



DCTD Staff Highlight: Paula Jacobs, PhD



Paula Jacobs, PhD
Associate Director, Cancer Imaging Program, DCTD, NCI, NIH

Born in Vicksburg, MS, Paula Jacobs, PhD, attended the Massachusetts Institute of Technology and was one of only 20 women in her freshman class of 900. Paula majored in chemistry there, then received graduate degrees from Tufts University and Northeastern University. After post-doctoral fellowships in chemistry and radiology, Paula spent 30 years in industry developing nanoparticle magnetic resonance imaging agents. She joined NCI in 2006 as a contractor supporting the Cancer Imaging Program (CIP). Transitioning to federal staff, she was appointed to Deputy Associate Director of CIP in 2009, Acting Associate Director in 2011, and finally Associate Director in 2012. Paula discusses some important events in cancer imaging research during her time at NCI.

What are some activities that you've been involved in at NCI?

I have spent most of my time at NCI in these areas: lowering regulatory barriers to investigational imaging agents, facilitating community access to data to develop clinical

decision-making tools, machine learning and artificial intelligence to extract hidden information from clinical images, and improving standardization of imaging.

What did you first focus on when you arrived at NCI?

NCI held only one imaging IND (Investigational New Drug) application when I arrived, despite many promising candidates. I worked closely with FDA, particularly with Dwaine Rieves, MD, Director, Division of Medical Imaging Products, FDA at the time, and who now volunteers with CIP. We now have 10 INDs, and multicenter trials in NCI's National Clinical Trials Network with investigational imaging drugs are ongoing.

Is there an important milestone that occurred during your time at NCI?

We filed the first (and still only) NDA (New Drug Application) at NIH, responding to a nationwide shortage of Technetium-99m (Tc-99m). Tc-99m is a radioisotope used for bone scans, which is important

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for diagnosing bone metastases in breast and prostate cancer patients. Its 6-hour half-life makes stockpiling it impossible. Around 2007, supply of this important isotope became problematic, so I prepared an NDA for the alternative **Sodium Fluoride F18** (NaF F18), which is more expensive than Tc-99m, but produces better images and can be made in large quantities in academic and commercial cyclotrons. With this NDA approved, other institutions submitted generic drug applications (Abbreviated NDA). Now there are 23 NDAs that supply NaF F18 from over 120 sites. Since short-lived radiopharmaceuticals cannot be centralized like a regular drug that sits on a shelf, its availability throughout the country has greatly impacted patient care.

Can you describe the history and impact of The Cancer Imaging Archive on cancer research?



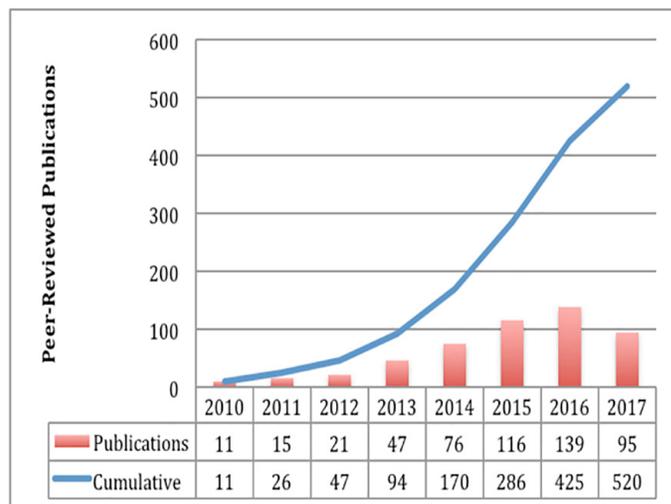
The Cancer Imaging Archive (TCIA) is a publicly accessible, large archive

of de-identified cancer medical images. TCIA started with a small group of radiologists who located and characterized lesions in a collection of **lung images**, with a goal to develop consensus guidelines for a computed tomography (CT) resource and a database of CT lung images. NCI's Center for Biomedical Informatics and Information Technology developed software for the resource, and as more images were added to the archive, we soon needed a more user-friendly version. Jim Tatum, MD, my predecessor in CIP, started the process, and the main archive came online in 2011. We were determined to make this resource freely available, and most of the collections are totally barrier-free, which means no data use agreement, no registration, no permissions required.

