSAL NO.	DURATION (months) Proposed / Granted
PRINCIPAL INVESTIGATOR / PROJECT DIRECTOR **Allen Holder**				AWARD NO.	

A. SENIOR PERSONNEL: PI/PD, Co-PI's, Faculty and Other Senior Associates (List each separately with title, A.7. show number in brackets)	NSF Funded Person-months CAL	ACAD	SUMR	Funds Requested By proposer	Funds granted by NSF (if different)
1. **Allen Holder - PI**	0.00	0.00	3.00	$ 21,000	$
2. **Arthur D Hanna - CO-PI**	0.00	0.00	1.50	10,500	
3. **Bill Salter Jr. - CO-PI**	0.00	0.00	0.00	0	
4. **Paul X Uhlig - CO-PI**	0.00	0.00	1.50	10,500	
5.					
6. ( ) OTHERS (LIST INDIVIDUALLY ON BUDGET JUSTIFICATION PAGE)	0.00	0.00	0.00	0	
7. (4) TOTAL SENIOR PERSONNEL (1 - 6)	0.00	0.00	6.00	42,000	
B. OTHER PERSONNEL (SHOW NUMBERS IN BRACKETS)					
1. (3) POST DOCTORAL ASSOCIATES	0.00	0.00	3.00	10,500	
2. (0) OTHER PROFESSIONALS (TECHNICIAN, PROGRAMMER, ETC.)	0.00	0.00	0.00	0	
3. (0) GRADUATE STUDENTS				0	
4. (18) UNDERGRADUATE STUDENTS				54,000	
5. (0) SECRETARIAL - CLERICAL (IF CHARGED DIRECTLY)				0	
6. (3) OTHER				6,000	
TOTAL SALARIES AND WAGES (A + B)				112,500	
C. FRINGE BENEFITS (IF CHARGED AS DIRECT COSTS)				14,688	
TOTAL SALARIES, WAGES AND FRINGE BENEFITS (A + B + C)				127,188	
D. EQUIPMENT (LIST ITEM AND DOLLAR AMOUNT FOR EACH ITEM EXCEEDING $5,000.) $ 8,500					
TOTAL EQUIPMENT				8,500	
E. TRAVEL 1. DOMESTIC (INCL. CANADA, MEXICO AND U.S. POSSESSIONS)				32,400	
2. FOREIGN				0	
F. PARTICIPANT SUPPORT COSTS 1. STIPENDS $ 72,000 2. TRAVEL 10,800 3. SUBSISTENCE 0 4. OTHER 0					
TOTAL NUMBER OF PARTICIPANTS (18) TOTAL PARTICIPANT COSTS				82,800	
G. OTHER DIRECT COSTS					
1. MATERIALS AND SUPPLIES				0	
2. PUBLICATION COSTS/DOCUMENTATION/DISSEMINATION				0	
3. CONSULTANT SERVICES				3,000	
4. COMPUTER SERVICES				0	
5. SUBAWARDS				0	
6. OTHER				24,000	
TOTAL OTHER DIRECT COSTS				27,000	
H. TOTAL DIRECT COSTS (A THROUGH G)				277,888	
I. INDIRECT COSTS (F&A)(SPECIFY RATE AND BASE)					
TOTAL INDIRECT COSTS (F&A)				18,000	
J. TOTAL DIRECT AND INDIRECT COSTS (H + I)				295,888	
K. RESIDUAL FUNDS (IF FOR FURTHER SUPPORT OF CURRENT PROJECTS SEE GPG II.C.6.j.)				0	
L. AMOUNT OF THIS REQUEST (J) OR (J MINUS K)				$ 295,888	$
M. COST SHARING PROPOSED LEVEL $ 0	AGREED LEVEL IF DIFFERENT $				

PI/PD NAME **Allen Holder**	**FOR NSF USE ONLY** INDIRECT COST RATE VERIFICATION		
ORG. REP. NAME*	Date Checked	Date Of Rate Sheet	Initials - ORG

C ***ELECTRONIC SIGNATURES REQUIRED FOR REVISED BUDGET**

Budget Summary
Title: Mathematical Computation with Applications in Medical Physics
Program: Computational Science Training for Undergraduates in the Mathematical Sciences

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Salary for Senior Personnel The investigators at Trinity and St. Mary's Universities do not request financial support during the academic year since directing the Reading and Research course will be part of their standard educational responsibilities. They are requesting summer support in the amount of $7,000 for the lead investigator, Dr. Allen Holder, and $3,500 for Drs. Uhlig and Hanna, per summer. This amount is based on 2 weeks of salary (4 weeks for the lead investigator) and covers the educational responsibilities and the administrative overhead of the lead investigator. This funding will begin the summer of 2008 and will continue through the summer of 2010.

