PROTON COMPUTED TOMOGRAPHY FOR CLINICAL APPLICATIONS

A Research Proposal

To

Loma Linda University

Medical School Research Support Committee

Principal Investigator: Reinhard W. Schulte, M.D., Assistant Professor of Radiation Medicine

Co-Principal Investigator: Kambiz Shahnazi, Ph.D., Medical Physicist

Co-Principal Investigator: Vladimir Bashkirov, Ph.D., Research Physicist

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Principal Investigator

Date signed: January 10, 2002

Principal Investigator Name: Reinhard W. Schulte

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Principal Investigator Name: Reinhard W. Schulte

ABSTRACT

Description of Project Research. Proton radiation therapy is a highly precise form of cancer therapy, which requires accurate knowledge of the dose delivered to the patient and verification of the correct patient position with respect to the proton beam to avoid damage to critical normal tissues and geographical tumor misses. In existing proton treatment centers dose calculations are performed based on x-ray computed tomography (CT) and the patient is positioned with x-ray radiographs. The use of x-ray CT images for proton treatment planning ignores fundamental differences in physical interaction processes between photons and protons and is therefore inherently inaccurate. Further, x-ray radiographs depict only skeletal structures; they do not show the tumor itself. Ideally, one would image the patient directly with proton CT by measuring the energy loss of high-energy protons that traverse the patient. The development of proton CT is the goal of our project.

Product Outcomes and Deliverables. The aim of the first project year is to perform studies to prove the feasibility of a conceptual approach to proton CT. These studies will include theoretical Monte Carlo simulations using GEANT, experimental studies on a water phantom with embedded inhomogeneities and development of a reconstruction algorithm to generate two-dimensional proton CT images.

BUDGET (Year 1)

Salaries & Fringe				
Title	**Name**	**Effort**	**Months**	**Total**
Principal Investigator	Reinhard Schulte	20%		0
Co-Principal Investigator	Kambiz Shahnazi	20%		0
Co-Principal Investigator	Vladimir Bashkirov	20%		0
Undergraduate Students	to be selected	20%	6	5,000
Graduate Student	Margio Klock	100%	2	5,000
			Salaries	10,000
Equipment				
Water phantom (design, parts, manufacture)				1,000
Turntable				200
Computer for data reconstruction				2,500
			Equipment	3,700
Supplies				
Laboratory notebooks				100
Dosimetry film				100
Electronic parts				100
Mechanical parts				200
			Supplies	500
Travel				
Students from UCSC to LLUMC				600
			Total	$14,800

Budget Justification

Dr. R. Schulte, M.D., M.Sc. principal investigator of the project, will lead this project in close collaboration with the co-principal investigators Kambiz Shawanazi, Ph.D and Vladimir Bashkirov, Ph.D. Dr. Shawanazi is an experienced researcher in the field of CT reconstruction algorithms. Dr. Bashkirov has extensive experience in Monte Carlo simulation of detector performance and data acquisition system development. No salaries are requested for these senior investigators.

Undergraduate students from the Santa Cruz Institute of Particle Physics (SCIPP) will perform most of the experimental and theoretical work. Our collaborators at SCIPP have agreed to provide us with undergraduate students who will help with the Monte Carlo simulations and the collection of experimental data. These students will work under the supervision of Dr. Bashkirov.

Margio Clock is a graduate student from the Department of Physics, Centro Federal de Educacao Tecnologica do Parana, Curitiba, Brazil. Margio and his thesis supervisor, Prof. Reuters Schelin have agreed that he would come to LLUMC to work with us on the development of a proton CT reconstruction algorithm. He will work under the supervision of Dr. Shawanazi. We are requesting partial salaries for these young investigators.

For the experimental work, we will need to design and manufacture a simple water phantom

with embedded inhomogeneities. The phantom will be mounted on a manual turntable for angular positioning. A fast computer will be required for Monte Carlo calculations and data reconstruction. A total of $3,200 is requested for equipment.

To support the experimental work we will need electronic and mechanical parts, and laboratory notebooks, CDs etc. We are also requesting travel money of $150 per trip for four roundtrips to LLUMC for the students from UC Santa Cruz.

