James Cox, M.D.

Interview #32

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James Cox, M.D.

Interview #32

Interview Profile

Interview Information Submitted in: 2013

Interview Information:

Three interview sessions: 3 January 2013, 12 April 2013, 23 April 2013
Total approximate duration: 5 hours 30 minutes
Interviewer: Tacey A. Rosolowski, Ph.D.

First interviewed in 2004, Lesley Brunet.

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About the Interview Subject:

Radiation oncologist, James A. Cox (b. 16 July 1938, West Virginia) came to MD Anderson in 1988 to serve as Vice President of Patient Care and Physician-in-Chief ('88-'92). He is a Professor in the Department of Radiation Oncology. Dr. Cox has been instrumental in advancing the design of clinical trials and in establishing many trials to demonstrate the effectiveness of radiation therapy in combination with chemotherapy and surgery. Through work conducted both at MD Anderson and with the Radiation Therapy Oncology Group (RTOG), his research has focused on many types of cancer, including lung cancer, lymphomas, esophageal and prostate cancer. Since 1998, Dr. Cox has been active in developing proton therapy at MD Anderson and opening the Proton Therapy Center in 2006. He has since worked on trials to compare proton therapy with conventional radiation treatments. He is also demonstrating the effectiveness of this therapy in reducing patients' side effects, tumor size, and survival.

Dr. Cox served as Head of the Division of Radiation Oncology from 1995 to 2010.

Major Topics Covered:

Personal and educational background

MD Anderson research culture

Clinical trials: controversy over, ethical issues;

The Radiation Oncology Group

Radiation oncology at MD Anderson; the Division of Radiation Oncology

Research: cancers, body areas, design of clinical trials; effectiveness of proton therapy

The Proton Therapy Center: history of

Regional care centers; sister institutions

MD Anderson presidents and views on growth

A note on transcription and the transcript:

This interview had been transcribed according to oral history best practices to preserve the conversational quality of spoken language (rather than editing it to written standards).

The interview subject has been given the opportunity to review the transcript and make changes: any substantial departures from the audio file are indicated with brackets [ ].

In addition, the Archives may have redacted portions of the transcript and audio file in compliance with HIPAA and/or interview subject requests.

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Original Interview Profile #32: James Cox, M.D.
Submitted by: Tacey A. Rosolowski, Ph.D.
Date revised: 3 July 2014

This interview of radiation oncologist, Dr. James A. Cox (b. 16 July 1938, West Virginia) was conducted over three sessions in the early part of 2013 (approx. duration, 5:30). (Dr. Cox was first interviewed in 2004 by Lesley Brunet.) Dr. Cox came to MD Anderson in 1988 to serve as Vice President of Patient Care and Physician-in-Chief ('88-'92). From '95 to 2010 he served as Head of the Division of Radiation Oncology. He is also a Professor in the Department of Radiation Oncology and holds the Hubert L. and Olive Stringer Distinguished Chair in Oncology in Honor of Sue Gribble Stringer. Since 1998, Dr. Cox has been active in developing proton therapy at MD Anderson, and the sessions take place in Dr. Cox's office at the Proton Therapy Center located south of MD Anderson's main campus, on Old Spanish Trail. Tacey A. Rosolowski, Ph.D. serves as interviewer.

Dr. Cox received his AB in Chemistry and Biology in 1960 from Kenyon College, Gambier, OH, and in 1965 was awarded his M.D. from the University of Rochester School of Medicine and Dentistry, Rochester, NY. He undertook Fellowships in Clinical Oncology and Therapeutic Radiology at Penrose Cancer Hospital, Colorado Springs, CO ('63-'64), then interned at the University of Chicago Pritzker School of Medicine in Chicago, Illinois ('66-'69). A final clinical fellowship in Therapeutic Radiology took him to the Institut Gustave-Roussy in Villejuif, France ('69-'70). In 1974, after holding serving as assistant professor on the faculty in Radiology at Georgetown University Hospital in Washington, D.C., Dr. Cox took up a position as Associate Professor in the Department of Radiology at the Medical College of Wisconsin, Milwaukee, Wisconsin. He became a full professor in 1977. In 1985, Dr. Cox joined the Department of Radiation Oncology at Columbia University College of Physicians and Surgeons in New York, where he stayed until 1988, when Dr. Charles LeMaistre recruited him to come to MD Anderson to serve as Vice President of Patient Care and Physician-in-Chief ('88-'92). He also served as Chair of the Department of Radiation Oncology and Head of the Division of Radiation Oncology ('95-2010). Through work conducted both at MD Anderson and with the Radiation Therapy Oncology Group (RTOG), Dr. Cox has been instrumental in advancing the design of clinical trials and in establishing many trials to demonstrate the effectiveness of radiation therapy in combination with chemotherapy and surgery. His research has focused on many types of cancer, including lung cancer, lymphomas, esophageal and prostate cancer. Since the opening of the Proton Therapy Center in 2006, he has worked on trials to compare proton therapy with conventional radiation treatments. He is also demonstrating the effectiveness of this therapy in reducing patients' side effects, tumor size, and survival.

In this interview, Dr. Cox talks speaks at length about his commitment to clinical trials as a means of improving patient care, covering many issues such as biases against clinical trials, ethical dimensions of such studies, and the specific studies he has conducted with conventional and with proton therapy. He also gives insight into the development of the Department and Division of Radiation Oncology, which was technologically behind the times when he assumed leadership. He discusses the development of the Proton Therapy Center and the role of

radiation oncology in establishing regional care centers that have expanded MD Anderson's reach.

James Cox, M.D.

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James Cox, M.D.

Interview #32

Segment Summaries

Interview Session One: 3 January 2013

Segment 00A
Interview Identifier

Segment 01
Early Memories and a Visual Mind
A: Personal Background

Story Codes
A: Personal Background
A: Character, Values, Beliefs, Talents
C: Funny Stories
C: Portraits

In this segment, Dr. Cox talks about childhood memories of West Virginia and Dayton, Ohio, where he recalls blackouts during WWII and his parent's Victory Garden. He recalls his early inclination for the sciences and talks about the strongly visual field he ultimately selected as well as some of the visual qualities of his own thinking. In addition to appreciating Early Renaissance art and Gothic architecture, he admits that he loves women's fashion, particularly enjoying features of design and proportion. His visual sensibilities focus on structure, he notes.

Segment 02
Clinical Research in MD Anderson Culture; The Radiation Therapy Oncology Group; and Specific Clinical Trials
A: The Researcher

Story Codes
A: The Researcher
A: The Clinician
B: MD Anderson Culture
B: Controversy
B: Research, Care, and Education in Transition
B: MD Anderson History
B: Institutional Politics
D: Understanding Cancer, the History of Science, Cancer Research
D: The History of Health Care, Patient Care

B: Critical Perspectives on MD Anderson
C: Professional Practice
C: The Professional at Work
D: On Research and Researchers
C: Research, Care, and Education

In this segment, Dr. Cox talks about his focus on clinical research. He begins by explaining why clinical research has been less appreciated at MD Anderson than laboratory or translational research. (As an instance of how clinical research can transform a field, he cites studies comparing the effectiveness radiation therapy vs. chemotherapy plus radiation.) Most clinical studies of radiation therapies were started by the Radiation Therapy Oncology Group (RTOG), and MD Anderson faculty was an important participant in these studies. Dr. Cox sketches the history of the RTOG, explaining its central role in organizing studies and gathering research statistics for twenty institutions. Dr. Cox explains that he viewed the RTOG as his laboratory, during his years of administrative service, and he served as senior investigator, though others were more hands-on participants.

Dr. Cox reflects on his skills in research design, offering as an example these skills, ideas he summarized in "Design and Implementation of Ion Beam Therapy," a chapter in the book, *Ion Beam Therapy: Fundamental Technology, Clinical Applications* (Springer, 2011). He explains what is meant by good research design and lists several factors that contribute to a successful clinical trial.

Dr. Cox then compares laboratory to clinical studies and notes that, in general, laboratory researchers are more directive in trials, while clinical researchers tend to be more cooperative. He says that there is a give and take in clinical research that would not be comfortable for most senior laboratory investigators

Segment 03
An Education Leading to Clinical Study
A: Educational Path

Story Codes
A: The Researcher
A: Personal Background
A: Professional Path
A: Inspirations to Practice Science/Medicine
A: Influences from People and Life Experiences
C: Evolution of Career
A: The Researcher
C: Formative Experiences

Here Dr. Cox explains the path that led him to clinical work in radiology. Dr. Cox became interested in cancer during his second year in medical school, while taking pathology, and he describes his first autopsy of an individual who had died from stomach cancer. He was fascinated by the cellular destruction and compares it to being "fascinated with a fire."

Dr. Cox next talks about the curriculum he followed at the University of Rochester School of Medicine and Dentistry (Rochester, NY) and his year at the Penrose Cancer Hospital in Colorado Springs, where he saw how helpful radiation therapy could be in combination with

surgery. This convinced him to return to U of R to train with Dr. Juan del Regato in radiation oncology. He talks about his shift to the residency program at Penrose, where he became involved in a B-04 trial on breast cancer run by Dr. Bernie Fisher.

Segment 04
Challenges of Clinical Trials: Informed Consent
A: The Researcher

Story Codes
B: Institutional Processes
B: Institutional Mission and Values
B: Ethics
D: Ethics
A: Professional Values, Ethics, Purpose
C: Professional Practice
C: The Professional at Work
A: The Administrator
D: Understanding Cancer, the History of Science, Cancer Research
D: The History of Health Care, Patient Care

Dr. Cox explains that, while in his residency at Penrose, he became interested in the issues involved when obtaining the collaboration of patients in a study. He then discusses informed consent at length, describing the issues involved and making reference to the Tuskegee syphilis case as a summary of the ethical issues at play. To demonstrate his ideas about informed consent, Dr. Cox describes a trial on cancer of the esophagus. While patients treated with radiation or surgery had some results, pairing chemotherapy with radiation therapy has such profound results that they “couldn’t ethically continue the trial.”

Dr. Cox explains that the Data Safety Monitoring Committee makes recommendations to stop any trial that is not ethically sound. Dr. Cox talks about several cases in which trials were conducted without any informed consent, and talks about the ethical and philosophical issues involved. He notes that informed consent was not a prominent issue until the 1970s, though now Institutional Review Boards are “out of hand.”

Segment 05
The Radiation Therapy Oncology Group
A: The Administrator

Story Codes
A: The Researcher
A: Overview
A: Definitions, Explanations, Translations
D: Understanding Cancer, the History of Science, Cancer Research
B: Devices, Drugs, Procedures
A: Activities Outside Institution
B: Beyond the Institution
D: Understanding Cancer, the History of Science, Cancer Research
D: The History of Health Care, Patient Care
D: Business of Research

Dr. Cox begins this segment with a brief history of the ROTG, founded in the late sixties, after several individuals running clinical trials created centers to gather statistics and manage trial operations. In the late sixties, the NCI gave instructions and funds to draws the disparate centers together. Dr. Cox became involved in 1978 or '79 and soon became vice chair for research strategy. He lists the areas of research the ROTG followed: hypoxic desensitizers and hypothermia; chemotherapy; and fractionization. He explains that he evaluated the results of studies. He speaks about an MD Anderson study treating cancer of the cervix with a combination of radiation and chemo.

Dr. Cox describes how technologies of radiation therapy have evolved and how this evolution has been influenced by the NCI's interest. (Dr. Cox feels the NCI has a prejudice in favor of chemotherapy, thus making less money available for radiation and surgery, even today.)

Segment 06
Radiation Oncology at MD Anderson
A: Overview

Story Codes
A: Overview
A: Definitions, Explanations, Translations
A: The Researcher
A: The Clinician
B: Information for Patients and the Public
B: Building/Transforming the Institution
B: Multi-disciplinary Approaches
B: Controversy
C: Portraits

Dr. Cox briefly describes how radiation is used to kill cancer cells and mentions a few of the first studies to investigate its effects.

Dr. Cox then talks about the Dr. Gilbert Fletcher's role in developing radiation therapy and its use at MD Anderson. He discusses the challenges Dr. Fletcher faced during this time when surgeons believed that the best treatment was to surgically remove cancer. Dr. Fletcher eventually convinced the MD Anderson community that radiation therapy could be successfully combined with surgery for positive patient outcomes. Dr. Cox talks about the attitudes of several surgeons: Dr. William MacComb, Dr. Richard Jesse, and Dr. J. Ballantyne.

Dr. Cox describes Dr. Fletcher's strong will, his unique form of genius, and his honesty even about toxicities of radiation levels. He notes that MD Anderson people "had great affection for him."

Segment 07
Leadership Experience
A: The Administrator

Story Codes
A: Professional Values, Ethics, Purpose

B: MD Anderson Culture
B: The MD Anderson Brand, Reputation
A: Military Service
B: Professional Path
B: MD Anderson Culture
B: MD Anderson Mission and Values

Dr. Cox reviews the experiences that led to the many leadership roles he has held during his career. He begins by noting that when he entered the military under the Berry Plan, there was a shortage of career people in radiation oncology and, at the age of thirty two, he became Head of the Radiation Oncology Service at Walter Reed Hospital, though he had served in administrative roles in smaller arenas.

Dr. Cox offers comments on the qualities of MD Anderson and why he has stayed at the institution so many years, noting that it offers "the best cancer care anybody can get."

Interview Session Two: 12 April 2013

Segment 00B
Interview Identifier

Segment 08
Early Clinical Studies
A: The Researcher

Story Codes
A: The Researcher
A: Overview
A: Definitions, Explanations, Translations
B: MD Anderson Culture
D: On Research and Researchers
D: Understanding Cancer, the History of Science, Cancer Research
D: The History of Health Care, Patient Care
C: Professional Practice
C: Patients, Treatment, Survivors
C: Healing, Hope, and the Promise of Research
D: On Research and Researchers

Dr. Cox begins the discussion of his research career with his residency. He explains that hypotheses in clinical research derive from the care of patients. Survival is the "immutable endpoint" that determines whether a treatment is successful, but survival does not tell you why a treatment is successful. Early in his career, Dr. Cox developed an approach to determine why treatments succeed, though he observes that many of the questions he asks about patterns of failure are irrelevant from other perspectives (e.g. medical oncology).

Dr. Cox describes studies done in the 70s with lung cancer to determine why treatments failed. When he became involved in the Radiation Therapy Oncology Group (RTOG) his style of

designing studies influenced the group. All of the ROTG studies during his ten years with the group used survival as the endpoint. Returning to his residency years, Dr. Cox talks about his studies of cancer of the breast and cervix. Dr. Cox notes that his view of clinical trials was strongly influenced by his mentor, Dr. Juan del Regato.

Segment 09
Research Focused on a Range of Body Areas
A: The Researcher

Story Codes
A: The Administrator
A: The Researcher
C: Professional Practice
C: The Professional at Work
A: Overview
A: Definitions, Explanations, Translations
D: On Research and Researchers
D: The History of Health Care, Patient Care

Dr. Cox summarizes the range of research he administered on fractionation while involved with the RTOG: lung cancer, head and neck cancers, cervix and brain. He also discusses the key importance of adding chemotherapy to patients' treatment regimens to get the best results.

Dr. Cox next explains that while he was Chair of the RTOG he was able to move combined treatments forward in the NCI and other organizations. He explains why the NCI is biased toward chemotherapy. He also comments on NCI politics is influencing how gynecologic cancers will be investigated.

Dr. Cox next comments on other cancer studies he oversaw during the period when he was Vice President for Patient Care under Dr. Charles LeMaistre [Oral History Interview].

Segment 10
Lung Cancer and Uncommon Lymphomas
A: The Researcher

Story Codes
A: The Researcher
C: Discovery and Success
C: Patients
C: Patients, Treatment, Survivors
C: Healing, Hope, and the Promise of Research
C: The Scientist at Work
A: Overview
A: Definitions, Explanations, Translations
B: Devices, Drugs, Procedures
D: Understanding Cancer, the History of Science, Cancer Research

Dr. Cox describes the research he undertook when left the position of Vice President for Patient Care and returned to his full-time faculty position, beginning with his new role as "the lymphoma

person." He explains the lymphoma trials that combined radiation and chemotherapy and that resulted in a successful response as well as a genetic translocation that will give rise to a genetic marker. He notes studies of radiation and chemotherapy in uncommon lymphomas.

Dr. Cox next explains how he was involved in teasing out the natural history of unusual lymphomas to understand them as distinct cancers. He uses testicular lymphoma as an example, describing how this cancer is treated with both radiation and chemotherapy. Patients with this cancer were rarely cured before this approach was developed: with this treatment, the cancer is eliminated in 50% of cases. Dr. Cox conducted this work between 1992 and 2000.

Dr. Cox then explains that he always saw cancer as more than one disease: he explains what it means to understand this at the molecular and cytogenetic level, eventually resulting in diagnoses being rendered by biochemical, molecular or genetic findings. He notes that his work at MD Anderson was tightly linked to his work with the RTOG. He continues, explaining that he returned to work with lung cancer in the late nineties. He mentions that lung cancer still has the highest death rate among all cancers, though mortality from lymphoma is increasing and Dr. Cox explains this is largely attributed to environmental chemicals. He explains the "modest progress" that he and the lung group at MD Anderson have made combining drugs, radiation, and surgery. Dr. Cox explains his work using prophylactic cranial irradiation to decrease the risk of brain metastasis from small cell carcinoma and notes that studies were also done to determine if this irradiation increased the risk for neuropsychological complications.

Segment 11
Documenting the Benefits of Proton Therapy
A: The Researcher

Story Codes
A: The Researcher
A: Overview
A: Definitions, Explanations, Translations
B: Devices, Drugs, Procedures
C: Healing, Hope, and the Promise of Research
C: Discovery and Success
D: On Research and Researchers

Dr. Cox explains a difficulty with proton therapy: the advantages can be seen on paper and modeled by computer, but "we don't yet have the evidence that people want." He describes the kinds of treatment advantages that proton therapy provides, particularly the reduction of toxicity.

Dr. Cox explains a study showing that proton therapy avoided toxicity in treatment of 15 patients with cancer of the tongue, then describes the next step of this research: to demonstrate the differences between two dimensional and three dimensional, conformational therapy. He explains that proton therapy offers these advantages because the beam can be targeted to hit very isolated structures.

Segment 12
Multidisciplinary Conferences at MD Anderson Lead to More Effective Treatment Plans
A: The Researcher

Story Codes
B: Building/Transforming the Institution
B: Multi-disciplinary Approaches
B: Institutional Mission and Values
B: Institutional Processes
B: MD Anderson Culture
A: The Clinician
C: Patients
D: On Care

Dr. Cox notes that proton therapy treatment focuses heavily on lung cancer and lists other cancers being studied, explaining that the study of esophageal cancer puts all the modalities together. This leads Dr. Cox to talk about the Tumor Board and Thoracic Conference –weekly multi-disciplinary meetings where specialists from different disciplines discuss cases and treatment options for patients. He explains that surgical techniques have improved so much that surgery is now also being integrated into the treatment modalities. He then describes the history of the conferences, which go back to the earliest years of MD Anderson and have proliferated through the entire institution. Dr. Cox describes how these meetings educated everyone, e.g. by having specialists from a wide range of fields talk to a radiologist, a pathologist, or someone conducting research on molecular markers. (He acknowledges that attendees are self-selected).

Dr. Cox affirms that the multi-disciplinary meetings have affected the culture of MD Anderson: Multi-disciplinary care is a hallmark of MD Anderson care. He explains that that the salary pool on which compensation is based at the institution insures that there is no economic incentive behind treatment decisions. "We function as a team" for all patients.

Dr. Cox explains that not everyone embraces multi-disciplinarity and that, in the past, MD Anderson faculty who worked on the disease sites tended to talk only to one another. When he brought in the RTOG, the multi-disciplinary focus has a definite impact on the institution. Dr. Cox closes this section by noting some other multi-disciplinary organizations and by explaining that MD Anderson may not be helped by some of the NCI's recent decisions on how to restructure cooperative groups.

Interview Session 3: 23 April 2013

Segment 00C
Interview Identifier

Segment 13
The Regional Care Centers and Sister Institutions
B: Building the Institution

Story Codes
B: Beyond the Institution
B: Building/Transforming the Institution
B: Multi-disciplinary Approaches

D: Fiscal Realities in Healthcare
B: The MD Anderson Brand, Reputation
B: Institutional Mission and Values
B: Institutional Processes
B: Devices, Drugs, Procedures
B: Critical Perspectives on MD Anderson
C: Patients
B: MD Anderson History

Dr. Cox gives an overview of issues involved in setting up regional care centers and sister institutions. He begins by noting that Radiation Oncology backed away from involvement in MD Anderson-Banner because of concerns that MD Anderson would have no hand in quality control for patient care. He next talks about setting up the first regional care center in Bellaire (1998/99): the regional care centers were originally established to provide radiation therapy.

Dr. Cox explains that for thirty years the treatment plans for all MD Anderson patients are created by way of a peer-review process that insures high quality care and results.

Dr. Cox next lists some other satellite centers and describes the lessons learned about recruitment and competition from within the communities. He concludes that, in general, the quality of the care centers has stood the test of time and paved the way for medical oncology and laboratory services to be offered at the sites as well. He summarizes the convenience that the care centers offer to patients. Next he describes the financial and administrative relationships between the care centers and MD Anderson. Dr. Cox then comments on the sister institutions in Orlando, Florida and Madrid, Spain, noting the importance of quality control and oversight of faculty for the success of such initiatives.

Segment 14
Head of the Department and Division of Radiation Oncology
A: The Administrator

Story Codes
A: The Administrator
C: Professional Practice
C: The Professional at Work
B: Building/Transforming the Institution
A: Definitions, Explanations, Translations
D: Technology and R&D

Dr. Cox explains his dual role as Head of the Department and Division of Radiation Oncology, first discussion his Departmental goals of expanding the faculty and creating a strong and highly specialized department. He also notes that the department was technologically out of date when he took over, and he explains the upgrades he introduced: a modern system for treatment planning, a CT simulator, and the transition from 2-D to 3-D treatments. The department next combined 3-D treatment planning with computer assisted treatment planning to refine patient protocols. Dr. Cox explains how the Department established a dosimetry school as the program grew. The Department next developed intensity modulated radiation therapy.

Segment 15
The Division of Radiation Oncology
B: An Institutional Unit

Story Codes
B: Controversy
B: Institutional Politics
A: Obstacles, Challenges
B: Building/Transforming the Institution
B: Multi-disciplinary Approaches
B: Growth and/or Change
C: Leadership

Dr. Cox describes challenges that he faced in developing the Division of Radiation Oncology. a change in attitude toward buying new equipment greatly helped move the Division forward. He describes a communication gap that existed with Ken Hogstrum, Chair of the Department of Radiation Physics (who focused on education over patient care and research), a problem resolved when Dr. Cox removed him. Dr. Cox describes some of the changes that took place as Dr. Hogstrum and a number of his supporters left, emphasizing that the individuals recruited to replace them shared his goals of developing the technological base of the Division as well as the 'research portfolio,' which went from effectively no research to over a million dollars of research funding. Dr. Cox ends this segment with comments on his administrative approach.

Segment 16
The Division of Radiation Oncology—Strategic Planning and Growth
B: An Institutional Unit

Story Codes
B: Building/Transforming the Institution
B: Multi-disciplinary Approaches
B: Growth and/or Change
B: Institutional Processes
B: MD Anderson Culture
C: Leadership

Dr. Cox summarizes the growth of the division between '97 and 2007, when he retired: from seventeen to fifty full-time faculty and from 240 to 600 patients seen per day. He notes that the Division made a lot of money for the institution and achieved a high level of credibility from good planning. He sketches the yearly strategic planning meetings the Division held each year, noting that the main goal of all planning was to ensure that the Division was the best in all areas. He explains that a second goal was to create a supportive environment for everyone, and believes that they were successful in achieving that. At the end of this segment, Dr. Cox offers reasons for the separation of Departments within the Division of Radiation Oncology.

Segment 17
The Proton Therapy Center
B: An Institutional Unit

Story Codes

A: Overview
A: Definitions, Explanations, Translations
A: The Researcher
A: The Clinician
B: Building/Transforming the Institution
B: Multi-disciplinary Approaches
B: Growth and/or Change
B: Obstacles, Challenges
B: The Business of MD Anderson
C: Discovery and Success
B: MD Anderson Mission and Values
D: Technology and R&D
B: Devices, Drugs, Procedures
B: Industry Partnerships
B: Beyond the Institution

Dr. Cox notes that the use of intensity-modulated radiation therapy was a starting point for thinking about how advanced technology could be used to concentrate radiation beams on a tumor. The idea to construct a Proton Therapy Center began in 1998, when Dr. Cox spoke to John Mendelsohn about the possibility, and Dr. Mendelsohn then went to the UT System. Though the University of Texas System would not fund it, Leon Leach [Oral History Interview, Dan Fontaine and others were enthusiastic and looked for other funding sources. Dr. Cox explains what created the enthusiasm for proton therapy, given the absence of any studies to confirm its benefits or advantages over other types of therapy. Dr. Cox believes that his credibility in the institution spurred the administration to embrace the idea.

