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Letfullin served as senior researcher at the Lebedev Physics Institute of the Russian Academy of Sciences (Samara branch), 1993-2002, and research associate at Mississippi State University, 2002-04. His research activities have included the electrodynamics of super-high-energy pulsed chemical lasers based on photonbranched chain reactions; the auto-wave effect of photon-branched chain reactions; the effect of giant laser energy gain; optical effects of diffractive multifocal focusing of radiation; theoretical modeling of laser light interaction with biological systems containing nanostructures; development of new dynamic modes for treating cancer cells by laser-activated nanoheaters; nanoparticle optics; laser heating and evaporation of nanostructures; and optical breakdown of aerosols.

Letfullin has published over 150 articles and conference proceedings and 11 book chapters on chemical lasers, diffractive optics, ultrashort laser physics, nanotechnology, nanomedicine and aerosol physics. He owns 4 patents in laser technology and optical engineering and has presented 38 invited seminars, colloquia and talks on scientific research and higher education. He is a member of the Optical Society of America, Society of Photo-Optical Instrumentation Engineers and American Society for Engineering Education.

Letfullin earned his bachelor's degree in physics, and a master's degree in optics and spectroscopy at Russia's Samara State University. He received his doctorate in laser physics from Saratov State University in Russia, followed by postdoctoral studies in optics at Mississippi State University.

Medical Physics Curriculum for Undergraduate Engineering Students

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Abstract

Medical physics demands expertise from a wide variety of disciplines and combines areas such as medical imaging, radiation therapy, nuclear oncology, even a new rapidly-growing field of nanomedicine. Medical physicists often have a physics or engineering background, but at the same time possess knowledge about radiation-tissue interactions and good general knowledge of biology, anatomy and physiology. The training of professionals and contributing to this technological field requires multidisciplinary education. In this paper, we are striving to enrich the science, technology, engineering and mathematics (STEM) students by developing an undergraduate program in medical physics. We discuss the new curriculum and the research/design sequence in medical physics for the undergraduate students. This innovative program will offer to undergraduate students both course work and intensive research experiences to better prepare them to lead the discovery of superior diagnostic techniques and treatments of diseases.

Introduction

A huge demand for competent Medical Physicists and Medical Dosimetrists exists in the country. Also, there is a challenge in training of qualified professions in these arenas. To address these challenges in medical physics education we propose to introduce the professions of Medical Physics and Medical Dosimetry at the junior level of the Bachelors in Science Program at Rose-Hulman.

Today's challenges in Medical Physics (MP) education and workforce development are to:

- Train the next generation of scientists and clinicians in a multidisciplinary environment.
- Invent and train to use novel MP products to fight life-threatening diseases.
- Expand the talent pool for translation and commercialization of novel MP treatment/diagnostic technologies.
- Bring relevant information to the public regarding new developments in MP.

The formalized training for Medical Physics and Medical Dosimetrists has been fragmented. Medical physicists require at minimum a Master's Degree in Medical Physics. Currently, there are nearly 20 Medical Physics graduate programs in the country. The curriculum for these programs ranging from 33 credit hours to 56 credit hours. These programs may fall under the Department of Physics, Department of Medicine, Department of Engineering, and Department of Health Sciences. This range of curriculum requirements and program oversight has made it difficult to set a minimum standard as far as the education that the aspiring Medical Physics student may receive. The American Association of Physicists in Medicine (AAPM) has just released a Task Group Report (Report # 197) that outlines the recommendations for Graduate Program curriculum. This supersedes the original recommendations set forth in TG-79. It will take most current graduate programs 5 years to modify their curriculum to meet these new changes. CAMPEP (Commission of Accredited Medical Physics Academic Programs) has also put out recommendations for Graduate Schools. The demand for formalized Medical Physics Programs internationally is high.

The formalized training programs for Medical Dosimetrists are very fragmented as well. Currently there are only 4 Medical Dosimetrist graduate programs. There is no standard established for this graduate discipline. The Medical Dosimetrist is filling a larger role today due to the increasing technologies that are afforded to the Radiation Oncologist. These roles now include assistance with target/tumor contouring, advanced dosimetry calculations, and medical physics assistant work. These increased responsibilities promote the need for a higher education standard that can be delivered with undergraduate and graduate programs. There are less than 10 B.S. level Medical Dosimetry programs. The entrance requirements for Medical Dosimetry range from an Associates Degree to a BS degree. The certifying board for Medical Dosimetrist is the MDCB (Medical Dosimetry Certification Board). They currently offer 3 routes for board approval. They will be increasing the standards for entry into the field.