Other Support

Dr. Bashkirov's salary is supported by a research grant from the National Medical Technology Testbed (NMTB) for the development of nanodosimetry. His work on the silicon microstrip detector system and data acquisition system will equally serve the nanodosimetry project and the proton CT project.

The silicon detector system that will be used to perform experimental studies for this project has been developed with funds of the nanodosimetry project. Use of this system for the proton CT project will not interfere with the progress of the other project.

CURRICULUM VITAE

Reinhard W. Schulte, Principal Investigator

Born:	1954, Neheim-Huesten (now Arnsberg), Germany
Education:	1978, University of Dortmund, Germany, Physics Diploma (M.Sc.)
	1986, Cologne University, Germany, Doctor of Medicine (M.D.)
	1992, Hannover Medical School, Germany, Radiologist

ACADEMIC APPOINTMENT

1995	Assistant Clinical Professor at the Loma Linda University School of Medicine, Loma Linda, California, USA.

NONACADEMIC POSITIONS

1994-1995	Clinical Research Assistant at the Loma Linda University Medical Center, Loma Linda, California, USA.
1989-1994	Postdoctoral Research Fellow at the Loma Linda University Medical Center, Loma Linda, California, USA.
1987-1989	Resident in Radiation Oncology, Department of Radiotherapy and Special Oncology, Hannover Medical School, Hannover, Germany
1985-1987	Resident in Diagnostic Radiology, Katharinen Hospital, Unna, Germany

RESEARCH GOALS AND INTERESTS

Main Goal: To study physical, biological, and clinical aspects of proton radiation in order to understand its main interactions with living organisms, and ultimately to improve the outcome of cancer therapy or prevent the induction of cancer.

Mathematical models of radiation response and risks.

Measurement of ionization clusters at the DNA level (nanodosimetry).

Stereotactic proton radiosurgery.

Patient immobilization and alignment.

FUNDED RESEARCH PROJECTS

1. Development of a Particle-Tracking Silicon Microscope, 2002. Collaborative project of LLU Radiobiology Program and UC Santa Cruz funded by NASA. Duration: ongoing (co-principal investigator)
2. Development of nanodosimetry for biomedical applications, 1997. Multi-institutional research project funded by the National Medical Technology Testbed and the U.S. Army. Duration: ongoing (principal investigator).

3. Development of functional proton radiosurgery for Parkinson's disease and other functional disorders of the brain, 1999. Research and development project funded by the Henry L. Guenther Foundation. Duration: ongoing (co-principal investigator).
4. Development of small-field proton radiosurgery, 1996. Research and development project funded by the Henry L. Guenther Foundation. Duration: 1 year (principal investigator).
5. Development of novel small-field radiation techniques for pituitary adenomas, 1989. Postdoctoral Fellowship award by the DFG (German Research Society). Duration: 2 years.

SELECTED PUBLICATIONS (JOURNAL ARTICLES, BOOK CHAPTERS)