Dr. Cox next sketches the partnership between public and private sources created to fund the initiative, with Hitachi as the vendor. He notes that his wife, Dr. Ritsuko Komaki, served as a mediator to help MD Anderson people deal with cross-cultural issues that arose during negotiations with Hitachi. He then explains what they requested in the design of the proton source and the challenges that arose as Hitachi dealt with their specifications, noting in particular how difficult it was to get three computer systems to work together.

Segment 18
Research at the Proton Therapy Center; the Future
B: An Institutional Unit

Story Codes
A: Overview
A: Definitions, Explanations, Translations
A: The Researcher
A: The Clinician
B: Building/Transforming the Institution
B: Multi-disciplinary Approaches
B: Growth and/or Change
B: Obstacles, Challenges
B: The Business of MD Anderson
C: Discovery and Success
D: Technology and R&D
B: Devices, Drugs, Procedures

B: Beyond the Institution
B: Controversy
D: Understanding Cancer, the History of Science, Cancer Research
D: The History of Health Care, Patient Care
C: Patients
C: Discovery and Success

Dr. Cox notes that the Proton Therapy Center project was started in May 2003. Since 2006, when the first patient was treated, 4400 patients have been seen, with virtually all patients involved in research studies. Dr. Cox explains that there is a master protocol for studying increasing dosages and the degree to which normal tissue is spared. Specific protocols have been created to compare proton therapy and intensity-modulated radiation therapy on non-small cell lung cancer and for cancer of the esophagus. Next Dr. Cos explains the reasons why individuals question the value of proton therapy. Some are anti-technology. Some admit that it looks valuable on paper, but question whether the effects are real; some say that, in principle, there is value, but there are too many technical uncertainties to warrant going ahead with it. Others accurately state that no randomized trials have been conducted to definitely prove that proton therapy is superior to x-rays. These studies are underway now. Dr. Cox says that the main benefits are fewer side effects for the patient. In some cases physicians are able to deliver higher doses of radiation, which may result in better tumor control. Dr. Cox says that all of these objections make it difficult to get papers accepted in journals so good results can be demonstrated.

Dr. Cox affirms that the Proton Therapy Center has been very successful. The Center is also in the process of expanding uses for patients, so proton therapy will be part of treatment for many diseases and stages of disease. He anticipates that eventually 20% of MD Anderson patients will be treated with proton therapy. He explains how patients are identified for proton therapy (curative uses, rather than palliative). The Proton Therapy Center will be upgrading certain functions, taking advantages of developments Hitachi has recently made.

Dr. Cox observes that the regional care centers have not referred as many patients for proton therapy as he would have expected and that they would like to treat even more patients. As the segment closes, explains that the original investors pulled out of the project and MD Anderson owns 51% of the interest in the Center.

Segment 19
The MD Anderson Presidents
B: Key MD Anderson Figures

Story Codes
B: Critical Perspectives on MD Anderson
C: Portraits
A: Personal Background
B: MD Anderson in the Future

Dr. Cox begins with observations about Charles LeMaistre, who recruited him to serve as Vice President of Patient Care, “a good title, bad job,” as he says. Cr. Cox explains that he and Dr. LeMaistre had very different orientations toward MD Anderson administration. Dr. LeMaistre was interested in issues related to the UT System, Dr. Cox says, then explains why he believes that Dr. LeMaistre didn’t fully understand what was going on at the institution.

Dr. Cox says that during Dr. LeMaistre's tenure, the institution was on the verge of greatness, but couldn't take the next step because many faculty were "living in silos."

Dr. Cox next talks about John Mendelsohn, who was very aware of what was going on in the institution (at least during the first years). He then turns to Ronald DePinho, whom he admires for his grand aims and desire to change the institution in a major way. He offers his view of the Moon Shots Program, which he sees advancing team science, though he has no expectation that is will eliminate the cancers at which the various sub-programs are aimed.

Segment 20
Contributions to MD Anderson
A: View on Career and Accomplishments

Story Codes
A: Contributions
A: Activities Outside Institution
A: Career and Accomplishments
B: The MD Anderson Brand, Reputation
A: The Researcher
B: Institutional Mission and Values
C: Portraits
C: Personal Reflections on MD Anderson

Dr. Cox talks about his contributions to MD Anderson: he spurred clinical research and therefore contributed to the care of patients. Administratively he believes he helped foster collegiality across departments and division, making faculty comfortable with multi-disciplinary work styles. Dr. Cox recalls that Gilbert Fletcher set a very high standard for radiation oncology at MD Anderson. Dr. Cox says that he has contributed to maintaining that stature, one that differs from any other cancer center in the world.

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

James Cox, MD

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Chapter 00A
Interview Identifier

Tacey Ann Rosolowski, PhD
00:00:00
I am Tacey Ann Rosolowski, and I am interviewing radiation oncologist Dr. James Cox for the Making Cancer History Voices Oral History Project run by the MD Anderson Cancer Center in Houston, Texas. Dr. Cox was first interviewed in 2004 by Lesley Brunet Dr. Cox came to MD Anderson in 1988 as the institution's physician in chief. From 1995 to 2011 he served as head of the Division of Radiation Oncology. He is also a professor in the Department of Radiation Oncology and holds the Hubert L. and Olive Stringer Distinguished Chair in Oncology in honor of Sue Gribble Stringer. This interview is taking place in Dr. Cox's office at the Proton Therapy Center located south of MD Anderson's main campus at the intersection of Old Spanish Trail and Fannin Street in Houston. This is the first of two—perhaps more—planned interview sessions. Today is January 3, 2013, and the time is 1:06. So thank you Dr. Cox for participating in this project.

James Cox, MD
00:01:08.430
It is my pleasure.

Interview Session: 01
Interview Date: January 4, 2013

Chapter 01
A: Personal Background
Early Memories and a Visual Mind

Story Codes
A: Personal Background
A: Character, Values, Beliefs, Talents
C: Funny Stories
C: Portraits

Tacey Ann Rosolowski, PhD
00:01:09.575
And I am looking forward to speaking with you and tracing through—as you said you have had four different careers at MD Anderson, so I am looking forward to teasing apart what those are. But I wanted to start just for the record with some background. If you could tell me where you were born and when.

James Cox, MD
00:01:29.038
I was born in Steubenville, Ohio July 16, 1938.

Tacey Ann Rosolowski, PhD
00:01:38.262
And did you grow up in that area?

James Cox, MD
00:01:40.823
No. I think we only lived there probably for six months or a year and then moved to Charleston, West Virginia where my father had a job working for a small insurance company located in Cincinnati, Ohio. And I lived there for—I guess—the better part of seven or eight years and moved then to Dayton, Ohio, which is where I consider, by and large, I have grown.

Tacey Ann Rosolowski, PhD
00:02:20.635
As you look back at that time—your growing up years—are there significant people or significant experiences that you feel shaped your intellectual perspective or your commitment to the particular fields of research and care that you have devoted yourself to?

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James Cox, MD
00:02:47.822
Well not from the period in Charleston particularly—that was during the war, however, and I do remember the blackouts. Our house overlooked the carbine and carbon chemical plant in the middle of the Kanawha River, and it was lighted brightly. It seemed always to serve as an ideal place to locate if they wanted to bomb something. And I couldn't imagine—in retrospect—I can't imagine somebody wanting to bomb something in Charleston, West Virginia, but if there were anything to bomb that would have been it.

Tacey Ann Rosolowski, PhD
00:03:42.280
How did that have an influence on you?

James Cox, MD
00:03:44.945
Well the war itself had an influence. My father, who was partially blind, did not serve in the military, but we had a so-called victory garden. We grew vegetables. We didn't have much money, and we made due with what we had. We had chickens, and the chickens gave us eggs. It gave us an occasional chicken.

Tacey Ann Rosolowski, PhD
00:04:23.795
And there were meat rationings.

James Cox, MD
00:04:26.256
Yes. So I remember that time as a complicated time for the world, but it did not really affect the happiness of my childhood. I mean—I started in school, I did not go to a kindergarten. There was not any kindergarten where I went—or I mean where I lived. So I started in the first grade, then I think by the third grade or so we moved to Dayton, Ohio. And in Dayton I had grade school teachers who—and high school teachers—who had effects. I got my one and only C in my life in high school in Latin. And I found that I had a natural inclination towards the sciences. That was not anything from any particular background. I mean—my sister had no inclination towards the sciences. I had one sister five years older than I.

Tacey Ann Rosolowski, PhD
00:05:50.973
What about the fact that you ended up going into a field that is very visual? When did you realize that that was an important part of the sciences you were interested in?

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James Cox, MD
00:06:12.404
I think probably the visual aspect of my—of science for me was more of a—more of a tool than it was an end point. The only other thing I have ever done visually that might be considered the least bit artistic would be photography, which I am not a particularly adept photographer, but I have taken pictures that I enjoyed reflecting trips. But you know, like other things, I used the visual part as the tool since I am not in diagnostic imaging—diagnostic radiology but use the images from diagnostic radiology in planning the treatment of patients with cancer. I would say it was not really at the forefront of my scientific thinking at all.

Tacey Ann Rosolowski, PhD
00:07:36.799
So do you consider yourself a visual thinker or—?

James Cox, MD
00:07:40.295
Yes. I do. I am a visual person. I am affected by—yeah—I am affected by how things look, and as a really remote aside—and you will have to think whether you want to include this at all—speaking of being visual—my—a major avocation is women's fashion.

Tacey Ann Rosolowski, PhD
00:08:24.314
How interesting. How interesting.

James Cox, MD
00:08:27.248
And I buy about eighty percent of my wife's clothes, and I enjoy fashions, but I do not think I would ever have any talent to draw or to do—to create fashion. There is a man who owns a boutique in Rice Village that I think has a wonderful job. He owns what was originally a women's boutique and now has extended to include men's clothing. And I think he has got a great job. He picks—he selects styles to sell.

Tacey Ann Rosolowski, PhD
00:09:11.772
So is it color? Is it proportion? Is it design? What is the visual element that grabs you?

James Cox, MD
00:09:19.007
I think it is probably proportion and design—also color, but it is—my interests in art are quite varied and do not fit particularly easily in any of that. I mean—I love the impressionists, but I also like the art of the—well—the early Renaissance in northern Europe.

Tacey Ann Rosolowski, PhD
00:09:57.163
The reason I am asking you is often visual thinkers do not have a good way of talking about the way their brain works—you know—we do not have a lot of language for that in this culture. But with people who work in surgery or work with interventional radiology—and Sidney Wallace talked a lot about his own visual thinking.

James Cox, MD
00:10:23.353
Oh, well he is—Sid Wallace has visual abilities that are extraordinary as an artist—

Tacey Ann Rosolowski, PhD
00:10:28.088
As an artist.

James Cox, MD
00:10:30.352
—and of course he brought that to interventional radiology.

Tacey Ann Rosolowski, PhD
00:10:34.211
Sure.

James Cox, MD
00:10:34.945
I am a huge admirer of him.

Tacey Ann Rosolowski, PhD
00:10:37.462
But—you know—those gifts can also work inside the mind even if they do not express themselves in a more art or external form, so do you see things in schematic forms? Do you see systems in color? I mean—how does your own mind work when you are working on—you know—in your own field?

James Cox, MD
00:10:59.597
I think probably it is more inclined towards structural rather than color. I love the—probably if there is one art form that I will travel hundreds of miles to see is the gothic architecture—early gothic architecture—not the flamboyant, but the architecture of the twelfth, thirteenth, early fourteenth centuries. And I—the churches and the abbeys and not necessarily only the large structures but—and I like the structure. I find it fascinating, but I have not thought about that relative particularly to what I do professionally.

Tacey Ann Rosolowski, PhD
00:12:12.446
Well I won't—maybe we can return to the question again later if you would like to think about it.

James Cox, MD
00:12:17.210
All right.

Tacey Ann Rosolowski, PhD
00:12:18.776
I mean—I am just always curious because it is part of how people work and part of (both speaking at once).
James Cox, MD
00:12:22.754
That is an interesting question, and I had not particularly thought along those lines relative to what I do professionally.

Tacey Ann Rosolowski, PhD
00:12:31.255
When did you realize that you had some kind of visual sensitivity or interest?

James Cox, MD
00:12:41.407
It probably became most striking to me when I lived in France in the later part of when I was in—sorry—after I finished my residency training program—I lived for a year in Paris and travelled—I have been so far as (???)(inaudible) and throughout France and to some degree in England and Belgium and Germany. And I think there it was—especially the architectural possibilities, but also—I mean—of course the museums were incredibly rich, and on Sundays many of them were free. I had three kids under six!

Tacey Ann Rosolowski, PhD
00:12:41.407
Oh—wow.

James Cox, MD
00:13:46.907
So travelling around at that time was not easy, but I did it a lot.

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Chapter 02
A: The Researcher
Clinical Research in MD Anderson Culture; The Radiation Therapy Oncology Group; and Specific Clinical Trials

Story Codes
A: The Researcher
A: The Clinician
B: MD Anderson Culture
B: Controversy
B: Research, Care, and Education in Transition
B: MD Anderson History
B: Institutional Politics
D: Understanding Cancer, the History of Science, Cancer Research
D: The History of Health Care, Patient Care
B: Critical Perspectives on MD Anderson
C: Professional Practice
C: The Professional at Work
D: On Research and Researchers
C: Research, Care, and Education

Tacey Ann Rosolowski, PhD
00:13:58.840
In your former interview with Lesley Brunet you talked about selecting your specialty and coming to MD Anderson, so I did not necessarily want to cover those details unless there was something that you felt I needed to have in my mind before we go further?

James Cox, MD
00:14:19.393
I don't think so. I mean—I probably covered it well at that—or adequately at that time.

Tacey Ann Rosolowski, PhD
00:14:27.823
Okay. I wanted to talk about—one thing you did not talk about during that period was really your own research program. So is that one of the research dimensions or one of the professional dimensions that you mentioned earlier?

James Cox, MD
00:14:44.594
Well—yes.

Tacey Ann Rosolowski, PhD
00:14:47.439
So maybe we could talk a bit about that.

James Cox, MD
00:14:51.311
My work in clinical research which is generally much less appreciated in an environment like this than laboratory research or translational research that uses the laboratory even for clinical benefit. And then people think—well—designing and getting people to participate in and analyzing clinical trials is really pretty pedestrian stuff, but I don't think it is.

Tacey Ann Rosolowski, PhD
00:15:32.074
Why is there that assumption about clinical research?

James Cox, MD
00:15:36.971
Well—it is just there. I mean—if you ask a lot of people in the laboratory—if you ask Josh Fidler [Oral History Interview], if you ask Margaret Kripke [Oral History Interview] coming from two very different directions, they would not pay the same degree of respect to clinical research that they would to the laboratory studies. Even though clinical research is what determines the care of patients far more immediately than what is going on in the laboratory. And when you have a clinical trial that is published in the *New England Journal of Medicine* or *JAMA* or in *Lancet* or—it is usually in one of those journals—it can truly change the practice of medicine or change the research environment for future studies, and if it does either of those or both I think it is pretty profound stuff.

Tacey Ann Rosolowski, PhD
00:16:53.621
Can you give me an example of—?

James Cox, MD
00:16:55.036
Well, an example comes to mind that is pretty fundamental, but it evolved over a considerable period of time, and that is the combination of chemotherapy and radiation therapy together relative to radiation therapy alone. And in virtually every site that was studied, the combination of cytotoxic drugs now—I do not mean hormones, but cytotoxic drugs—that is true in hormones too—but cytotoxic drugs and radiation therapy prove to be superior to radiation therapy alone in survival. I mean—not just in control of the tumor or some other earlier or secondary end point, and this is true in cancer of the esophagus, cancer of the lung, tumors in the head and neck, cancer of the cervix. And in other sites like cancer of the larynx and cancer of the anal canal it had a big difference in avoiding the surgical procedure that would lead to major morbidity like laryngectomy or abdominoperineal resection resulting in a colostomy. So in each of those it proved to be superior, and each of those trials was not easy to mount. And there was resistance—there were pockets of resistance here at MD Anderson to participating in those trials. At that time, or during much of that period of time outside of MD Anderson, I was chairing the Radiation Therapy Oncology Group, and most of those trials were either started and subsequently published where the RTOG was the major participating group, and that is natural because it was the only group that was asking radiation therapy related questions by and large. Now there were a few exceptions but—

Tacey Ann Rosolowski, PhD
00:19:49.547
Can I ask you—I mean—just to interrupt to get a sense of how this worked. So these trials were founded through the Radiation Therapy Oncology Group, which was the organizing body for them—was that the idea? And then there were you and others from MD Anderson who participated? I am just trying to get a sense of how the RTOG (both speaking at once).

James Cox, MD
00:20:11.916
The RTOG has been in existence since the late 1960s. And it was the organizing group—it also managed the statistical center and the operations for about 20 institutions that contributed large numbers of patients. And they were mostly academic institutions—major academic institutions, but not all of the major academic. They included—for example—the University of California San Francisco—UCSF. They included Washington University in St. Louis, Thomas Jefferson in Philadelphia, eventually—although not at the very beginning—the University of Pennsylvania, and they included NYU. And only after I came to MD Anderson did MD Anderson join.

Tacey Ann Rosolowski, PhD
00:21:44.196
Why? Why was that delay in place?

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James Cox, MD
00:21:52.731
Well I think the previous leadership in MD Anderson was interested in—Lester Peters—was interested in laboratory research. I think he felt whatever clinical research were to—clinical research that should be done should be done at MD Anderson, and then if somebody else picked it up and wanted to do it on a national basis, that was for them to do. But the RTOG had these 20 more or less core institutions, and then they had another 150-200 institutions scattered throughout the United States and Canada that participated. So they were able to recruit large numbers of patients, and I kind of—during that period of time—I kind of viewed that as my laboratory. So I was sort of the senior investigator for most of those trials but more as a facilitator helping other people to succeed. The vast majority of the trials that were published from that period, my name was not there as the senior author. So it turned out to be a very worthwhile thing, but in terms of academic recognition—you know—ten or fifteen years later who would know? They might know—oh yeah Jim Cox chaired the RTOG for a decade, but—you know—what does he have to show for it? And there were a few trials that I participated very heavily in.

Tacey Ann Rosolowski, PhD
00:24:01.000
And these were also trials that were combining chemotherapy with radiation?

James Cox, MD
00:24:07.720
Many of them. Many of them.

Tacey Ann Rosolowski, PhD
00:24:11.429
I read as I was doing background research for this interview that you said that you have a particular strength in putting together research studies—somehow an investigational method, and I wondered if you could talk a little bit more about what you meant by that? What is a good research design, and where does the science stop and art begin?

James Cox, MD
00:24:37.001
It is interesting—I published a book chapter for a different purpose. The title of it kind of goes to the question that you are asking. This is in a book called *Ion Beam Therapy*—so it is relatively recent. But the title of the chapter is *Design and Implementation of Clinical Trials of Ion Beam Therapy*, and it goes through what are the critical elements. Among them are having hypotheses that not only I feel are worth testing, but that the community of participating physicians has come to the conclusion—or perhaps I have helped them come to the conclusion—that these are questions that are worth answering because to do an effective clinical trial you have to have a good question. You have to have a group of investigators interested enough in that question to contribute their patients to the study because it takes extra time and effort always to ask patients to participate in clinical trials. Now that takes extra expense usually. And then oftentimes there is some countervailing view of what should be done and the details of radiation therapy such as fractionation, the details of the chemotherapy in terms of what drugs and what doses, and there are a lot of details in there that have to be worked out usually needing other people as leader to help move that forward. It is the sort of thing that I cannot tell them what to do; they have to be motivated to say, "Yes, this is worth doing." It would totally fail in the Congress of the United States. Anyhow—and then you have—and those questions are not answered quickly. Usually a trial ideally would answer this question within three years, but they rarely do. And some may take five years or even ten years. And it is still a worthwhile trial unless some other hypotheses come forward that are so much more compelling that they want to drop doing that study. Usually the study is worth completing. And so you need those elements, and I have outlined them in that chapter.

Tacey Ann Rosolowski, PhD
00:28:08.890
Are those elements—to what degree are those elements different from the good design elements of laboratory research? And I am—is there—in those differences—is there something about those differences that helps contribute to the prejudice against clinical research?

James Cox, MD
00:28:25.691
I think in laboratory studies the director of the laboratory is much more directive. He or she much more likely tells the people in the laboratory what to do. Occasionally there will be a colleague that is sort of working on something that might be adjacent or maybe complementary in the same general laboratory, but usually it is post-doctoral fellows, graduate students, people who the director of the laboratory is directing. And that is different from what happens in cooperative groups.

Tacey Ann Rosolowski, PhD
Among whom are peers—right?

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James Cox, MD
00:29:34.466
Really are peers each with their own constituency, each with their own body of patients, and where it is much more collaborative science than what goes on in the laboratory. And maybe the fact that it is collaborative science is one of the things that is looked down on.

Tacey Ann Rosolowski, PhD
00:30:03.472
Yeah it doesn't—it kind of doesn't fit the mold of the lone researcher—

James Cox, MD

Right.

Tacey Ann Rosolowski, PhD
00:30:07.114
—pushing back the frontiers.

James Cox, MD
00:30:09.120
That is right.

Tacey Ann Rosolowski, PhD
Yeah.

James Cox, MD
00:30:09.120
That is right. And there may be many other reasons. But one of the other reasons is that it is usually done by clinicians. And there are the clinicians and there are the laboratory scientists, and laboratory scientists always wish that they were making as much money as the clinicians, but they would not want to give up the fact that what they are doing is autonomous or at least semi-autonomous and much more at the forefront.

Tacey Ann Rosolowski, PhD
00:30:58.802
This may be an unfair question, but do you see that there are kind of different personalities attracted to laboratory versus clinical research? I mean—or is that too general of a statement to make?

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James Cox, MD
00:31:20.595
I think in general that is true. There is a give and take in clinical research that would not be comfortable to most senior laboratory investigators. So I—yeah—I think there is a difference.

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Chapter 03
A: Educational Path
An Education Leading to Clinical Study: A Fascination for Cellular Destruction

Story Codes
A: The Researcher
A: Personal Background
A: Professional Path
A: Inspirations to Practice Science/Medicine
A: Influences from People and Life Experiences
C: Evolution of Career
A: The Researcher
C: Formative Experiences

Tacey Ann Rosolowski, PhD
00:32:07.117
Where do you think you cultivated your abilities to set up these groups and discover how to answer those fundamental questions or needs that you identified earlier?

James Cox, MD
00:32:27.505
I think it happened pretty early in medical school. When I was in college I did laboratory studies with amphibians, and I found it very fascinating. One of the things that I liked about it is I did these studies mostly with one colleague who was interested in the same kind of things. And it is probably worth noting that he went on to a career in the laboratory and I went to medical school, but we both had great fascination for what we were doing—working in the laboratory of a guy—or we were working with a senior investigator who had sort of given us the opportunity to work with some of the systems that he had worked with. And we were learning pretty fundamental things. I mean we were trying to make antibodies at a time when it was really hard to do. But then when I went to medical school, I became interested in cancer when I was a second-year medical student taking a course in pathology. What I saw happening clinically fascinated me more than what was going on, let's say, in the laboratory in biochemistry—things like that.

Tacey Ann Rosolowski, PhD
00:34:55.998
Tell me about what it was that interested you so much.

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James Cox, MD
00:35:05.032
The first autopsy in which I participated—and at that time they did autopsies far more frequently than they do now—the first autopsy I attended—or in which I participated—was a man who died of cancer of the stomach. You were able to observe quite directly how the tumor had spread within the abdomen, how it involved the liver in ways that were very obvious, and we had been reading about various fundamental pathologic processes—inflammation, degenerative processes, and so on. This was something that I found fascinating—maybe a little bit fascinating like you would find watching a fire fascinating because it was somebody who had died from a disease that was not able to be stopped.

Tacey Ann Rosolowski, PhD
00:36:43.549
Like cellular conflagration.

