Final Report for Period: 09/2007 - 08/2008
Submitted on: 11/30/2008
Principal Investigator: Lee, Eva K.
Award ID: 0313169
Organization: GA Tech Res Corp - GIT
Submitted By:
Lee, Eva - Principal Investigator
Title:
ITR/AP(CCR): Investigation of Computational Optimization in Brachytherapy Cancer Treatment

Project Participants

Senior Personnel

Name: Lee, Eva
Worked for more than 160 Hours: Yes
Contribution to Project:

Post-doc

Graduate Student

Name: Cha, Kyungduck
Worked for more than 160 Hours: Yes
Contribution to Project:
Kyungduck Cha worked on cancer treatment optimization as his PhD thesis research.

Name: Gupta, Kapil
Worked for more than 160 Hours: No
Contribution to Project:

Name: Maheshwary, Maheshwary
Worked for more than 160 Hours: Yes
Contribution to Project:
Sid Maheshwary worked on hypergraphic structures as part of his PhD thesis research.

Name: Wu, Tsung-Lin
Worked for more than 160 Hours: No
Contribution to Project:
Tsung-lin learnt of modeling of cancer treatment, and the mathematics that involves in dose-escalation and tumor control probability analysis.

Undergraduate Student

Technician, Programmer

Other Participant

Research Experience for Undergraduates

Organizational Partners

Memorial Sloan Ketting Cancer Center

Dr. Marco Zaider offered the necessary clinical experience to provide guidelines for us in designing mathematical models that are realistic for use in brachytherapy cancer treatment. He also helped to evaluate plans and provided feedback on their quality and clinical relevance.

Other Collaborators or Contacts

Yes, the PI has initiated other cancer research collaboration with Joe Deasy at Washington University.

Activities and Findings

Research and Education Activities:

Research:

This project addresses the fundamental problem of treatment planning for brachytherapy treatment of cancer. This medical procedure involves placement of radioactive sources either in or near tumors. It can be used as a definitive treatment for cases where the tumor is confined to the diseased organ; or as an adjuvant treatment along with external beam radiation therapy and/or surgery. The research involves development of mathematical models for treatment planning, theoretical investigation of these models, and algorithmic design for solving large-scale and dense MIP problem instances.

Education:

Supervised PhD students in this research project, and subsquently, two PhD theses were completed. Further, Kyungduck Cha's thesis: Cancer Treatment Optimization was awarded Honorable Mention in the 2008 INFORMS George Dantzig Dissertation Competition.

Selected Presentations:

Cha, Integer Programming Strategies for Large-scale Cancer Instances, INFORMS Washington DC 2008.

Cha, Cancer Treatment Optimization, Georgia Dantzig Dissertation Competition, INFORMS Washington DC 2008.

Maheshwary, Parallel Branch-and-Cut Algorithm for Solving Market-Share Instances, INFORMS Washington DC 2008.

Large-Scale Optimization Strategies for Optimal Cancer Treatment Design, SIAM Optimization Conference, Boston May 2008.

Cha, Integer Programming Strategies for Large-scale Cancer Instances, INFORMS Seattle 2007.

Maheshwary, Computational Advances in Generating Hypergraphic Cutting Planes, INFORMS Seattle 2007.

Keynote presentation: Operations Research advances Cancer Therapeutics, INFORMS Seattle, Nov 2007.

Plenary presentation: Robust Optimization to Accommodate Effects of Systematic Treatment Uncertainties, Fields Institute Research in Mathematical Science, Oct 2007.

Plenary presentation: 4D-Image-Guided Treatment Planning Optimization for Managing Organ Motion in Radiotherapy Planning, 2007 International Conference on ``Medical Radiations: Research and practice,'' Marrakech Morocco Apr 2007.

Maheshwary, Facets of Conflict Hypergraphs -- Theory and Computation, INFORMS Pittsburgh Nov 2006.

Computational Optimization for Cancer Therapeutics, Operations Research Symposium, Hong Kong University Jun 2006.

Facets of Conflict Hypergraphs -- Theory and Computation, INFORMS 2006 International Conference, Hong Kong Jun 2006.

