OMB No. 0925-0001/0002 (Revised on 5/30/2018)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors. Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Hristov, Dimitre

eRA COMMONS USER NAME (credential, e.g., agency login): HRISTOV.DIMITRE

POSITION TITLE: Associate Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
Bulgarian National University, Sofia, Bulgaria	M.Sc.	1992	Physics
McGill University, Montreal, Canada	Ph.D.	1998	Medical Physics

A. Personal Statement

The development of novel imaging and image-guidance techniques for cancer related investigations and interventions has been a main focus of my research effort. In particular, as a Medical Physics Faculty at McGill University, I conducted research on free-hand 3D ultrasound-image guidance for radiotherapy simulation and pre-treatment verification. This research resulted in technology licensed and commercialized by Resonant Medical Incorporated, Montreal, CA (currently marketed by Elekta Ltd). Later on as a Senior Physicist with the System Concepts and Innovation team at Siemens Oncology, I contributed to the development of Megavoltage Cone-Beam CT which became a commercial product. At Stanford, I have initiated and led a project on 2D/3D angiography guidance for frameless stereotactic radiosurgery of arteriovenous malformations. This project resulted in clinically used simulation and planning system. I also led a multi-disciplinary research effort (robotics, computer science and medical physics) in collaboration with Philips Ultrasound Investigations on tele-robotic 3D ultrasound for real-time soft tissue guidance concurrent with radiation beam delivery. The expertise and technology that we have developed for 4D ultrasound imaging and analysis have been instrumental in enabling the data acquisition and analysis for an ongoing NIH-R01 funded patient study as well as all other 4D CEUS studies currently ongoing at Stanford.

B. Positions and Honors

Positions and Employment

1997–1998	Medical Physicist, Radiation Oncology, Montreal University Hospital Center
1998–2001	Assistant Professor, Medical Physics Unit and Department of Oncology, McGill University
2001–2003	Senior Clinical Medical Physicist, Department of Oncology, King Faisal Specialist Hospital and Research Center
2003–2004	Senior Staff Physicist, Siemens Medical Systems, System Concepts, Oncology Care Systems
2005–2007	Clinical Collaboration Manager, Siemens Medical Systems, Innovations, Oncology Care Systems
2007–2017	Assistant Professor, Radiation Oncology, Stanford University Medical Center
2017- present	Associate Professor, Radiation Oncology, Stanford University Medical Center

Other Experience and Professional Memberships

1997-present	Canadian Organization of Physicists in Medicine (COMP)
2003-present	American Association of Physicists in Medicine (AAPM)

2009-present American Society for Therapeutic Radiology and Oncology (ASTRO)
2014-present Faculty member, Stanford Cancer Center Institute
2013-present Section Editor, Journal of Applied Clinical Medical Physics, 01/2016-01/
2013-2018 Therapy Imaging Subcommittee (American Association of Physicists in Medicine)

Honors

2000–present Member of the Canadian College of Physicists in Medicine

C. Contribution to Science

1. In the last decade, intensity modulated and volumetrically modulated external beam delivery techniques have dramatically improved external beam radiation therapy as these techniques have allowed sculpting complex dose distributions resulting in lower toxicity rates while maintaining probabilities of cure. However, since these techniques have been confined to mono-isocentric and mostly co-planar trajectories a significant opportunity for further improvement in external beam delivery has remained uncovered. Some of my recent publications have addressed this opportunity by exploring the potential of non-isocentric non-coplanar delivery trajectories. We have proposed and reported on novel fully dynamic non-isocentric Trajectory Modulated Arc Therapy (TMAT) employing concerted couch, gantry, and collimator leaf motions concurrent with beam delivery. For accelerated partial breast irradiation (APBI) in prone position, we have shown that in comparison to state-of-the art non-coplanar iso-centric intensity modulated delivery, TMAT resulted in marked reduction of the breast tissue volume irradiated at high doses. Thus TMAT may be an important venue for achieving better cosmetic outcomes in external beam APBI. These publications have introduced new paradigm and direction for further improvement of external beam radiation delivery. I served as the primary investigator on all of these studies.

a. Fahimian B, Yu V, Horst K, Xing L, Hristov D. Trajectory modulated prone breast irradiation: a LINAC-based technique combining intensity modulated delivery and motion of the couch. Radiother Oncol. 2013 Dec; 109(3):475-81. doi: 10.1016/j.radonc.2013.10.031. PubMed PMID: 24231240.
b. Yu VY, Fahimian BP, Xing L, Hristov DH. Quality control procedures for dynamic treatment delivery techniques involving couch motion. Med Phys. 2014 Aug; 41(8):081712. doi: 10.1118/1.4886757. PubMed PMID: 25086522.
c. Jieming Liang, Todd Atwood, Rie von Eyben, Benjamin Fahimian, Erika Chin, Kathleen Horst, Karl Otto, Dimitre Hristov, Trajectory Modulated Arc Therapy: a Fully Dynamic Delivery with Synchronized Couch and Gantry Motion Significantly Improves Dosimetric Indices Correlated with Poor Cosmesis in Accelerated Partial Breast Irradiation, International Journal of Radiation Oncology*Biology*Physics, Available online 25 April 2015, ISSN 0360-301 http://dx.doi.org/10.1016/j.ijrobp.2015.04.034.