Salary for Postdoctoral Student Dr. Salter will hire a postdoctoral student in medical physics in 2007, and about 1/15 of this position will be dedicated to the goals of this grant, which equates to $3,500 per year. In particular, this individual will be responsible for creating the patient data needed for the numerical experiments, and under the direction of Dr. Salter, this person will take the lead on the publications for the medical physics literature. This person will travel with Dr. Salter to San Antonio at the beginning of each summer so that s/he can assist the summer projects.

Peer Tutor Salary We will support 6 senior peer-tutors each academic year. Each will be paid on an hourly basis of $10 per hour, for 15 weeks per semester and up to 10 hours per week. This is a maximum of $1,500 per student per semester, which accounts for $18,000 per year.

Salary for System Administration The department of Radiation Oncology at the University of Utah supports a system administrator, and this person will manage the Beowulf cluster for this proposal. We anticipate that this will be approximately 1/15 of his or her overall salary, for a total of $2,000 per year.

Fringe Benefits The fringe benefit calculation uses three different rates. The per year calculation is detailed in the following table.

Institution	Amount/Description	Rate	Total
Trinity University	7,000 Summer Salary for lead PI	17.65%	1,236.00
St. Mary's University	7,000 Summer Salary for two faculty	24%	1,680.00
The Huntsman Cancer Institute	5,500 Postdoc and Sys. Admin. Salary	36%	1,980.00
Total			4,896.00

Equipment Although we will have the power of a 30 machine Beowulf cluster, we still need to collect substantial amounts of data onto a single machine to interact with other software such as CPLEX. The numerical research of the past few years has shown that even moderate clinical cases require a single process to have 3+ Gigabytes of memory, and 32-bit architecture is limited to approximately 2 Gigabytes. Having a single 64-bit machine with sufficient memory is crucial to the goals of this proposal. We are asking for $\$8,500$ to purchase one 64-bit server and the supporting software of CPLEX, AMPL and MATLAB. This machine will become the lead node of the Beowulf cluster.

Domestic Travel These funds are requested in four parts:

- **Conference Travel:** We are requesting funds to travel to 3 domestic conferences per year, such as the joint meetings of the AMS and the MAA, SIAM optimization, the national meeting of INFORMS, and the national meeting of the AAPM. This accounts for $3 \times \$1,200 = \$3,600$ per year.
- **Travel from Utah to San Antonio:** Dr. Salter will make 3 week long trips to San Antonio to help direct the beginning of each semester. His postdoc will also make the trip once per year (at the beginning of the summer). We estimate that each of these trips will cost $\$1,000$, and we are requesting $\$4,000$ per year to cover these expenditures.
- **Travel from San Antonio to Utah:** Twice during the 3 years covered by this grant we are requesting funds to support a week long visit to The Huntsman Cancer Institute for the investigators who reside in San Antonio. This travel is hugely valuable to the research goals of this proposal because it will allow the investigators to work as one unit. We anticipate the cost of this trip being $\$1,000$ per person, and are asking for $3 \times \$1,000 = \$3,000$ in 2008 and 2010.
- **Travel to Awardees Meeting** As indicated in the proposal guidelines, we are requesting $\$1,200$ to attend an awardees meeting annually.

Participant Stipends We will support 6 students over each summer at a rate of $\$4,000$ per student per summer. This accounts for $\$24,000$ per year. Housing costs are covered by Trinity University.

Participant Travel We expect many of the seniors to speak about their research. After all, welcoming young researchers into the academic community is a stated goal of the grant, and we expect undergraduates to be the lead speaker on at least half of the talks. One venue will be the annual meeting of the Texas section of the MAA. We hope to take as many participants as possible and are requesting $\$1,200$ per year to support this trip. Additionally, we expect at least two students to present their research at national conferences and are asking for an additional $2 \times \$1,200 = \$2,400$ of funding to support this travel.

Consulting Services At the beginning of the 2009-2010 academic year we will undergo an external review by an expert in mathematical computation. We will cover this person's expenses and pay them $\$2,000$ for their evaluation. We estimate the entire cost of the review to be $\$3,000$.

Colloquium Support We request the support for 5 colloquium speakers per semester (10 per year). We will cover the speakers travel and pay them a $300 honorarium. The requested amount per year is $10 \times \$800 = \$8,000$.

Current and Pending Support
Title: Mathematical Computation with Applications in Medical Physics
Program: Computational Science Training for Undergraduates in the Mathematical Sciences

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Dr. Holder is listed as Senior Personnel on Trinity's pending NSF-REU grant in mathematics. This grant has been funded for 9 years, and if if refunded in its full request, it will be funded for 3 more (2007-2009). The total request of this grant is $261, 154. Dr. Holder is one of 6 personnel on this proposal, and only 3 are needed per summer. He supported this grant 5 of the last 6 summers and has worked with 13 undergraduates on topics in optimization and computational biology. He has published 2 articles with these student, with a third article in submission. The first of these articles appeared in *Operations Research Letters* and was the 4th most requested article in this journal from 2000 to 2004. If this CSUMS proposal if funded, he will excuse himself from all responsibilities of the REU grant to focus on the objectives of this proposal.