Plenary presentation: Large-Scale Optimization Strategies for Optimal Cancer Treatment Design, Fields Institute Research in Mathematical Science, June 2006.

2006 Mathematician Ambassador: Targeting tumors: advances and challenges, the 2006 mathematician selected by the American Mathematical Society to meet individually with congressional leaders on Capital Hill to present and promote mathematical advances and applications to medicine and to lobby for funding to NSF, June 2006.

Panel presentation: Optimization in Medicine and HealthCare,
NSF/NIBIB HealthCare Systems Engineering Workshop, NSF Headquarters, June 2006.

Keynote presentation: Research Challenges in Medicine and HealthCare, The 31st Conference on Mathematics of Operations Research, Lunteren, The Netherlands Jan 2006.

Facets of Conflict Hypergraphs -- Theory and Computation, INFORMS San Francisco Nov 2005.

Plenary presentation: Integer Programming in Radiation Therapy,
Workshop on Optimization in Medicine, University of Coimbra Portugal Jul 2005.

Incorporating Biological Metabolite Information within Treatment of Prostate Carcinoma and Analysis of Dose Escalation Effect, competitive reviewed selection, 48th Annual meeting American Society for Therapeutic Radiology and Oncology, Pittsburgh Nov 2006.

EK Lee, Computational Challenges in Cancer Advances and Biomedical Informatics. Washington University St. Louis, School of Medicine, St. Louis Apr 2005.

EK Lee, Panel presentation: A 21st Century Frontier: Advances in Treatment of Cancer, Georgia Tech: Innovating Here and Now. Washington D.C. Nov 2004.

EK Lee, Panel presentation: Cancer Treatment and Design: Optimization in Radiation Planning and Delivery: Myth or Reality, 46th Annual meeting American Society for Therapeutic Radiology and Oncology, Atlanta Oct 2004.

EK Lee, Media discussion: Overview of Cancer Research, Biotechnology: A 21st Century Frontier: CASE Media Fellowship, Atlanta May 2003.

EK Lee, Panel: New Trends and Challenges in Computer-Assisted Medical Research and Practice, DIMACS Workshop on Medical Applications in Computational Geometry, New Jersey Apr 2003.

EK Lee, Large-Scale Biocomputing for Cancer Diagnosis and Optimal Treatment Design, Georgia Tech Annual Supercomputing Conference SC2004, Pittsburgh Nov 2004.

EK Lee, Incorporating Biological Metabolite Information Within Treatment of Prostate Carcinoma, 46th Annual meeting American Society for Therapeutic Radiology and Oncology, Atlanta Oct 2004.

EK Lee, Automated Data Collection and Integration for Cancer Treatment Design and Clinical Quality Evaluation Investigation, Joint BECON\footnote{NIH's Bioengineering Consortium}/BISTIC\footnote{Biomedical Information Science and Technology Consortium} 2004 Symposium Biomedical Informatics for Clinical Decision Support: A Vision for the 21st Century, NIH Bethesda Jun 2004.

EK Lee, An NTCP-Driven, MR-Guided Dose Escalation Study For Permanent Prostate Implants, Whitaker Foundation Grantee Conference, La Jolla Aug 2003.

EK Lee, Facets of Conflict Hypergraphs -- Theory and Computation, INFORMS Colorado Oct 2004.

EK Lee, New Features in a General MIP Solver (MIPSOL), INFORMS Atlanta Oct 2003.

EK Lee, Computational Science for Oncological Research, Emory-GA Tech Cancer Research Advance, Jan 2004.

EK Lee, Bioinformatics, Modeling, and Biocomputing, Emory-GA Tech Planning Symposium on Quantitative Medicine, Dec 2003.

Findings:

We have developed realistic and practical mathematical models to describe the physical planning of brachytherapy, which involves the determination of an ``optimal'' configuration of radioactive sources to be implanted in/near the tumor. There is a finite, but extremely large, set of possible source configurations to choose from (determined by medical devices), making treatment planning an extremely difficult combinatorial problem. We use the technology of mixed integer programming (MIP) to model this problem.