James Cox, MD
00:36:46.569
Yeah. Really. And so that is when I became interested in oncology. It was long before I was interested at all in radiation oncology. I mean—I was interested in cancer. And that gradually developed throughout my medical school experience as a third-year student. I saw patients with various types of cancer and leukemia. What I did not see ever were patients with cancer that had been successfully treated because they weren't in the hospital. So partly—well—let me step back—there was a lot of encouragement for students at the University of Rochester—where I went—to take a year out of medical school and to work—to take a year out of medical school. The pathologist—and they were the ones who were driving this push towards taking a year out of medical school—wanted the students to work in the autopsy rotation where there were never quite enough people to keep up with all the work to be done or in the laboratories of the pathologists who were interested in various aspects of pathophysiology. And so they wanted them to take the year out between the second and third year of medical school. I did not want to do it at that time, but I wanted to take a year out after my third year of medical school, and I wanted to work in a cancer hospital.

I applied to several cancer hospitals, and the only one where I got an enthusiastic response was the very small Penrose Cancer Hospital in Colorado Springs that was run by a radiation oncologist. He gave encouragement to come there, and I went there and spent a year. He had never had a student spend that much time. And it was—when I saw what radiation therapy could do and surgery could do in curing patients with cancer, because I was seeing them come back for follow up having been successfully treated. That was all the more encouragement that not only was there this terrible disease, but you could make it go away. That was pretty exciting.

Tacey Ann Rosolowski, PhD
00:40:21.658
And I am thinking too—you know—going back to that topic we were talking about earlier—there was that built in collaboration with the radiologist and then with the surgeon in that marriage very early.

James Cox, MD
00:40:37.124
Yeah. It was. So we—so after I had been there for about three quarters of the year, I went to Dr. [Juan A.] del Regado, and I said, "I would like to come back here and train in radiation oncology after I do my internship and would there be a place for me?" And of course they didn't have anything like the match at those times. So he said yes—we would have a place for you. So I went back to the University of Rochester and used the experience that I had in Colorado Springs to—plus additional work that I did at the University of Rochester—to write an honors thesis for medical school. I was able to graduate with a doctor of medicine with honors—there were only two of us in the class. Then I went to the University of Chicago Hospital for internship and then went back to Colorado Springs.

Tacey Ann Rosolowski, PhD
00:41:58.932
Why did you choose radiology rather than surgery?

James Cox, MD
00:42:13.716
I think it was the influence of Dr. del Regado. He was a very charismatic man—a small man. He was probably somewhere between 5'4" and 5'5" tall, but he had an enormous personality. He was a mentor, and then over the years we stayed friends—very close friends—until the time he died. We had one major problem that we disagreed on, the Vietnam War. But we got over that.

Tacey Ann Rosolowski, PhD
00:43:22.956
Who was for and who was against?

James Cox, MD
00:43:26.068
He was for—I was against.

Tacey Ann Rosolowski, PhD
Okay.

James Cox, MD
00:43:28.959
I was in the Army at the time. I had volunteered for the draft—no, no—I wasn't in the Army at that time. Yeah—actually I was. I had volunteered for the draft when I was an intern at his recommendation so that I might be a candidate for what was called the Berry Plan, which was a plan where they would let people go into the service and serve for two years in a specialty that the military needed, and radiation oncology was one of those specialties. So I ended up being—when I went on active duty—I ended up being stationed at Walter Reed in DC.

Tacey Ann Rosolowski, PhD
00:44:25.798
So can you sketch for me how your research evolved? I mean—we talked about sort of the hiatus—if you will—that you took when you were, I guess, burdened with administrative responsibilities here at MD Anderson and were really working with the Radiation Therapy Oncology Group in more of an organizational or consultative fashion. So how did your more hands-on—you as principle investigator—research evolve?

James Cox, MD
00:44:54.513
Well it was very much a part of the RTOG at that time. I did not have any active research program going on at MD Anderson at that time.

Tacey Ann Rosolowski, PhD
00:45:07.417
I was actually thinking about earlier—how your research started before you even came here.

James Cox, MD
00:45:27.026
Well it was also influenced by people in the field that I got to know—del Regado being one of them. I mean—when I was a resident at Penrose we were involved in what subsequently, I think, came to be known as the BO4 trial of the NSABPN—the National Surgical Adjuvant Breast—later Breast and Bowel Project—which was run by a surgeon, Bernie Fisher.[Dr. Bernard] We were injecting patients who had just had a mastectomy—I guess—with drugs in the perioperative period trying to prevent metastasis. That was part of the work that was done. And then there were trials of their getting postoperative radiation to the breast. Then I became interested in the process of how you used the clinical information to pose questions and how you involve the collaboration of patients in the answer of those questions because patients became collaborators too.

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Chapter 04
A: The Researcher
The Challenges of Clinical Trials: Informed Consent

Story Codes
B: Institutional Processes
B: Institutional Mission and Values
B: Ethics
D: Ethics
A: Professional Values, Ethics, Purpose
C: Professional Practice
C: The Professional at Work
A: The Administrator
D: Understanding Cancer, the History of Science, Cancer Research
D: The History of Health Care, Patient Care

Tacey Ann Rosolowski, PhD
00:45:07.417
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Tacey Ann Rosolowski, PhD
00:46:45.310
How so?

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James Cox, MD
00:47:23.817
Well because you were asking them to participate in a laboratory—in a clinical investigation, and then there is the whole big area of the ethics of clinical trials, which I also became very interested in and involved with to some degree. Although it was not a part of informed consent in those early years, it subsequently became clear that in the informed consent was the commitment that you would—that the patients would be able to know the results of what happened to them as a group, and if the results were profound and striking it might even—you know—it might even change what would be done for them, but that is pretty rare. And then by chance when I was—there are many digressions, and I do not want to get too involved in them, but when I was active with the American College of Radiology at first as a member of the steering committee and then later as a chancellor, one of the people that I got to know was a guy named Paul Gebhard who is lawyer—who was the lawyer for the College of Radiology at the time, and then an amicus brief, and I do not remember the exact case, but he was the first person to put in print the words informed consent.

Tacey Ann Rosolowski, PhD
00:49:48.546
In what year was that?

James Cox, MD
00:49:49.749
Well I think it was in the late '50s. I have got a brief reference to it somewhere in something that I wrote because we did a—when I was with the RTOG one of the sort of—I don't know how we got the *Red Journal* involved with it. I guess maybe I was—was I already editor in chief of the *Red Journal*? I guess in the late '90s on the anniversary of—on one of the anniversaries of the infamous trial on syphilis in the African-American men from Tuskegee, we actually held a meeting in Tuskegee and had part of—had several—I think three or four papers contributed to the *Red Journal*—you may be familiar with it. This is the journal I am talking about. It's over there next to you too.

Tacey Ann Rosolowski, PhD
00:51:31.688
Radiation Oncology?

James Cox. MD
00:51:33.273
Yeah. It's this. *International Journal of Radiation Oncology*. One of the issues had the sculpture of Booker T. Washington outside—see that Tuskegee anniversary on the cover, and in that I wrote about the history—it was an editorial, so it was not long. So it was sort of taking the old history from the syphilis trials and how things had changed since that time. And in that editorial I referenced the work of Paul Gebhard and his use of the term informed consent for the first time in the legal arena.

Tacey Ann Rosolowski, PhD
00:52:51.237
So this was—this idea of informed consent—it seems like it was evolving and actually becoming kind of a theoretical piece of how you were seeing the design of experiments with seeing patients as collaborators?

James Cox, MD
00:55:01.335
Yeah. It was. I mean—I think—certainly my whole view of informed consent changed, but that was part and parcel of the evolving interest in clinical research and philosophical and mechanical and the administrative and the scientific and the results. And then when we got the results of probably the earliest trial I recall, it was a trial in cancer of the esophagus, which was at that time a disease that killed almost everybody that was afflicted. And we treated them with radiation therapy or they were treated surgically, and the results were terrible with both. And there were various ways of trying to combine radiation therapy and surgery, and they by and large did not work. And putting chemotherapy together with radiation therapy had really quite a profound effect. I mean—there were people who were cured of the disease. And so a clinical trial was done that compared chemotherapy and radiation therapy versus radiation therapy alone, and the results were so strikingly different that they had to stop the trial. They could not ethically continue it anymore and—

Tacey Ann Rosolowski, PhD
And what year was this about?

James Cox, MD
00:55:07.998
I think the first publication was probably about somewhere around—somewhere between 1990 and 1992 and probably the more definitive publication was in *JAMA* in about '99.

Tacey Ann Rosolowski, PhD
00:55:26.459
And you were involved with this trial?

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James Cox, MD
00:55:28.730
I was heading the RTOG when the results of that trial came out. It was started in the ‘80s. I was involved in the RTOG in the ‘80s, but I was not directly involved with the start of the trial. But when it came out and we had the results that required us to stop the trial, I was involved with that.

Tacey Ann Rosolowski, PhD
00:55:55.213
So how did that work? The results came out, and did—were they sent to a committee?

James Cox, MD
Uh-hunh (affirmative).

Tacey Ann Rosolowski, PhD
Did you convene a committee?

James Cox, MD
00:56:02.213
This was where we—very early times when we had the Data Safety Monitoring committees. And the Data Monitoring—we had to present the results to the Data Monitoring committee, which were all independent people. They were not RTOG members. They were absolutely independent, and you presented the studies to them, and they indicated whether—their recommendation—I mean—they could not say do this or do that, but their recommendation was either to stop the trial or to continue it on. If the results were sufficiently similar, they would say continue it. And if the results were strikingly different, they would say, "You have got to stop because you cannot enroll people in a study where you know the results of the other arm are much better." So there are some interesting philosophical and ethical issues related to clinical trials. There was a time when nobody paid attention to those at all. I mean—some of the most famous people in the United States accomplished terrific things by doing things with patients where the patients had no say in it whatsoever, and there wasn't any idea of informed consent. I think of the trials of treating burns in patients—the trials that were done in Boston in—I think in the '50s—by Francis Moore and others in terms of how to manage serious burns. They did things with those patients that were not—well—there was no consent involved. They just did them. And sometimes they were successful, and sometimes they were totally unsuccessful. But the patients were going to die anyhow, and so they figured we got to do something. That drove a lot of the decision-making before the idea of informed consent came about. And the informed consent really—I believe—was not prominent—it did not begin to become prominent until the early '70s. It was at the early '70s when there was the discovery of what had been done in Tuskegee and the just awful thought that people had—men had not been treated for syphilis when they knew that there was a medication that could cure them. And then the whole idea of informed consent developed and institution review boards developed, and then maybe institution review boards got out of hand as they have here. But that is a whole interesting story all on its own. I remember there is a wonderful article written by Atul Gawande—you know him?

Tacey Ann Rosolowski, PhD
Uh-hunh (negative).

James Cox, MD
01:00:08.587
It was—it is actually a biography of Francis Moore. And Gawande covers the history of what Moore and his colleagues did in treating burn patients in Boston and how they did things by trial and error. And when the trials were successful, they profoundly changed the practice of medicine. And Francis Moore was kind of a wild man—I mean—he did things that I think people thought were pretty crazy, but they cured some people and changed medicine. And later on Francis Moore became one of the people who were most strict about not wanting to see that done in the future.

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Tacey Ann Rosolowski, PhD
01:01:39.428
Interesting.

James Cox, MD
He was one who was most strict about informed consent and not doing things on patients for which there was no approval by anybody. In his later life he went—anyhow Gawande does a wonderful job. It was published in *The New Yorker*, and it is a great piece.

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Chapter 05
A: The Administrator
The Radiation Therapy Oncology Group

Story Codes
A: The Researcher
A: Overview
A: Definitions, Explanations, Translations
D: Understanding Cancer, the History of Science, Cancer Research
B: Devices, Drugs, Procedures
A: Activities Outside Institution
B: Beyond the Institution
D: Understanding Cancer, the History of Science, Cancer Research
D: The History of Health Care, Patient Care
D: Business of Research

Tacey Ann Rosolowski, PhD
01:02:10.061
It sounds really interesting. I was wondering if you would tell me more about the involvement with the Radiation Therapy Oncology Group? You talked about how that was established in the late ‘60s you said?

James Cox, MD
Uh-hunh (affirmative).

Tacey Ann Rosolowski, PhD
And who was involved in founding that organization? When did you really get involved?

James Cox, MD
01:02:28.074
It was a guy named Simon Kramer, and he was actually—he was a—not a contemporary. He was a bit younger than Dr. del Regado, but they were on many national committees together. Simon Kramer, Gilbert Fletcher from Anderson, Henry Kaplan from Stanford, Morton Kligerman from Yale—they were all sort of contemporaries in the sense that they were frequently involved at the National Cancer Institute in the treatment and evaluation of policy. And so Kaplan had started a trial on Hodgkin's disease in about '65 and pulled together a unique set of individuals who were interested in doing it, a statistical setter, an operations setter and so on—a whole self-contained construct. Del Regado did the same thing with cancer of the prostate, but Kaplan's was with Hodgkin's. Del Regado did the same thing with cancer of the prostate a couple years later—pulled together—you know—had its own statistician, its own operations setter. And Simon Kramer went to the National Cancer Institute to get funding for yet another study that involved actually chemotherapy and radiation therapy for cancer of the head and neck, and the leadership at NCI said wait a minute—we cannot just do this for every idea that comes along from somebody who is notable, form a national group—and by that time there were a few national groups. They had come out of the recognition at the National Cancer Institute that you could not address questions with just the patients in a single institution—not even NCI. And so they pushed for the formation of cooperative groups. And I think NSABP was one of the earliest with Bernie Fisher.

Tacey Ann Rosolowski, PhD
01:05:13.436
NSABP stands for?

James Cox. MD
01:05:14.779
National Surgical Adjuvant Breast Project. That was one of the earliest. And the Eastern Cooperative Oncology Group or ECOG was a little later than that. And then there was the Southwest Oncology Group. So there was some experience with these groups developing, and the NCI leadership at the time said form one of these groups. So Kramer did.

Tacey Ann Rosolowski, PhD
01:05:51.195
So the idea—just to pick up a little piece—the idea of bringing together multiple institutions was simply that you needed the patient numbers?

James Cox, MD
01:06:00.162
Yes.

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Tacey Ann Rosolowski, PhD
Okay.

James Cox, MD
It was.

Tacey Ann Rosolowski, PhD
01:06:05.743
So when did you become involved with the group?

James Cox, MD
01:06:09.300
I became involved with the group in I think 1978 or ’79 when I was in the Medical College of Wisconsin. Actually we were developing a good strong department at that time, and they encouraged us to join. And we joined, and to this day the Medical College of Wisconsin is one of the leading institutions in the RTOG. But I was involved, and relatively soon after that I became one of the—I forget what it was called—vice chair for research strategy or something like that.

Tacey Ann Rosolowski, PhD
01:07:10.211
And what did that entail?

James Cox, MD
01:07:12.262
It entailed interacting with the various disease site areas. So there was the group treating tumors of the central nervous system, head and neck, lung, cervix, esophagus—anyhow so there was—oh and prostate. So there was brain, head and neck, thorax, GI, GU, and GYN. And so it was interacting with each of those groups to sort of stimulate the evolution of the research questions. After that experience I was elected to chair of the group in 1987, and with it went a big grant, and I have forgotten how much money it was. It would have been a lot more now, but it is probably four or five million dollars, and that was to be distributed throughout the institutions for participation in these clinical trials.

Tacey Ann Rosolowski, PhD
So what were some of the most significant initiatives and findings that were taking place while you were there at that time?

James Cox, MD
01:09:00.898
Well in—and they were mostly in the area of chemotherapy and radiation therapy together. There was a big interest—oh there were some blind alleys of course—so there was a big interest in drugs that were called hypoxic sensitizers, and oxygen—the lack of oxygen is what makes tumors resistant to radiation therapy. So if you had drugs that would counteract that—that would work in the tumors to make them more sensitive to radiation, tumors would be controlled better. So there are several years of work on hypoxic cell sensitizers.

Tacey Ann Rosolowski, PhD
01:09:55.661
And was this one of the blind alleys?

James Cox, MD
01:09:57.280
This was one of the blind alleys. It just never went anywhere. Another one was hypothermia. You know—the biology was really incredibly strong. The ability to monitor heat distribution and delivery was very poor. It just did not work. But adding chemotherapy together with radiation therapy did work. And so it became one of the areas of considerable interest. The other thing that was of great interest was what was called fractionation, which is splitting the dose that is delivered into large doses each time or small doses each time, giving it once a week or giving it two or three times a day, and there was a lot of interest in that. And that has continued to go, but that has sort of reached a plateau and took a background place to the work with chemotherapy and radiation therapy together. So—I mean—I was involved in all of those and also involved in shutting them down and stopping them when they weren't going anywhere, which was not a very popular thing to do.

Tacey Ann Rosolowski, PhD
01:11:35.877
So you were reviewing all the research—

James Cox, MD
Yeah.

Tacey Ann Rosolowski, PhD
—and the results, and then deciding who got money and (both speaking at once)?

James Cox, MD
01:11:40.686
Deciding—you know—sort of coming to the group—we met semi-annually—coming to the group and saying we cannot afford to do this anymore. We are going nowhere with this strategy, and we've got limited resources. We've got to use those resources otherwise. So we shut down the hypothermia program. We shut down the hypoxic sensitizer program, and we moved more into fractionation and into chemoradiation. The first big success was in cancer of the esophagus. The second big success was in cancer of the nasopharynx. And then the one that really got MD Anderson turned on more than any others was actually cancer of the cervix. Patricia Eifel and Mitch Morris, who was here—I don't know if you still know that name—but Mitch Morris was a gynecological oncologist, very active in GYN oncology, and he and Patricia actually were the lead people in the nation in pushing the concept of chemoradiation versus radiation therapy alone for cancer of the cervix. Chemoradiation was clearly superior. And so that was another winner for that particular approach. Then they were doing one for cancer of the anal canal where the end point they were looking at was avoiding colostomy. They did one for cancer of the larynxcancer where it was avoiding laryngectomy. There were others.

Tacey Ann Rosolowski, PhD
01:13:49.139
Was there—so on the one hand, you have the trials going on, which is thinking about how to most effectively use what was available either with radiation technology and then with chemotherapy—was there something happening at the same time with the technology of radiation therapy that was adding complexity to this mix or adding other factors?

James Cox, MD
01:14:15.502
Yeah. There was, but it was not really being addressed as—I mean aside from hypothermia—it was not being addressed as a technology assessment approach, but hypothermia was being added to standard radiation therapy.

Tacey Ann Rosolowski, PhD
01:14:40.765
Now is just hypothermia meaning you chilled the patient, or was there something else going on?

James Cox, MD
01:14:44.931
No. You tried to heat the tumor.

Tacey Ann Rosolowski, PhD
Okay. Got it.

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James Cox, MD
01:14:48.195
Now you could try to heat the patient, and actually Joan Bull, who is over at the UT Health Science Center, she was one of the leading people in the country in doing total body hyperthermia. The goal was that if you got the tumor up to a certain temperature, then radiation therapy and even chemotherapy were more effective.

Tacey Ann Rosolowski, PhD
01:15:16.335
Meaning that with the increase in temperature the processes would take place faster? Or what would make the tumor more sensitive with more temperature?

James Cox, MD
01:15:27.385
Well there were a lot of biologic studies trying to address that question. There were a lot of biochemical changes that took place when the temperature got a little higher and radiation or chemotherapy was added. Some of those biologic processes are still considered pretty important—the whole idea of heat shock proteins and—

Tacey Ann Rosolowski, PhD
01:16:07.686
What are those?

James Cox, MD
01:16:09.388
Well they supposedly develop when you get to a certain temperature, and they have various interactions in the tumor, and they are still being studied. So, but back to your question about technology evolution and technology assessment, there were advances in technology going on in the field primarily with external radiation therapy—with treatment from the outside. But they were never—I mean there were simulators that came in, and there were imaging modalities that came in, but they were not formally evaluated. One of the reasons for it was that there was no interest at the National Cancer Institute in having them evaluated at that time. And the funding came for the RTOG and these other cooperative groups came from the National Cancer Institute. And—you want some water?

Tacey Ann Rosolowski, PhD
I've got some down here.

James Cox, MD
01:17:53.021
And so the ideas had to go through the Cancer Therapy Evaluation Program—CTEP. And if the people who were leading CTEP were not interested in the question that you wanted to address, then they were not going to approve funding for it. So it wasn't just—the decisions about research strategy were not confined or limited to the RTOG. They had to be sold—if you will—to the leaders at CTEP. Now the leaders at CTEP were all medical oncologists. They did not know anything about radiation oncology. There were usually one or two very good, very prominent radiation oncologists that were there as consultants, but they did not participate much in making those decisions. And that is still true to today, that the somewhat grim statement about NCI is that it is a National Chemotherapy Institute. There is some interest in surgery, some interest in radiation therapy—not very much—and very little money that is allocated to either one. There is just a huge desire to hit another or hit some home runs with drug therapy. And now the drug therapy of course has multiplied many fold with the availability of biologic agents. And we have tried with the proton work—we have tried to see if there was any interest in clinical investigations of proton therapy. There is interest, but the interest is split among various agencies of the federal government. The National Cancer Institute is only one agency that has any interest in it, and they do not have a huge interest in it—again—for the same reason that it is not a drug.

Tacey Ann Rosolowski, PhD
01:21:12.758
And why is there this prejudice towards drugs? I mean—is it a money thing? Or is it simply the history of who has been in power there?

James Cox, MD
01:21:24.340
Yeah. It is strictly who has been in power at NCI. Yeah.

Tacey Ann Rosolowski, PhD
01:21:37.291
Interesting. I hadn't heard that before.

James Cox, MD
No?
Tacey Ann Rosolowski, PhD
No. Uh-hunh (negative).

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James Cox, MD
01:21:46.242
I was on the board of scientific counselors of the Division of Cancer Treatment, and CTEP—the Cancer Therapy Evaluation Program—is under that division. We would spend tens of millions of dollars looking for a new exciting drug in some—you know—forest in Thailand, and it was harder than hell to get any money to do any kind of research involving radiation therapy. They just were not—that was not what they wanted to do. They wanted the next—I don't know—vincristine or vinblastine—they wanted the next drug that would be—that would hit a home run and take care of cancer. They have become a lot more sober about that possibility I think, but I think the interest is still the same. The people who work there in the sort of radiation research program are having to struggle with that internally all the time. So the people that are in the radiation research program would like us to investigate proton therapy, but there's—they don't have a good handle on the funds which stimulates such research.

Tacey Ann Rosolowski, PhD
01:24:04.310
Let alone in the strategic kind of way. Interesting.

James Cox, MD
Right.

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Chapter 6
A: Overview
Radiation Oncology at MD Anderson and Memories of Gilbert Fletcher

Story Codes
A: Overview
A: Definitions, Explanations, Translations
A: The Researcher
A: The Clinician
B: Information for Patients and the Public
B: Building/Transforming the Institution
B: Multi-disciplinary Approaches
B: Controversy
C: Portraits

Tacey Ann Rosolowski, PhD
01:24:10.532
Let me go back to something really basic because you made a couple statements that I realize that I am probably much less educated about this than I need to be. How would you describe what radiation oncology is to a lay person? I mean, what is it as an intellectual discipline, and then what is (???)(inaudible)?

James Cox, MD
01:24:38.452
It's the use of ionizing radiations to kill cancer cells. One of the reasons why fractionation became such a big deal early on was when they first applied ionizing radiations they did it—you know—just for a long period of time with x-rays or later on with radium by just putting it on the skin—let's say—and leaving it there. And what happened was essentially a burn—not a thermal burn and it wasn't immediate—but it evolved into what would develop a crust and eventually a hole and be quite morbid. In France there were a couple of investigators that looked at what happened if you just gave three shorter applications instead of one, and it had a huge effect that was positive. They used the testes as the basis for a rapid cell renewal system that would be similar to a tumor, and they found that they could stop spermatogenesis without causing the necrosis of the scrotal skin whereas if they gave one application it would cause necrosis—I mean—it would cause death of the skin, but it would not turn out spermatogenesis. So it was the whole idea of selective cell killing and sort of looking at selective cell killing and dose distributions in the body by various—in various ways that is much of the history of radiation therapy. And really only in the last twenty years—well—I shouldn't say that because the original interest goes back probably forty years, but mostly in the last twenty years that there has been the biggest interest in chemotherapy and radiation therapy together.

Tacey Ann Rosolowski, PhD
01:27:33.299
Because originally radiation therapy was really partnered with surgery—is that the case or—?

James Cox, MD
01:27:41.305
Yeah. It was, but not very—yes, it was. That is correct. Not what is very good. Not with very good results and not with necessarily very good strategy.

Tacey Ann Rosolowski, PhD
01:28:12.629
So it sounds like maybe that was a partnership by default because there wasn't anything else available at the time really—is that the case?

James Cox, MD
01:28:17.807
Yeah. That is to some degree true. The very earliest clinical trial that was ever done in the United Kingdom was the use of postoperative x-ray therapy following mastectomy for cancer of the breast. There are still investigations going on in that whole general arena now with the intact breast, but it is amazing. That was begun in the late forties.