1. Bashkirov V., Schulte RW. *Dosimetry system for the irradiation of thin biological samples with therapeutic proton beams.* Phys. Med. Biol. 2002 47:1-21.
2. Schulte R., Bashkirov V., Shchemelinin S., Garty G., Chechik R., Breskin A.. *Modeling of radiation action based on nanodosimetric event spectra.* Physica Medica 2001, Vol. XVII, Suppl. 1:177-80.
3. Schulte RW. *Nuclear data for neutron and proton radiotherapy and for radiation protection.(book review)*. Radiat Res. 2001 56:223-4.
4. Nardi E, Schulte R. *Confining proton beams with longitudinal magnetic fields: Monte Carlo calculations.* Med Phys. 2000 27:2369-71.
5. Schulte RW, Fargo RA, Meinass HJ, Slater JD, Slater JM. *Analysis of head motion prior to and during proton beam therapy*. Int J Radiat Oncol Biol Phys. 2000 47:1105-10.
6. Schulte RW, Slater JD, Rossi CJ Jr, Slater JM. *Value and perspectives of proton radiation therapy for limited stage prostate cancer*. Strahlenther. Onkol. 2000 Jan;176(1):3-8.
7. Levy R.P., Schulte R.W., Slater J.D., Miller D.W., J. M. Slater. *Stereotactic radiosurgery--the role of charged particles*. Acta Oncol 1999;38(2):165-169.
8. Shchemelinin S., Breskin A., Chechik P., Colautti, and R. W. Schulte. *First measurements of ionisation clusters on the DNA scale in a wall-less sensitive volume*. Rad. Protect. Dos. 1999;82(1):43-50.
9. Slater J.D., Yonemoto L.T., Rossi C.J. Jr., Reyes-Molyneux N.J., Bush D.A., Antoine J.E., Loredo L.N., Schulte R.W., Teichman S.L., and J.M. Slater. *Conformal proton therapy for prostate carcinoma.* Int J Radiat Oncol Biol Phys 1998;42(2):299-304.
10. Vatnitsky, S. M., Schulte R. W., et al. *Radiochromic film dosimetry for verification of dose distributions delivered with proton-beam radiosurgery*. Phys Med Biol 42, 1887-98, 1997.
11. Schulte R.W. Prediction of cellular effects of high- and low-LET irradiation based on the energy deposition pattern at the nanometer level. In: "Microdosimetry. An Interdisciplinary Approach". D.T. Goodhead, P. O'Neill, H.G. Menzel, (Eds.). The Royal Society of Chemistry, Cambridge, UK, pp 211-214, 1997.
12. Schulte R.W., *Early and late responses to ion-irradiation*. In: Ute Linz (Ed.) Ion Beams in Tumor Therapy, Chapter II.7, Chapman & Hall, London, 1995, pp. 53-62.

Curriculum Vitae

NAME	POSITION TITLE , ROLE ON PROJECT
Kambiz Shahnazi, Ph.D.	Postdoctoral Scientist, Co-Principal Investigator

PROFESSIONAL PREPARATION

INSTITUTION AND LOCATION	MAJOR/AREA	DEGREE	YEAR
Ohio State University	Engineering	M.Sc.	1988
University of Connecticut	Electrical Engineering	Ph.D.	1997

APPOINTMENTS AND PROFESSIONAL EXPERIENCE

2001–present Medical physicist/dosimetry, Department of Radiation Medicine, Loma Linda University Medical Center.

1998–2001 Postdoctoral fellow (medical physicist), Yale University-Backus Hospital,
Adjunct position: Analog and digital circuits design and laboratory, University of New Haven.
Study of AAPM's TG51 and TG21 protocols; Study of orthovoltage and TG61 protocols.
Investigation of microdensitometer and Gaf-Chromic film for high spatial resolution study of ^{125}I and ^{192}Ir.

1997–1998 Postdoctoral Associate, Diagnostic Radiology, Yale University.
Optical tomography for 3D Imaging using Polymer Gels; LabView Program, Instrumentation with high voltage system for cell study.

1994-1997 Researcher, Department of Electrical Engineering, University of Connecticut.
Remote Sensing of atmosphere using heterodyning technique; signal processing and data acquisition. Supported by the National Science Foundation - Atmospheric Science, and University of Connecticut.

1990-1994 System and Design Coordinator, Vallylab Inc., a Pfizer company.

RECENT PUBLICATIONS

1. K. Shahnazi and J. Gore," Optical tomographic scanning system for detection and monitoring," SPIE International Symposium, Vol. 3534, Nov. 1998.
2. K. Shahnazi and L. Lynds, " Heterodyne Measurements of Stratospheric Ozone using a Single Sideband Tunable CO_2 Laser," Proceedings of SPIE, Vol. 3380, April 1998.
3. K. Shahnazi, "Frequency Modulation Spectroscopy with a Tunable CO_2 Sideband Laser: ozone detection", Applied Optics, Vol. 37, No. 12, April 20, 1998.
4. K. Shahnazi, L. Lynds, P.K. Cheo, "Simplified Tunable Single Sideband CO_2 Laser Spectrometer," Optical Engineering, May 1997.
5. J. Gore, K. Shahnazi, Report on Optical Scanner and 3D dosimetry study - National Institute of Standard and Technology (NIST) 1997.