Theoretical investigation of the underlying polyhedral structure of the MIP models was conducted via the construction of conflict hypergraphs. Hypergraphic structures such as hypercliques, hyper-oddholes and hyperwheels have been identified, and necessary and sufficient conditions for the associated inequalities to be facet-defining to the polyhedra of interest were studied. Resulting theorems of cutting planes were subsequently implemented, and tested to determine their effectiveness in the solution process.

Independent computational tools aimed at solving the difficult dense MIP instances from this class of problems, as well as from other applications were investigated. Dense MIP instances, even small ones, have proven to be intractable by leading computational solvers. Computational approaches newly established include matrix reduction techniques, penalty branching strategies which take advantage of the geometry of the seed locations, aggregate branching which focuses on reduced-cost and multiple branches with sets of variables instead of variable dichotomy.

Resulting plans from our MIP approaches have been shown to be clinically acceptable and of higher quality in tumor control and normal tissue dose reduction, compared to plans designed by existing commerical planning systems.

Training and Development:

The project provided Ph.D. and undergraduate students hands-on research experience in interdisciplinary areas of engineering and medicine. Each student works closely with the PI as well as well-known cancer researchers. PhD students involved in this project took classes in their main engineering disciplines as well as those in cancer biology and biotechnology disciplines. They were also working towards a minor in bioinformatics during their graduate studies. Two students completed their PhD thesis research in 2008.

Outreach Activities:

The project offers opportunities for Ph.D. and undergraduate students to work in interdisciplinary areas of engineering and cancer biotechnology. Each student works closely with the PI as well as well-known cancer researchers. PhD students involved in this project both took classes in their main engineering disciplines as well as in cancer biology and biotechnology disciplines. They were also working towards a minor in bioinformatics during their graduate studies.

The PI is involved in high-school recruiting and has presented her work in interdisciplinary areas to some of the high-schoolers.

The PI presented a talk entitled 'A 21st Century Frontier: Advances in Treatment of Cancer' which described computational and engineering techniques and their applications to cancer treatment at 'Georgia Tech: Innovating Here and Now', a public alumni event (approx. 300 attendees from very diverse fields) held in Washington DC, November 2004.

Several plenary talks were given by the PI on various high-profile workshops and conferences, attended by audience from diverse fields:

-Keynote presentation: Operations Research advances Cancer Therapeutics, INFORMS Seattle, Nov 2007.

-Plenary presentation: Large-Scale Optimization Strategies for Optimal Cancer Treatment Design, Fields Institute Research in Mathematical Science, June 2006.

-2006 Mathematician Ambassador: Targeting tumors: advances and challenges, the 2006 mathematician selected by the American Mathematical Society to meet individually with congressional leaders on Capital Hill to present and promote mathematical advances and applications to medicine and to lobby more federal funding for NSF, June 2006.

-Panel presentation: Optimization in Medicine and HealthCare,
NSF/NIBIB HealthCare Systems Engineering Workshop, NSF Headquarters, June 2006.

-Keynote presentation: Research Challenges in Medicine and HealthCare, The 31st Conference on Mathematics of Operations Research, Lunteren, The Netherlands Jan 2006.

-Plenary presentation: Large-Scale Integer Programming for Radiation Therapy Treatment Planning, Modeling and Optimization conference:

Theory and Applications (MOPTA), Windsor Ontario Canada Jul 2005.

Furthermore, the results of this project have attracted media attention and resulted in newspaper/media reports on the findings, as well as TV filming of the work for national broadcast (see one-time publication for details of these reports and TV segments). Thus this research and its impact has reached the public through various means of news, television, and medical magazines.

