OMB No. 0925-0001 and 0925-0002 (Rev. 12/2020 Approved Through 02/28/2023)

# BIOGRAPHICAL SKETCH

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NAME: **Graves, Edward Elliot**

eRA COMMONS USER NAME (credential, e.g., agency login): **Graves.Edward**

POSITION TITLE: Associate Professor, Division of Radiation Physics, Department of Radiation Oncology, Stanford University School of Medicine, Stanford, CA

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 *(if applicable)* | Completion Date MM/YYYY | FIELD OF STUDY |
|---|---|---|---|
| University of California, Berkeley | B.S. | 05/1996 | Bioengineering |
| University of California, Berkeley and San Francisco | Ph.D. | 05/2001 | Bioengineering |
| Massachusetts General Hospital | Postdoctoral | 07/2003 | Molecular Imaging |

**A. Personal Statement**

My research focuses on understanding tumor and normal tissue radiation response through the development and application of molecular imaging techniques. To this end my group has developed a variety of methods of noninvasively detecting and quantifying molecular and physiologic aspects of radiation and tumor biology, including tumor cell migration and proliferation, immune responses, oxygen concentrations, hypoxia-regulated gene expression, and metabolism. In addition, in order to evaluate the relevance of these molecular factors to clinical radiation therapy, we have developed technology for the delivery of clinically-similar image-guided conformal radiotherapy to small animals and applied it in preclinical systems to understand the biological effects of these treatments.

Ongoing and recently completed projects that I would like to highlight include:

**Ongoing Research Support**

RRADICAL, Varian Medical Systems, Inc.
Gensheimer (PI), Role: Translational Research Co-Chair
09/09/16 – 09/08/22
A phase II trial of addition of radical-dose radiation therapy to anti-PD1 immunotherapy for non-small cell lung cancer patients

R01 CA219994, NIH
Idoyaga (PI), Role: Co-investigator
09/15/17 – 08/31/22
Effect of Radiotherapy on Dendritic Cell Subsets: Implications for Immunotherapy

2R44 CA217607-03, TibaRay, Inc./NIH
Bhardwaj and Loo (PI), Role: Senior/Key Person
09/01/19 – 08/30/22
Practical Implementation of an Ultra-rapid FLASH Radiation Therapy Linac Beamline

P01 CA244091-01, University of California, Irvine/NIH
Loo (PI), Role: Co-investigator
06/01/20 – 05/31/25
Increasing the therapeutic index of brain tumor treatment through innovative FLASH radiotherapy

2021-SCI-CIA-Pham, Stanford Cancer Institute
Pham (PI), Role: Co-Investigator
09/01/20 – 02/28/22
Universal Sterilization of Blood Products through Next-Generation Ultra-High Dose Rate Linear Accelerator Irradiation

2021-SCI-CIA-Dirbas, Stanford Cancer Institute
Dirbas (PI), Role: Co-Investigator
03/01/21 – 02/28/22
Preclinical model for evaluating FLASH radiotherapy for breast cancer

R01EB030493, NIH
Wu (PI), Role: Co-Investigator
09/20/21 – 06/30/24
Focused kV X-ray Modulated Conformal Radiotherapy for Small Targets

R21CA256708, NIH
El Kaffas (PI), Role: Co-Investigator
2/01/22 – 01/31/24
Novel Mechano-Acoustic Enhancement of Immunotherapy

**Completed Research Support**

P01 CA67166 (NCX), NIH/NCI
Giaccia (PI), Role: Leader, Core B
06/01/13-05/31/19
Hypoxia: Molecular Studies and Clinical Exploitation

R01 CA197136, NIH/NCI
Graves (PI)
09/01/15 – 08/31/21
Radiation-Induced Tumor Cell Migration

R01 CA19829104, NIH
Rankin (PI), Role: Co-Investigator
04/01/16 – 03/31/21
Preclinical Testing of a Novel Therapy Targeting AXL in Advanced Kidney Cancer

T29IP0443, UCOP
Loo (PI), Role: Co-investigator
04/01/19 – 03/31/21
Immune mechanisms of FLASH radiotherapy: a new paradigm for lung cancer cure

199214, Stanford Cancer Institute
Graves (PI)
09/01/20 – 08/31/21
Synergizing CAR-T Cell Therapy with Radiation for the Treatment of Brain Tumors

Citations:

1. Rafat M, Aguilera TA, Vilalta M, Bronsart LL, Soto LA, von Eyben R, Golla MA, Ahrari Y, Melemenidis S, Afghahi A, Jenkins MJ, Kurian AW, Horst K, Giaccia AJ, **Graves EE**. Macrophages Promote Circulating Tumor Cell-Mediated Local Recurrence Following Radiation Therapy in Immunosuppressed Patients. Cancer Research 2018; 78(15):4241-4252. PMC6072588.