Curriculum Vitae

NAME	POSITION TITLE , ROLE ON PROJECT
Bashkirov, Vladimir, Ph.D.	Postdoctoral Scientist, Co-Principal Investigator

PROFESSIONAL PREPARATION

INSTITUTION AND LOCATION	MAJOR/AREA	DEGREE	YEAR
Moscow Inst. of Engineering and Physics	Exp. Physics	M.Sc.	1979
Moscow Inst. of Engineering and Physics	Exp. Nuclear Physics	Researcher	1983
Moscow Inst. of Engineering and Physics	Particle Physics	Ph.D.	1997

APPOINTMENTS AND PROFESSIONAL EXPERIENCE

1999–present Postdoctoral Research Fellow, Loma Linda University Medical Center, Loma Linda, CA. Development of nanodosimetry for biomedical applications.

1997-1998 Work on proposal of a new tracker and particle identifier (by *dE/dx*) for ZEUS experiment luminosity upgrade - project science leadership, MC simulation, experimental tests, software development (DESY, Hamburg, Germany)

1996 Development of TRD for a space application in future AMS experiment at ALFA space station - development of MC simulation software, experimental tests (CERN, Switzerland)

1992-1995 Commissioning of Transition Radiation Detector at ZEUS experiment - hardware and software development, data taking and treatment, MC software development and physics analysis (DESY, Hamburg, Germany).

1991-1992 Work on experimental tests of ATLAS TRT detector - hardware and software development, data handling and MC simulation (CERN, Switzerland).

1989-1991 Participation in development and experimental test of a calorimeter and scintillation light registration technique at ultra-low (<10mK) temperature for dark matter search experiment (Milan, Italy).

1981-1989 Design, MC simulation, construction and commissioning of a low background experiment for double-beta decay search (Moscow)

1979-1981 Participation in experiments at Protvino accelerator - DAQ, hardware and software development.

1978 –1979 Participation in mu-nucleon atom production experiments at Dubna accelerator - data taking and off-line analysis.

RECENT PUBLICATIONS

1. Bashkirov V., Schulte RW. Dosimetry system for the irradiation of thin biological samples with therapeutic proton beams. Phys. Med. Biol. 2002 47:1-21.
2. Schulte R., Bashkirov V., Shchemelinin S., Garty G., Chechik R., Breskin A. Modeling of radiation action based on nanodosimetric event spectra. Physica Medica 2001, Vol. XVII, Suppl. 1:177-80.
3. Bashkirov V. Particle identification by relativistic rise of time above threshold in gaseous detectors. Nucl. Instrum. Meth. A 433 (1-2): 560-563 AUG 21 1999

Research Plan

A. Specific Aims

The objective of this project is to perform theoretical and experimental work on proton computed tomography (pCT). This will serve as a preclinical study for the implementation of pCT on one of the existing LLUMC proton gantries.

Our feasibility study involving theoretical and experimental work in cooperation with other research institutes will provide data for performance prediction and optimization of a pCT system. It will also provide information for design and manufacture of pCT used for clinical applications in cancer detection and proton radiation treatment planning.

The project is based on the hypothesis that pCT is superior to conventional computed tomography (CT) in terms of the accuracy of range calculations of protons in tissue, the anatomical detail of tumor and normal-tissue interfaces, and the dose delivered to the patient at equivalent levels of geometric resolution.

B. Background and Significance

Proton radiation therapy spares more healthy tissue and allows higher tumor doses than conventional radiation therapy. This is possible due to the characteristic of the proton depth dose curve: a relatively low entrance dose is followed by a high-dose peak, the Bragg peak, which can be positioned in the tumor tissue. Beyond the Bragg peak the dose fall-off is very steep, i.e., from 90% to 20% of the peak dose within a few millimeters. Precise and conformal radiation therapy with protons therefore requires a very accurate prediction of the position of the Bragg peak within the patient.

The range of protons in tissue depends both on the initial proton energy and on the composition of the tissue in the beam path. The ability of a medium to decrease the kinetic energy of a charged particle is described by the average energy loss per unit path length. This quantity, which is called the *stopping power*, depends mainly on the density of the medium traversed by the particle. Thus, the range of the protons is controlled by the integrated stopping power in the tissues along the proton beam path.