Journal Publications

Easton T, Hooker K, Lee EK, "Facets of the Independent Set Polytope", Mathematical Programming B, p. 177, vol. B98, (2003). Published,

Lee EK, Zaider M, "IntraOperative Dynamic Dose Optimization in Permanent Prostate Implants", International Journal of Radiation Oncology, Biology and Physics, p. 854, vol. 56(3), (2003). Published, 12788195

Lee, EK, "Generating cutting planes for mixed integer programming problems in a parallel computing environment", INFORMS JOURNAL ON COMPUTING, p. 3, vol. 16, (2004). Published, 10.1287/ijoc.1030.002

Lee, EK; Sofer, A, "Operations research in medicine - Computing and optimization in medicine and life - Preface", ANNALS OF OPERATIONS RESEARCH, p. 1, vol. 148, (2006). Published, 10.1007/s10479-006-0088-

Lee, EK; Zaider, M, "Mixed integer programming approaches to treatment planning for brachytherapy - Application to permanent prostate implants", ANNALS OF OPERATIONS RESEARCH, p. 147, vol. 119, (2003). Published,

Lee, EK; Sofer, A, "Untitled - Preface", ANNALS OF OPERATIONS RESEARCH, p. 13, vol. 119, (2003). Published,

Lee EK, Zaider, M, "Operations Research Advances Cancer Therapeutics", Interfaces, p. 5, vol. 38(1), (2008). Published,

EK Lee, Maheshwary S, "Facets of conflict hypergraphs", Mathematics of Operations Research, p. , vol. , (2008). Submitted,

Lee EK, Deasy JO, " Optimization in intensity-modulated radiation therapy", SIAG/OPT Views-and-News, Optimization in Medicine, p. 20, vol. 17(2), (2006). Published,

Books or Other One-time Publications

M Zaider, EK Lee, "Treatment planning for low dose rate and high dose rate brachytherapy", (2004). Book, Published
Editor(s): Ed. Dicker, Merrick, Gomella, Valicenti, Waterman, Gomella
Collection: Basic and Advanced Techniques in Prostate Brachytherapy
Bibliography: Chapter 12, CRC Press

EK Lee, M Zaider, "Optimization and Decision Support in Brachytherapy Treatment Planning", (2004). Book, Published
Editor(s): M Bandeau, and F Sainfort
Collection: Handbook of Operations Research/Management Science Applications in Health Care
Bibliography: Chapter 28, Kluwer Academic Publishers, Hillier International Series in OR/MS

TV news report on Lee's research, "Technology Improves Prostate Cancer Treatment", (2005). TV reports, Published
Collection: ABC TV and News Report
Bibliography: Mar 9

TV journalist: profile of Lee's research, "Curing Prostate Cancer", (2004). TV news segment, Published
Editor(s): The American Institute of Physics and American Mathematical Society
Collection: TV news for Discoveries Breakthroughs -- Inside Science
Bibliography: TV news segment broadcasted nationwide on Science News

Newspaper report profile, "Engineering Meets Biology in Tackling Tumors", (2004). Book, Published
Collection: Atlanta Business Chronicle's Health-Care Quarterly
Bibliography: February

Journalist's report on Lee's research., "The Long and Short of Inverse Planning", (2007). journalist's report in medical magazine, Published
Collection: Medical Imaging Magazine
Bibliography: January

Journalist's report on Lee's research., "Combined metabolic and therapeutic imaging improves tumor therapy", (2005). Journalist's report on medical magazine, Published
Collection: Diagnostic Imaging
Bibliography: January 10

Cha, Kyungduck, "Cancer Treatment Optimization", (2008). Thesis, Published
Bibliography: April

Web/Internet Site

URL(s):

http://www.isye.gatech.edu/~evakylee/medicalor

Description:

This website features (bio)medical research projects conducted by the PI, including this NSF-sponsored project. It also includes inter-disciplinary graduate programs of Operations Research in Medicine, and Bioinformatics, as well as undergraduate premed programs. Funding from NSF is acknowledged.

Other Specific Products

Product Type:

Patents

Product Description:

``Improved Brachytherapy Treatment Planning Method and Apparatus,"
Provisional application No. 60/162,236. US   Utility patent: 6,530,873 B1 issued Mar 11, 2003.

Sharing Information:

This patent has been licensed to a medical software company. System developed is now available for use in clinics nationwide.

Product Type:

INFORMS Franz Edelman Award

Product Description:

This work is awarded the 2007 INFORMS Franz Edelman award, the highest and most prestigious award in the field of Operations Research. It's considered the "superbowl" and the award recognizes outstanding examples of operations research (O.R.) projects that have transformed companies, entire industries and people?s lives.