2. Ultrasound is a non-ionizing real-time soft-tissue imaging modality widely used in cancer interventions with potential to provide target visualization during beam delivery when accurate tracking is most critical. To enable the incorporation of ultrasound imaging in the radiotherapy process I have initiated and led the development and the feasibility evaluation of a number of novel technologies: ultrasound-to-computed tomography hardware fusion, operator-free imaging, and automatic motion detection and tracking. My initial research in this domain has been licensed and implemented in a commercial ultrasound image guidance system (Clarity, Elekta Ltd) clinically used for ultrasound guidance in radiation therapy. More recently we introduced and demonstrated the feasibility of telerobotic ultrasound imaging as means for real-time guidance during delivery. This work has opened a new research area currently explored by several academic and industrial R&D teams. I served as the primary investigator in all of these studies.

a. Schlosser J, Salisbury K, Hristov D. Telerobotic system concept for real-time soft-tissue imaging during radiotherapy beam delivery. Med Phys. 2010 Dec;37(12):6357 67. PubMed PMID: 21302793.
b. Schlosser J, Salisbury K, Hristov D. Online image-based monitoring of soft-tissue displacements for radiation therapy of the prostate. Int J Radiat Oncol Biol Phys. 2012 Aug 1;83(5):1633-40. doi: 10.1016/j.ijrobp.2011.10.049. Epub 2012 Jan 26. PubMed PMID: 22285664.
c. Schlosser J, Hristov D. Radiolucent 4D ultrasound imaging: System design and application to radiotherapy guidance. IEEE Trans Med Imaging 2016;35:2292-2300.

d. Schlosser J, Gong RH, Bruder R, Schweikard A, Jang S, Henrie J, Kamaya A, Koong A, Chang DT, Hristov D. Robotic intrafractional us guidance for liver sabr: System design, beam avoidance, and clinical imaging. Med Phys 2016;43:5951.

3. Contrast-enhanced dynamic ultrasound imaging is accessible tool for assessing tumor vasculature and vascular response to treatment but current 2D imaging is fundamentally limited in quantification because of sampling errors. We have adapted technologies we have developed for ultrasound guidance in order to enable the exploration of novel 3D imaging approaches for assessment of tumor angiogenesis in three dimensions which in turn can further expand the role of functional and molecular ultrasound imaging for detection and monitoring cancer. We have shown that this new volumetric imaging is highly reliable and allows assessment of tumor angiogenesis more accurately than traditional 2D imaging. I served as a co-investigator in these studies providing the required technical (acquisition and analysis) capabilities.

a. Wang H, Kaneko OF, Tian L, Hristov D, Willmann JK. Three-dimensional ultrasound molecular imaging of angiogenesis in colon cancer using a clinical matrix array ultrasound transducer. Invest Radiol 2015;50:322-329.
b. Wang H, Hristov D, Qin J, Tian L, Willmann JK. Three-dimensional dynamic contrast-enhanced us imaging for early antiangiogenic treatment assessment in a mouse colon cancer model. Radiology 2015;277:424-434.
c. El Kaffas, A., et al. (2017). "Quantitative Three-Dimensional Dynamic Contrast-Enhanced Ultrasound Imaging: First-In-Human Pilot Study in Patients with Liver Metastases." Theranostics **7**(15): 3745-3758.
d. Zhou, J., et al. (2017). "Early prediction of tumor response to bevacizumab treatment in murine colon cancer models using three-dimensional dynamic contrast-enhanced ultrasound imaging." Angiogenesis **20**(4): 547-555.

Complete List of Published Work in My Bibliography:

http://www.ncbi.nlm.nih.gov/sites/myncbi/1d5FXVQavx25z/bibliography/48084964/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

Reference Number: R01 CA195453 Kamaya/Hristov/El-Kaffas (Co-PIs) 04/2016-04/2020
NIH/NCI
Title: 3D Dynamic Contrast-Enhanced Ultrasound for Monitoring Chemotherapy of Liver Metastases
This research project is the first clinical trial to assess the feasibility and reproducibility of a novel tracking-assisted dynamic volumetric perfusion US imaging in patients with colorectal cancer and evaluate whether biomarkers derived from such imaging can potentially serve as early predictor of response to therapy. Upon successful completion, this trial will lay the foundation for future clinical trials using volumetric perfusion ultrasound imaging for better monitoring of cancer therapy in patients with various other cancer types even beyond colorectal cancer
Role: Co-PI