New Curriculum Development – MP Program for Engineering Physics Students

In order to prepare the next generation of scientists and clinicians in this field, we must reengineer our educational approach. We are striving to enrich the science, technology, engineering and mathematics (STEM) education of undergraduate students by developing a MP program in engineering college like a Rose-Hulman Institute of Technology (RHIT). This innovative program will offer to undergraduate students both course work and intensive research experiences to better prepare them to lead the discovery of superior diagnostic techniques and treatments of diseases. In this paper, we discuss the new curriculum and course syllabus for the MP undergraduate program to be developed at RHIT.

Rose-Hulman Institute of Technology is a four-year undergraduate college offering degrees in engineering, mathematics and science. The current student body consists of 1,900 students (1,810 undergraduate and 90 graduate), of which 20% are female.

RHIT already has a well-formed curriculum for interdisciplinary training in biophysics and biomedicine, which includes lecture courses, focused training sessions and seminars. Indeed, students have been taking a new course called *Cancer Biology* along with courses in nanotechnology; have pursued new interdisciplinary research themes with co-mentors from the biological and physical sciences; have developed and filed new intellectual property in the field of nanobiomedicine; and have been accepted into graduate medical physics programs. Based on the new course *Principles of Nanomedicine*, a set of interdisciplinary laboratories has been developed and offered for Rose-Hulman students by the Department of Physics and Optical Engineering (PHOE) and Department of Applied Biology and Biomedical Engineering, which cover the basic principles and practice of photonics, laser physics and nanoscience to address fundamental questions in health science.

We have organized and managed research on biophotonics and nanomedicine at RHIT for six years (2004-2010), during which time 40 undergraduate students have participated in a wide range of cancer-related projects. Currently, we are developing a multidisciplinary program in biophotonics at the PHOE department which is supported by a grant of \$100,000 from the Lilly Endowment (2007-2010) and Saint Louis Institute on Nanomedicine: Phase 1 (2009-2010) and Phase II (2010-2011). This research-educational program focuses on physics, optics, laser

science and nanotechnology in biological and health-related research. This study enables our undergraduate and graduate physics, optical, applied biology and biomedical engineering students to have the option to pursue open-ended multidisciplinary research projects in bio- and nanophotonics at the cutting-edge areas of photonics. The specific focus of that project is to develop biophotonics-based technologies for the detection of cancer biomolecules and targeted treatments of cancer patients. The biophotonics lab space has been used to host these projects.

The biophotonics laboratory is equipped with diagnostic tools including the spectrophotometer Evolution 300, powerful transmitting/fluorescent microscope Olympus IX71, with CCD camera and QCapture software for getting cell images, 3D medical imaging ORS Visual software. Presently, students and faculty have several ongoing research projects in spectroscopy and imaging of biological cells, including leukemia blood cells.

This work done by individual faculty at RHIT leads to the next level in the development of multidisciplinary engineering education for STEM undergraduate students – designing an undergraduate MP program at RHIT though collaboration with Radiological Technologies University (RTU). We have developed a collaborative relationship RTU supporting the growth of the MP discipline. Together, RHIT and RTU can bring high-end Radiological equipment (Imaging, Therapy, and Computer Based Systems) to the RHIT campus. Additionally, the RHIT students will get exposed to a very promising and satisfying medical field where they can utilize their knowledge gained at RHIT.

Radiological Technologies University is a premier and rapidly growing graduate school. RTU was formed in CY2009 and offers 3 graduate programs in the following disciplines: Medical Physics, Medical Dosimetry, and Medical Health Physics. The curriculum follows those

recommendations as set forth in the AAPM Task Group #197 Report. RTU's program offers 3 advantages over other programs. First, RTU has a clinically oriented faculty who specialize in all of the subset of the Medical Physics arena. Secondly, the school solely focuses on the Radiological technologies and introduction of new clinical technologies into the curriculum is rapid. Third, RTU has well established relationships with the major Radiation vendors to include those that manufacture linear accelerators, imaging equipment, testing equipment, and treatment planning software developers.