Sharing Information:

The optimization models and algorithms guide doctors toward the most effective dose provided by each radioactive seed, the shape of the organ being treated, the locations of tumor cells within the organ and critical structures for which radiation dose should be limited, the sensitivity of tissues to radiation, and the expected shrinkage of the organ after treatment. The system?s goal is to provide consistent tumor-killing radiation doses to the tumor cells while limiting potentially damaging doses to nearby critical structures.

Using our approaches, the resulting system allows for real-time (intra-operative) treatment of prostate cancer. It offers significantly safer and more reliable treatment outcomes. In addition, it eliminates the need for pre-operative simulation and post-implant dosimetric analysis, resulting in savings of hundreds of millions of dollars per year in the US alone. Post-treatment quality of life is improved through drastic reduction (up to 45-60 percent) of complications. The reason for this is twofold: a) treatment plans thus devised deliver less radiation to adjacent healthy structures, and b) the ability to perform mid-implant re-planning eliminates the unavoidable discrepancies between planned and actual seed placement in the target. This has a profound impact on the cost of managing treatment-associated morbidity. The procedure uses approximately 20-30 percent fewer seeds and 15 percent fewer needles (used to place seeds inside the prostate gland). As a result, the operating-room time is shortened, and the entire procedure is less invasive. The system has the potential to establish standards and guidelines for cancer treatment quality control and quality assurance of the implantable plan.

Wide distribution of our system should allow consistent treatment planning across different clinics, and significantly reduce variability in treatment plan quality. The next phase of this effort will expand the applicability of our system to other forms of brachytherapy, such as treatment of breast, cervix, esophagus, biliary tract, pancreas, head and neck, and eye.

Product Type:

INFORMS George Dantzig Dissertation Award

Product Description:

Kyungduck Cha: "Cancer Treatment Optimization"

Sharing Information:

This PhD thesis work has been awarded "Honorable Mention" for the 2008 INFORMS George Dantzig Dissertation Award.

Contributions

Contributions within Discipline:

This clinical problem opens up the opportunity for advancing a new and different facet of the mathematical programming/OR frontier. Many of the computational integer programming advances in the last 50 years have been strongly motivated by challenges arising from industrial applications. These applications result in large-scale super sparse constraint matrices (<= 1 percent) where methodologies now exist that offer good solutions. However, the treatment planning instances have totally dense constraint matrices, and existing solution techniques in commercial MIP solvers are unable to solve them. As a result, we initiated a theoretical investigation that led to the introduction of the concept of conflict hypergraphs and their use in generating cutting planes to assist in the MIP solution process. The resulting computational strategies not only improve solution times for these cancer instances, but also help to solve some intractable, small (10 constraints and 250 variables) yet totally dense market-share instances (Cornejuols and Dwande 1999, Easton, Hooker, and Lee 2003).

Thus, this collaboration advanced the frontiers of knowledge in integer programming. First, conflict hypergraphs provide a rich and complex construct for theoretical investigation of the independent set polytope, a structure embedded as a subsystem in many MIPs. Second, from a computational standpoint, we offer new directions related to separation strategies for hypergraphic structures. In particular, new computational strategies for hypercliques, hyperoddholes, hyperwebs, and hyperanti-webs and parallel cutting plane algorithms are currently under development. These will aid in the solution of other difficult dense MIP instancesùinstances that are intractable using currently available strategies. Third, the study of the dense MIP problem is important in its own right in the field of integer programming and operations research. Thus, our study establishes a new research frontier to the field of mixed integer programming where new theory and computational advances can be pursued.

Contributions to Other Disciplines:

The contribution of our work is multiple folds towards cancer patient care:

A. Cost Savings

Our system eliminates the cost of the pre-treatment simulation session, including imaging, pre-plan treatment design by an expert planner, labor, and facility usage. Cost savings are estimated to be $5,000 per patient. This does not factor in further savings to the patient, e.g., costs of time off from work for the simulation session and hospital waiting time.