2. Ali R, Apte S, Vilalta M, Subbarayan M, Miao Z, Chin FT, **Graves EE**. $^{18}$F-EF5 is predictive of radiation response in preclinical models of cancer. PLoS One 2015; 10(10):e0139425. PMC4592127.
3. Vilalta M, Rafat M, Giaccia AJ, **Graves EE.** Recruitment of circulating breast cancer cells is stimulated by radiotherapy. Cell Reports 2014; 8:402-409. PMC4121080.
4. Zhou H, Xu J, Rodriguez M, van den Haak F, Zhu X, Xian Y, Nelson G, Jogani R, Keall PJ, **Graves EE.** Development of a MicroCT-Based Image-Guided 3D Conformal Radiotherapy System for Small Animals. International Journal of Radiation Oncology Biology Physics 2010; 78:297-305. PMC2906632.

**B. Positions, Scientific Appointments, and Honors**

**Positions and Scientific Appointments**

| | |
|---|---|
| 2021 – 2022 | Invited Faculty, Hokkaido University (no formal duties or funding) |
| 2012 – present | Associate Professor (with tenure), Departments of Radiation Oncology and, by courtesy, Radiology, Stanford University, Stanford, CA |
| 2012 – present | Member, Radiation Research Society |
| 2011 – present | Member, World Society of Molecular Imaging |
| 2010 – present | Peer reviewer, Cancer Prevention and Research Institute of Texas |
| 2008 – present | Founding member, AAPM Small Animal Conformal Irradiation working group |
| 2008 – present | Member, American Association of Physicists in Medicine |
| 2008 – present | Member, American Society of Radiation Oncology |
| 2006 – present | Peer reviewer, Department of Defense Breast Cancer Research Program |
| 2004 – 2012 | Assistant Professor, Department of Radiation Oncology, Stanford University, Stanford, CA |
| 2003 – 2010 | Member, Society for Molecular Imaging |
| 2003 – 2004 | Acting Assistant Professor, Department of Radiation Oncology, Stanford University, Stanford, CA |
| 2001 – 2003 | Postdoctoral fellow with Ralph Weissleder, Massachusetts General Hospital, Charlestown, MA |
| 1996 – 2001 | Graduate student researcher with Sarah Nelson, University of California, San Francisco, CA |
| 1995 – present | Member, Tau Beta Pi (national engineering honor society) |
| 1995 – 1996 | Research assistant with Dr. Leon Chua, University of California, Berkeley, CA |

**Honors**

| | |
|---|---|
| 2021 – 2022 | Invited Collaborative Researcher, Global Center of Biomedical Science & Engineering (GCB), Hokkaido University |
| 2001, 2002 | NIH Postdoctoral Training Grant recipient |
| 2000 | First prize, student poster competition, ISMRM Cancer Workshop |
| 2000 | Achievement Rewards for College Scientists scholar |
| 1998 | UC Berkeley Block Grant recipient |
| 1996 – 1999 | NIH Predoctoral Training Grant recipient |

**C. Contribution to Science**

1. My research centers on applications of emerging functional and molecular imaging techniques to study the radiobiology of cancer and normal tissue and to improve the efficacy radiotherapy of cancer. These efforts balance engineering of novel methods to image biologically and clinically important aspects of the tumor microenvironment with application of these techniques to understand how cells and tissues respond to radiation. This work has included basic research on the effects of radiation on tumor cell migration, evaluations of the ability of imaging methods to detect hypoxia and the role of oxygenation in preclinical studies, and investigation of the prognostic performance of clinical imaging modalities. This variety of studies demonstrates the multidisciplinary nature of my laboratory and its approach to solving problems in the basic and clinical sciences.
    a. Vilalta M, Brune J, Rafat M, Soto L, **Graves EE**. The role of granulocyte macrophage colony stimulating factor (GM-CSF) in radiation-induced tumor cell migration. Clinical and Experimental Metastasis 2018; 35(40):247-254. PMC6064390.
    b. Rafat M, Aguilera TA, Vilalta M, Bronsart LL, Soto LA, von Eyben R, Golla MA, Ahrari Y, Melemenidis S, Afghahi A, Jenkins MJ, Kurian AW, Horst K, Giaccia AJ, **Graves EE**. Macrophages Promote