Tacey Ann Rosolowski, PhD
01:29:03.846
Now when Gilbert Fletcher was here you had an opportunity to meet him?

James Cox, MD
Uh-hunh (affirmative).

Tacey Ann Rosolowski, PhD
You did? Yes? Okay. I know that he was very controversial, meaning kind of a flamboyant figure too as far as I understand, but do you think—what were the controversies surrounding his work? And understand please the spirit in which I am asking this because it is not really—you know—I mean—colorful characters are colorful characters, but what I am wondering is what were the issues really about radiation therapy that were driving these controversies and creating tension within MD Anderson about the use of radiation therapy?

James Cox, MD
01:29:49.993
Well, the main controversy was the effectiveness of radiation therapy relative to surgery, and probably the single greatest area of disagreement and acrimony was with Fletcher and William McComb, who was the head of head and neck surgery. McComb came from Memorial Hospital in New York now called Memorial Sloan Kettering, and his idea was you could not cure anything with radiation therapy. You had to cut it out. And Fletcher, who had seen examples as I had of things—patients being successfully treated with radiation therapy with good long-term results, knew that that was not the case and knew that some of the operations that were being done by McComb and his colleagues were very morbid and were unnecessary because you could cure the same patients with radiation therapy. Fletcher fought like hell to get that across and eventually he succeeded. Now he succeeded partly because—I guess—McComb died. I don't know when he died. But his successor—and I don't know if it was his immediate successor or if there was somebody in between—but his successor was Richard Jesse, and Jesse was a much more open person and was willing to look at the results and advantages of radiation therapy and then figure out how to combine radiation therapy and surgery together to achieve the best results for the patient. So he was more of the—if you will—current philosophy or culture of MD Anderson that says ultimately it is really what is best for the patient that should drive everything we do, and anything else should take second place. And so Dick Jesse—and he was so respected by everybody—by Fletcher, by all the people in head and neck surgery, by people in other departments, he was a real leader. So that kind of gradually put that set of issues to bed, although when I first came to MD Anderson there were some carryovers from the McComb period, primarily Jay Ballantyne [Dr. Alando]. I don't know if you know that name.

Tacey Ann Rosolowski, PhD
01:33:33.563
I recognize it but not enough to (both speaking at once).

James Cox, MD
01:33:35.502
Yeah. Well, Ballantyne was one of the last head and neck surgeons that thought he could do anything and should do it—could do anything and should do everything. And then eventually he died too.

Tacey Ann Rosolowski, PhD
01:33:57.364
That was really kind of an old guard perspective.

James Cox, MD
01:33:59.825
It was the earliest people in the history of MD Anderson because there was McComb in head and neck surgery, Lee Clark in general surgery, Fletcher, and then Felix Rutledge in gynecology. Now because radiation therapy and especially radium therapy was a standard part of gynecologic treatment of cancer of the cervix and endometrium, Fletcher and Rutledge came to working together much more easily, and they evolved the joint clinics as actually did the people in head and neck cancer.

Tacey Ann Rosolowski, PhD
01:34:46.310
I actually didn't realize that. How was radium used to treat gynecologic cancers at the time?

James Cox, MD
01:34:52.233
It was put in the uterus.

Tacey Ann Rosolowski, PhD
In what form?

James Cox, MD
01:34:57.851
They were usually tubes of radium—and you know what a wine cork looks like?

Tacey Ann Rosolowski, PhD
Uh-hunh (affirmative).

James Cox, MD
Well they would put the wine corks inside the vagina, and then they had a tube of some various lengths that would go into the uterus itself, and that would be used to sort of surround the area where the cancer of the cervix was, and it was shown to be curative as far back as 1920.

Tacey Ann Rosolowski, PhD
01:35:31.842
Really? I had no idea.

James Cox, MD
01:35:41.901
Yeah. I might even have a picture. Here, move it over there. Okay.

Tacey Ann Rosolowski, PhD
All right. There I go.

James Cox, MD
But in the—

Tacey Ann Rosolowski, PhD
01:35:51.697
I have to say it always surprises me when I hear stories like this because when evidence is mounting and there is a demonstrative effect from using something and yet there is an entire discipline that is resisting it—it just seems very strange. You know—again—how slow cultures are changed, how slow disciplines are to change.

James Cox, MD
01:36:20.348
Well, one of the problems with surgery and radiation therapy was that at some institutions surgeons were the ones who used the radium to treat cancer, and so they thought they knew everything about it.

Tacey Ann Rosolowski, PhD
I see.

James Cox, MD
01:36:41.292
Let me see if I can find it. I'm not finding the chapters. Somewhere it's buried in here—I'm sorry I can't just pull it out right now.

Tacey Ann Rosolowski, PhD
01:37:27.645
Oh, that's all right. I can search—or we can look for it afterwards—after the recorder is turned off. What were your impressions of Gilbert Fletcher?

James Cox, MD
01:37:49.075
My impressions of him—well I had two different impressions. One, I knew that he was a very strong-willed man who would argue with anybody about anything if he believed strongly in it. And del Regado was very similar in that regard. And strangely, as time would prove, they evolved a considerable amount of respect for each other. So one of Fletcher's longtime associates—a guy who was here for many, many years—Bob Lindberg—did his residency with del Regado, and del Regado's whole idea of a residency was you spent three years with him and then you ought to go to another place with a different philosophy, and you ought to spend at least one year there and only then were you fully trained. Not a bad idea. So he encouraged Bob Lindberg to come to MD Anderson and work with Fletcher. And so—I mean—he had a lot of respect for Fletcher, and I had a lot of respect for Fletcher although I knew him to be a tough

customer. Then I worked with one of Fletcher's trainees when I was in the Army, and he was a fabulous, smart, terrific guy—Len Shukovsky—Leonard Shukovsky. And so Len and I were in the Army together, and we argued a lot and so on and so forth, but we really got along well. I mean—I sort of brought my viewpoint from del Regado, and he brought the experiences with Fletcher. And—again—there ended up a lot of respect on both sides. I spent an evening at his home with Fletcher visiting, and so that was another impression of Fletcher. And then when I went to the Medical College of Wisconsin, I needed a favor relative to a certificate of need thing, which I won't go into, that had to do with high-energy x-rays, and I asked Fletcher to write a letter for me. He was very generous, and he wrote a letter. And so we were friends almost from the very beginning. Then when I came to Houston I used to visit him, and I would go by his office and see what was going on. Then when he developed leukemia I would visit him at home. But he was an interesting character.

Tacey Ann Rosolowski, PhD
01:41:45.995
How would you describe his intelligence—his genius—you know his—how—?

James Cox, MD
01:41:51.025
He was a genius in many ways. His grasp of physics was great. His grasp of human radiation biology was even greater, and his observational skills were extraordinary. So he examined patients far more frequently than people do now, and he watched the evolution of how tumors respond. He was particularly interested in head and neck and cancer of the cervix. And so in both cases you could observe what was happening to the tumor as it was responding to radiation therapy. So he was really a very careful observer and with that a real scholar about what was happening. He was incredibly honest. So when they did treatments at MD Anderson that ended up being toxic, let's say, or having bad effects—usually long-term effects—he would publish them. He would not shy away from the fact that they had done things that were not good for the patients, and he published them so that other people would not do the same things. So—I mean—he had many, many skills. And the people who were around him—you know—as tough as he could be—they had great affection for him. I mean—I found that out when I came here. I had more than a few people say how much Fletcher meant to them personally. There were a handful of people who did not feel that way, but I saw every reason to think that he was an extraordinary man. I mean—he was a leader. He was a leader within the institution. He had the respect of even people who did not agree with him.

Interview Session: 01
Interview Date: January 4, 2013

Chapter 07
A: Overview
Leadership Experience

Story Codes
A: Professional Values, Ethics, Purpose
B: The Leader
C: Leadership
B: MD Anderson Culture
B: The MD Anderson Brand, Reputation
A: Military Service
B: Professional Path
B: MD Anderson Mission and Values

Tacey Ann Rosolowski, PhD
01:44:53.589
Were there any lessons that you learned from him [Gilbert Fletcher] after having—you know—arrived at this institution and meeting him and setting yourself on your own leadership path here?

James Cox, MD
01:45:05.660
Well I had done some of this stuff before. I mean I had been—in terms of leadership, such as it might be—when I was in the Army, I said I went in and I was in the Berry Plan and one of the reasons was they did not—they were so short of regular Army—that is to say career Army people in the field of radiation oncology. After I had been there for a year, the last one of those people retired from the Army, and so I became the head of the radiation oncology service at Walter Reed. And I was 32. Then I became head of the radiation oncology service at Georgetown at 34 and then at the Medical College of Wisconsin at 36.

Tacey Ann Rosolowski, PhD
01:46:28.498
That is unusually young—isn't it?

James Cox, MD
01:46:30.784
Pretty young. And then I was at the Medical College of Wisconsin for many years. So I had done kind of radiation oncology administration in smaller arenas before being here. I don't think I learned anything brand new from Fletcher because I knew him from afar, but I was impressed all over again that he was a very—you know—special human being. I knew his history, and I talked with his wife about how he evolved in the field because he was not trained in radiation oncology like I was. He was trained in radiology, and then he kind of took a tour throughout Europe. He visited several places, and he was so quick to glean the essence of what these places were doing that was valuable, and he brought that back to MD Anderson. That was what he put in place. So he was a very special guy, and—you know—I had a lot of respect for him always.

Tacey Ann Rosolowski, PhD
01:48:31.890
We have only five minutes left in the session today. Would you like to say anything else today? Or do you want to close off and then make another time?

James Cox, MD
01:48:44.451
Well I don't know that we have talked about things that are of interest to you or things that you think—if you would like quick comments about anything I will provide you with any quick comments.

Tacey Ann Rosolowski, PhD
01:49:07.497
I am not sure if I have any quick, quick, quick questions.

James Cox, MD
01:49:14.330
I have had a wonderful career here, and I had some disappointments early on and some disagreements early on—things where people said or might have said, "Why did you stay here?" Certainly I had many opportunities to go other places, and I stayed here because as I practiced—you know—as I got out of the administrative realm and practiced radiation oncology here, I realized that this is the best cancer care that anybody can get and that to go to any other place would be to move into an arena where the cancer care was not as good, and that just was not an appealing thing. So—you know—I could have been vice chancellor for this or dean of that or so on and so forth—there were many opportunities, but I chose to stay doing what I did. And there are some regrets that go along with that—you know—it doesn't get the recognition that you would get if you had been the dean of something or other and you get into the Institute of Medicine or you get recognitions of that sort, but it has been a good run. So I am happy for it. And if you want to talk about things—if you have anything else you want to know I would be happy to spend more time talking with you.

Tacey Ann Rosolowski, PhD
01:51:46.159
Oh I have plenty more I would like to know about. One thing I wanted to ask you—actually I can close off the recorder here and just take some notes for my own review purposes. So I just wanted to say officially for the record thank you for spending your time today.

James Cox, MD
01:52:04.916
We have gone right along without any interruption for a couple hours at least.

Tacey Ann Rosolowski, PhD
Yes.

James Cox, MD
01:52:11.222
It has been fun. Thank you.

Tacey Ann Rosolowski, PhD
Oh good.

James Cox, MD
I've enjoyed it.

Tacey Ann Rosolowski, PhD
01:52:15.967
I'm glad. I did too. I'm learning a lot. Well I'm turning off the recorder at—let's see—2:57.

(end of audio)

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

James Cox, MD

Session 2— April 12, 2013

Chapter 00B
Interview Identifier

Tacey Ann Rosolowski, PhD
00:00:05.625
This is Tacey Ann Rosolowski, and today I'm at the Proton Therapy Center in the office of Dr. James Cox, and we're in our second session. The time is about 11:25, and the date is April 12, 2013. So thank you Dr. Cox for agreeing to do this session. We were strategizing before I turned on the recorder and decided that today would be a good day to devote to the discussion of the research that you have done. I'm hoping that we can go back to fairly early—the research that you first conducted when you first came to MD Anderson and even if there's a relevance in tracing the roots of that in your previous positions and tracing the evolution of that research career and story.

Interview Session: 02
Interview Date: April 12, 2013

Chapter 8
A: The Researcher
Clinical versus Basic Research; Focusing Research on Patterns of Failure Studies

Story Codes
A: The Researcher
A: Overview
A: Definitions, Explanations, Translations
B: MD Anderson Culture
D: On Research and Researchers
D: Understanding Cancer, the History of Science, Cancer Research
D: The History of Health Care, Patient Care
C: Professional Practice
C: Patients, Treatment, Survivors
C: Healing, Hope, and the Promise of Research
D: On Research and Researchers

Tacey Ann Rosolowski, PhD
00:00:28.201
We were strategizing before I turned on the recorder and decided that today would be a good day to devote to the discussion of the research that you have done. I'm hoping that we can go back to fairly early—the research that you first conducted when you first came to MD Anderson and even if there's a relevance in tracing the roots of that in your previous positions and tracing the evolution of that research

James Cox, MD
00:01:02.241
Well it starts back as early as my residency, and it is all clinical research. Now a side comment about clinical research is that it is not very highly respected academically.

Tacey Ann Rosolowski, PhD
00:01:34.582
Yeah, you were talking about the last time we spoke.

Interview Session: 02
Interview Date: April 12, 2013

James Cox, MD
00:01:38.313
So for somebody to spend a career doing that, you could say, "Well, that's a lot of wasted time." And it is if you look at it from the point of view of a basic scientist, where to design a discrete experiment in the laboratory, carry it out over a period of weeks or months or maybe a couple years, and then have a paper to write or more papers to write because the research has been based on a specific hypothesis. Now in clinical research, I think the hypothesis derives, at least to a considerable degree, from the care of patients. And I think in caring for patients, one comes up against questions that are not adequately answered. One can develop a hypothesis about what that might be.

Tacey Ann Rosolowski, PhD
00:03:00.195
Can you give me an example?

James Cox, MD
00:03:06.624
Well an example that goes back far but also comes to the present time is when people do clinical trials, the ultimate endpoint is survival. And that is an immutable endpoint. Nobody can argue with being alive or dead. Any of the other endpoints are less crisp, I guess—they're not as definitive. Well that tells you whether you have been successful in a certain kind of treatment, but it doesn't tell you anything about why. And so early on I developed an approach that said, "Okay. If we're failing in treatment, why are we failing? Is it because we have not eradicated the local tumor? Is it because if we were treating with radiation therapy, we have not had a large enough field so the tumor's recurred at the margin of the field that we treated? Or the tumor has spread." Now in some quarters—and I think this is true in much of medical oncology—those questions are immaterial because their paradigm for the treatment of cancer is leukemia, which is disseminated from the very beginning. And so they don't find it very useful to ask about patterns of failure. But I've been doing that all of my career, and I can continue to be doing that with the proton effort now. We've uncovered some interesting things. If you fail to eradicate the local tumor, is it because the dose—I'm talking now entirely about radiation therapy—is it because the dose was not enough? Or was there uncertainty in the dose distribution? And of course disseminated disease speaks for itself. Well I started to this with cancer of the lung in the 1970s.

Tacey Ann Rosolowski, PhD
00:06:11.098
What prompted you to begin asking questions in that way?

Interview Session: 02
Interview Date: April 12, 2013

James Cox, MD
00:06:18.556
It was, in part, my training. It was, in part, the discussions with Dr. del Regado, my mentor. He didn't frame it in the way that I just did, but he did ask, "Why did we fail?" And that's an important question. It's an important question for anybody that's dealing with local treatment. It would be a similarly important question for a surgeon who's trying to remove a tumor and ideally remove it all. Or the sidelight of it is the consequences of treatment, the toxicity, the functional deficits. So that's another side of the treatment equation. And so having an approach to that—as far as research strategies are concerned—when I became involved with the Radiation Therapy Oncology Group in the very late 1970s, I brought those questions to the group, and over time that helped color some of the research that went on with the group. Although all of the phase three studies that were designed at the time when I led the group during that ten-year period, all of them had survival as the endpoint. Now that is not true at the present time. It's not true in studies that are being done here, but still I contend that it's the ultimate endpoint. Still it doesn't give you the answer of why you succeed or fail. And you're happy to succeed so you pass that off, but if you fail, there's a reason. And as time went on, I guess that carried some weight as far as being selected to become chair of the RTOG.

Tacey Ann Rosolowski, PhD
00:08:49.740
Uh-hunh (affirmative). When you were a resident, what were the studies that you were doing that helped you frame this approach?

James Cox, MD
00:08:57.820
One of the studies I was doing had to do with cancer of the breast. Another one had to do with cancer of the cervix, actually very early cancer of the cervix—what's now called—well we call it carcinoma in situ. It now goes primarily by the title intraepithelial neoplasia—what's this?

Tacey Ann Rosolowski, PhD
Shall I pause the recorder? Do you need to—

James Cox, MD
No. Okay, I know what they need. I have to do something.

Tacey Ann Rosolowski, PhD
Okay, I'll just pause the recording.

James Cox, MD
Yeah.

[The recorder is paused.]

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Tacey Ann Rosolowski Ph,D
00:09:54.603
Let me just get this back on. Okay, we're recording again. So you were talking about the breast and cervical cancer that you were working on as a resident.

James Cox, MD
Uh-hunh (affirmative).

Tacey Ann Rosolowski, PhD
And what were the studies that you were running? What exactly were you doing?

James Cox, MD
00:10:10.248
Well they had treated a series of patients with intraepithelial neoplasia with radiation therapy at that time which was not—this is in the very, very early days of treatment of intraepithelial cancer of the cervix. The standard treatment was hysterectomy . We were trying to spare patients a hysterectomy and give them an opportunity, actually, to still bear children. And so it was not my hypothesis, but that of my mentor, that you could do this with very localized radiations delivered only to the cervix. So I pulled all those patients together, wrote them up. It was a retrospective study. It was prospective on his part, but for me it was just gathering the data. Now interestingly, the study that we were doing on cancer of the breasts was to go back and review all of the patients that had been treated at the Penrose Cancer Hospital and have the path reviewed and try in a very primitive way at that time to understand better the findings in pathology that would predict recurrence or no recurrence. Unfortunately, that never got completed because my mentor was interested in something else, and we just never got it completed.

Tacey Ann Rosolowski, PhD
What was the—

James Cox, MD
00:12:01.243
But it was the discussions with him about that, whether it was with lymphomas or whether it was cancer of the prostate. All of those were situations where we asked that question. In about 1983, actually, I had a symposium at the Medical College of Wisconsin that was published in a NCI—it wasn't called an NCI monograph—I think it was called Cancer Treatment Symposium. We had some funds to invite some people from around the country, and many of the people working in cancer came and addressed this issue—patterns of failure. It was published. Many people have told me over the years that it was a really remarkable body of data because we asked them to come not just with opinions; we asked them to bring data. They did, and it was a rich resource. But that was a carryover of this effort on patterns of failure.

Interview Session: 02
Interview Date: April 12, 2013

Chapter 09
A: The Researcher
Research Focused on a Range of Body Areas

Story Codes
A: The Administrator
A: The Researcher
C: Professional Practice
C: The Professional at Work
A: Overview
A: Definitions, Explanations, Translations
D: On Research and Researchers
D: The History of Health Care, Patient Care

Tacey Ann Rosolowski, PhD
00:13:29.452
Uh-hunh (affirmative). How did that focus [on patterns of failure in radiation treatments] evolve as you began to undertake your own studies that you can see from the beginning?

James Cox, MD
00:14:01.565
Well the other area of interest—and they kind of went together—was the area that's called fractionation. That is—you split up the dose of radiations that you give a patient to exploit the differences between the cancer cells ability to—the inability of the cancer cells to recover between doses of radiation and the ability of normal tissues to recover. And if you don't give too big a dose at one time, you can exploit that difference. So I was working in that area.

Tacey Ann Rosolowski, PhD
00:14:52.746
And what kind of cancer?

James Cox MD
00:14:54.846
That was primarily cancer of the lung, head and neck, cervix. It seems to me there was another—brain. This was in the context of the RTOG by that time, and we mounted a series of trials looking at fractionation and found that some fractionation experiments just didn't seem to help. Others, and cancer of the lung, did seem to help.

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Interview Date: April 12, 2013

Tacey Ann Rosolowski, PhD
00:15:41.086
When I was looking at the array of body areas that you focused on, they're so different. I'm wondering what—I'm sure this is a terribly naive question—but what are the unique challenges that each of these areas of the body presents to the radiation oncologist?

James Cox, MD
00:16:02.259
Well the challenges are similar for each of the areas, and that is basically to improve the control of the tumor locally because radiation therapy is a local treatment means. And so that went together with the patterns of failure analyses. For many, there are disease sites where you're trying to improve the tumor locally. As it turned out, a much more important approach, which did not come from our work—that came from the work of people in the Netherlands adding chemotherapy simultaneously with radiation therapy and then comparing that with radiation therapy alone. It turned out that that was a much more powerful way to approach controlling the disease than the altered fractionation. That's proven to be true in many disease sites. One of the first ones was cancer of the esophagus and then cancer of the lung, head and neck, cervix, and all these areas where we did the chemotherapy and radiation therapy at the same time. The chemotherapy plus concurrent radiation therapy was better than radiation therapy alone, and that was measured by survival in every case.

Tacey Ann Rosolowski, PhD
00:18:05.324
What were some of the figures that you came up with—the survivorship rates?

James Cox, MD
00:18:10.345
Well for example, one of the biggest ones—and this didn't come from the group in the Netherlands as a starter—was cancer of the esophagus, where the results with radiation therapy alone, with relatively high doses, were poor—very poor. Well, when we did the randomized trial, at three years no patient was alive that was treated with radiation therapy alone, and a lesser dose of radiation combined with chemotherapy led to a survival of about twenty-five percent, which is a long way from what you would like it to be, but it's very different than zero. And so that was one of the ones. Later on we did head and neck, initially looking at preserving the larynx—preserving function and later on looking at survival.

Tacey Ann Rosolowski, PhD
00:19:28.626
Now were these all accommodations with chemo, or did you also work with people in surgery on this?

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James Cox, MD
00:19:35.246
The one for head and neck was with the surgeons because if there wasn't a very favorable response by a certain point in time, then they would go on to a laryngectomy.

Tacey Ann Rosolowski, PhD
00:19:52.660
Uh-hunh (affirmative). I think I remember talking to Dr. [Kent] Gifford about this.

James Cox MD
00:19:57.361
Right. He was very much involved. Dr. [Kie Kian] Ang was very much involved.

Tacey Ann Rosolowski PhD
00:20:01.959
Tell me about that collaboration. When did that take place, and what exactly did you do for that study?

James Cox, MD
00:20:09.252
Well, in the RTOG they had done a study in the Veterans Administration system where they compared chemoradiation—where they did chemoradiation for cancer of the larynx that otherwise would be completely removed—the larynx would be removed. So if they did chemoradiation and there was a favorable response, then they would go on to pursue chemoradiation and avoid surgery. If there was not a favorable response, they would proceed to surgery. So that was the study that was done largely by Dr. Ang and the Veterans Administration system. We took one step back from that and said, "Well, if we did chemotherapy and radiation therapy together, would it be better than radiation therapy alone?" And it did prove to be better. The chemoradiation was better primarily in larynx preservation because if that failed, they went on to laryngectomy, and the survival was pretty much the same in both groups. One of the interesting things that we did that involved very much the investigators at MD Anderson—and I will give you the expurgated view of that—was to look at concurrent chemoradiation for cancer of the cervix, and a disease that is pretty curable with radiation therapy of the lung. And it turned out that the chemoradiation was clearly superior. That has now become the standard throughout the world.

Tacey Ann Rosolowski, PhD
00:22:43.601
When were those findings made?

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James Cox, MD
00:22:46.148
Oh I think that was published in—those findings were published in the early 1990s. And that's become a standard ever since.

Tacey Ann Rosolowski, PhD
00:23:06.689
Who were your collaborators on that project?

James Cox, MD
00:23:08.654
Well actually I was chairing the RTOG, so officially I wasn't a collaborator. Although Dr. Eifel would acknowledge that I did a huge amount of work in moving that forward, both within the RTOG and within the National Cancer Institute because all of those studies had to be approved by part of the NCI called the Cancer Therapy Evaluation Program and within that a branch called the Clinical Investigations Branch. They were not as sympathetic to what we were doing as we wanted them to be.

Tacey Ann Rosolowski, PhD
Why was that?

James Cox, MD
But eventually they came around.

Tacey Ann Rosolowski, PhD
00:24:00.295
And was that—I think you mentioned last time that there was a bias in the NCI and maybe other organizations towards surgery and chemo. Am I remembering that correctly?

James Cox, MD
00:24:12.307
Well, at the NCI it's a bias primarily toward chemo because the cooperative groups were started to investigate leukemia.