In the United States, there will be an estimated 218,890 new cases of prostate cancer in 2007. The American Brachytherapy Society 2005 statistics show that approximately 30 percent of patients are treated using brachytherapy, 30 percent external beam radiation, 25 percent surgery, and 15 percent with other modalities. Thus, nationwide, when all clinics adopt intra-operative real-time planning, the potential annual cost savings would total 328 million dollars per year (218,890 Î 0.3 Î 5,000).

Moreover, observing the clinical trend, it is expected that the proportion of patients who choose brachytherapy will increase because its side effects are generally less severe when compared to external beam radiation therapy and surgery, and because of its effectiveness for early-stage diagnosis (New York Times 2006). Brachytherapy is most effective for early-stage diagnosis; this is the trend in the United States where annual physical examinations of male patients include vigorous early screening. Compared to surgery, brachytherapy has a similar five-year recurrence rate (20 percent); however it preserves the organ and its functionality for sexual potency. The latter is of special concern to younger early-stage prostate cancer patients who still look forward to fathering children.

Real-time intra-operative treatment planning will provide significant savings in countries other than the United States. In 2000, the incidence rate of prostate cancer was roughly 550,000 worldwide; traditionally, brachytherapy is used more widely in other parts of the world because of its treatment convenience (a half-day procedure) and relatively low side effects.

Intra-operative planning with dynamic dose correction provides superior post-implant dose analysis and has eliminated the traditional post-operation CT scan. This contributes to additional savings of roughly 131 million dollars per year for brachytherapy treatment of prostate cancer alone.

Our OR-planning system results in a reduction of 20-30 percent of seeds compared with traditional pre-planning methods. Each seed costs approximately $20-50, and each implantation involves 60-200 seeds. Assuming that an average of 100 seeds are implanted per patient via pre-planning, with a cost of $30 per seed, then a 20 percent reduction in seed usage by applying our system would lead to a per-patient savings of $600, and an annual cost savings of $39 million nationwide (218,890 Î 0.3 Î 600). There is no additional labor cost because a clinical physicist must be in the operating room for any implantation procedure. In addition, it makes use of equipment that is standard in every operating room; therefore, there is virtually no additional cost associated with this procedure.

B. Quality of Care and Quality of Life for Patients

Our process improves patient quality of care and quality of life significantly as we describe below.

1. In comparison to traditional computer-aided approaches, and other ad hoc heuristic algorithms, the system we developed consistently returns plans with the prescribed dose delivered to 98 percent of the prostate, and it improves conformity ranges (a measure of how closely the prescription isodose curve matches the target tumor contour) from 10-20 percent. The latter improvement translates to a reduction in toxicity and complications to normal tissue exterior to the prostate, including fewer external ulcers, and less bladder and rectum bleedingùside effects that may require surgical corrections.

2. Clinical evidence shows a significant reduction in average urethra dose and duration of symptom persistence (as documented in clinical papers). Thus, our system results in fewer patients requiring medications and urologic intervention for symptom management; those who do experience side effects generally require shorter periods of intervention. This has a profound impact on both health care costs and quality of life of the treated patient.

3. The procedure uses approximately 20-30 percent fewer seeds and 15 percent fewer needles. Thus, the procedure time is shortened; and it is less invasive because fewer needles are inserted into the body during implantation. This results in faster recovery.

4. The national distribution of our system and the increasing number of centers performing prostate implants in the United States indicate that its potential clinical significance is far-reaching. Plans can be created rapidly during implantation. The viability of being able to re-optimize in real time based on the actual location of the deposited seeds allows modification of plans when unforeseen difficulties occur during an operation. These modifications can potentially correct any areas of tumor under dosage prior to completion of the brachytherapy procedure (or correction due to implantation error by an inexperienced clinician). In addition, the operator will become more cognizant of what the real-time dose to the urethra and rectum is, and can make dynamic adjustments of the intra-operative plan to ensure that the final dose delivered to these structures remains as low as possible without any compromise of the target coverage. This helps to ensure a uniform quality of care among patients.

5. The ability to perform (superior) planning intra-operatively results in the elimination of the need for the simulation session. This results in less inconvenience (including time off from work for the simulation and hospital waiting time) for patients.