RTU is developing a 2 year Medical Physics Residency program that will follow both CAMPEP and AAPM TG-90 Report guidelines. RTU's education model allows for quick expansion to the international markets. Currently, RTU has begun work to put regional campuses in the following locations: Orlando, Florida; San Diego, CA; Mumbai, India; Bejing, China; Rio DeJenero, Brazil; Tokyo, Japan; Kiev, Ukraine. In addition, 2 European sites are being evaluated.

RTU maintains close relationship with the professional organizations of each discipline, major vendors in the field, and large cancer centers in the US. RTU is active in the grant process and will collaborate with major Engineering & Physics disciplines nationally and internationally to fill the demand that is needed in these fields. These professionals will see rapid growth in their disciplines due to: increased technologies, retirement of baby boomer generation, aging population (more cancers). RTU and Rose Hulman will be actively engaged to promote the Medical Physics and Medical Dosimetry professions.

At Rose-Hulman, we strive to recruit the good quality students. They typically represent the top ten percent of their high-school class. They are hard-working, focused and creative students. As teachers, we recognize the need to foster these qualities in our students through exposure to cutting-edge multidisciplinary research for the purpose of enhancing their creativity, while providing the opportunity to learn new laboratory techniques, instrumentation and computer simulations in cancer nanomedicine. This gap in training undergraduate students in multidisciplinary area of cancer nanomedicine will be reached through the following activities described below.

At Rose-Hulman Institute of Technology, we currently study biological and health-related systems using advanced laser and photonics-based techniques. For example, some biomedical courses are currently offered for RHIT students in the Physics and Optical Engineering (PHOE), Electrical and Computer Engineering (ECE), Chemistry and Applied Biology and Biomedical Engineering (ABBE) departments, like the OE/BE435 biomedical optics course, PH302 biophysics course, and BE340 biomedical instrumentation course. We are proposing to unite these efforts into a single multidisciplinary MP program for Engineering Physics (EP) students. The proposed curriculum for the new course/lab development is briefly described below.

<u>Curriculum</u>.

The medical physics minor can be created on the basis of the courses are already offered at Rose without almost adding new courses. A couple core Medical Physics courses like Diagnostic Radiology, Nuclear Oncology can be added to the curriculum or introduced into the existing courses like Biophysics. The lab portion of the proposed MP program will be performed in Biophotonics lab: currently nine labs can be offered for these courses.

The proposed curriculum for the MP program consist of two main parts: part A is compulsory for all EP students, and part B is specific for the students specializing in medical physics.

7

Part B.	Proposed	curriculum	for engin	eering	physics	concentration	in nanomedicine	e.
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Required courses:	Description	Hours	
PH302	Biophysics	4	
ECE 497	Medical Imaging Systems	4	
AB 451	Cancer Biology	4	
Additional			
Required courses:	Description	Hours	
OE 535/BE 535	Biomedical Optics	4	
EP570	Basic Principles of Photodynamic Therapy and Nanomedicine	4	
BE 560	Tissue-Biomaterial Interactions	4	
BE 340	Biomedical Instrumentation	4	
EP 480 (New)	Radiation Dosimetry	4	
Total	32		
And the research/design sequ	uence in Medical Physics/Cancer Nanomedicin	ie	

New Nanomedicine Course Development

In order to help our undergraduate students seize those emerging opportunities in nanotechnology, we are developing materials to support a sophomore-level college course in cancer nanomedicine. The target audience includes science, engineering and mathematics students who have completed at least one year of calculus, physics and chemistry. This four-credit course, entitled *Basic Principles of Photodynamic Therapy and Nanomedicine*, has 30 lectures and 10 lab sessions. In addition, many of the modules are sufficiently self-contained to

allow them to be used as supplementary material in more traditional courses at the sophomore and junior levels.

This course provides a comprehensive introduction to the rapidly-developing field of cancer nanomedicine. It emphasizes cooperative learning approaches involving strong student participation with research assignments, reports and presentations. Nanomedicine involves many science disciplines including physics, optics, chemistry, biology, computers and nanoscience, providing an excellent avenue for introducing students to the truly interdisciplinary nature of much of what takes place in scientific research. The course addresses the need to prepare our graduates to be successful in light of multidisciplinary research.