Tacey Ann Rosolowski PhD
Oh, I see. Okay.

James Cox, MD
00:24:25.800
Since the vast majority of the physicians at NCI are medical oncologists and a handful—a small handful are surgeons, and an even smaller group are radiation oncologists, the view of the chemotherapy lobby, if you will, is vastly stronger.

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Tacey Ann Rosolowski, PhD
00:24:54.818
Were the sources of resistance to the treatment you were proposing in this study different, or did that come from the same bias?

James Cox, MD
00:25:17.001
They were different in one way. The RTOG didn't have an NCI approved actual committee on gynecologic cancer. There was a separate cooperative group—the gynecology, oncology group—that was doing those studies. And from the NCI perspective, all of those studies ought to be done by that group and not by the RTOG. I had to lobby very hard to get it started by the RTOG and even to get it continued because in the middle of all this, we had a once-every-five-year review. There was a chance that they would make us close down the study. But they didn't, fortunately. But it did require a lot of effort, both within the group and within NCI. It was highly successful. Another one that was done, which again, in this case, didn't involve a big survival advantage because, like the larynx study, you could do surgery afterwards, and it would help correct the failure. That was for cancer of the anal canal, and there the goal was to avoid colostomy. There was a separate trial in cancer of the nasopharynx where surgery doesn't come into the picture at all, but radiation therapy is quite effective. Perusing chemotherapy and radiation therapy at the same time led to a much better result with cancer of the nasopharynx. So we had all of these series of trials that were carried out—either started or came to fruition during the period that I chaired the group. A lot of them were published afterwards.

Tacey Ann Rosolowski, PhD
00:27:45.922
So this sounds like a really, really fruitful time for MD Anderson work, certainly.

James Cox, MD
00:27:52.749
It was. And the interesting part of that is going back to when I first came here, and the position I was in—vice president for patient care—I think I related to you that it turned out to be, from my view, not a very satisfactory position. The thing that kept me sane was the research efforts with the RTOG.

Tacey Ann Rosolowski, PhD
00:28:23.373
Now tell me about setting up the connections with these different researchers during that unsatisfying period when you were VP, but nonetheless obviously helping to forward these collaborations and careers of other MD Anderson faculty.

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James Cox, MD
00:28:44.469
Well it was generated from the radiation oncologists and the surgeons. The medical oncologists were not the primary players during that time in these studies.

Tacey Ann Rosolowski, PhD
00:29:09.513
Why do you think that was? Why do you think medical oncology was—

James Cox, MD
00:29:13.377
Well, they were involved, but they were not testing new drugs, so it was not of paramount interest to them. Their goal, by and large, is to test new drugs and try to see if they get better results. Sometimes the results are only measured in the shrinkage of a tumor, then to have it return rather quickly. Or, in patients that have widespread disease, to improve survival by a matter of weeks or a few months. So the endpoints for drug studies are very different than the endpoints for radiation studies. We do not consider response an important endpoint. Local control of the tumor within the field of irradiation becomes the primary endpoint for radiation studies.

Tacey Ann Rosolowski, PhD
00:30:33.715
So you were saying it was the radiation oncologists and the surgeons who were really the prime movers behind this. So who are some significant people that you (???)(inaudible, speaking at once) connections with.

James Cox, MD
00:30:47.082
Well in the head and neck arena, it was Dr. Ang—Kian Ang—and Helmuth Geopfert [Oral History Interview]. The collaboration has always been—well almost always—it depends on far back you want to go. But in recent years, there's always been a strong collaboration between the head and neck surgeons and the radiation oncologist. And so Geopfert was a champion with us along with Kian Ang, Moshe Maor. And then in the lung studies, it was Dr. [Wuan Ki] Hong [Oral History Interview] and as far as feeding into them, Dr. [Jack] Roth in surgery, and then Dr. [Ritsuko] Komaki. The three of them served as a resource for the implementation of these trials. There were a few other medical oncologists involved—Jin Soo Lee, who is now in a leadership position in a cancer center in South Korea. Then in the cervix area it was Patricia Eifel in radiation oncology and Mitch Morris who left the institution years ago to pursue a career. He was the gynecologic oncologist who was most involved with the cervix studies. In fact, the publication that came out, he was the first author. Then he went off in the field of information technology. That interested him. I don't think he ever practiced after that, but I don't know for sure. But he was very actively involved. And then—what else? Those were the main ones where

positions from MD Anderson were very actively involved in these studies.

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Chapter 10
A: The Researcher
Lung Cancer, Uncommon Lymphomas, and Other Cancers

Story Codes
A: The Researcher
C: Discovery and Success
C: Patients
C: Patients, Treatment, Survivors
C: Healing, Hope, and the Promise of Research
C: The Scientist at Work
A: Overview
A: Definitions, Explanations, Translations
B: Devices, Drugs, Procedures
D: Understanding Cancer, the History of Science, Cancer Research

Tacey Ann Rosolowski, PhD
00:33:30.279
When were you able to return to design your own studies or collaborate very closely in more than a facilitative role in doing studies?

James Cox, MD
00:33:41.994
When I returned to the full-time faculty in 1992. So after four years in the position of vice president for patient care and physician in chief, then I returned. And at that point, Dr. Peters—Lester Peters—who had the division at that time, needed somebody to succeed Dr. Fuller—Lillian Fuller in the lymphoma arena. I had a lot of interest and had done a lot of work in that area. So I became the lymphoma person for awhile.

Tacey Ann Rosolowski, PhD
00:34:35.107
And what did you do in the studies?

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James Cox, MD
00:34:37.721
Well, I worked very closely with Fernando Cabanillas and other colleagues in the lymphoma department. We designed some trials—and pathologists, there were pathologists as well—designed some trials to look at trying to see if radiation therapy or chemotherapy—one or the other, and we did a randomized comparison—were able to achieve a molecular complete response. The study that we were looking at had a translocation at two different chromosomes. It gave rise to a market that we could follow over time in these studies. So we pursued that for quite awhile.

Tacey Ann Rosolowski, PhD
00:35:51.250
So that sounds like—was the discovery of that marker really significant?

James Cox, MD
00:35:58.306
Well the discovery of the marker was done by—I'm trying to remember who discovered that translocation and that marker. One of the people—and I don't remember his name—was a guy who served as a consultant in the O.J. Simpson trial in California. He was a molecular biologist who—he was involved. But what we did, we had a colleague in pathology that had developed a way of expanding this marker—amplifying this marker—so that we could test patients to see whether they had it or not and to look at it following treatment. We'd look at it before treatment and then following treatment. So we did those studies for a while. And then—what else?

Tacey Ann Rosolowski, PhD
00:37:22.117
Do we need to pause?

James Cox, MD
No, let me see.

Tacey Ann Rosolowski, PhD
Okay.

James Cox, MD
Sorry.

Tacey Ann Rosolowski, PhD
That's all right. So the other areas of your work in lymphoma were—?

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James Cox, MD
00:37:47.695
Well we were looking at seeing about the role of radiation therapy and chemotherapy in uncommon lymphomas—lymphomas of the stomach, orbit, Waldeyer's ring—the ring around the pharynx. Small bowel—

Tacey Ann Rosolowski, PhD
00:38:20.088
What's the orbit?

James Cox, MD
Eyes. Where the eyes—

Tacey Ann Rosolowski, PhD
In the eyes. Okay. Uh-hunh (affirmative). And you said small bowel?

James Cox, MD
00:38:26.670
Small bowel, thyroid—these are all tumors that are not common. So to know what happened when we saw those patients—they didn't fit well in just calling them lymphomas because each one had a distinct natural history, and we were trying to tease out that natural history and also the response to treatment.

Tacey Ann Rosolowski, PhD
00:38:58.456
One of the things that's come up in a number of interviews is just the fact that given the critical mass of patients who come to MD Anderson, you actually have the opportunity to see unusual cancers.

James Cox, MD
That's right.

Tacey Ann Rosolowski, PhD
00:39:13.736
I'm curious, in this case with this study of the very unusual cancers with unusual natural histories, what did that help you understand about the diseases (???)(inaudible, speaking at once) in general?

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James Cox, MD
00:39:28.277
Well, I think one of the things it did was help not only us, but everybody in the lymphoma group to realize that each one of these was a distinct entity, that to lump them together—let's say as large-cell lymphoma, was not sufficient to understand the natural history and the way of solving the problem. An example that was—one of the more dramatic examples was testicular lymphoma, which occurs in men almost entirely over the age of sixty, whereas the other testicular tumors all occur very much earlier in life. It turned out that those tumors, although they spread to lymph nodes nearby, weren't the main problem. The main problem was that it spread to the central nervous system. It spread to the brain and the spinal cord, and you had to treat the entire cerebrospinal axis. So it led to our giving chemotherapy intrathecally inside the thecal sac. Along with chemotherapy—and it also led to giving radiation therapy, not to the regional lymph nodes, but to the opposite testis because that was another sanctuary area where the drugs didn't reach an adequate concentration, so we needed to treat the opposite testis to prevent the tumor from coming back.

Tacey Ann Rosolowski, PhD
00:41:29.030
And what were the results that you were able to get from that?

James Cox, MD
00:41:30.873
They were very much better. Those patients were rarely cured before adopting this approach. And afterwards—I don't know what the numbers are because I haven't stayed on top of it as it's evolved—but I think well over half the patients or more—the tumor was eliminated. Now these are older men, so the survival was not an endpoint that was easy to draw any conclusions, but being able to eliminate all evidence of disease was the goal there.

Tacey Ann Rosolowski, PhD
00:42:22.956
And obviously without surgery and preserving function—

James Co,x MD
Right—with no surgery. That was one example.

Tacey Ann Rosolowski, PhD
00:42:32.210
And the dates around the time that you were doing these unusual lymphomas?

James Cox, MD
00:42:38.289
I would say it was between about '92 or '93 up until about 2000.

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Tacey Ann Rosolowski, PhD
00:42:58.943
Of course this is important for historical record, but I'm also asking because one of the things that's really struck me as a non-specialist coming in and talking to all of you, is that it's starting to come clear to me how there was this huge shift in understanding cancer not as one monolithic entity, but actually as multiple diseases and then as a kind of moving target that can literally morph.

James Cox, MD
00:43:30.487
Well, even in something like lymphoma, where saying a patient has lymphoma doesn't tell me
anything. It's really what kind, how they present, it's all of these subtypes. And there are many, many subtypes of lymphoma that are very different. Now more and more they're characterizing them at the molecular level or at the cytogenetic level, and that is helping them find ways of at least categorizing them and then monitoring them. So increasingly to have the molecular or cytogenetic signature of these lymphomas helped a better understanding.

Tacey Ann Rosolowski. PhD
00:44:33.476
What was it like for you as a scientist who was trained pretty much in one way of seeing cancer, and then having the concept of the disease so radically altered?

James Cox, MD
00:44:46.027
Well, for me it wasn't a big deal because I—from the time of my pathology course in medical school, it was clear that cancer was not one disease—it was hundreds. And then when you got down to something more narrow like lymphoma, lymphomas were not one disease—they were maybe dozens. And cancer of the lung, more and more we're understanding is not one disease—it's different ones. The more we understand it at the molecular level, the more discrete entities we're able to come up with—and discrete treatments. So I think as time goes on, increasingly, instead of having the diagnosis rendered by the microscope, by light microscopy—
I don't think we'll do away with light microscopy, but I think it will be dependent upon the biochemical or molecular or cytogenetic findings that give the diagnosis.

Tacey Ann Rosolowski, PhD
00:46:16.729
What I was hearing as you were describing the very different natural histories of those unusual or rare cancers, lymphomas was the contour—it's starting to take shape of individualized therapy, personalized care and all of that.

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James Cox, MD
Uh-hunh (affirmative).

Tacey Ann Rosolowski, PhD
00:46:34.776
So it's just fascinating how that was evolving and being put together by all these different—

James Cox, MD
00:46:42.098
—and more and more. Obviously you know that it's moving in that direction towards individualized therapy and one of the areas that needs to be worked on much more, but there isn't funding readily available for it is the platform of local treatment with radiation therapy and molecular agents given at the same time.

Tacey Ann Rosolowski, PhD
00:47:22.775
What are some other significant studies that you were working on in the '90's and—I'm just continuing your research story.

James Cox, MD
00:47:33.862
Well it was interwoven between what I was doing here at MD Anderson and what I was doing at the RTOG because there was this big overlap. I was at Anderson—I would say all throughout the '90's I was doing one thing, mostly with lymphoma patients, and then at the end of the '90's, more with cancer of the lungs. And there it was designing trials, trying to look at altered fractionation plus chemotherapy for different types of cancer of the lung.

Tacey Ann Rosolowski, PhD
00:48:23.796
Maybe I should just ask you, what are the figures for lymphoma and lung cancer nationwide? Is it increasing? Is it decreasing?

James Cox, MD
00:48:36.891
Lung cancer is decreasing in frequency in men. I think it's still going up or plateauing in women. But the death rate for lung cancer is the highest in both men and women. Cancer of the lung kills more women than cancer of the breast.

Tacey Ann Rosolowski, PhD
00:49:09.274
And that's the highest death rate among all the cancers?

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James Cox, MD
Uh-hunh (affirmative).

Tacey Ann Rosolowski, PhD
Wow.

James Cox, MD
00:49:20.217
Right. Lymphoma, which was much lower on the list early, has been increasing in frequency slowly over the last couple decades. I don't know what the latest figures are, but it's been increasing.

Tacey Ann Rosolowski, PhD
00:49:45.622
Is there any sense about why that is?

James Cox, MD
00:49:48.665
There's a lot of speculations.

Tacey Ann Rosolowski, PhD
Are you willing to share some of those? (laughs)

James Cox, MD
00:49:54.339
Well, one, for example, is in the states where a lot of chemicals, primarily pesticides or similar kinds of chemicals, are used in the agricultural industry or in ranching and so on. Those states have had the highest increase in lymphomas, and one of the leading figures in lymphomas is from a bit of an unlikely place—Nebraska. Jim Armitage is recognized as one of the leading people in the country, but they see a lot of lymphoma patients in Nebraska, which doesn't have a very high population. (laughs)

Tacey Ann Rosolowski, PhD
00:51:09.621
Right. But those obviously have huge agricultural—

James Cox, MD
00:51:13.080
And so that's one connection. That's the main one that comes to mind for me.

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Tacey Ann Rosolowski, PhD
00:51:26.006
So in the early ’90s you focused on lymphoma and then later lung.

James Cox, MD
Uh-hunh (affirmative).

Tacey Ann Rosolowski, PhD
And what were—did you go through the significant—did the lung studies that you spoke about earlier cover what you were doing in the late ’90s?

James Cox, MD
00:51:43.016
No—I started out doing investigations in cancer of the lung, primarily these patterns of failure kinds of studies. But then I had very little to do with it except through the RTOG during the early ’90s. And then in the late ’90s I got very involved with the group here, and I’ve stayed involved with that group ever since with trying to put drugs together with radiation, some cases with surgery to try to achieve better results with cancer of the lung. I think we’ve made some modest progress, but not as much as I would like. As the chemotherapy gets better—we found this out with small-cell carcinoma of the lung—as the chemotherapy gets better, the local treatment becomes more important. That’s a bit counterintuitive because with small-cell carcinoma, it was so responsive to chemotherapy, they thought you didn’t need radiation therapy and did a series of studies and found out that you do.

Tacey Ann Rosolowski, PhD
00:53:17.174
What are the drugs that are used?

James Cox, MD
00:53:18.523
Primarily cisplatin—for small-cell carcinoma of the lung, primarily cisplatin and etoposide. For the non-small-cell—squamous and adenocarcinomas—well now they’re making a distinction, especially between those now—happily, something I’ve argued for, for a long time. Between adenocarcinoma and squamous, the main drugs are cisplatin and Paclitaxel for squamous and cisplatin and pemetrexed for adenocarcinomas. And then—it’s especially with the adenocarcinomas that you find these molecular abnormalities—EGFR, ALK, and drugs that can be used in patients with those abnormalities.

Tacey Ann Rosolowski, PhD
00:54:37.709
Were there some studies during this period and also during the lymphoma period that you were particularly excited about or surprised by?

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James Cox. MD
00:55:04.419
Surprised by—I don't know that there were studies in cancer of the lung that were particularly surprising. The combination of radiation therapy and chemotherapy for small-cell lung cancer was very gratifying—it was not surprising.

Tacey Ann Rosolowski, PhD
00:55:47.220
And the results there were—?

James Cox, MD
00:55:49.762
—were a lot better than they had been with the previous studies, but still they have a long way to go. With small-cell carcinoma, you could probably cure somewhere between a quarter and a third of the patients, but that leaves an awful lot of patients where there was a long way to go. And then the other area that we focused on—from the patterns of case studies—was looking at brain metastases, and finding that with small-cell carcinoma of the lung, the frequency of brain metastases was extremely high. If we gave very modest doses of radiation therapy to the brain when there was no obvious evidence of brain metastases, then that would decrease—greatly decrease the risk of brain metastases. Ultimately, when the large trials were done—and they were done jointly between institutions in Europe and the Unites States—it turned out that that so-called prophylactic cranial irradiation actually improved survival, which again was a surprise—not to me—but to a lot of my colleagues in medical oncology. They were very surprised. They thought that the irradiation of the brain carried a grave risk of neuropsychological problems. We studied that prospectively. Dr. Komaki was the lead person on that. Who did that neuropsychological study? I'm blanking on her name. They did it before and after and found that there wasn't very much effect from the brain irradiation. But the patients with small-cell carcinoma had abnormalities at the very beginning before any treatment, which was a new finding.

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Chapter 11
A: The Researcher
Documenting the Benefits of Proton Therapy

Story Codes
A: The Researcher
A: Overview
A: Definitions, Explanations, Translations
B: Devices, Drugs, Procedures
C: Healing, Hope, and the Promise of Research
C: Discovery and Success
D: On Research and Researchers

Tacey Ann Rosolowski, PhD
00:58:31.218
Uh-hunh (affirmative). Now when you said surprised or that you weren't surprised, it sounds to me that you weren't surprised because you really believe in the ability of radiation to do this. Am I interpreting that correctly?

James Cox MD
00:58:47.817
Well, I don't know if I believe it. I take it back, you're probably quite right. (laughter) I'm in a situation now—and you're going to want to come to that eventually—where proton therapy, because we can see the advantages on paper or in the computer, we can see that the dose distributions that avoid normal tissues have to decrease the risk of complications because it avoids the tissues where complications occur. But we don't have the evidence that people want and they're in a great hurry for—comparing protons versus x-rays.

Tacey Ann Rosolowski PhD
01:00:00.240
Uh-hunh (affirmative). Talk to me about what you are seeing on paper and on computer that creates these advantages.

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James Cox, MD
01:00:08.874
Well, you're seeing that you're able to spare normal structures. For lung we're able to spare the lung, the normal lung—and the heart and the esophagus better than we can with even the most sophisticated x-rays, which would be IMRT or intensity-modulated radiation therapy. Is that going to play out in the advantage of either reducing toxicity or improving tumor control? I think the main difference there is going to be a difference in survival because I think it's going to be a combination of controlling the tumor and avoiding toxic effects on the lung. But in head and neck, Steven Frank, one of my colleagues, is taking the lead in treating patients with cancer of the oropharynx—that's tonsil and base of tongue, mostly tonsil and base of tongue—tonsillar fossa and base of tongue, showing that by using protons with the scanning beam, he's able to avoid toxicity in the tongue. When they treat such patients with IMRT, they have to spread the dose out, so a lot of the dose goes into the oral cavity. That is incredibly adverse in terms of altering people's lives—interfering with the quality of life. He has shown with just a handful of patients—15 patients—that there's an ability to avoid that toxicity in the oral cavity that is very striking.

Tacey Ann Rosolowski, PhD
01:02:47.678
And his name again?

James Cox, MD
01:02:50.442
Steven Frank.

Tacey Ann Rosolowski, PhD
01:02:59.951
Thank you. What was the research that you did after the lung studies in the '90s or continuing with them into the 2000s that brought you to the interest in the proton center or in proton therapy?

James Cox, MD
01:03:13.022
Well, I'm not sure that the lung studies brought me into the interest in the proton center. Actually the study—that I didn't do, it was done by other people at MD Anderson—that shed the greatest light on showing the difference between the older kind of 2D treatment versus a 3-dimensional conformal therapy to a higher total dose showed that the patients who were treated to the higher total dose did better in terms of biochemical freedom from progression, and that was one of the earliest studies that showed that difference. Then it seemed obvious that by avoiding the normal structures that caused toxicity when treating cancer to the prostate and giving a higher dose, you can improve survival. Then on paper or in the computer, proton therapy is the ultimate way to do it—maybe not the ultimate way, but a way very different than anything that can be done with x-

rays because protons stop and can be made to stop wherever you want them to stop in the body. And so that was the genesis in my interest in proton therapy because I knew that in the future so much more could be done. And then, when we started developing the portfolio of clinical investigations for proton therapy, cancer of the lung was at the top of my list because I thought we could make a lot of progress there, and we have, but we don't have enough patients treated in comparison with IMRT that have been followed long enough to say anything.

Tacey Ann Rosolowski, PhD
01:05:59.605
How would you like to proceed next? Because obviously there's lots going on with the Proton Therapy Center and the research in the different studies, but I want to make sure that we fill in the blanks so that we know how you moved up to working with that. Do you feel we've covered the research that you've done prior to the Proton Center adequately? Or are there some other studies you'd like to mention?

James Cox, MD
01:06:34.993
Well, we could talk for a long time about all of those studies. I think we've covered it generally. It was a mix. If you look at the overlap if you were to try a Venn diagram, you would see the studies that were being done in the RTOG overlapping that were being done at MD Anderson. In lymphoma there was no overlap, but with lung there was a great deal of overlap. Then I got directed into studies also of cancer of the esophagus, which really is a story of putting all modalities together of the surgery and the radiation therapy and the chemotherapy—chemotherapy and radiation therapy being given at the beginning, and then following that was surgery.

Interview Session: 02
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Chapter 12
A: The Researcher
Multidisciplinary Conferences at MD Anderson Lead to More Effective Treatment Plans

Story Codes
B: Building/Transforming the Institution
B: Multi-disciplinary Approaches
B: Institutional Mission and Values
B: Institutional Processes
B: MD Anderson Culture
A: The Clinician
C: Patients
D: On Care

Tacey Ann Rosolowski, PhD
01:07:47.021
What were the discussions like with your collaborators in figuring out how to do this?

James Cox, MD
01:07:55.617
Well, we have a tumor board that's—we can call it a tumor board. We have a thoracic conference every Tuesday afternoon, and then they have a separate conference on cancer of the esophagus at noon on Tuesday, and discussions in those groups with the interested parties and the people who are actually treating the patients. Those kind of interchanges led to the efforts in that direction—and some efforts that were done really didn't make it very much effect. For example, induction chemotherapy turned out not to be very valuable. Chemoradiation is very valuable prior to surgery. But it's so effective, some have argued, "Well, do you need the surgery at all?" And in the past I would have argued, "Probably not." But the surgeons have become so good, and they can do that surgery, which is really, really big surgery, in a very sophisticated way and avoid most major complications—that having surgery, to me, as part of the equation is very compelling.

Tacey Ann Rosolowski, PhD
01:09:48.438
When did these weekly conferences start? Maybe I should ask, how did they start?

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James Cox, MD
01:09:58.804
Well no, the very earliest ones started in the early years of MD Anderson treatment. There were two groups—the gynecologic oncologist and the radiation oncologist. That was one. And the head and neck surgeons and the radiation oncologist, that was another. In both cases, the medical oncologist didn't play very much of a role. The thoracic conference started right around the time that we arrived, and it started—it was a joint effort between Dr. Hong, Dr. Roth, and Dr. Komaki.

Tacey Ann Rosolowski, PhD
01:10:54.650
And what was the logic for them?

James Cox, MD
01:10:58.971
There were two pieces that—many patients required at least two, if not all three disciplines involved. And secondly, and this was Dr. Roth's and Hong's strong push, that every patient ought to be on protocol; every possible patient should be on a study.

Tacey Ann Rosolowski, PhD
01:11:25.684
Did some people disagree with that?

James Cox, MD
01:11:33.274
There were some people who didn't care. They wouldn't object, but they weren't going to go out of their way to do it, but they were influenced by that conference. And whether it was Dr. Roth in surgery who—very, very highly respected person. The other surgeons in the department then, they couldn't really object to it very easily. The same thing is true with Dr. Hong. And the same thing is true with Dr. Komaki. Now, since that time, those kind of conferences have proliferated throughout the whole institution. There are ones dealing with brain and spine and sarcoma. The various GI sites—colon.

Tacey Ann Rosolowski, PhD
01:12:52.202
And what do they add to patient care and then also to the intellectual drivers of research?