C. Accessibility, Training, Quality Control, and Quality Assurance

As is well-documented in clinical literature, there is great variability in the experience of human planners who design brachytherapy treatment plans, both within and among institutes/clinics/hospitals. This variability, combined with the highly complex and labor intensive nature of traditional computer aided planning methods, results in huge variability in planning procedures, quality of plans, and ultimately treatment outcomes.

Two significant benefits of the automated computerized planning system that we have developed are the potential removal of the operator-dependent quality of the resulting plans, and its prospect to establish standards and guidelines for cancer treatment quality control and quality assurance. Availability of the system nationwide will significantly reduce the vast variability in planning quality because different clinics will be able achieve the same high-quality plans.

Another benefit relates to its use as a training tool. Unavoidably, as part of the medical training in learning the techniques of seed implantation (not the treatment planning but the actual physical implantation of seeds into the patient's body), mistakes can be made. The advantage of the on-the-fly, multi-stage re-optimization is that it allows for dynamic dose correction and rapid re-optimization; the resulting partial plan can be amended so as to achieve the desirable clinical properties. The re-optimization thus benefits both the doctor/resident who is learning the physical techniques as well as the patient who still receives a good result because deficiencies in the initial placement can be corrected by later implanted seeds. Psychologically, this allows trainees to focus on mastering the techniques without fearing the result of a bad experience.

As we described above, there is virtually no additional cost associated with this procedure, making it accessible (affordable) to the broad clinical community.

Scientific Advances
The collaborative effort between clinical researchers and operations research scientists resulted in scientific advances on two diverse fronts: medical advances and OR advances.

Specifically, in medical advances:

A rapid operator-independent intra-operative treatment planning system provides the groundwork for advancing the technological frontier of brachytherapy. It opens up opportunities to conduct complex clinical investigations that may otherwise be impossible, as evidenced in our study of the tumor shrinkage and seed displacement analysis and 30-day extended dose-control planning (Lee and Zaider 2001a), and on biological MRS-guided dose escalation (Zaider, Zelefsky et al. 2000, Lee and Zaider 2004, 2006). The OR modeling paradigm provides great flexibility in modeling the clinical problem realistically, and the rapid solution engine objectively returns the best possible plans.

The system will serve as a basis for facilitating the standardization of brachytherapy treatment planning in prostate cancer. It also will serve as a foundation on which to base automated computerized treatment planning for general brachytherapy, a process involved in the treatment of a variety of cancers (breast, cervix, esophageal, brain, and sarcoma) throughout the body. Finally, the system can be used as a tool to carry out research that requires the generation of high-quality, unbiased plans in a timely manner.

Contributions to Human Resource Development:

The project offers opportunities for Ph.D. and undergraduate students to work in interdisciplinary areas of engineering and cancer biotechnology. Each student works closely with the PI as well as well-known cancer researchers. PhD students involved in this project took classes in their main engineering disciplines as well as in cancer biology and biotechnology disciplines. They were also working towards a minor in bioinformatics during their graduate studies. Two students completed their PhD thesis in 2008.

The PI is involved in high-school recruiting and has presented her work in interdisciplinary areas to some of the high-schoolers.

The Center for Education Integrating Science, Mathematics, and Computing (CEISMC)is a partnership uniting the Georgia Institute of Technology with many other educational groups, schools, corporations, and opinion leaders throughout the state of Georgia, toward one common goal: to ensure that K-12 students in Georgia receive the best possible preparation in science, mathematics, and technology as they seek their place in the modern world. Lee was interviewed for her advances in mathematics and medicine.

http://www.ceismc.gatech.edu/gazette/content/2007_06_lee.aspx

The PI presented a talk entitled 'A 21st Century Frontier: Advances in Treatment of Cancer' which described computational and engineering techniques and their applications to cancer treatment at 'Georgia Tech: Innovating Here and Now', a public alumni event (approx. 300 attendees from very diverse fields) held in Washington DC, November 2004.

Furthermore, the results of this project have attracted media attention and resulted in newspaper/media reports on the findings, as well as TV filming of the work for national broadcast (see one-time publication for details of these reports and TV segments). Thus this research and its impact has reached the public through various means of news, television, and medical magazines.

Contributions to Resources for Research and Education:

Two book chapters on related topics were published, and four others are currently under preparation.