For optimum accuracy of proton range determinations it would be best to measure a three-dimensional matrix of stopping power values in the irradiated tissue using pCT. This could be accomplished by measuring the energy loss of protons passing through the tissues from many different directions. Although the idea of pCT is not new, and previous experimental work has been published [1-3], pCT is currently not available, probably due to the lack of rotating proton gantries in the past and the limitations of data processing speed. Instead conventional CT has been used for proton treatment planning, which involves conversion of photon attenuation measurements into stopping power using a calibration curve [4,5]. The accuracy of the calibration curves is one of the main limiting factors determining the accuracy of proton range calculation for proton treatment planning.

With the development of proton gantries, first at LLUMC and now in several other proton treatment centers, and the orders-of-magnitude increase in computing power and speed, technical obstacles for the development of pCT have been overcome. Direct measurement of proton stopping power distribution with pCT has the potential to improve the accuracy of predicting the position of the Bragg peak and is, therefore, of great importance for precise proton radiation treatment planning.

Besides the determination of proton ranges, other parameters of proton transport through tissues need to be known with good accuracy. Multiple Coulomb scattering leads to a widening

of proton beams with increasing depth, and nuclear interactions result in the loss of primary protons and the exposure of tissues to secondary particles, typically of higher biological effectiveness. Common treatment planning algorithms ignore these effects or treat them in a simple manner that often is inadequate for precise dose calculations. Measurement of these parameters with pCT would allow incorporation of these important parameters into future treatment planning algorithms based on Monte Carlo transport calculations.

There are other potential advantages of pCT. Conventional CT images derive their tissue contrast from attenuation differences of photons as they pass through the body. This attenuation is proportional to the square of the average atomic number, *Z*, of the tissues traversed. Bones, consisting mainly of high-atomic calcium, are relatively easy to distinguish from soft tissues. On the other hand, the composition of most tumors is very similar to normal soft tissues and their normal-tissue boundaries are, therefore, difficult to delineate. Accordingly, visualization of tumors is usually accomplished by intravenous injection of high-*Z* contrast media, which accumulate in some but not all tumors. Since these contrast media also increase the CT values of normal tissues to a certain degree, they interfere with the conversion of CT values to stopping power, further compromising the accuracy of proton range calculations. By means of pCT it is possible to detect subtle differences in the density of the tissues on the beam path. Tumor tissue typically has a higher density than surrounding normal tissue, and therefore it may be possible in many cases to detect the tumor boundaries in pCT images obtained for treatment planning without the need to inject contrast medium.

Beyond the use of pCT for treatment planning, it could also be used to verify the accuracy of dose delivery on a day-to-day basis. It is likely, and will be investigated within this project, that the dose given to the patient during a pCT investigation is sufficiently low so that it could be performed for each proton dose fraction. The pCT images could then be used to verify the correct positioning of the patient with respect to the proton beam and to detect changes in the patient's anatomy during the treatment course; for example, due to tumor shrinkage and weight loss or gain of the patient.

In summary, we conclude that the development of pCT would be of great importance for future proton treatment planning. The current trend of an increased demand for proton treatments of irregular tumors or tumors located near sensitive organs and the steadily increasing number of proton treatments worldwide emphasize the importance of the development of proton computed radiography for clinical applications in cancer therapy.

C. Previous Work

C1. Position- and Energy-Sensitive Single Particle Detection

Within our nanodosimetry project, we have developed a system for position and energy measurements of single protons that is currently implemented into the nanodosimeter and is also well suited to study the concept of a proton CT. The current system comprises two carefully aligned silicon "modules" located in front of and behind the object to be imaged. Each module consists of a pair of single-sided silicon micro-strip detector planes with their strips oriented at right angles. Figure 1 shows one of the two modules. These four detectors provide information about the primary particle track from the strip-hit information as well as the particle's energy, which can be determined via the specific energy deposition measured with each detector plane.