James Cox, MD
01:13:01.796
They add a lot. To patient care, sometimes they help make a determination of the best way to treat the patient. And it evolves in a discussion. It's not obvious. We were, I guess, trying to figure out where to go next. Is that right?

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Tacey Ann Rosolowski, PhD
01:13:44.455
Well, I actually was hoping you would say a bit more about these conferences and what they added.

James Cox, MD
01:13:51.885
Oh the conferences, yeah.

Tacey Ann Rosolowski, PhD
Because you said that first of all it helped make a determination about the best way to treat patients.

James Cox, MD
01:13:59.290
And plus it helped support the clinical research activities of enrolling the patients on treatment. Plus, it was educational for everyone when we had some of the people who are expert—including the pathologist—who are expert in these molecular markers, in the biomarkers. That's something that is not discussed very much in the radiation oncology community here or nationally. But it was an ongoing education, and pretty much all—the medical oncologist, some more than others—Dr. Tsao, Anne Tsao, Vassiliki Papadimitrakopoulou, Merrill Kies—all of these people in the discussions about molecular abnormalities, and are there drugs that can be used that are directed toward them. All of that was a great education for the rest of us that attended the conference. So it had an educational, a patient care advantage, and then it had a clinical research advantage. So all of the conferences go in those directions.

Tacey Ann Rosolowski, PhD
01:15:35.251
Now is it self-selecting who attends those?

James Cox, MD
Yes.

Tacey Ann Rosolowski, PhD
Because I'm just—

James Cox, MD
It is.

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Tacey Ann Rosolowski, PhD
01:15:42.113
Yeah, as you were describing it, I'm thinking you really have to have an openness to be there. And would you say that those conferences attract a certain type?

James Cox, MD
Yes.

Tacey Ann Rosolowski, PhD
01:15:56.380
And how would you characterize that person?

James Cox, MD
01:15:58.799
Well they attract a certain type, and if you have an hour in the middle of the day or at the end of the day, somebody has to ask themselves, "Is it valuable to go to the conference or should I stay at my desk and get caught up on all the things that I have to do?" So there are a lot of people who never come, and there are some people who come most of the time, and there are a handful of people who are there all the time unless they're out of town. And the other advantage is that there's usually a pathologist and somebody from diagnostic imaging at each one of those conferences. So it's not just the treatment side, but it's also the path and the diagnostic imaging side. And all of that's educational too. I think I get a great deal out of going to those conferences. And I really encourage our residents to go to them, but they are now pretty much all over the institution and all of the major disease-site areas.

Tacey Ann Rosolowski, PhD
01:17:33.271
Do you think they've affected the culture of MD Anderson at all?

James Cox, MD
01:17:43.802
Yes.

Tacey Ann Rosolowski, PhD
How so?

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James Cox, MD
01:17:46.489
Well I think multidisciplinary care of the cancer patient is a hallmark of MD Anderson. It's not that it's not done other places, but it's not done as readily and willingly—it's not embraced with the same degree of commitment at other places than it is here. Now part of that is also the financial structure of MD Anderson, where all of the positions are salaried. So at these conferences, there's no economic incentive for somebody to recommend something other than that which is best for the patient. So doing something which is best for the patient, that has not only benefits for the patient, but it has benefits for the institution because then—I don't know how many thousands of times I've heard people want to go to MD Anderson because it's the best and they know that they're going to get the best care. And in many cases, they know they're going to have input from anybody that can help. I very frequently tell patients when I see them first, "We function as a team. We're a multidisciplinary team and we're going to call upon anybody at the institution to consult that would be an advantage for you as a patient." And they've come to—so that has become the culture. And that's a big change over the time when I first came here. Now the thing that's missing is that there's some groups—and we probably ought to talk about some of this off the record—(laughs)

Tacey Ann Rosolowski, PhD
01:20:10.665
Let me know when you want me to—

James Cox, MD
01:20:11.992
—but there are some groups that talk to themselves and have convinced themselves of something, but they're ignored nationally because they're just not considered—the work that they're doing is not considered cutting edge or broadly relevant or suitable for export into the community. And I can give you examples of that—but later. (laughs)

Tacey Ann Rosolowski, PhD
01:20:59.433
Understood. So I'm trying to get a sense of the balance or the evolution. When you arrived, how was the culture different from what you see now?

James Cox, MD
01:21:17.617
More frequently than today, the people in a discipline or in a disease-site area were talking just to each other. They were not even talking to the people outside the institution. Now with my coming, I brought the institution into the RTOG. That included the surgeons and the medical oncologist and, of course, colleagues in radiation oncology. I think that had a favorable effect on the institution. It really got the discussion of what they were doing much more broadly throughout the cancer world outside of MD Anderson.

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Tacey Ann Rosolowski, PhD
01:22:16.515
I can see why you see the RTOG and the work at MD Anderson as being part—

James Cox, MD
01:22:24.720
They're linked.

Tacey Ann Rosolowski, PhD
Yeah, they're very linked.

James Cox, MD
01:22:27.993
—very strongly linked. Now there are groups—there are a handful of positions that are involved with the Southwest Oncology Group. I think that's the only—oh, of course, the Gynecologic Oncology Group, the GOG. But now they're restructuring the cooperative groups at the National Cancer Institute level, and there are certain groups that are going to be forced to fit together. They don't necessarily include all of the groups that might be of greatest interest to the RTOG or MD Anderson. We'll have to see how that goes. It's in its early phase of development and it's very much a work in progress that it's hard to know if it's going to be at all successful.

Tacey Ann Rosolowski, PhD
01:23:49.187
Uh-hunh (affirmative). We're almost at noon and earlier you said you need—

James Cox, MD
Yeah, I'm going to have to go.

Tacey Ann Rosolowski, PhD
Okay. All right. Well thank you for your time today.

James Cox, MD
We're at a pretty good stopping point I think.

Tacey Ann Rosolowski, PhD
01:23:58.809
Okay. And I'm turning off the recorder at 12:00 noon.

James Cox, MD
Okay, great.

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(End of Audio 2)

THE UNIVERSITY OF TEXAS
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Making Cancer History®

James Cox, MD

Session 3— April 23, 2013

Chapter 00C
Interview Identifier

Tacey Ann Rosolowski, PhD
Let me just put an identifier on, and then we will be ready to roll. Okay—we are recording. And this is Tacey Ann Rosolowski, and today I am at the Proton Therapy Center for my third session with Dr. James Cox. Today is April 23, 2013, and the time is 10:31. So thanks Dr. Cox.

Interview Session: 03
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Chapter 13
B: Building the Institution
The Regional Care Centers and Sister Institutions

Story Codes
B: Beyond the Institution
B: Building/Transforming the Institution
B: Multi-disciplinary Approaches
D: Fiscal Realities in Healthcare
B: The MD Anderson Brand, Reputation
B: Institutional Mission and Values
B: Institutional Processes
B: Devices, Drugs, Procedures
B: Critical Perspectives on MD Anderson
C: Patients
B: MD Anderson History

Tacey Ann Rosolowski, PhD
01:30:10.551
And we were just talking about how today we are going to focus on your administrative roles, and you said you wanted to start at the end. So where would you like to start today?

James Cox, MD
00:00:27.185
Well I want to start at the end only because of the Banner component that I don't really think that I played any significant role in that.

Tacey Ann Rosolowski, PhD
00:00:36.641
Okay.

James Cox MD
00:00:40.121

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I initially had discussions with Dr. [Thomas W.] Burke [Oral History Interview] about the role that the head of radiation oncology might assume relative to Banner, but it was clear that that role which I envisioned as something similar to what we do in the regional care centers nearby was not going to be that way. It was going to be a role where we would not appoint a faculty. We would not have—I mean—ostensibly we would have control if they got into trouble, but—I mean—we would not really have control. And that has been the case. I hear almost nothing about them. Matt Callister, who is a trainee of ours, is heading the program there. He is a very, very good person. And aside from his visiting from time to time I have almost no interaction with him. Now it is possible—I think Dr. [Thomas A.] Buchholz has had more interaction after I left the division head position, but I don't identify that.

Tacey Ann Rosolowski, PhD
00:02:03.520
Well what was the relationship that you had envisioned and that you would have wanted to work for?

James Cox, MD
00:02:08.349
Well it would be the same one that we have with the regional care centers where each of those people at—at least the radiation oncology part of the regional care centers—are faculty members of ours. And so we are responsible for evaluating them. We expect regular interactions with them, and we are in charge of the quality assurance program with them. We started that—did we ever touch on how we started the regional therapy (both speaking at once)?

Tacey Ann Rosolowski, PhD
00:02:54.033
No. Not at all.

James Cox, MD
00:02:56.946
Okay. Well, I'm sorry to be going backwards then.

Tacey Ann Rosolowski, PhD
00:02:59.600
No—that's quite all right.

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James Cox, MD
00:03:05.619
Anyhow—there was an occasional discussion of MD Anderson doing something in the community, but it was just discussion. In 1998 or 1999 I became aware of two things simultaneously. One was that a former trainee of ours whom we all held in high regard was finishing her military obligation. She was stationed in—I think in Biloxi, Mississippi, and so she was wanting to come back to the Houston area. Her husband is a dentist, and they were wanting to return to the Houston area. At the same time we became aware of a facility in Bellaire that had—for lack of any other laborious description—had fallen on hard times. They had had difficulty staffing it. It had had—I think—problems with some results in patients that were not good—not satisfactory. And they were—the person who was leading that—a physicist—was interested in selling it. So we didn't sell it; we leased it. But that was the beginning of the entire regional care center program, and for many years the only activities in the regional care centers were radiation therapy. So when—and I was cautioned not to do that—that it was a mistake. It was a facility that had a bad reputation. It was going to tarnish the reputation of the institution, and I think by that time I had enough credibility with the senior leaders of the institution that they were willing to give us a chance to do it.

Tacey Ann Rosolowski, PhD
00:05:48.469
What was the need at the time for the regional care centers, particularly in radiation?

James Cox, MD
00:05:52.823
Well there were two needs. One is that the individual who was moving back to Houston was either going to be part of it or was going to be part of our competition.

Tacey Ann Rosolowski, PhD
00:06:05.073
Who was this individual?

James Cox. MD
00:06:08.848
Elizabeth Bloom. And she is still very active—not there anymore. And she is an outstanding person.

Tacey Ann Rosolowski, PhD00:06:16.472
Is that B-L-U-H-M?

James Cox, MD
00:06:18.769
B-L-O-O-M.

Tacey Ann Rosolowski, PhD
Okay. Thank you.

James Cox, MD
00:06:21.531
Liz took it on with enthusiasm and worked very hard, and we worked hard to bring the facility up to a presentable state to actually get new equipment put in there. In time it evolved in a way that made her happy and made us satisfied. And we were pleased with it (both speaking at once). Itt never built up to a very large number of patients, but it was successful.

Tacey Ann Rosolowski, PhD
00:07:06.059
What was the need from the patient care end?

James Cox, MD
00:07:08.589
Well, because patients often do not like to come to the Texas Medical Center. They find it confusing, intimidating, expensive, and if they can get their care closer to where they live and in a more comfortable, convenient environment as far as parking and things like that, they vastly prefer that. And it turned out that many of the patients that were treated there were actually seen in our multi-disciplinary care centers at MD Anderson—a program that involved radiation therapy was mapped out for them. And then they were given the option of being treated there. And some of them chose to be treated at the main center, and some of them chose to be treated there. And Liz did an excellent job. We did—we reviewed just as we do with every other patient—we reviewed—you know, a peer review of every patient that she treated. And she welcomed that, and it went very well. I wouldn't say it was without any bumps, but from a professional side it was quite smooth.

Tacey Ann Rosolowski, PhD
00:08:42.550
So is that peer review process—that is something that is done only with the development of treatment plans in the regional care centers? I am just trying to get—

James Cox, MD
00:08:52.347
No. It is done with every patient treated here.

Tacey Ann Rosolowski, PhD
00:08:54.306
With every patient (???)(inaudible)—oh wow.

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James Cox, MD
00:08:55.464
Every patient treated in our department has a peer review by other faculty members.

Tacey Ann Rosolowski, PhD
00:09:02.646
Wow. Wow.

James Cox, MD
00:09:03.698
And that is—I don't know if that is unique to MD Anderson—it probably isn't now, but it is something that has been true at MD Anderson for at least thirty years—maybe longer.

Tacey Ann Rosolowski, PhD
Wow.

James Cox, MD
00:09:19.489
And it is very valuable because suggestions are made that sometimes change the course of treatment for a patient or at least fine tune it so that subtle distinctions are picked up by various people, and recommendations are made, and they are followed through. We do it here—every patient that is treated at the Proton Center is—undergoes peer review.

Tacey Ann Rosolowski, PhD
00:09:56.006
And that seems like a really key piece for regional and satellite care centers for quality control.

James Cox, MD
00:10:03.103
It is.

Tacey Ann Rosolowski, PhD
00:10:05.162
Yeah. Is that something—was that kind of the gold standard for you?

James Cox, MD
Uh-hunh (affirmative).

Tacey Ann Rosolowski, PhD
00:10:09.902
I mean—that was absolutely essential?

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James Cox, MD
Yes.

Tacey Ann Rosolowski, PhD
Okay.

James Cox, MD
00:10:14.022
Yes. And then by invitation—we did not go seeking it out in the community—by invitation we established a relationship with St. Luke's Medical Center in the Woodlands, and then eventually I think it is CHRISTUS in Clear Lake and then I think another CHRISTUS facility in Katy. Then we had a brief stint at Fort Bend that did not work out well, and we went on to Sugar Land where we have a facility now with one and now—almost all of those places two faculty members.

Tacey Ann Rosolowski, PhD
00:11:08.433
Now what were the various lessons you learned in each of—setting up programs in each of those places?

James Cox, MD
00:11:19.956
It varied. There was generally enthusiasm on the part of the practitioners in the facilities, and they welcomed the presence of radiation therapy from MD Anderson, but there were certain things they didn't want to do. They did not want to have our pathologists involved or our diagnostic imaging people involved, and it took a long time to get over that. For Bellaire that was no issue, but in The Woodlands it was an issue, and it was a bigger issue as we went to Fort Bend. There were competitors in the community that really, really did not like us at all—in fact—in one case one of the competitors wanted to hire the radiation oncologist that we had at the facility and offered—I seemed to recall offered her more or less $1 million. We talked about it—she said no. But—I mean, it shows the degree to which there was competition in the community and not a uniform acceptance by any means. In some cases the people in the community established a radiation therapy facility quite close by for purposes of competition. But—anyhow—the tie-in with Anderson, the peer review, the quality of what we did in general has stood the test of time, and we are proud of it. Of course, it served as the basis for going into—then having medical oncology go into the same facility that first happened at Clear Lake, and it was very successful there. Having the laboratory go in there with the—able to obtain blood products and do blood tests. And then the pathologists were able to be involved. Some of that was facilitated by the electronic medical record. As it evolved it became easier to do those things in the community with the same record keeping approach and the same standard and everything that we have here.

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Tacey Ann Rosolowski, PhD
00:14:13.572
Was that originally part of the plan to have all of those services in the regional care centers?

James Cox, MD
00:14:19.965
No. I think it was only after we showed success in Bellaire that it sparked the interest of a couple people. The gynecologist who had moved into the community on their own in some ways, but soon after that, and then Dr. Burke wanted to see it develop that way. Sorry. So medical oncology was next; the last to come in were the surgeons. And now there are—I think there are surgeon jobs in all of those centers, mostly surgeons dealing with cancer of the breast. I would say there is a preponderance of treatment of cancer of the breast in those centers, but pretty much everything is treated.

Tacey Ann Rosolowski, PhD
00:15:37.532
And what is the value for—when I was talking to Leon Leach [Oral History Interview], he was talking about the regional care centers as a strategic kind of opportunity. How do you see the regional care centers serving MD Anderson—you know (both speaking at once).

James Cox, MD
00:15:51.065
Well—it's not so simple. It helps the patients. I mean, it's good for the patients in terms of their convenience. There are certain things that we do that it is difficult to do—that are difficult to do in the regional care centers, especially as it involves coordination of several specialties. I mean—concurrent chemotherapy and radiation therapy and surgery—it becomes more complicated. And that is especially true for cancer of the esophagus, lung, and head and neck. But the other thing is that it undoubtedly takes some patients away from MD Anderson that would otherwise come here to the main center. And the way the—I don't know quite how to say it—the way the attribution of financial benefit from those centers to MD Anderson is recognized—is not very satisfactory from my side. When we were overseeing the radiation therapy practices in these centers, we kept separate books on that. We knew exactly how many patients were treated. We knew what the income was, we knew what the expenses were, and we had control of it. Then it was taken over by the institution, and it all flowed into a black box. And we can keep track of what happens with radiation therapy at the regional care centers, but I don't know if any of the other disciplines do or not.

Tacey Ann Rosolowski, PhD
00:18:47.205
So how does it work? I mean the idea is that the regional care centers—the payment—does flow back to the institution, and then the institution decides what portion of that goes back to the regional care center. And how—?

James Cox, MD
00:18:59.875
Well—no—it's—they have their budget. They have to justify anything that they want or need. They have to justify an extra nurse. They don't have any control. The control comes from the institution, and the institution doesn't always see the same need that is seen at the regional care center, so there can be differences of opinion about what the needs are in the regional care centers. I think most of that has become ironed out, but at the beginning that was a big problem.

Tacey Ann Rosolowski, PhD
00:19:43.666
Were there some themes in what the administration didn't recognize as a need? You know part of their learning curve is how to do this.

James Cox, MD
00:19:54.593
They did not know what was important that was missing, and some of it may be obvious, but some of it was a hard sell to them. We could say we needed an extra clerk to have—to be there for the patients when they checked in at a certain time of day. They would say, "Well—why do you need that?" And you'd say, "Well, we need it because we need it." And they would say, "Well, why?" And to try to document in some laborious way why you need what those people working there felt was obvious. You know—there was a disconnect, and there may still be, I just do not see it any more. I think that has become smoothed out as there has sort of been a head administrative framework developed for the regional care centers with Peter Pisters as a surgeon being the person responsible ultimately for it and a very reasonable guy, and I think one that tries very hard to do the right thing. So I think as an intermediary who has spent a lot of time—as we say—in the trenches, it is not so hard to make a case to him for the needs at one center or another as it is to somebody who has never taken care of a patient.

Tacey Ann Rosolowski, PhD
00:21:54.076
Do you think that the regional care centers had a positive effect on MD Anderson's public profile?

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James Cox, MD
00:22:04.283
Yeah, I think they have. I think they have—certainly in the greater Houston area they have and in Albuquerque where we reached out the first time outside the state. It has had a very positive effect in Albuquerque. Now there are two other what might be called regional care centers, but they were there before any of the stuff that we started in 1999. One was in Orlando; one was in Madrid. Those were governed entirely locally, in some cases with a good business sense and in some cases like Madrid with a weak approach to business. Or—you know—I mean—it seemed weak to us. Plus, we had no quality control over what they did at all. We do now a little bit more in Orlando—we have some people who go there and review patients already treated, but it is not a prospective review. We don't have any of that in Madrid. And I don't know to what extent we have that at Banner. I mean—maybe I should know, but I just don't. So I dare say in my view Banner has developed more in the direction of the Orlando/Madrid model than it has the similar approach to what we have done with these regional centers around Houston, and quality control and control of the faculty—and that also means control of physics support. We think it is critical, and that is done in a consistent way in the regional care centers around Houston. That is not done in any consistent way in Madrid. Again—it is better now in Orlando as it's evolved over the last few years. So it has all started out with the discussion of Banner because I wanted to disavow any knowledge of Banner, but then one of the administrative things that I was heavily involved with was the early years of the development of the regional care centers.

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Chapter 14
A: The Administrator
Head of the Department and Division of Radiation Oncology

Story Codes
A: The Administrator
C: Professional Practice
C: The Professional at Work
B: Building/Transforming the Institution
A: Definitions, Explanations, Translations
D: Technology and R&D

Tacey Ann Rosolowski, PhD
00:25:24.364
And this was—this was after you were department chair (both speaking at once)—this is when you were division head?

James Cox, MD
00:25:30.660
Yeah. Now a department chair and division head were one and the same when I took over in—

Tacey Ann Rosolowski, PhD
00:25:40.004
'95?

James Cox, MD
00:25:43.418
'95. And they stayed linked until, I believe, 2007.

Tacey Ann Rosolowski, PhD
00:25:54.925
That is what I have down here, and then the title changed.

James Cox, MD
00:25:58.274
And then there was a separate department chair and a separate division head.
Tacey Ann Rosolowski, PhD
00:26:03.888
So there was a restructuring of the department at that time? Was there?

James Cox, MD
00:26:11.896
No. There was a dividing up of work.

Tacey Ann Rosolowski, PhD
00:26:18.590
Oh—okay. So how did that all work? What was the change?

James Cox, MD
00:26:20.717
I mean a lot of—the heavy load that falls upon the department chair and the person who shared both titles was evaluation of faculty, and that—you know—there is a requirement that the faculty are evaluated annually, and that forms are filled out, and questions are answered about have they done this and what—what contributions have they made and so on. And then that evaluation is supposed to match up with any recommendations for merit increases. In a more complicated way it is supposed to match up with how people use their time. In other words, are they spending only twenty percent of their time doing academic activities or are they more heavily involved in research that they are doing maybe in a laboratory in which case it may be a fifty/fifty designation. There are a very small number of individuals who spend twenty percent of their time clinical and eighty percent of their time in the lab, but those are specifically designated within the institution as physician-scientists. So there are only a few of those in radiation oncology, I think maybe four or five.

Tacey Ann Rosolowski, PhD
00:28:17.968
So what was the scope of your—well—tell me how you came to become department chair in ’95.

James Cox, MD
00:28:26.580
They were linked together. They were just—it was one job—department chair and division head (both speaking at once).

Tacey Ann Rosolowski, PhD
00:28:33.182
Okay. So it was simply just a more limited title at that point. So what was the scope of your responsibilities?

James Cox, MD
00:28:42.867
Well—you know—in that position you did everything.

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Tacey Ann Rosolowski, PhD
00:28:46.858
Yeah. How big was the department in ’95?

James Cox, MD
00:28:48.842
In 1995 there were seventeen faculty. I think there were probably fifteen full-time physicists. There was only a pretty small symmetry group. The symmetrists are sort of a bridge between the physicists and the physicians. So—well, there were things that we did and not necessarily in chronological order, but in an order of some importance we expanded the faculty as we expanded the number of patients that we were treating. And we expanded the number of patients we were treating in part to keep up with the expansion and other disciplines in surgery and medical oncology throughout the institution. In doing that and recruiting the right people and having them in the right place and governing all that because we are so highly specialized that people who take care of patients with cancer of the prostate never treat a patient with cancer of the breast. And people who take care of patients with cancer in the head and neck do not treat patients with cancer of the lung even though it is a few centimeters away. So we are super specialized, and getting the right people into those right specialization areas is a challenge both for recruitment and retention.

Tacey Ann Rosolowski, PhD
00:31:02.778
When you say the right people—what were you looking for?

James Cox, MD
00:31:07.120
Well you are looking for people who are interested in that area who will make a contribution who have expressed some strategies or goals that would make them contribute in a favorable way to the group. And rarely—I don’t know if I should say rarely—infrequently has the role of one entirely of taking care of patients. The goal is to have academic interests, academic accomplishments and to evaluate faculty on the basis of those accomplishments as well as the patient care.

Tacey Ann Rosolowski, PhD
00:32:08.084
What did you envision for the department and division when you took over in ’95?

James Cox, MD
00:32:14.106
Well, the other thing that was lacking was that it was technologically pretty much out of date. And so approaches to equipment—new equipment, new—

Tacey Ann Rosolowski, PhD
00:32:36.549
Why was there—why was it out of date? Why hadn't there been a commitment to keeping up?

James Cox, MD
00:32:42.560
Well, I'm not sure I can answer that for certain. I believe it was the interest of my predecessor as department chair and division head that his interest was primarily in the laboratory, and I think he took pretty good care of what went on in the laboratory, but I think he was less interested in the breadth of activities in a clinical domain. And so—and at the same time the same was true—I guess—in physics. So it was a—there needed to be some changes in those areas. I mean—Dr. [Lester] Peters left and went back to Australia. Dr. [Ken] Hogstrum and I were together for a while. He was not as open to that movement of technology as I was hoping to see.

Tacey Ann Rosolowski, PhD
00:34:01.398
What was going on in technology that you wanted to grab hold of?

James Cox, MD
00:34:06.062
Well—for example—we didn't have modern computer systems for treatment planning. They had a home-grown system that they were sort of married to, but there were commercial systems now becoming available that were much more sophisticated, and that other people in the community and private practice in the community had these systems and were able to do things that we were not able to do.