<u>The aim of the course</u> is to study the basic mechanisms of laser light interaction with cancer cells containing nanostructures for photodynamic therapy and diagnosis of cancer. The ultimate goal is to acquire skills in computer modeling of physical principals for selective nanophotothermolysis of cancer cells involving nanooptics, heat-mass transfer around laser-heated intracellular nanostructures, cell ablation, microbubble dynamics and nanocluster aggregation.

<u>This is a science-oriented multidisciplinary course</u> where the students secure solid training in research techniques, including the development of sophisticated numerical simulation methods for solving complex problems in cancer nanomedicine, research skills working on regular assignments, presenting their results, getting experience in writing research reports/papers, and experimental skills in using an ultrashort laser and spectrophotometer, and in developing an image of the biological cells by using a fluorescent microscope.

Nanomedicine Laboratory Development

Hands-on-experience is equally important in training undergraduate students in this multidisciplinary area, and to this end we are developing the laboratory component to the cancer nanomedicine course. This entails eight two-hour labs: two spectrophotometer labs, two imaging labs, one femtosecond laser lab, two biomedical optics labs, and one virtual 3D imaging lab. We have developed a lab syllabus, lab manual and detail instructions for the lab report format.

The goal of the **spectral labs** is to train undergraduate students on how to operate the spectrophotometer Evolution 300, find an ideal setting for taking data, and look at the sensitivity of the device by measuring the spectrum of the different biological samples. The field of optics offers several technologies that may be developed to serve as cancer detection devices or specific therapeutic agents. Progress towards the development of these new optical technologies in cancer diagnosis and therapy requires the investigation of the optical (spectral) properties of normal and cancerous cells. The difference in absorption spectra of normal and carcinoma cells could be used as an effective and accurate technique for cancer diagnosis.

The goal of **imaging labs** is give undergraduate students practical experience in using the Olympus IX71 microscope, CCD camera and QCapture software, and in obtaining normal and cancerous cells images.

The goal of the **ultrashort laser** lab is to train undergraduate students to perform *in vivo* experiments with cancer cells targeted by gold nanoparticles/nanorods irradiated by a femtosecond pulsed laser, with post-laser viability studies including microscopy and spectrophotometry.

The goal of the **biomedical optics** labs is to study the scattering and absorption of the laser light by biological tissues.

The goal of the **virtual 3D imaging lab** is to learn how to use ORS Visual software, which provides a fast and powerful advanced visualization/PACS viewer solution. It allows the review and analysis of 2D, 3D and 4D images of human anatomy generated with computed tomography, magnetic resonance, ultrasound and positron emission tomography imaging data. With this productivity-enhancing tool, physicians can easily navigate within these images to better understand disease conditions.

Performing Undergraduate Research in Nanomedicine

We want to integrate research and education by training undergraduate students in this emerging area, bringing the latest scientific developments to classrooms, and training the next generation of scientists and teachers. This has a much broader impact on the healthy development of education, science and technology in the U.S. Such a broader impact will be realized through training a group of undergraduates in research. By developing the research skills, abilities and interests of a group of undergraduates early in their post-secondary experience, we are contributing to an emerging pattern of early involvement in research. This allows students to progress farther and encourages them to pursue advanced degrees and enter scientific research and teaching professions. Besides its long-term impact on the field, this program should serve as a model for other institutions to recreate, particularly modest and small universities interested in expanding their research potential.

Our research focuses on the theoretical and experimental development of two important components of the futuristic vision for cancer treatment by nanoparticles: detection technologies

for cancer proteins and cancer cell-targeted therapies. Nanoscale devices carrying therapeutic payloads and delivered within close proximity of the tumor *in vivo* can play a significant role in increasing the effectiveness of the treatment, while decreasing the severity of side effects. Such techniques should be particularly helpful in regard to organs that are difficult to access because of a variety of biological barriers, including those developed by tumors. For example, nanoparticles are capable of crossing the blood-brain barrier due to their small size, and thus are an excellent candidate for non-invasive treatment of brain tumors.