Using a prototype system, we have demonstrated that the accuracy of proton coordinate measurements is better than 0.1 mm. Furthermore, the energy of protons passing the detector system can be derived from the signal of each silicon strip detector for proton energies above 20

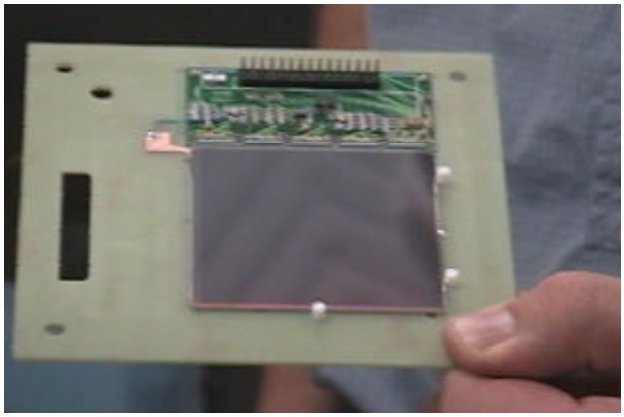

Fig. 1. One of the two existing silicon modules. The 6.4cm x 6.4 cm silicon strip detector and the readout electronics are visible.

MeV. In addition, there is an applicable region below about 3 MeV, where the particle stops in the detector and energy can be measured directly. In the energy range of 3-20 MeV the signal of at least one of the two detectors planes will be within the measurable range, and thus will provide sufficient information to reconstruct the energy of the proton. At high energies, i.e., above 100 MeV, the detector signal is a relatively weak function of incident proton energy. However, for the purpose of our experiment, we will adjust the initial proton energy such that the exit energies will fall below 100 MeV.

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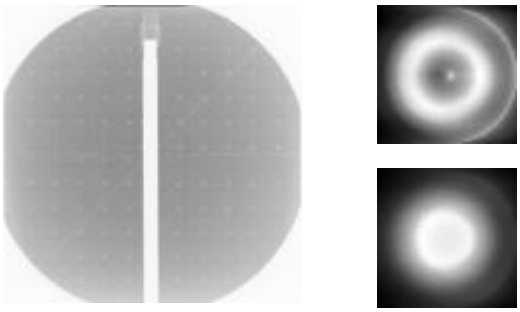
C3. Image Acquisition and Reconstruction on the LLUMC Proton Gantry

We have started to test and develop our abilities to reconstruct radiographic projections similar to those obtained with computed tomography using the LLUMC proton gantry. For this purpose we used the digital x-ray radiography system that is installed on the gantry. A digital radiograph was taken of a cylindrical metal object (Figure 2a). The digital image was sent to our



a b

Fig. 2. (a) Digital x-ray radiograph of a cylindrical test object taken with on one of the LLUMC proton gantries. (b) Reconstruction of two tomographic images showing cross-sectional views of the object.

collaborators at the Department of Physics, Centro Federal de Educacao Tecnologica (CEFET) do Parana, Curitiba-PR, Brazil. This group has experience in the development of reconstruction algorithms for CT images based on x-ray cone beam geometry. Assuming cylindrical symmetry of the object, a cross-sectional image was reconstructed, as shown in Figure 2b. The group at CEFET expressed interest in supporting us to develop a similar algorithm based on proton projection radiographs.

D. Experimental Plan

D1. Conceptual Approach to Proton CT

Figure 3 outlines the concept of the pCT we propose. The system utilizes an energetic proton beam that can penetrate the image object. The beam will be delivered by one of the rotating LLUMC proton gantries. It will be widened using existing scattering foils on the proton beam line to form a 3-D cone covering the volume of interest.

The position of protons passing through the object will be detected by a system of silicon microstrip detectors positioned in front of and behind the object. For reconstruction of the proton track, one needs to measure the entry point on the proximal side and also the exit point on the distal side of the object. This can be accomplished by placing two 2D-position-sensitive microstrip detectors MS_1 and MS_2 sufficiently close to the object. Using a second set of detectors, MS_3 and MS_4, one can also determine the scattering angle of the transmitted proton and its lateral displacement from the original trajectory.