CIP gathered brain tumor clinical images associated with The Cancer Genome Atlas (TCGA) genomic data. We helped develop radiologist evaluations of these images – rigorous semiquantitative expert radiologist

“structured” readings amenable to statistical analysis. Groups of radiologists self-assembled, and CIP set up the readings and software for the investigators. The participants were the first to publish correlations of imaging phenotypes to the related genomic and clinical data from TCGA. **The brain image reading manual** is publicly available, and others for breast, lung, and renal cancer will be available in the future. Compared to a tumor biopsy that has limited tissue for research, tumor images show the whole tumor and the changes over time and treatment.

Currently 83 collections are available in TCIA – 41,000 patients, close to 20 terabytes of data, from 31 million individual images. More than 500 papers (that we know of) have been published using TCIA data. TCIA is a published journal, and each collection has a Digital Object Identifier (DOI), providing investigators a citation for their data on their CV.



Publications based on TCIA data since its inception

TCIA and CIP grants also support research in standardization, repeatability, and reproducibility of cancer imaging, critical for clinical care. For example, a patient may be diagnosed in one hospital by an imaging test, and then have post-treatment imaging done at another hospital – if the images aren't reproducible, we cannot tell if any differences are real. Sharing data in TCIA advances the development of advanced computer algorithms

Staff Highlight... continued

to improve reliability and clinical utility. CIP's grant-based **Quantitative Imaging Network** (QIN) encourages standardization and data sharing, changing the research culture to data collaboration instead of sequestration. All QIN members participate in cross-institutional collaboration and data sharing, a key vision of the late Larry Clarke, PhD, a CIP Branch Chief.

What do you see as the future of TCIA?

TCIA is a key player in the **Applied Proteogenomics Organizational Learning and Outcomes** (APOLLO) network, a collaboration between NCI, the Department of Defense, and

the Department of Veterans Affairs to integrate genetic and protein information in cancer. CIP prospectively receives and curates patient images and histology slides from APOLLO studies. TCIA will also be an integral part of the Cancer Data Commons now being developed to integrate all types of cancer data. Another initiative will include animal tumor images from patient-derived xenografts (PDXs) from **NCI's Patient-Derived Models Repository** in TCIA. We in CIP made a philosophical choice to make cancer images and data totally available, and I feel like we've made a difference to the research community.

Spotlight: Researchers Address Challenges of Small Cell Lung Cancer

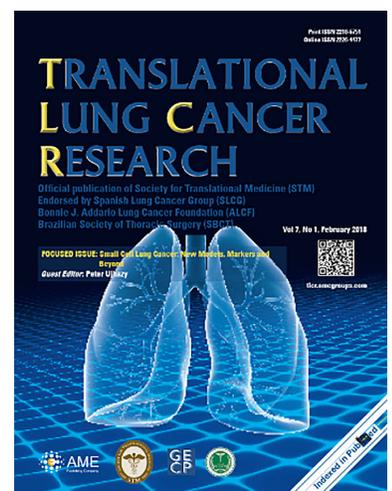
The **Small Cell Lung Cancer Consortium** (SCLC-C) was established in 2017 in response to the Recalcitrant Cancer Research Act of 2012 and is dedicated to solving this difficult clinical problem. It is estimated that worldwide more than 250,000 people die of this disease yearly. The momentum in SCLC research is growing, and the number of publications per year almost tripled since 2008. The goal of the Consortium is to harness this interest and energy by establishing a collaboration comprised of several funding mechanisms to advance research in this field. The SCLC-C includes scientists and physicians from seven U01 projects devoted to either early detection/diagnosis or therapy, one U24 infrastructure grant, 10 NCI-funded SCLC grants (separate from the U mechanisms), and NCI intramural investigators focused on the disease.

NCI hosted the first Annual Small Cell Lung Cancer Consortium Meeting on March 15-16, 2018 to hear the latest research from the Consortium members and to plan future collaborations. The SCLC-C meeting topics included molecular pathology, detection, oncogenesis/tumor biology, models, therapeutics, and emerging targets. Among special guests, NCI welcomed its former director, Dr. Harold Varmus, who was awarded a U01 in the Consortium and presented his

project deriving SCLC-like cells from human embryonic cells. The NCI meeting organizers included Dr. Eva Szabo, Division of Cancer Prevention (DCP) and Drs. Suzanne Forry and Peter Ujhazy, DCTD for the scientific aspects, and Ms. Tamara Walton and her team in DCTD and staff in DCP for the logistics.

The SCLC therapy U01 Funding Opportunity Announcement (**PAR-16-049**) for the Consortium remains open, and the final application date is in November 2018. Funding of these additional therapy grants will solidify the Consortium with its final collaborators.