Reference Number: 1 R01 CA17655301A1 Xing (PI) 06/01/2014-05/31/2020
NIH/NCI
DASSIM-RT and Compressed Sensing-Based Inverse Planning
The goal of this project is to establish a novel paradigm of dense angularly sampled and sparse intensity-modulated radiation therapy (DASSIM-RT). In this scheme, the redundant or dispensable modulation of the incident intensity-modulated beams is removed effectively by using a compressed sensing (CS) technique. The delivery time saved in this way is used to increase the angular sampling for improved dose conformality. By balancing the angular sampling and intensity modulation, DASSIM-RT enables us to fully utilize the technical

capabilities of modern digital linacs to produce highly conformal dose distributions that can be delivered efficiently.
Role: co-Investigator

Reference Number: 1R01CA22366701A1 Xing (PI) 06/01/2018-05/31/2023
NIH/NCI
Radioluminescence dosimetry solution for precision radiation therapy
The goal of this project is to create a clinically translatable solution for more accurate and reliable quality assurance (QA) measurements of linear accelerators in radiation therapy by developing a novel radioluminescence imaging technique. Upon success the research will substantially improve the safety, quality and efficiency of radiation oncology practice, and enable patients to truly benefit from modern radiation therapy modalities such as VMAT and IMRT and SBRT.
Role: co-Investigator

Completed Research Support

Reference Number: N/A Hristov (PI) 12/01/2014-12/01/2018
Bio-X Interdisciplinary Initiatives, Stanford University
Radiation sensitized nanocarriers for MR-guided radiation therapy and drug delivery
The goal of the project is to investigate the feasibility of a novel chemo-radiotherapy approach employing radiation-induced delivery of therapeutic load from MRI detectable nano-carriers.
Role: PI

Reference Number: N/A Hristov (PI) 09/01/2014– 09/01/2017
Funder: Elekta Ltd
Comparison of intra-fractional prostate motion detection using Clarity ultrasound system versus MV failure detection technique
The goal of the project is evaluate the accuracy of real-time ultrasound tracking in comparison to current radiographic-based tracking techniques.
Role: PI

Reference Number: N/A Hristov (PI) 11/17/2014-11/16/2015
Philips Healthcare
Ultrasound Guidance of Radiation Therapy
The goal of the project is evaluate the utility of 3D B-mode US imaging for adaptive radiotherapy.
Role: PI

Reference Number: 1R41CA17089 Hristov (PI) 09/24/2012- 08/31/2015
NIH/NCI STTR Phase 1
Robotic Ultrasound Image Guidance for Radiation Therapy
The goal of this project is to establish feasibility of the imaging component of the proposed ultrasound guidance system, and to inform any design changes to the acquisition system that may be needed. Furthermore the development of a real-time image-guidance system necessitates the development of image-based tracking algorithms. Thus the investigators hope to use and learn from the data in two ways:
Role: PI

Reference Number: Hristov (PI) 09/1/2012-08/31/2015
Siemens Medical Solutions, Inc
Motion Evaluation and Modeling for Quantification of PET and Perfusion CT Imaging Bio-Markers of Response Therapy
Role: PI

Varian Medical Systems 10/15/2012- 10/15/2014
Pilot Study of Dynamic Accelerated Partial Breast Irradiation Technique

The goal of this study is to evaluate Dynamic Accelerated Partial Breast Irradiation (DAPBI), an alternative to IMRT and 3D-CRT, which has shown to cause high rates of moderate-to-severe late normal tissue toxicities.
Role: PI

No Reference # Hristov (PI) 04/01/2011-03/31/2013
Philips Healthcare
Ultrasound Guidance of Radiation Therapy
Role: PI

No Reference # Hristov (PI) 03/01/2011-02/29/2012
Friends for an Earlier Breast Cancer Test
X-ray Stimulated Fluorescence for Early Detection of Breast Cancer
The goal of this study is to investigate the feasibility of using X-ray Stimulated Fluorescence phenomenon as a basis for an imaging system for early detection of breast cancer.
Role: PI

NIH PAR09028 Rebecca Fahrig (PI) 04/01/2010-03/31/2012
National Center for Research Resources
Axiom-Zeego Shared Instrument Grant
The goal of this study is to procure Axiom Zeego instrument and develop an accompanying program to share instrument capabilities and knowledge across projects and departments.
Role: Co-Investigator

II Pd-56 Hristov (PI) 10/01/2010-09/30/2012
Bio-X Interdisciplinary Initiatives, Stanford University
Tele-robotic system for real-time soft-tissue image guidance of stereotactic body radiation therapy
The goal of this study is to develop a telerobotic system for remote ultrasound imaging and guidance concurrent with radiation beam delivery.
Role: PI

No Reference # Hristov (PI) 09/01/2011-08/31/2012
Center for Biomedical Imaging at Stanford
Magnetic Resonance Imaging of Radiation-Activated Alginate Nanoparticle Drug/Sensitizer Delivery
The goal of this study is to investigate the feasibility of synthesizing alginate nanoparticle carriers of therapeutic and imaging load along with MR imaging for the detection of radiation-induced load release.
Role: PI