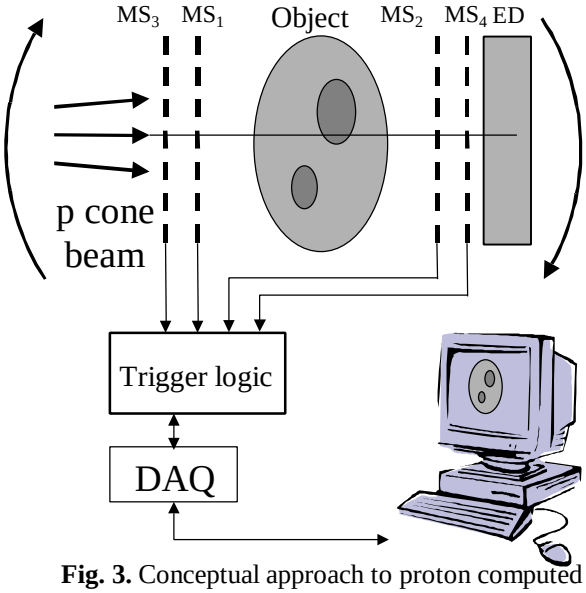


Fig. 3. Conceptual approach to proton computed tomography. MS = silicon microstrip detector; DAQ = data acquisition system; ED = energy detector

The microstrip detectors, indirectly by measuring the deposited energy, also provide information about the energy of the protons. However, for the required degree of energy resolution a separate energy detector (ED), e.g., a solid state detector or inorganic scintillator, will be required to measure the energy of traversing protons.

A dedicated trigger system identifies primary protons passing through the patient and suppresses background events. Protons that are only detected in the upstream detectors but not in the detectors behind the patient indicate the loss of protons due to inelastic nuclear reactions. The distribution of integral energy loss, scattering angles, lateral displacements, and nuclear interaction probabilities will provide useful information about the density and atomic composition of the imaged volume.

Installation of the described system on a rotating proton gantry will enable the capture of proton projection radiographs from many projection angles. This information can then be used to reconstruct a 3D map displaying physical properties of the imaged object relevant for proton treatment planning.

D2. Experimental Work

To test the conceptual approach, we will use the central beam line in the LLUMC proton research room and the existing silicone microstrip modules. The horizontal beam line provides monoenergetic proton beams up to 250 MeV with excellent energy stability. The experimental setup, a simplified version of the conceptual approach in Figure 3, is shown in Figure 4. The two silicon detector modules will be installed on an optical bench together with scattering foils that spread the narrow proton beam to an appropriate cone size. The wide proton beam will pass through a water-filled phantom with embedded inhomogeneities of known density and relative positions with respect to the detector system. The density of the inhomogeneities will be confirmed independently using proton range measurements. To provide multiple projection angles, the phantom will be mounted on a turntable. A trigger and data acquisition system, which has been developed for the nanodosimetry project, will also be used to collect and store the raw data of the multiple projection images of the phantom. A dedicated software program for reconstruction of pCT images based on the raw data will be developed during the project.

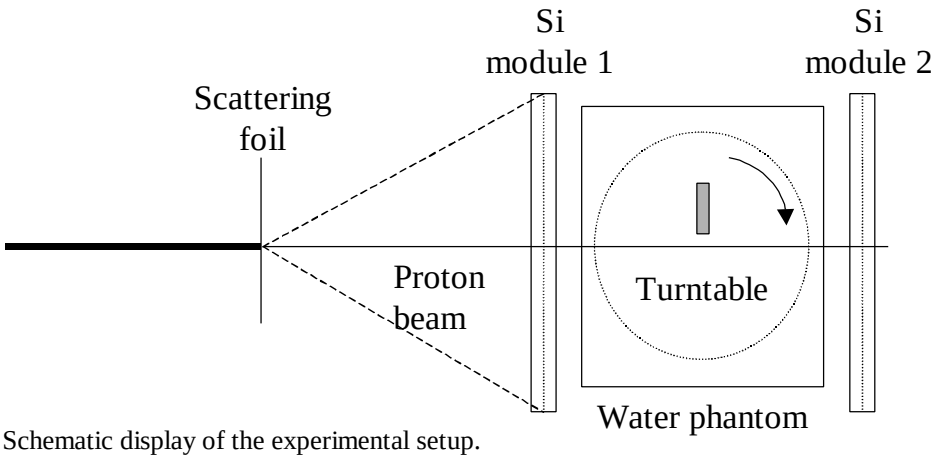


Fig. 4. Schematic display of the experimental setup.

By placing relatively dense inhomogeneities into the phantom, we will be able to evaluate energy differences between protons that traversed the inhomogeneities and those that did not. This should enable us to reconstruct 2D CT images of sufficient detail to prove the principle of the method. One should note that, since we only have two detectors, we cannot measure the entrance and exit angle of the protons with this initial version of the system, which will compromise the geometric resolution to a certain degree. During this first year, the importance of the angular measurements will be evaluated using theoretical calculations.