Drs. Hanna, Uhlig, and Salter have no current or pending funding.

Facilities, Equipment and Other Resources
Title: Mathematical Computation with Applications in Medical Physics
Program: Computational Science Training for Undergraduates in the Mathematical Sciences

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Both Trinity and St. Mary's Universities have received infrastructure grants in the past 10 years to modernize their classrooms (Trinity received a $75,000 Texas Infrastructure grant and St. Mary's received $2.1 million in Title V funds). All classrooms have modern projectors and computer access. Furthermore, the students at St. Mary's University purchase laptops as part of their tuition, and learning to harness modern technology is part of the University's curriculum. Both campuses have campus wide Internet access, including wireless access, and numerous computer labs. Trinity also has two labs that each have 30+ linux machines. Access to the computing resources required by this proposal is universal among both student populations.

The primary computing resource for the clinically based numerical experiments is the Beowulf cluster at The Huntsman Cancer Institute (HCI). We will prototype modules on local machines at Trinity and St. Mary's Universities, and once tested, we will include them as part of the operational code on the cluster at the HCI. Access to the operational code will be restricted to control the haphazard development that would ensue from universal access. However, any student needing access to the cluster will have access. We expect one of the student teams to focus on distributive computing, and they will have access to the cluster.

The HCI has access to several commercial treatment systems, and since this is somewhat uncommon for a clinic, this is especially important to mention. Different commercial systems use different optimization routines and often develop different treatments for the same patient. Having access to several will allow us to make wide-scale comparisons that typically would not be possible. The HCI will use these systems to build a test bank for problems that will allow us to make comparisons on the same patient information.

Both Trinity and St. Mary's University have exceptional undergraduate libraries, with access to research libraries through various consortiums. Research articles are typically available within a few days via interlibrary loan. We further have direct access to the research libraries at The University of Utah and The University of Texas at San Antonio. Availability of research materials is assured.

ST. MARY'S UNIVERSITY

October 12, 2006

Dr. Allen Holder
Department of Mathematics
Trinity University
1 Trinity Place
San Antonio, TX 78212

Dr. Holder,

I am happy to provide a letter of support for the collaborative project proposed by you and two of our faculty, Dr. Paul Uhlig, Department of Mathematics, and Dr. Arthur Hanna, Department of Computer Science. The Computational Science Training for Undergraduates in the Mathematical Sciences Program at the National Science Foundation complements our goal in the Undergraduate Research Program at St. Mary's University to increase research opportunities for our students.

The research connection to medical physics is a good match to St. Mary's faculty and students since our largest majors are biology and biochemistry. A significant number of our science graduates go on to medical and dental schools and to doctoral research programs. Additionally, our new five-year academic affairs strategic plan places high priorities on undergraduate research and faculty scholarship. This project will support both of these major goals.

St. Mary's University and Trinity University have enjoyed many years of partnership and collaboration. We look forward to the approval of this proposal and to the ensuing exchange of students, faculty, and great ideas.

Best wishes,

Susan McCarthy

Susan McCarthy, Ph.D.
Assistant to the Vice President
for Academic Affairs and
Director, Academic Grants

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ONE CAMINO SANTA MARIA
SAN ANTONIO, TEXAS 78228-8586
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MEMORANDUM

TO: ALLEN HOLDER, MATHEMATICS

FROM: J. PAUL GIOLMA, CHAIR, IRB

SUBJECT: IRB EXEMPTION FOR IMAGE ANALYSIS STUDY

DATE: 10/11/06

CC: DIANE SMITH, ACADEMIC AFFAIRS

This memorandum provides exemption from further Trinity IRB involvement, except as provided for below (duration and status reporting).

Dr. Holder is studying structures in images provided by Huntsman Cancer Institute under a NSF grant. Dr. William Salter, PhD. (University of Utah/Huntsman) has indicated that the images used are obtained retrospectively for this study. Images are stripped of identifying information, and Dr. Holder has no access to such information.

For IRB exemption, DHHS Regulation 46.101.b requires:

(4) Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

Dr. Holder, identified as the investigator here, does not have access to patient identification. His work is therefore exempt under DHHS Regulation 46.101.b (4).

Dr. Douglas L. Hall
St. Mary's University
One Camino Santa Maria
San Antonio, Texas 78228
DHall@StMaryTX.edu

October 14, 2006

To the CSUMS Program Directors,

The Computer Science Department at St. Mary's University unreservedly supports the CSUMS proposal being submitted by Dr. Arthur Hanna and his colleagues at Trinity University, St. Mary's University, and The Huntsman Cancer Institute. Dr. Hanna has regularly involved his undergraduate students in his research efforts and the proposed CSUMS project will afford another significant opportunity for St. Mary's undergraduate research.