The SCLC-C wrote a selection of articles for the February 2018 edition of **Translational Lung Cancer Research**, entitled, "Small Cell Lung Cancer: New Models, Markers, and Beyond." Peter Ujhazy, MD, PhD, Translational Research Program, edited the series and co-authored the preface, "**Small Cell Lung Cancer: Updates and New Concepts.**"



News about DCTD Programs and Activities

Program Updates

New Resource for Researchers: Clinically Annotated Data and Specimens from Phase III Trials



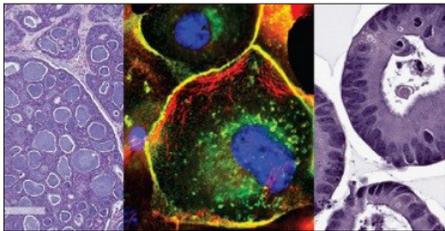
On April 2, 2018, NCI announced the availability of a new research resource for the scientific community: [NCTN Navigator](#). Navigator is an online resource that contains a unique inventory

of specimens that have associated patient clinical data obtained over the length of the clinical trial. Navigator

is intended for investigators who have typically conducted exploratory correlative analyses and are now seeking specimens to validate their hypotheses. The Navigator inventory is currently

limited to published adult phase 3 studies that evaluated cancer treatments and includes data from more than 90 trials, 60,000 patients, and 850,000 specimens. Specimens from pediatric trials are expected to be added in the next year. [An NCI Cancer Currents blog](#) post describes Navigator in more detail.

Additional Cancer Types and Rare Cancers Now Available in NCI's Patient-Derived Models Repository



[NCI's Patient-Derived Models Repository](#) (PDMR) is a national repository of early-passage, molecularly characterized, clinically annotated patient-derived xenografts (PDXs) developed from patients with solid tumors. Since April 2017, more than 160 public models

have been made available to the research community. In March 2018, several [new models](#) were added to the PDMR, including cancer types not previously available and some rare cancers. Read the recent [NCI Cancer Currents blog](#) on the PDMR.

Publications and Outreach

Peer-reviewed Publications

Ahmed MM, Coleman CN, Mendonca M, Bentzen S, Vikram B, Seltzer SM, Goodhead D, Obcemea C, Mohan R, Prise KM, Capala J, Citrin D, Kao G, Aryankalayil M, Eke I, Buchsbaum JC, Prasanna PGS, Liu FF, Le QT, Teicher B, Kirsch DG, Smart D, Tepper J, Formenti S, Haas-Kogan D, Raben D, Mitchell J. [Workshop Report for Cancer Research: Defining the Shades](#)

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H, Luznik L, Smith BD. [A Multi-Center Phase I Trial of Ipilimumab in Myelodysplastic Syndrome Patients following Hypomethylating Agent Failure](#). *Clin Cancer Res.* 2018 May 1. Epub ahead of print.

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a KMT2A Partial Tandem Duplication Targeted Therapy: Results of Phase 1 Study NCI 8485. *Haematologica.* 2018 Mar 22. Epub ahead of print.

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Srivastava AK, Hollingshead MG, Govindharajulu JP, Covey JM, Liston D, Simpson MA, Peggins JO, Bottaro DP, Wright JJ, Kinders RJ, Doroshov JH, Parchment RE. [Molecular Pharmacodynamics-Guided Scheduling of Biologically Effective Doses: A Drug Development Paradigm Applied to MET tyrosine Kinase Inhibitors](#). *Mol Cancer Ther*. 2018 Mar;17(3):698-709.

Ujhazy P, Lindwasser OW. [Small Cell Lung Cancer: Updates and Concepts](#). *Transl Lung Cancer Res*. 2018 Feb;7(1):1-3. Full selection of articles from the Small Cell Lung Cancer Consortium and edited by Peter Ujhazy, MD, PhD in the February 2018 edition of [Translational Lung Cancer Research](#), entitled, "Small Cell Lung Cancer: New Models, Markers, and Beyond."

Cancer Currents Blog Posts

[Rucaparib Approved as Maintenance Treatment for Some Recurrent Ovarian Cancers](#); **Elise Kohn, MD**, Cancer Therapy Evaluation Program; May 4, 2018.

[NCI Expands Repository of Cancer Research Models: A Conversation with Drs. Doroshov and Evrard](#); **James Doroshov, MD, DCTD Director**, and **Yvonne Evrard, PhD**, Frederick National Laboratory for Cancer Research; April 20, 2018.