D3. Theoretical Work

Several physical factors determine the spatial and energy resolution of pCT. When traversing a medium, protons undergo multiple small deflections due to interaction with the nuclear Coulomb field of the target atoms. This so-called multiple Coulomb scattering limits the spatial resolution of pCT, but on the other hand provides information on the target material since the scatter angle is a function of the atomic number of the target nuclei [6].

The energy loss of a proton traversing an object is subject to statistical fluctuations, denoted as *range straggling*. This phenomenon limits the density resolution of pCT. Range straggling depends on the atomic and mass number of the target nuclei and on the thickness of the object [7], and from this point of view it provides useful information about the target composition.

The total number of protons traversing the object is attenuated by inelastic nuclear interactions. This effect not negligible: for example, in a 250 MeV proton beam slowing down in water, secondary particles produced by nuclear interactions contribute 20% to the absorbed dose. For pCT, the most important aspect of these nuclear interactions is that they remove primary protons from the beam, thereby increasing the data acquisition time for a given level of accuracy. On the other hand, measurement of the rate of particle loss from the primary beam depends on the incident energy and the mass number of the target nuclei [8], and can, therefore, provide additional information about the target composition.

We will use the Monte-Carlo code GEANT to study the influence of these physical factors on the performance of pCT in general and our experimental setup in particular. The GEANT code permits incorporation of other codes for the treatment of nuclear interactions, while the transport of protons is performed by GEANT itself. Comparisons will be made between theoretical predictions and experimental results.

Using the theoretical calculations we hope to answer the following questions:

1. What is the dependence of spatial and density resolution on incident proton energy?
2. What spatial and density resolution can be reached with pCT for a reasonable data acquisition time?
3. How much would additional measurement of entry and exit angles of the protons improve the spatial resolution of pCT?
4. What would be the typical dose to a patient undergoing a pCT?

D4. Future Prospects

If our experimental and theoretical work indicates that pCT is feasible, we will make an effort to fully develop and implement this new technology on one of the LLUMC proton gantries. Discussions with colleagues at our Proton Therapy Cooperative Group meetings indicate that there is great interest in the realization of pCT. We expect this effort to take about three to five years.

There are currently 23 proton facilities operating worldwide and there are plans to construct additional 20 facilities (Figure 5). Market research indicates a potential for 140 facilities in the U.S. alone over the next two decades. Modern proton accelerators, which have been shown to work reliably in a hospital environment, are now available on the market. The opening of the hospital-based facility at LLUMC 10 years ago has demonstrated the value of protons in radiation therapy. Other hospital-based facilities, which are likely customers for one or several proton computed tomography systems, have been constructed more recently or are in the planning stage.

Fig. 5. Existing and proposed proton facilities.

E. Literature Cited

1. Cormack A. M. and A. M. Koehler. Quantitative proton tomography. Phys. Med. Biol. **21**:560-69, 1976.

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3. Hanson K.M., Bradbury J. N., Cannon T. M., Hutson R. L., Laubacher D. B., Macek R. J., Paciotti M. A., and T. A. Taylor. Phys. Med. Biol. **26**:965-983, 1981.

4. Chen G.T., Singh R. P., Castro J. R., Lyman J.T., and J. M. Quivey. Treatment planning for heavy ion radiotherapy. Int. J. Radiat. Oncol. Biol. Phys. **5**:809-1819, 1979.

5. Schneider U., Pedroni E., and A. Lomax. The calibration of CT Hounsfield units for radiotherapy treatment planning. Phys. Med. Biol. **41**:111-124, 1996.

6. Mustafa A.A. and Jackson D.F. Small-angle multiple scattering and spatial resolution in charged particle tomography. Phys. Med. Biol. **26**:461-472. 1981.

7. Payne M.G. Energy straggling of heavy charged particles in thick absorbers. Phys. Rev. **185**:611-623, 1969.

8. Sihver L., Tsao C. H., Silberberg R., Barghouty A. F., and T. Kanai. Calculations of depth-dose distributions, cross sections and momentum loss. Adv. Space Res. **17:**105-108, 1996.