Tacey Ann Rosolowski, PhD
00:34:36.530
What does a system like that do?

James Cox, MD
00:34:39.089
It stores the characteristics of the beams that you have. You know—if you have an accelerator and it has got two photon beams and 6 electron beams—those beam characteristics are measured and stored in the computer. And then you capture—and that was the other thing that was missing—we did not have a CT simulator, so we were using old fashioned simulation. And so we needed to get CT simulators to use which then that information could be put into the computer, and it could be planned in three dimensions. So we went from doing two-dimensional treatment to three-dimensional treatment at virtually every site—some earlier than others. And then as time went on and the field moved forward, we went from the three-dimensional planning which was based on CT and MR—those two major approaches, and then that combined with the computer-assisted treatment planning systems or the computerized treatment planning systems, and with that was the development of a much more sophisticated dosimetry program. We developed a dosimetry school, and for the first couple of years we could train the dosimetrists, but they did not want to stay and work here.

Tacey Ann Rosolowski, PhD
00:36:54.158
Why didn't they?

James Cox, MD
00:36:56.210
Well—I don't know. I guess the work environment was not as comfortable as they would like, but—so that changed over time.

Tacey Ann Rosolowski, PhD
00:37:07.872
Now is the dosimetry school still in existence?

James Cox, MD
00:37:10.770
Oh yeah.

Tacey Ann Rosolowski, PhD
I had no idea.

James Cox, MD
00:37:12.217
It is very vigorous.

Tacey Ann Rosolowski, PhD
Wow.

James Cox, MD
00:37:15.515
I've forgotten how many students there are—probably fifteen maybe. We have a therapy school and a dosimetry school, and they are both excellent, and the people who are trained are in very high demand.

Tacey Ann Rosolowski, PhD
00:37:34.229
And these are all things that were started when you were division head?

James Cox, MD
00:37:37.695
The therapy school was already there, but the dosimetry school was not. And so it was started—I recruited—actually Robin Famiglietti, who is now the division administrator who came and started the therapy school, started the therapy program, expanded it greatly, did a wonderful job in developing it, and now it is a gem of the department or division.

Tacey Ann Rosolowski, PhD
00:38:17.392
Were there other technological initiatives—technologies available that you brought to MD Anderson?

James Cox, MD
00:38:25.137
Well—I mean—those—I think those were the major ones. There were similar kinds of technological developments in the area of brachytherapy—that is where you put sources in the body—but probably the major ones were computerized dosimetries so that we could go from 2-D to 3-D, and then the imaging that fit into that kind of dosimetry. And then as time went on we went on to intensity-modulated radiation therapy, which was another more sophisticated way of planning and delivery, and it was dependent upon getting new accelerators that had the capability of delivering IMRT.

Tacey Ann Rosolowski, PhD
00:39:28.444
What does that mean—intensity-modulated?

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James Cox, MD
00:39:32.169
It means that you can target a tumor and deliver unequal doses with the beams that come in from various different directions, often five to nine different directions, and they sum in a way so that it gives a high-dose to the tumor, but it avoids the nearby normal tissues. And it is now our preferred way of treating—I would say the majority of patients that we treat with curative intent in any site—maybe not every site. But like in head and neck it is the only way we do it now.

Tacey Ann Rosolowski, PhD
00:40:18.719
It sounds like it has a similar function to the proton therapy in that it can target and not (both speaking at once)—

James Cox, MD
00:40:24.954
Yeah. It does. It does.

Tacey Ann Rosolowski, PhD
00:40:27.980
Yeah—go into healthy tissues.

James Cox, MD
00:40:30.117
Yes. It does. And, in fact, it was a challenge on the part of some of the people who were doing so well with IMRT—especially our head and neck team—were doing so well with IMRT that they didn't have any interest in protons. Now that has changed or at least is in the process of changing so that now some of the areas that are treated under the title or rubric of head and neck are now being treated only—well not only but preferentially with protons.

Tacey Ann Rosolowski, PhD
00:41:15.359
Tell me about some of the kind of key moments of change or growth in the division when you were head.

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James Cox, MD
00:41:24.994
I'm not sure there were moments so much as it was a continuum. I probably—I think that probably the first thing that changed was an approach to buying equipment. There were those who felt that it was good to have different kinds of equipment from different vendors because there were research opportunities. This was among the physicists. I didn't agree with that, and I had some problems with the physicists on that because if we had equipment that replicated each other—if one piece of equipment went down and we could change over and patients would never lose a treatment, and we evolved in that direction. So there was a change there. And then the equipment itself evolved, and we sort of kept up with what were the latest capabilities that the equipment itself provided like these multi-leaf collimators where you could shape the beam with devices inside the head of the linear accelerator, and that is especially important for IMRT. And so you got accelerators that had that. And then there were others that had imaging devices attached to the accelerators. We used to call it OBI—on-board imaging, but now pretty much every accelerator has on-board imaging, so we don't talk about it anymore. It's just part of what an accelerator does because we set up the patients with imaging before we treat them. So all of this was in evolution, but I think changing the approach to buying accelerators was a big change early on, changing the approach to dosimetry systems was a pretty big change, and some of the physicists bought into that, and some didn't at the beginning because they were interested in their own research area that involved that. A lesson there that the institution is learning now is that you can develop something within your department or within your institution, and it is not only state of the art it is ahead of state of the art. But then companies come along, and they can devote absolutely everything that they do to developing the same thing, and it can quickly go beyond what our department can do or what the institution can do. And so now that's coming up with the electronic medical record. They are going to change the electronic medical record from what we have now to a commercial system sooner or later. I am not sure exactly when that is going to take place. So that was very much true for the treatment planning systems also.

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Chapter 15
B: An Institutional Unit
The Division of Radiation Oncology

Story Codes
B: Controversy
B: Institutional Politics
A: Obstacles, Challenges
B: Building/Transforming the Institution
B: Multi-disciplinary Approaches
B: Growth and/or Change
C: Leadership

Tacey Ann Rosolowski, PhD
00:45:23.064
I wanted to ask you—it is the second time you mentioned that the physicists—there was kind of a communication gap there or a disconnect—do you want to talk more about that in the department?

James Cox, MD
00:45:44.027
Well it is a delicate area. I mean—the fact of the matter is that the head of physics at that time and I did not see eye to eye with where we needed to go, and I eventually realized that I couldn't get to where we wanted to go with him.

Tacey Ann Rosolowski, PhD
00:46:07.845
What were the differences in opinion—viewpoint?

James Cox, MD
00:46:11.240
It was more—it was more an almost full-time concentration on education as the main part of what a physicist should do rather than patient care and research. That was the main difference. And certainly there's nothing that I have against education. I think it's terribly important, but it could not be at the expense of everything else. So I think that was the most fundamental thing. And then there was the business of equipment and wanting to move into new equipment, and there was—just a hesitancy to do that, and we just weren't moving.

Tacey Ann Rosolowski, PhD
00:47:09.294
Who was the person who was head of radiation and physics at the time?

James Cox, MD
00:47:12.722
Ken Hogstrom.

Tacey Ann Rosolowski, PhD
00:47:16.999
And so how did you resolve that? Get around it?

James Cox, MD
00:47:20.822
I got rid of him. That is why I am a little hesitant—because when I got rid of him there were other people who were personally very tied to him that left. So we had a real changeover of the physics group. Some stayed and continued to make a really important contribution, some very talented people left. And we brought in Radhe Mohan who was the—had been the head of clinical physics at Memorial Sloan Kettering and then the head of the department of physics what is now called Virginia Commonwealth Institution—Virginia Commonwealth University—then it was called the Medical College of Virginia. When Radhe came he was very much on the same wavelength that I was as far as developing both the clinical or the technological aspects about the department and the research portfolio of the department. So we went from having no externally funded research to several million dollars' worth of externally funded grants, and that's not counting contributions from companies that wanted us to do certain kinds of research with them.

Tacey Ann Rosolowski, PhD
00:49:31.035
Now when you said the research portfolio, what was in that portfolio? What did you envision as sort of an idea balance?

James Cox, MD
00:49:39.219
Well I envisioned—I didn't necessarily have a goal of a certain kind of research, and it has taken several forms. The idea of having people spend a significant portion of their time working in new areas where they could apply for grants to the National Cancer Institute or the Department of Defense or the Department of Energy where it would be peer-reviewed and externally funded—I think that was an important goal that we achieved, and Dr. Mohan deserves a lot of credit for that. In the process, he brushed up against some people in the division. And—you know—it wasn't entirely smooth, but in general things went in a very positive direction. Administratively—my approach—whether it is with residents or faculty or even department heads—and there are of course two other departments in the division besides radiation oncology. There is experimental radiation oncology and radiation physics. So my approach has been to hire good people, not tell them what to do, but support the ideas and directions that they want to go,

and I think that leads to happier, more productive individuals, although sometimes it can lead off into tangents. And if we have reviews of the activities, eventually that gets sort of corrected with time. And it gets corrected by peer-review. I mean external reviewers.

Tacey Ann Rosolowski, PhD
00:52:19.314
How did you develop that kind of leadership or administrative approach?

James Cox, MD
00:52:25.053
Pretty much that has been my approach all along from the beginning. When I was at the Medical College of Wisconsin I was recruiting people, and there were several things that I liked to do myself in terms of clinical activities—take care of patients with head and neck cancer, with cancer of the prostate, with lymphomas. Well, in order to recruit people that I wanted I had to give that up to them, and I often sort of kept a hand in and was sort of involved with it, but I had to give that up. And ultimately about the only thing that was left that nobody wanted was cancer of the lung. So I ended up working in that area. And one of my colleagues twenty-five years ago said, "You are wasting your time doing research on cancer of the lung because it's just hopeless, and you're not going to get anywhere, and it's just going to bury you." So—anyhow—it did not, but I—that has been my approach. Sometimes selecting the people has not been correct, although I think my sense of evaluation of people is pretty good. And I have few regrets—a few—but I have relatively few regrets about the people that I have recruited, and the people who are here now I think are fabulous (both speaking at once).

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Chapter 16
B: An Institutional Unit
The Division of Radiation Oncology—Strategic Planning and Growth

Story Codes
B: Building/Transforming the Institution
B: Multi-disciplinary Approaches
B: Growth and/or Change
B: Institutional Processes
B: MD Anderson Culture
C: Leadership

James Cox, MD
00:54:38.581
So, anyhow, we went from seventeen full-time faculty and by the time I—let's see from '97 let's say to 2007 when we split the division department into a separate department and a separate division, and obviously they are not separate, but we had over fifty faculty.

Tacey Ann Rosolowski, PhD
That's amazing.

James Cox, MD
00:55:16.789
We had gone from treating 240 patients a day in '97 to treating about 600 patients a day now with absolutely advanced technology and still with peer-review.

Tacey Ann Rosolowski, PhD
00:55:43.366
What has that represented for the institution?

James Cox, MD
00:55:59.056
By and large they have been happy. We have made a lot of money for them. They have been supportive, and I think probably I have made—and the people that I've hired that have worked with me closely have made reasonable estimates of what we were going to do, let's say, in planning a budget, and we have been pretty accurate in doing that. So we have maintained a high level of credibility in terms of our planning.

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Tacey Ann Rosolowski, PhD
00:56:48.689
What kind of revenue stream are we talking about here? What kind of money does the division of radiation (both speaking at once)?

James Cox, MD
00:57:01.228
Right now I am not entirely sure. I think from the technical side—that is to say that which flows to the institution as opposed to PRS—gosh I don't know—it's been so long since I've looked at the figures with a high level of interest that I want to say in general the whole portfolio is of the order of—maybe $250 million or more.

Tacey Ann Rosolowski, PhD
00:58:04.862
I was asking because in one of the articles that I read for background research the author was saying that you were interested in looking at strategic planning issues with the division. And so I was—

James Cox, MD
We did that regularly.

Tacey Ann Rosolowski, PhD
00:58:17.187
So how did that work? And with what result?

James Cox, MD
00:58:20.726
Well—we got people together once a year, and we set aside a certain amount of time to look at various components that included our educational program that included research, and the research of course included ERO physics as well as the clinical department. In the clinical department there were people doing research that was actually in the laboratory, but they were clinicians doing research in the lab.

Tacey Ann Rosolowski, PhD
00:59:13.518
What were the strategic planning goals?

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James Cox, MD
00:59:16.906
They differed each year. I mean we developed—we had a meeting one time in the midst of this where somebody from outside of the institutions challenged—what is your goal? And I said, "It's to be the best, it's to have the best division or department of radiation oncology in the world—bar none." And I think we have done it. So in each area it was how can we enhance what we are doing? Accepting the fact that we are doing really well here, how can we make it better? Don't rest on your laurels—think about how you can move forward in a more positive direction. Now it is true in every part of the division. There is another piece of it—and I may have mentioned this before in other context—and this is not part of strategic planning, although it underlies strategic planning. We wanted to have a department that is absolutely as supportive as it possibly could be for the people who work within it, so something that I have said frequently is absolutely our top priority in everything we do is the patient. Nothing gets in the way of that. And if you do strategic planning with some goals, the goals have to point in that direction, but second only to the patients is taking care of each other. I have emphasized that over and over again, and I think that has become part of the culture I believe.

Tacey Ann Rosolowski, PhD
01:01:59.862
What are some things that you did or fostered to create a supportive environment?

James Cox, MD
01:02:07.885
I have very little patience for people who are trying to intimidate each other. And that is true among the residents, it is true with the faculty, it is true throughout the entire department, so occasionally there would be people who would sort of—in one way or another—put unnecessary or inappropriate pressures on other people. You might say brow beat them. And I just—I would talk with them and say, "Just don't do it." Now I would not do it in public, and so a lot of times they wouldn't know I had even done it, and the other people wouldn't know. They might complain to me and say, "Why haven't you done something about this?" And I would say, "But I have." And sometimes it was not obvious for a while. So that was one major thing, and it included faculty.

Tacey Ann Rosolowski, PhD
01:03:31.139
Well, in general I think the people who are hired at MD Anderson are pretty high intensity independent people.

James Cox, MD
01:03:39.190
Yeah. They are.

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Tacey Ann Rosolowsk,i PhD
01:03:40.729
And that must create some unusual challenges of getting people to work together, leaderships—you know—is that something you have found?

James Cox, MD
01:03:50.317
Well, I think if people enjoy doing what they're doing, if they are working in a supportive environment, then to be able to transmit that to the components that they are responsible for—you know—the other parts of the department and even within the institution because—I mean—we know many circumstances where people in other divisions were really, really unhappy with the leadership and really unhappy with the way things were done within their section. And sometimes the solutions were really obvious to me, but of course it wasn't my division so what could I do? On rare, rare occasions I went to John Mendelsohn about it, but not on any kind of routine basis.

Tacey Ann Rosolowski, PhD
01:05:10.844
Is there anything else you would like to say about your time as division head?

James Cox, MD
01:05:19.856
You know there is a publication, and I have forgotten was the occasion is, but Robin Famiglietti—do you know Robin?

Tacey Ann Rosolowski, PhD
01:05:41.991
Uh-hunh (negative). I'll just pause here.
James Cox, MD
01:05:44.322
Yeah. I think so. So Robin would have the publication. They did—and I cannot remember what the occasion was. I guess maybe it was we started doing an annual report, and I think maybe the first one that was done was more than an annual report. And I suspected this was in—I think it was after we separated the departments, so I think it was probably somewhere between 2007 and 2009. But there was an annual report, and I think it documents what happened over time so that there are numbers put to the things that I have told you about how the division changed.

Tacey Ann Rosolowski, PhD
01:06:51.731
I didn't ask you why the departments were separated in the way that they were.

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James Cox, MD
01:07:01.345
That is a funny story. Well one—the amount of work to be done just got to be too great. At the same time you were trying—needing to do everything in regard to the faculty and to make sure people were doing what they needed to as far as taking care of patients. And then there was the issue of recruiting a new head of experimental radiation oncology and a new head of physics when Dr. [Radhe] Mohan stepped down as chair. So there were a lot of things to be done on the division head side as well as the department chair side. Plus the reality is that there was—in my mind—a natural successor, and that was Tom Buchholz, and he was being recruited away to another institution. And so I decided to separate it at that time, and then they would launch a national search, which they had to do. This was with the blessing of the president of course. They would have a national search with the hope that Dr. Buchholz would be selected, although there was another fine candidate from the outside—or actually who had been here before and who is in another state—they were finalists. And anyhow Buchholz was chosen through the usual search process—not a quick process—it took a year. But he knew he was a candidate, hopes that he could have that job, and he and I have a very close working relationship, and I have tried to be a mentor to him in many ways. And so it was in no small part a way of trying to keep him, and that was sort of decided at the time when he was getting stronger overtures from other institutions. At that same time it was happening in other divisions. They were separating the head of the division from the head of the department whether it was in pathology, diagnostic imaging, medical oncology, so there was ample precedent for it.

Tacey Ann Rosolowski, PhD
01:10:31.864
Was there an impact on how resources were allocated? Space? All of that? I'm just curious what effect it had.

James Cox, MD
01:10:40.907
Not a whole lot. There was not a whole lot of impact there. The impact had to do with sharing decision making, having some resources that previously had come to me as department chair that were already designated in that way by PRS—how PRS funds float. But it was more decision making, but it was also recruitment. He took a major role in recruiting the faculty. So it worked out well, and once he was well-established it made good sense for me to step down from that position, although now he's got this situation of being department chair and division head, which is not a comfortable situation, but with the sort of economic situation at the moment I don't think that is going to change right now.

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Chapter 17
B: An Institutional Unit
The Story of the Proton Therapy Center

Story Codes
A: Overview
A: Definitions, Explanations, Translations
A: The Researcher
A: The Clinician
B: Building/Transforming the Institution
B: Multi-disciplinary Approaches
B: Growth and/or Change
B: Obstacles, Challenges
B: The Business of MD Anderson
C: Discovery and Success
B: MD Anderson Mission and Values
D: Technology and R&D
B: Devices, Drugs, Procedures
B: Industry Partnerships
B: Beyond the Institution

Tacey Ann Rosolowski, PhD
01:12:09.510
Right. Right. Would you like to talk about the Proton Therapy Center now?

James Cox, MD
01:12:13.273
Sure.

Tacey Ann Rosolowski, PhD
01:12:15.514
How it all got started and—.

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James Cox, MD
01:12:21.493
As we evolved—as I described to you earlier. Technologically going from 2-D treatment planning and delivery to 3-D treatment planning and delivery to IMRT—it became abundantly clear just as you suggested that we could do a better and better job avoiding normal tissues and concentrating the beam on the tumor. And, in principle, the best way to do that is with protons because they can be made to stop, you can shape the proton beam so that it conforms to the tumor, and so it seemed obvious that was the logical next step. And there were a couple other facilities in the U.S. that were hospital-based, so—

Tacey Ann Rosolowski, PhD
01:13:46.168
When was this idea born really?

James Cox, MD
01:13:48.512
It was born around 1998 or less, and we went and talked to Dr. Mendelsohn who in turn talked to people at the University of Texas system, and we looked at what it would cost in a sort of global sense. And they said that sounds like a great idea—we are not going to spend the money to do that. It would—taking on that additional debt would mess up our bond rating, which is hallowed to them. So with the help of Mr. Leach, Dan Fontaine, and at that time the person who was very important—Mitch Latinkic, who was our division administrator—but primarily led by Leon and Dan. We looked for another way of getting funding, and the idea of developing a public/private partnership was born in those discussions, and we put out a request for proposal and had more than one proposal.

Tacey Ann Rosolowski, PhD
01:15:34.199
Can I stop you just for a second? I want to ask you what was it that convinced you and enabled you to convince John Mendelsohn and Leon Leach and (both speaking at once).

James Cox, MD
01:15:43.067
It was the results—it was the results that we were seeing as we went from 2-D to 3-D—even 2-D to 3-D.

Tacey Ann Rosolowski, PhD
01:15:55.684
So could you describe those results?

James Cox, MD
01:15:57.724
Well we were able to give higher doses and still not have higher side effects with the normal tissues, and we did a randomized study here in cancer of the prostate, and it showed that we could give higher doses and have a better result from that—a higher rate of freedom from progression.

Tacey Ann Rosolowski, PhD
01:16:28.103
So was the decision—I mean—I'm just wanting to make sure I get this correct—was the decision to embrace the proton therapy based on studies done with IMT or there were studies available from proton therapy that—

James Cox, MD
01:16:45.720
No—no. Studies were not available for proton therapy (both speaking at once). There were some studies available that showed the safety of using proton therapy, and those studies were done in physics research laboratories, but enough patients were treated—probably 40,000 or 50,000 patients were treated in those physics laboratories that showed that it was safe and that it worked and that you could spare the normal tissues, and it really had a big effect in some areas, especially children.

Tacey Ann Rosolowski, PhD
01:17:35.106
But the technology was pretty new so—there wasn't—

James Cox, MD
01:17:40.042
Oh the technology was very new. In these other places it had been developed in their facility—Mass General—it was developed at Mass General. They had treated patients at the heart and cyclotron laboratory—the physics laboratory for years, but they were going to take on placing proton capability at Massachusetts General Hospital, and Loma Linda University had started treating patients in 1991 with proton therapy. It hadn't published; they were not a very academic crew. But what we knew of what they had done was very favorable.

Tacey Ann Rosolowski, PhD
01:18:45.417
So what else did—I mean—just as sort of the background piece, because I know—I mean—Leon Leach and John Mendelsohn certainly would not have gotten on board with this if it hadn't—there had not been something very compelling in terms of what it offered for patient care, but then on the other side something compelling of what it would offer the institution financially.

James Cox MD
01:19:06.098
I don't think they were looking at it from the point of view of what it would offer the institution financially. I mean—they were looking at it as a resource to—they didn't want to lose money, but they were looking at it as a resource for the care of patients, and I think—if you asked others I am pretty sure they would say that it was the credibility that I had both with John [Mendelsohn] and with Leon [Leach] and Dan [Fontaine] that if I said that this would do this, and that this was a right thing to do, they would believe me. And they studied enough on it to—you know—to understand what I was talking about. But basically I think they believed what I said, and that was enough to move forward.

Tacey Ann Rosolowski, PhD
01:20:10.288
So you were talking about that process of creating that public/private partnership.

James Cox, MD
01:20:14.414
Right. So that was led by (both speaking at once)—that was led by Leon, who did a wonderful job. Leon and Dan especially, but the final thing on this was that it was Leon's. And developing the public/private partnership, and the private part of it was a joint enterprise between Sanders, Morris, Harris, the investment banking company, and The Styles Company, which had been—had a history of building and running healthcare facilities over many years. So they put together a proposal, they said that they would raise the money, that they had the knowledge to build the facility, and so we developed that partnership with them. Then it was a matter of finding who the—you know—who the vendor was going to be or what the company was going to be that would provide the proton source if you will. And that turned out to be Hitachi. And we looked at many others. We looked at the one that was involved with Loma Linda. We looked at the one in Belgium, which is Ion Beam Associates—IBA—and we visited them. And we visited Tsukuba University in Japan where Hitachi had built from scratch a proton facility, and it was seeing that and knowing the depth of Hitachi's capability. I don't know how many hundreds of billion dollar company with engineering capability, which is just enormous, and we worked out a proposal from them. It was not easy because of the difference in business cultures, but actually that is where my wife's role came in because she played a very important role in bridging with the Japanese.

Tacey Ann Rosolowski, PhD
01:22:52.092
And your wife's name?

James Cox, MD
01:22:53.803
Ritsuko Komaki—Dr. Komaki—K-O-M-A-K-I. She was absolutely instrumental in getting this. It turned out that one of the key people in Hitachi—actually the president of the company within Hitachi that was responsible for proton therapy, had been a high school classmate of hers.

Tacey Ann Rosolowski, PhD
Oh—how funny.

James Cox, MD
In Hiroshima.

Tacey Ann Rosolowski, PhD
01:23:28.838
It is a small world.

James Cox, MD
01:23:30.557
And—you know—again—it was the credibility that she had and through her that I had with him that made it possible. Otherwise, I think it would have fallen through.

Tacey Ann Rosolowski, PhD
01:23:48.662
What were some of the issues that were coming up to make the negotiations difficult?

James Cox, MD
01:23:51.879
The people who were negotiating from Hitachi and the United States couldn't say yes to anything; they could only say no, and they needed somebody to tell them that it was okay to say yes. The people from our side were exceedingly legalistic. They wanted penalties if you didn't reach this milestone or that milestone or so on, and that wasn't the way they were used to doing business in Japan. You know—it was not the matter of talking about penalties; it was saying if you said you were going to do something, you would do it, and not doing it was a matter of losing face, and that was driving them more than anything else here. The people here didn't understand anything about the idea of losing face. They wanted it all spelled out on paper that if you did not do this you would have to pay them that, though we finally got over all of that, signed the contracts in December of 2002 in Houston, and—

Tacey Ann Rosolowski, PhD
01:25:18.393
I have got this lawn mower coming back and forth.