[NCI Launches New Resource for Specimens and Data from Cancer Clinical Trials](#); **Jeff Abrams, MD**, Cancer Therapy Evaluation Program, **Irina Lubensky, MD**, Cancer Diagnosis Program, **Grace Mishkin, MPH**, Cancer Therapy Evaluation Program; April 2, 2018.

[Targeted Therapy Larotrectinib Shows Promise in Early Trials; Regardless of Cancer Type](#); **Nita Seibel, MD**, Cancer Therapy Evaluation Program; March 9, 2018.

[Can Oxygen "Microbubbles" Make Radiation Therapy More Effective?](#); **Eric Bernhard, PhD**, Radiation Research Program; February 20, 2018.

Interviews, Press, and Social Media

[Hilton Head Father Is Urging Senate to Boost Childhood Cancer Treatment Effort](#); **Malcom Smith, MD, PhD**, Cancer Therapy Evaluation Program; McClatchy DC Bureau; May 16, 2018.

[How to Ruin Cancer's Day](#); **Dan Xi, PhD**, Office of Cancer Complementary

and Alternative Medicine; Knowable; May 1, 2018.

[PARP Inhibitors Are Improving the Outlook of Hard-to-Treat Cancers](#); **James Doroshov, MD, DCTD Director**; The Scientist; April 1, 2018.

[NIH-Funded Study Shows Sorafenib Improves Progression-Free Survival for Patients with Rare Sarcomas](#); NCI Press Release; March 28, 2018.

[NCI Facebook Live Event: Rectal Cancer: Treatment, Research and Quality of Life](#); **Carmen Allegra, MD**, and **Andrea Denicoff, MS, RN**, Cancer Therapy Evaluation Program, and **Deborah Schrag, MD, MPH**, Dana Farber Cancer Institute; March 29, 2018.



["Appropriate Eligibility Criteria" Must Guide Selection of HIV-Positive Individuals for Cancer Trials](#); **Elad Sharon, MD, MPH**, Cancer Therapy Evaluation Program; Healio; March 26, 2018.

[How to Find Hidden Cancers? Doctors Try Glowing Dyes](#); **Paula Jacobs, PhD**, Cancer Imaging Program; Associated Press; March 14, 2018. [Companion USA Today video interview](#).

Conferences and Meetings

DCTD-supported research will be presented at the [ASCO 2018 Annual Meeting](#) (June 1-5, 2018; Chicago, IL). A full list of DCTD staff presentations is available on the [DCTD website](#).

The Cancer Imaging Program convened its 10th [Quantitative Imaging Network](#) (QIN) meeting on May 17-18, 2018. The QIN promotes research and development of quantitative methods to measure tumor response to therapies in clinical trials. At this year's meeting, **Angela Jarrett, PhD**, University of Texas at Austin, received the QIN Larry Clarke Young Investigator Award. Her presentation was entitled, "Predicting the response of breast cancer to neoadjuvant therapy using a mathematical model calibrated by quantitative MRI data."

Angela Jarrett, PhD receives the QIN Larry Clarke Young Investigator Award from Robert Nordstrom, PhD, CIP



On April 23, 2018, the Cancer Therapy Evaluation Program (CTEP) held its annual [Experimental Therapeutics Clinical Trials Network](#) (ETCTN) Portfolio Presentation meeting. This meeting is a venue for CTEP's Phase 1 and Phase 2 investigators to present their early phase clinical trial portfolios.

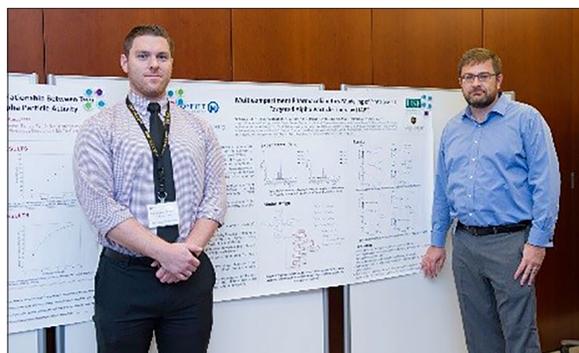


The goals of the ETCTN Portfolio Presentation meeting were to:

- bring together NCI CTEP and associated program staff with the leadership of the NCI CTEP Phase 1 and Phase 2 sites
- enable both NCI staff and ETCTN investigators to be apprised of ongoing and planned clinical trials within the ETCTN program
- promote improved scientific and clinical collaboration to enhance accrual to CTEP-sponsored trials
- facilitate alignment of ETCTN activities with CTEP's program goals

Staff in the Radiation Research Program and the Dosimetry Planning Committee convened a workshop on [Dosimetry of Systemic Targeted Radiopharmaceutical Therapy](#) (TRT) on April 19-20, 2018. Attendees from academic research and clinical centers, industry, and government agencies discussed the scientific, practical, and regulatory aspects of TRT dosimetry.