St. Mary's has a growing commitment to its nascent undergraduate research program directed by Dr. Tim Raabe. Quoting in part from www.StMaryTX.edu/URO

The mission of the St. Mary's undergraduate research program is to facilitate and increase the use of undergraduate research as a teaching and mentoring tool on the campus of St. Mary's University. The goals of the undergraduate research program are to increase the number of students participating in undergraduate research...assist the student, especially culturally or economically disadvantaged students, to realize his/her potential as a positive contributor to a field or discipline by completing a research project. The University sponsors the St. Mary's University annual Undergraduate Research Symposium and Creative Activities Exhibition.

I enthusiastically support the goals of this proposal. To ensure the success of the grant, the Computer Science department will allow Dr. Hanna to teach CS4375 (Advanced Topics: Mathematical Computing) as part of his teaching responsibilities for the duration of the grant. If there are any further questions, please do not hesitate to contact me.

Sincerely,

Dr. Douglas L. Hall

Mary Wagner-Krankel, Ph.D., Chair,
Department of Mathematics
St. Mary's University
mwagnerkrankel@stmarytx.edu

October 17, 2006

To the CSUMS Program Directors,

The Mathematics Department at St. Mary's University enthusiastically supports the CSUMS proposal being submitted by Dr. Allen Holder (PI) under which Dr. Paul Uhlig, our Associate Professor of Mathematics, would collaborate as a Co-PI. Dr. Uhlig has been a leader in our department as St. Mary's expands its emphasis on undergraduate research. The proposal, through Dr. Uhlig's activities, will support our department's efforts to grow the number of majors in our Mathematical Sciences degree programs (BS) especially in computer science, physics and biomathematics.

The department enthusiastically supports the goals of the proposal. To that end it will schedule Dr. Uhlig to teach MT 5160, 5260 and/or 5360 Independent Study as part of his teaching responsibilities for the duration of the grant. If there are any further questions, please do not hesitate to contact me.

Sincerely,

Mary Wagner-Krankel

Mary Wagner-Krankel

I am writing this letter to express my unqualified support for the attached NSF CSUMS grant application. Dr.'s Holder, Hanna, Salter and Uhlig have previously performed work on optimization of radiation therapy treatment plan quality in collaboration with and supported by my department, and I consider this work important and valuable to the medical community. The notion of leveraging the knowledge and experience gained on projects such as the one just mentioned toward the education and training of undergraduate students in mathematics seems only logical. Mathematical optimization of treatment delivery parameters has become an extremely important component of the treatment planning process in radiation oncology and there is clearly a need to grow our understanding in this area. The idea of training undergraduate mathematics students to facilitate this growth is, in my opinion, a wise use of available resources aimed at ultimately improving the quality of care that we are able to provide our patients.

Sincerely,

Dennis Shrieve MD

Professor and Chair

Department of Radiation Oncology

University of Utah – Huntsman Cancer Institute

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Roberto Hasfura
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Department of Mathematics
One Trinity Place
San Antonio, TX 78212
jhasfura@trinity.edu

October 14, 2006

To the CSUMS Program Directors,

The mathematics department at Trinity University wholeheartedly supports the CSUMS proposal being submitted by Dr. Allen Holder and his colleagues at St. Mary's University and The Huntsman Cancer Institute. Dr. Holder has had a tremendous impact on our students over the last few years with related research, and the proposed CSUMS initiative promises to advance this impact. Two immediate and important effects come to mind.

First, I have read numerous alumni surveys in the 7 years that I have been chair, and when asked what they would have changed about their education, the alumni have unequivocally stated that they left Trinity with little exposure to computer science. The goals of this proposal will help rectify this omission, and I hope and expect that many of our majors will take advantage of the educational opportunities in scientific computing provided by this grant.

Second, Trinity is undergoing a capital campaign, and one of the initiatives is to build interdisciplinary programs. This CSUMS proposal naturally supports this initiative since it is focused on the interdisciplinary area of medical physicist, which includes mathematics, computer science, physics and biology. Few projects could support so many disciplines. Also, Trinity has introduced a minor in Scientific Computing to support the interdisciplinary initiative, which includes two new courses in mathematics. We are in our first offering of the minor, and student participation is lacking. I perceive that funding this proposal will help solidify this curricular option, and hence, will make a long lasting impact on our scientific curriculum.

For these reasons I enthusiastically support the goals of this proposal, and to ensure its success the mathematics department will schedule Dr. Holder to teach MATH 3-90 (Readings and Conference) as part of his regularly scheduled teaching responsibilities for the duration of the grant. If there are further questions, please do not hesitate to contact me.

Sincerely,

Roberto Hasfura