James Cox, MD
01:25:24.043
That does not help you at all, does it.

Tacey Ann Rosolowski, PhD
Well he is looking like he is almost done. They could probably filter some of it out.

James Cox, MD
01:25:34.851
Then from that point on it was an intense thing with our physics team working together with Hitachi's engineers and physicists to describe exactly what we wanted in it—what capability we wanted in the unit here.

Tacey Ann Rosolowski, PhD
01:25:57.371
Because this was a complete custom build? I mean—(both speaking at once).

James Cox, MD
01:26:00.608
Oh yes.

Tacey Ann Rosolowski, PhD
Yeah.

James Cox, MD
Totally.

Tacey Ann Rosolowski, PhD
Yeah.

James Cox, MD
01:26:01.940
Well—it was not complete—I mean there was a very credible example at Tsukuba University, but we were asking capabilities of them that were not part of that.

Tacey Ann Rosolowski, PhD
01:26:17.166
And what did you—what were you asking?

James Cox, MD
01:26:19.023
We were asking for one thing—we were asking for what is called a pencil beam or scanning beam where you can sort of aim the proton beam into the tumor, and you did not have to have any devices to shape the beam or anything like that.

Tacey Ann Rosolowski, PhD
01:26:40.182
Interesting. Was that done manually or—?

James Cox, MD
01:26:41.563
No—by magnets.

Tacey Ann Rosolowski, PhD
By magnets. I see.

James Cox, MD
01:26:45.099
It avoided your having to do—put in these devices manually, which you did with the other—with passage scattering, which is what we call the other way of giving proton therapy where we have a proton beam that is broadened, and then you have to shape it with brass pieces and then with acrylic pieces that sort of partially absorb the protons so that it ends up with a distribution in depth that looks like the tumor.

Tacey Ann Rosolowski, PhD
01:27:20.441
Interesting.

James Cox, MD
01:27:21.811
But with the scanning beam you do not need those devices, but it is a very sophisticated thing, and there was no commercial vendor that had that.

Tacey Ann Rosolowski, PhD
01:27:33.597
Was that the main feature you were asking for, or were there others?

James Cox, MD
01:27:36.828
Well it was one of them.

Tacey Ann Rosolowski, PhD.
01:27:38.137
What were the others?

James Cox, MD
01:27:39.952
Oh—dose rates and sort of automation of various components.

Tacey Ann Rosolowski, PhD
01:27:53.466
Now how does it work? I mean—can you only—how many patients can you have receiving these beams at once?

James Cox, MD
01:28:00.693
You can only have one patient at a time.

Tacey Ann Rosolowski, PhD
01:28:02.148
Oh really?

James Cox, MD
01:28:02.148
We have four rooms. One patient being treated, and during that time the other patients are being set up, but then you have to switch from room to room because there is only one synchrotron, and it is producing beam all the time, but it is being extracted and sent into one room and then into another room with various energies. So the switching of energies had to be electronic, and the changing from one room to another had to be—it all had to be based on a computer that Hitachi had. But then we had two other computer systems, and therein lies part of the bumps in the road that we ran into. One was the treatment planning system where you had the beam characteristics stored as we talked about earlier—beam characteristics stored in the computer, and then we captured the CT images of the patient, and then the dosimetrists and physicists and physicians put together a plan to avoid normal tissues and to have a high dose at the tumor. So I mean—and the third computer was the record and verify system—the electronic record, and they were all produced by different manufacturers, and they all had to talk nicely to each other. And it took a lot of give and take before that happened.

Tacey Ann Rosolowski, PhD
01:30:03.330
It is always in the details.

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James Cox, MD
01:30:05.725
Right.

Tacey Ann Rosolowski, PhD
Yeah. So—

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Chapter 18
B: An Institutional Unit
Research at the Proton Therapy Center; the Future

Story Codes
A: Overview
A: Definitions, Explanations, Translations
A: The Researcher
A: The Clinician
B: Building/Transforming the Institution
B: Multi-disciplinary Approaches
B: Growth and/or Change
B: Obstacles, Challenges
B: The Business of MD Anderson
C: Discovery and Success
D: Technology and R&D
B: Devices, Drugs, Procedures
B: Beyond the Institution
B: Controversy
D: Understanding Cancer, the History of Science, Cancer Research
D: The History of Health Care, Patient Care
C: Patients
C: Discovery and Success

James Cox, MD
01:30:10.551
So we ramped up. We started in the—started building in May of 2003 and treated our first patients in May of 2006. We have now treated approximately 4,400 patients, and we have treated over 1,000 with the scanning beam. And still there is hardly—you know—there are only a handful of patients that have been treated with this scanning beam any other place.

Tacey Ann Rosolowski, PhD
01:30:52.173
So I assume—I mean are all of the patients—or the majority of patients who are receiving treatment involved in some sort of study?

James Cox, MD
01:31:01.408
Uh-hunh (affirmative). Yes.

Tacey Ann Rosolowski, PhD
And what kind of studies are you doing?

James Cox, MD
01:31:04.794
There are several. One is in—basically they are studies of trying to increase the dose or deliver the same dose to the tumor while sparing normal tissues and documenting the degree to which you are sparing normal tissues. So we have a master protocol that takes all of those patients into account, and then we have discrete specific protocols for various components. We are doing the only studies comparing proton therapy and IMRT. We have a protocol that we started in 2008 that is nearing its completion that is for non-small cell lung cancer, and then we have a relatively recent protocol within the last year or so comparing IMRT and protons for cancer of the esophagus, and then we have a new protocol—a new protocol that is being developed for the RTOG, which is also asking that same question—protons versus IMRT.

Tacey Ann Rosolowski, PhD
01:33:04.365
So this is still—since the number of patients is still pretty small, these must be fairly small studies.

James Cox, MD
01:33:10.398
Right. They are. I mean—

Tacey Ann Rosolowski, PhD
Are these all MD Anderson-based or are you collaborating?

James Cox, MD
01:33:14.220
The one with—the only randomized study the IMRT versus protons that is in conjunction with Massachusetts General Hospital. And then there are some other small studies with Mass General that involve radiating the liver, children—various tumors in children, and the base of the skull.

Tacey Ann Rosolowski, PhD
01:33:54.625
How long do you think—well—what is—is there a controversy right now about the value of proton therapy?

James Cox, MD
01:34:02.557
Oh yeah. Big.

Tacey Ann Rosolowski, PhD
01:34:03.923
And what is that based on? What is the conversation about?

James Cox, MD
01:34:11.215
Well—turn your recorder off and let me—

[The recorder is paused.]

Tacey Ann Rosolowski, PhD
01:34:16.593
All right. So we are recording again.

James Cox, MD

I think there are several reasons why people object to proton therapy. There is one group of people who are anti-technology. My wife, Ritsuko, ran into one in India when she was there at a meeting. A guy from England who simply said it is unnecessary, but then he said—you know—and IMRT is unnecessary, and he went on and on. Apparently none of the current technology seemed to be worth anything to him. So—okay—I mean if you are starting from that point I do not have much to say. There is another group that says, "Well—it looks good on paper in the computer, but how do we know it is real?" Well—we make actual measurements—our physicists make actual measurements for every patient before any treatment is given, so we know it is real. Plus we have examples of human dosimetry that have shown that it is also real. And so that does not hold water, although—again—there are people who believed that, and in this whole thing there is a lot of belief. Now the one thing that they can say which is accurate and is not believed is that proton therapy has never been shown in a prospective randomized trial to be better than x-ray therapy. And they are right. I mean—we are doing those studies now, and people have not done them before, and eventually those studies will be done and completed. But—and those are kind of purists, but they are right; there has not been any demonstration with prospective randomized comparisons.

Tacey Ann Rosolowski, PhD
01:37:23.118
What are the preliminary findings from the studies that are being run now?

James Cox, MD
01:37:27.106
Well—we are having fewer side effects.

Tacey Ann Rosolowski, PhD
01:37:32.792
Is that the main area of benefit? Or are there—?

James Cox, MD
01:37:35.621
Well, in some cases we are giving higher doses and still having fewer side effects, and we think that that will translate into better tumor control, and the side effects are—you know—especially important for children. I mean—my gosh—if you radiate any structure in a child—any growing structure—and all tissues in children are growing by and large—you run the risk of damage that is permanent and progressive. So anyhow those are the main—oh—and there is a third argument or fourth argument—whatever it is—that says okay, we understand in principle the value, but there are too many uncertainties in the physics and the dose distribution and the accuracy and all of this—too many uncertainties to be able to adopt this at this time. Now hiding behind that in many cases is a viewpoint that we are either not ever going to have proton therapy, or it is going to be so many years that we are going to have to be using x-rays for a very long time. And so there is the naysayer from the point of view of we won't be able to have that. And—again—it has made it difficult in several areas. It has made it difficult to have papers accepted in journals because one or another reviewer may come at it from any one of those directions that says—you know—this is just not true or not valuable, and it has been a surprise because people who say, "Well—we need data," and then you go to publish data and they do not want to accept the data, and the data is never perfect. I mean—it is always more fragmentary and incomplete than you would like it to be. But in the meantime the body of data will build if there are publications that can be looked at. So—anyhow.

Tacey Ann Rosolowski, PhD
01:41:14.930
That is surprising. Yeah. So what do you foresee in the future for the research and for the Proton Therapy Center?

James Cox, MD
01:41:25.110
Well, I think—the Proton Therapy Center here is being very successful. One of our main goals was to expand the indications for proton therapy beyond those that had been already investigated in the physics research facilities years ago—expand into other areas where protons would be valuable. And this could be in the head and neck, in the brain, of course children, in the abdomen where it is not used very much, possibly in the pancreas, certainly for the liver, and maybe for the rectum. So I think proton therapy is going to establish a place for the treatment of many diseases or many stages of disease so that it will possibly occupy as much as maybe twenty percent of all the patients that are treated with radiation therapy. It is not going to ever be close to one hundred percent. So—and I think there is enough recognition of that value throughout the world now that it is just—you know—the development of proton centers is going very rapidly.

Tacey Ann Rosolowski, PhD
01:43:24.831
So how do you determine which patients will receive proton therapy?

James Cox, MD
01:43:29.785
Well, one are these sort of protocols that we have developed where we have thought ahead which patients would—for which patients it would be valuable. And that is brain, children, lung, head and neck, esophagus, and with this we know what specific normal tissues we are trying to avoid, what side effects we are trying to avoid, and that is the goal. And we also know that there are some types of patients that we are not ever going to treat with protons. We are not going to do total-body radiation. We are not going to do whole-breast radiation in place of mastectomy. We're just not. And we are not going to use it by and large for just palliative care. It's not that we will never use it for symptom relief, but by and large it is to be used to treat patients with curative intent. If it's to be used for palliative care, it's to give a very high dose in an area where they are surrounding normal tissues that are really worrisome.

Tacey Ann Rosolowski, PhD
01:45:25.501
So do you see the center expanding, or how do you—where do you see it going?

James Cox, MD
01:45:30.187
Oh I think it will—I think it will stay pretty much the way it is probably for another year or two because there needs to be upgrades of certain things. Hitachi has made further developments as they have developed facilities for other institutions, so they have made progress in areas that we are interested in. We can do a better job of combining imaging with the proton therapy, which we do not have the best imaging in the room that we would like to have, and so we need to get that developed. But there are plans and a way to do that. So I think it will continue to develop and—

Tacey Ann Rosolowski, PhD
01:46:29.281
Now, in terms of the relationship of this center with other departments and services at MD Anderson, do you find that you work well with people—identifying patients of theirs that might be—

James Cox, MD
01:46:44.177
Yeah.

Tacey Ann Rosolowski, PhD
01:46:45.854
And so that communication process has been pretty smooth?

James Cox, MD
01:46:48.226
In general that has been quite favorable. We have not had—yeah—that has been quite favorable.

Tacey Ann Rosolowski, PhD
01:47:00.605
And I'm sure that will help a lot in feeding patients into your study—

James Cox, MD
01:47:08.629
Oh—it does.

Tacey Ann Rosolowski, PhD
Right.

James Cox, MD
It does help a lot.

Tacey Ann Rosolowski, PhD
Yeah. Is there anything else that you would like to say about—

James Cox, MD
01:47:12.033
Where we have not had great success is recognition in the regional care centers of the value of proton therapy, so we get very few referrals from the regional care centers.

Tacey Ann Rosolowski, PhD
01:47:25.517
What do you think that's about?

James Cox, MD
01:47:26.572
I don't know.

Tacey Ann Rosolowski, PhD
01:47:29.976
That's interesting.

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James Cox, MD
01:47:32.489
I don't have a good explanation for that. We have one person in Clear Lake who sends us patients—not high volume—but sends us patients on a regular basis, but she is the only one.

Tacey Ann Rosolowski, PhD
01:47:54.733
Who knows—that is interesting. Is there anything else you would like to say about the Proton Therapy Center? Or the process of developing it (both speaking at once)?

James Cox, MD
01:48:05.286
You know—I think it's been—well what has happened over the past few years is that the original investors have pulled out there—the financial commitments to them have been completed. I don't know what the financial breakdown of the various components of support for the Proton Center, but it is my understanding that there are Chinese investors that are involved in the last year, and there are—and MD Anderson now owns actually the majority. I mean—it has—I think it has fifty-one percent interest, and I believe that was bought out from Hitachi. So I think it is going okay. I think it is maybe not—we are not treating as many patients as they would like to see, but I think that will fluctuate over time.

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Chapter 19
B: Key MD Anderson Figures
The MD Anderson Presidents

Story Codes
B: Critical Perspectives on MD Anderson
C: Portraits
A: Personal Background
B: MD Anderson in the Future

Tacey Ann Rosolowski, PhD
01:49:33.710
I wanted to ask you some questions about relationships with the different presidents since you have worked with three of them now, and I know you were brought in by Charles LeMaistre [Oral History Interview] and was wondering if you could talk about him as an administrator—a leader—your working relationship with him. I know you had some questions and issues.

James Cox, MD
01:50:09.618
You know—in something like this I don't know what I should say because—

Tacey Ann Rosolowski, PhD
01:50:15.074
Well—the way I look at it is not so much telling tales out of school, but really an evaluation. You know—like what could have been done better, what was done okay—that kind of thing.

James Cox, MD
01:50:27.885
I think—as I have summarized it—and I think even to you—I came in with what seemed to be a great title that turned out to be a bad job. And the reason it was a bad job is that the division heads—the division heads felt I had a responsibility to them. I thought coming in that I had more of a responsibility to—that I was not limited by my responsibility to them.

Tacey Ann Rosolowski, PhD
01:51:28.092
And just for the recorder (both speaking at once)—
James Cox, MD
That it was more of a—that it was more of a leadership position than a management position, and it turned out to be purely a management position. And if the division heads did not like a decision that I would make, they would turn around and go to Dr. LeMaistre, and he did not dissuade them.

Tacey Ann Rosolowski, PhD
01:51:51.127
And just for the recorder I will say you are speaking about your period as vice president of patient care.

James Cox, MD
01:51:55.847
Yes.

Tacey Ann Rosolowski, PhD
Yeah.

James Cox, MD
01:51:57.222
Entirely. And then as time went on—you know—it became clear that we had a different orientation. He—actually LeMaistre was interested in issues that were related to the University of Texas system. I think he was proud to be president of MD Anderson. I think it served him from the point of view of posture within the community. I don't think that he really fully understood what was going on within the institution. Now, in fairness I will say that having come from the outside and having spent four years in that position of vice president for patient care, I did not fully understand what was happening throughout the institution until I went back to taking care of patients within MD Anderson and essentially was side-by-side with the people who were caring for patients in every division—pathology and diagnostic imaging—and only then did I understand what MD Anderson was all about.

Tacey Ann Rosolowski, PhD
01:53:44.182
Why do you think it's that way, that you can't get that view from an administrative position?

James Cox, MD
01:54:05.671
Dr. LeMaistre was not a cancer person. He did not come from a background where his primary specialization was with cancer. He was a pulmonary medicine physician. He had political clout in the arena of dangers of smoking. And the other people—you know—the other—the chief financial officer—the other people around Dr. LeMaistre were not physicians. And so—and the physicians that related to Dr. LeMaistre wanted something from him. The division heads wanted him to bless what they were doing. So it's hard to know within any institution if, in fact, you don't know what you don't know. Now, I mean, I can go anywhere and explain what is happening at MD Anderson, where its strengths and weaknesses are and what—and why I think it is a great place to work, and after I left that position of vice president for patient care I had

many opportunities to go other places—sorry—it is partly—it's maybe talking and partly it is I have got allergies.

Tacey Ann Rosolowski, PhD
01:56:08.589
It has been a rough season for them.

James Cox, MD
01:56:16.088
But—so I think it is hard. So after I left the position of vice president for patient care and was taking care of patients and working with the residents and working with the faculty within our own division—you know—I just came to appreciate the institution very well. I think at that time the institution was on the verge of greatness but was not there, and one of the reasons why they were on the verge of greatness but had not arrived at it is they spent too much time talking to themselves. So if you are in a big place, especially with some specialization, and if people are talking to themselves all the time and convincing themselves that the conclusions that they have come to about how to care for patients, about what the research shows so on and so forth, convincing themselves that they are right but are ignoring the rest of the world of cancer treatment—cancer research and cancer treatment outside it is easy to become limited. It is easy to be living in a silo.

Tacey Ann Rosolowski, PhD
01:58:12.711
Interesting.

James Cox, MD
01:58:17.963
And what I said to others during the time I was in that VP position was—well, and of course I was involved in the RTOG at the same time. I said you have got—you really have got people in other places, and I got some of them to come to the RTOG meetings and they became involved. I got some of them to come to the RTOG meetings, and they had a terrible time, and I think we talked about that, but I think the interplay between what was going on here and what was going on nationally became expanded quite a lot, and as it became expanded the institution became appreciated more and more and more. And then of course there were some high-profile people who came here or were benefactors, and that was good, and there were a lot of people who came here having gone either to Johns Hopkins or Mayo Clinic or Memorial in New York and then came here and said—you know—this is just a different place. The whole atmosphere is different. The whole approach to taking care of patients is different.

Tacey Ann Rosolowski, PhD
01:59:56.374
What were they identifying as being so unique?

James Cox, MD
02:00:04.663
The feelings of support of everybody within the institution for them and what they needed. So if they were wandering down the hall looking a little bit lost, somebody would come up to them and say, "Can I help you?" and in some cases would take them to where they needed to be, and that just did not happen in those other places. And that—to some degree that is a bit of Texas or Houston or southern hospitality, but it is a mindset that is very favorable in terms of caring for patients, and people are very impressed with that, and they should be.

Tacey Ann Rosolowski, PhD
02:00:58.975
What about John Mendelsohn [Oral History Interview] and your relationship with him?

James Cox, MD
02:01:05.140
I have always had an excellent relationship with John. I mean—he is a good, outstanding scientist, a real student of what is going on within the institution, or at least he was in the first many years. And I think because of that he had a great deal of credibility with most people within the institution. As I said in a meeting the other day, there are always within the faculty or the alumni or let's say the retirees—there are always a certain number of bomb throwers, and there always will be. So I think, notwithstanding the problems that he had with the bomb throwers, I think most people viewed him and continue to view him with great respect and an appreciation for him as a scientist. Maybe—maybe listening a little too closely to certain elements of people within the institution, and thereby not getting a broad enough view. And I think he was open to the broader view, but I think just on a personal basis he would get input from some people who gave him the view that served them well, which is not surprising—I mean—it happens to the President of the United States I am sure.

Tacey Ann Rosolowski, PhD
02:03:38.059
Right. Sure. What about Dr. [Ronald] DePinho?

James Cox, MD
02:03:40.234
Well I have not had nearly as much interaction with him. I mean he is an—I think he is an outstanding scientist. I think he is a visionary. I think he looks to change things in a major way, and I admire that. I appreciate a little bit the problems of working in the same institution with your spouse who is strong-willed, but I think she is a terrific scientist too. And I think—you know—they are a very good—wonderful addition to the institution.

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Tacey Ann Rosolowski, PhD
02:04:31.827
What are some of the issues that have come up for you with a spouse being employed at the same institution?

James Cox, MD
02:04:31.827
Oh—there have not been very many because actually I remember one time we were in clinic several years ago and somebody said to me, "I just learned that you are married to Dr. Komaki." I said, "Yes." They said, "Is that—we have been working together for five years, and I never knew that." So I think the majority of people have had that experience. There were—there was at least one person who really was anxious to do harm to us, but eventually that element disappeared, and so generally we have not had any difficulties. We have not been in the same kind of limelight that Dr. DePinho has and Lynda Chin.

Tacey Ann Rosolowski, PhD
02:06:03.040
What is your prognosis for the Moon Shots Program?

James Cox, MD
02:06:14.170
Well—on a positive note they are bringing together people and galvanizing them to try to arrive at creative solutions that have not previously been fully considered. Do I have any expectation that it's going to eliminate any of the forms of cancer at which it is aimed? No. It's not. So it will do—it will have a lot of benefit for interdisciplinary science, and that is good—team science—that is good. It will not achieve a grand goal. I remember it was Andy von Eschenbach—he first went into the position as head of the National Cancer Institute many years ago and had said we are going to cure cancer by 2015, and obviously we are not, and so I think the prognosis for the Moon Shots Program in that regard is pretty much the same. Cancer is too complicated, and it's too many diseases, and it's too fundamental, and I don't think we are going to do away with it. It is like doing away with inflammation. I don't think we will ever do away with inflammation or doing away with the degenerative diseases. You just cannot, but will we be able to help and do positive things? Yes.

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Chapter 20
A: View on Career and Accomplishments
Contributions to MD Anderson

Story Codes
A: Contributions
A: Activities Outside Institution
A: Career and Accomplishments
B: The MD Anderson Brand, Reputation
A: The Researcher
B: Institutional Mission and Values
C: Portraits
C: Personal Reflections on MD Anderson

Tacey Ann Rosolowski, PhD
02:08:32.908
I am aware that we are running over, so I wanted to ask you just a couple final questions. First of all, is there anything else that you would like to add about your experience at MD Anderson, your contributions?

James Cox, MD
02:09:00.225
I am a realist. I have done a lot at Anderson, and I have done a lot of which I am very proud of. On the other hand, when I have gone as one of the annual meet the professors at our national meeting and they are all residents sitting around a table—residents who are not from MD Anderson, and so I ask them, "So who was Gilbert Fletcher?" They don't know. "Who was Juan del Regado?" They don't know. "Who was Henry Kaplan?" Maybe one out of the whole group will have heard his name but will not know anything about him. So like those before me for whom I have great admiration that which I have done will disappear into the institution and hopefully become a part of its fabric, but it will not be identified with me.

Tacey Ann Rosolowski, PhD
02:10:34.532
What are some of those things that you are really glad you have accomplished?

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James Cox, MD
02:10:39.786
Well, I think I have spurred a lot of clinical research in the right direction through cooperative groups and also through the individual research approaches that we have taken. And there are those—my colleagues—we are involved in translational research, and I have not done any of the laboratory part of that, but I have been key to what has happened in the clinical part of it whether it's with the RTOG, whether it's with cancer of the lung or lymphomas or any of the disease-side areas in which I have been involved, but the main things I have accomplished in the research arena have been in clinical research, and the things in clinical research are what contributes to the care of patients. I mean—those are more immediate. They are perhaps not as revered scientifically as discrete pieces of research that will appear in the *Journal of Science* next month, but they have a beneficial effect on patients, and when you come right down to it that is where my heart is. And administratively I think I have—I think I have helped foster the collaboration with other divisions, other departments with very few exceptions so that I and my colleagues have a very comfortable working relationship in the multi-disciplinary realm. And going back historically, when Fletcher was the head of the division, through the force of his personality and what he accomplished clinically, he set a high standard for the role of and view of radiation oncology within MD Anderson. I believe I have contributed to maintaining that stature of radiation oncology within MD Anderson, and by and large I think that differs from any other cancer center in the world. So those are the things of which I am proud.

Tacey Ann Rosolowski, PhD
02:14:31.205
Is there anything else that you would like to add?

James Cox, MD
02:14:35.395
I think that is enough (laughter). That is probably a good place to stop.

Tacey Ann Rosolowski, PhD
02:14:40.090
All right, Dr. Cox. Well, thank you very much for taking the time to do these sessions. I really do appreciate it.

James Cox, MD
02:14:44.508
My pleasure.

Tacey Ann Rosolowski, PhD
I am turning off the recorder at 12:51.

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James Cox, MD
Oh my.

(end of audio)