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Dosimetry workshop attendees present their research

Conferences and Meetings ... continued

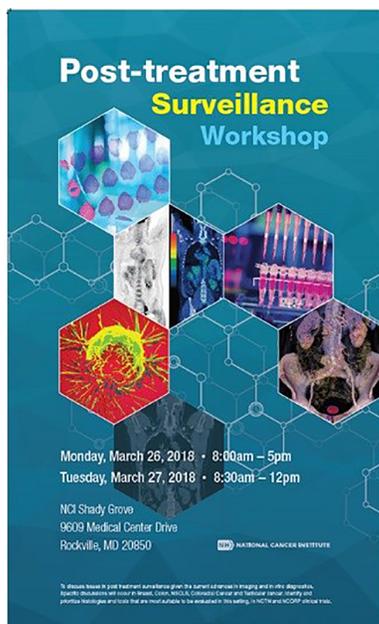
NCI's [Clinical Imaging Steering Committee](#) held a workshop, "Improving Brain Tumor Characterization with Advanced Neuroimaging Methods" from April 18-19, 2018. The workshop was co-chaired by **Drs. Lalitha Shankar**, Cancer Imaging Program, DCTD, **Dan Barboriak**, Duke Cancer Center, **Michael Knopp**, The Ohio State University, and **Neil Rofsky**, UT Southwestern Medical Center. The focus of the workshop was to discuss ways to improve the quality and standardization of standard of care neuroimaging in NCI trial consortia and to enhance the evaluation of advanced functional, molecular, and radiomic imaging techniques.

In October 2017, [CIP celebrated its 20th Anniversary](#). CIP highlighted its 20 years of research contributions to cancer research and vision for the future in a symposium on April 4, 2018.



Past and present CIP Associate Directors (l to r): James Tatum, MD, Dan Sullivan, MD, and Paula Jacobs, PhD

NCI convened a workshop on [Issues in Post-Treatment Surveillance](#) on March 26-27, 2018. The workshop attendees were asked to:



- Consider post-treatment surveillance in oncology, and how the management algorithm(s) changes with time, clinical evidence, and technological advances
- Discuss issues in post-treatment surveillance given the current advances in imaging and liquid biopsies
- Identify and prioritize histologies and tools that are most suitable to be evaluated in clinical trials in NCI's National Clinical Trials Network (NCTN) or NCI's Community Oncology Research Program (NCORP), or potentially in clinical registries
- Make recommendations for future clinical trials in non-small cell lung, breast, prostate, colon, and testicular cancer

A video of the meeting can be seen on NIH VideoCast ([Day 1](#) and [Day 2](#)).

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Conferences and Meetings ... continued

Staff from NCI, the National Institute of Arthritis and Musculoskeletal and Skin Diseases and The National Institute of Allergy and Infectious Diseases jointly organized a workshop entitled, “**Cancer, Autoimmunity and Immunotherapy**” on March 22-23, 2018. The goals of the workshop were to understand the biology of immune-related adverse events (irAEs), which have occurred in cancer patients being treated with immunotherapies, and how that might inform the study of autoimmune disease and to define the potential for the study of autoimmune disease to lead to greater understanding of the treatment and management of irAEs during and following cancer therapies. Watch both days of the workshop in NIH VideoCast: ([Day 1](#) and [Day 2](#)).



Norman Sharpless, MD, NCI Director, speaks at the NIH Conference on Cancer, Autoimmunity and Immunology

Alice Chen, MD, Developmental Therapeutics Clinic and **Nita Seibel, MD, Malcolm Smith, MD, PhD**, and **Elad Sharon, MD, MPH**, CTEP, participated in the April 20, 2018 FDA meeting, “**FDA/OCE Public Meeting on Relevant Molecular Targets in Pediatric Cancers: Applicability to Therapeutic Investigation FDARA 2017.**”



Malcolm Smith, MD, PhD, (far left) at FDA meeting