Circulating Tumor Cell-Mediated Local Recurrence Following Radiation Therapy in Immunosuppressed Patients. Cancer Research 2018; 78(15):4241-4252. PMC6072588.

c. Vilalta M, Rafat M, Giaccia AJ, **Graves EE**. Recruitment of circulating breast cancer cells is stimulated by radiotherapy. Cell Reports 2014; 8:402-409. PMC4121080.

d. **Graves EE**, Vilalta M, Cecic IK, Erler JT, Tran PT, Felsher D, Sayles L, Sweet-Cordero A, Le QT, Giaccia AJ. Hypoxia in Models of Lung Cancer: Implications for Targeted Therapeutics. Clinical Cancer Research 2010; 16:4843-4852. PMC2948600.

2. My group has also evaluated the ability of hypoxia imaging methods to stage cancer and to inform the delivery of cancer therapies including radiation, which are known to be hindered by the presence of tumoral hypoxia. This work has focused on evaluation of the sensitivity and specificity of optical and positron emission tomography (PET) measures of tumor hypoxia, and on the prognostic performance of preclinical and clinical PET images of hypoxia for patients undergoing radiotherapy.

   a. **Graves EE**, Hicks RJ, Binns D, Bressel M, Le QT, Peters L, Young RJ, Rischin D. Quantitative and Qualitative Analysis of [18F]FDG and [18F]FAZA Positron Emission Tomography of Head and Neck Cancers and Associations with HPV Status and Treatment Outcome. European Journal of Nuclear Medicine and Molecular Imaging 2016; 43(4):617-625. PMC4767583.

   b. Ali R, Apte S, Vilalta M, Subbarayan M, Miao Z, Chin FT, **Graves EE**. $^{18}$F-EF5 is predictive of radiation response in preclinical models of cancer. PLoS One 2015; 10(10):e0139425. PMC4592127.

   c. Cecic I, Chan D, Sutphin P, Ray P, Gambhir SS, Giaccia A, **Graves EE**. Oxygen sensitivity of reporter genes: implications for preclinical imaging of tumor hypoxia. Molecular Imaging 2007, 6: 219-228.

3. In order to study clinically relevant radiotherapy methods in preclinical studies, I have led the development of image-guided conformal radiation therapy systems suitable for use in small animal research. We developed a device based on a commercial micro-computed tomography (microCT) system capable of directing x-ray beams of varying widths to a target within a mouse, analogous to how conformal radiotherapy is delivered in the clinic. In addition, we have engineered a suite of Monte Carlo-based tools to model dose delivery to small animal tissues in order to quantify radiation doses produced by a variety preclinical irradiators, and have applied this technology in the basic radiobiology research described above.

   a. Zhou H, Xu J, Rodriguez M, van den Haak F, Zhu X, Xian Y, Nelson G, Jogani R, Keall PJ, **Graves EE**. Development of a MicroCT-Based Image-Guided 3D Conformal Radiotherapy System for Small Animals. International Journal of Radiation Oncology Biology Physics 2010; 78:297-305. PMC2906632.

   b. Bazalova M, Zhou H, Keall PJ, **Graves EE**. Kilovoltage beam Monte Carlo dose calculations in sub-millimeter voxels for small animal radiotherapy. Medical Physics 2009; 36:4991-4999. PMC2773455.

   c. **Graves EE**, Zhou H, Chatterjee R, Keall PJ, Gambhir SS, Contag CH, Boyer AL. Design and Evaluation of a Variable Aperture Collimator for Conformal Radiotherapy of Small Animals Using a MicroCT Scanner. Medical Physics 2007; 34: 4359-67.

**Complete List of Published Work in MyBibliography:**
http://www.ncbi.nlm.nih.gov/myncbi/browse/collection/41145464/?sort=date&direction=descending