To accelerate such efforts, we have performed theoretical modeling with experimental verification of laser-induced synergistic effects in cellular nanoclusters, including the bubbleoverlapping mode for selective killing of cancer cells. We have discussed the application of nanotechnology for laser thermal-based killing of abnormal cells (e.g., cancer cells) targeted with absorbing nanoparticles (e.g., solid gold nanospheres, nanoshells or nanorods) in the literature [1-7]. We have theoretically and experimentally demonstrated that the absorbed laser energy is quasi-instantaneously converted into heat, thereby rising the temperature of the nanoparticles and surrounding cell. Due to the heat, the threshold temperatures can be reached for various synergetic effects in a cancer cell volume, such as thermal coagulation, vaporization, sound production, bubbles and plasma generation. These effects can be used to increase the sensitivity of photoacoustic diagnosis or aid in therapy, such as selective photothermolysis [5,7], by selective thermal killing of tumor cells into which absorbing nanoparticles have been incorporated. The potential advantages of nanophotothermal sensitizers heated with short laser pulses may include: (1) selective cancer-cell targeting by means of conjugation of absorbing particles (e.g., gold nanospheres, nanoshells or nanorods) with specific antibodies; (2) localized tumor damage without harmful effects on surrounding healthy tissue; (3) absorption at longer

wavelengths in the window of transparency of most biotissues; (4) no undesired side effects (e.g., cytotoxicity or cutaneous photosensitivity); and (5) relatively-fast treatments involving potentially just one or several laser pulses.

Undergraduate students have been involved in all stages of our projects, providing them with extensive hands-on-experience in a wide variety of biological and physical techniques in cancer nanomedicine research. Over ten papers have been presented by Rose-Hulman undergraduate students at the following conferences: Butler University Undergraduate Research Conference (Indianapolis, IN); Annual Argonne Symposium for Undergraduates in Science, Engineering and Mathematics (Chicago, IL); Math, Engineering and Science Conference (Evansville, IN); and Annual American Society for Engineering Education IL/IN Section Conference.

Conclusions

The proposed curriculum has the potential to have a major influence on undergraduate education in medical physics because (1) the materials will have been piloted in two institutions with a variety of students, and (2) the materials are developed by experienced teachers familiar with the backgrounds of first- and second-year students. In addition, each of the institutions has its own network of peer institutions used for benchmarking, thus providing a multiplication factor for dissemination. One of the principal strategies is to foster integration of research and education through the programs, projects and activities scheduled in the curriculum, that infuse education with the excitement of discovery and enrich research through the diversity of learning perspectives.

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References

- [1] R. R. Letfullin, R. Colin and T. F. George, "Modeling Photothermal Heating and Ablation of Biological Hard Tissues by Short and Ultrashort Laser Pulses", *International Journal of Theoretical Physics, Group Theory and Nonlinear Optics* (July 2010).
- [2] R. R. Letfullin, C. B. Iversen and T. F. George, "Modeling photothermal therapy: Kinetics of thermal ablation of healthy, and cancerous cell organelles and gold nanoparticles" *Nanomedicine* (2010).
- [3] R. R. Letfullin, T. F. George, C. Duree and B. M. Bollinger, "Ultrashort Laser Pulse Heating of Nanoparticles: Comparison of Theoretical Approaches," *Advances in Optical Technologies* 2008, ID 251718-1-8 (2008).
- [4] R. Letfullin, V. Zharov, C. Joenathan and T. George, "Nano-Photothermolysis of Cancer Cells," SPIE Newsroom DOI: 10.1117/2.1200701.0634-1-2 (2007).
- [5] R. R. Letfullin, C. Joenathan, T. F. George and V. P. Zharov, "Cancer Cell Killing by Laser-Induced Thermal Explosion of Nanoparticles," *Nanomedicine* 1, 473-80 (2006).
- [6] R. R. Letfullin, V. P. Zharov, C. Joenathan and T. F. George, "Laser-Induced Thermal Explosion Mode for Selective Nano-Photothermolysis of Cancer Cells," in *Complex Dynamics and Fluctuations in Biomedical Photonics IV (Photonics West 2007: Biomedical Optics)*, edited by V. V. Tuchin, *Proceedings of SPIE* 6436, 64360I-1-5 (2007).
- [7] V. P. Zharov, R. R. Letfullin and E. Galitovskaya, "Microbubbles-Overlapping Mode for Laser Killing of Cancer Cells with Absorbing Nanoparticle Clusters," *Journal of Applied Physics* 38, 2571-81 (2005).