EK Lee, M Zaider, Optimization and Decision Support in Brachytherapy Treatment Planning. Chapter 28 in ``Handbook of Operations Research/Management Science Applications in Health Care," Editors: M Bandeau, and F Sainfort. Kluwer Academic Publishers, Hillier International Series in OR/MS. 2004.

M Zaider, EK Lee, Treatment planning for low dose rate and high dose rate brachytherapy. Chapter 12 in ``Basic and Advanced Techniques in Prostate Brachytherapy," Ed. Dicker, Merrick, Gomella, Valicenti, Waterman, Gomella. 1-84184-298-2, CRC Press, 2004.

Contributions Beyond Science and Engineering:

Using operations research approaches, our team has devised sophisticated optimization modeling and computational techniques for real-time (intra-operative) treatment of prostate cancer using brachytherapy (the placement of radioactive 'seeds' inside a tumor). The resulting system offers significantly safer and more reliable treatment outcomes. In addition, it eliminates the need for pre-operative simulation and post-implant dosimetric analysis, resulting in savings of hundreds of millions of dollars per year in the US alone. Post-treatment quality of life is improved through drastic reduction (up to 45-60 percent) of complications. The reason for this is twofold: a) treatment plans thus devised deliver less radiation to adjacent healthy structures, and b) the ability to perform mid-implant re-planning eliminates the unavoidable discrepancies between planned and actual seed placement in the target. This has a profound impact on the cost of managing treatment-associated morbidity. The procedure uses approximately 20-30 percent fewer seeds and 15 percent fewer needles (used to place seeds inside the prostate gland). As a result, the operating-room time is shortened, and the entire procedure is less invasive. The system has the potential to establish standards and guidelines for cancer treatment quality control and quality assurance of the implantable plan.

Wide distribution of our system should allow consistent treatment planning across different clinics, and significantly reduce variability in treatment plan quality. The system will serve as a basis for facilitating the standardization of brachytherapy treatment planning. It also will serve as a foundation on which to base automated computerized treatment planning for general brachytherapy, a process involved in the treatment of a variety of cancers (breast, cervix, esophageal, brain, and sarcoma) throughout the body. Finally, the system can be used as a tool to carry out research that requires the generation of high-quality, unbiased plans in a timely manner.

Categories for which nothing is reported:

To treat cervical cancer that has spread or that has come back after treatment . Radiation therapy may be used to treat cervical cancers that have spread to other organs and tissues. The types of radiation therapy most often used to treat cervical cancer areÂ If the cancer has not spread to distant areas, brachytherapy, which is discussed below, may also be given after the concurrent chemoradiation is complete. EBRT can also be used as the main treatment of cervical cancer in patients who canâ€™t tolerate chemoradiation, canâ€™t safely have surgery, or choose not to have surgery. It can also be used by itself to treat areas of cancer spread. Possible side effects of EBRT. Interstitial brachytherapy cancer treatment optimization in virtual reality. @inproceedings{MillerINTERSTITIALBC, title={INTERSTITIAL BRACHYTHERAPY CANCER TREATMENT OPTIMIZATION IN VIRTUAL REALITY}, author={S. Miller} }. S. Miller. The virtual reality (VR) brachytherapy system that we have designed and implemented will be presented. Brachy-therapy is a cancer treatment modality, whereby, needles are inserted into a patient to act as channels to deliver radioactive sources to the diseased tissue. The focus of this paper is on the advances that have been made on the system. More software tools h Brachytherapy is a local treatment and treats only a specific part of your body. It is often used to treat cancers of the head and neck, breast, cervix, prostate, and eye. What to Expect When Having Brachytherapy. What Happens Before Your First Brachytherapy Treatment. You will have a 1- to 2-hour meeting with your doctor or nurse to plan your treatment before you begin brachytherapy.Â Depending upon the type of treatment selected, we'll also go over special instructions for Ravi to follow. Ravi: Will I have side effects? Dr. Williams: You probably will have some side effects. The side effects you may have depend on the part of your body being treated. Side effects happen because radiation can injure healthy cells that are near the cancer cells it's destroying.