Medical Physics Navigator for Clinical Trials

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Medical Physics Navigator for Clinical Trials

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Disclosures

• Timothy Ritter: Therapeutic medical physicist at Virginia Commonwealth University and the Department of Veterans Affairs. Perform work under AHRQ grant 1R01HS026486-01.

• Paige Taylor: Therapeutic medical physicist; NIH funding, grant CA180803.

• Shruti Jolly: Professor at the University of Michigan. On the advisory boards for Varian and AstraZeneca; salary support from Blue Cross Blue Shield of Michigan (MROQC).
Session Learning Objectives

• Distinguish the different types of clinical trials, identify their important elements, and identify key personnel involved in trial success.

• Understand the steps involved in clinical trial credentialing.

• Identify how medical physicists can contribute to clinical trials.
Outline

1. Trial Overview
2. Medical Physics Roles
3. Trial Organizations
4. Trial Credentialing
5. Physician Perspective
A Little History

- One of the first clinical trials looked at scurvy, a vitamin C deficiency that devastated sailors.
- James Lind, a Scottish Physician, studied citrus fruits as a cure.
- 12 sailors were divided into six groups of two men each.
- The “two oranges and one lemon” arm showed significant improvement after a 6 day trial (then the fruit ran out!).
- “A Treatise of the Scurvy” (1753) was published and then ignored.

For more information: https://www.medpagetoday.com/blogs/revolutionandrevelation/74568
Purpose of Clinical Trials

“Clinical trials are research studies performed in people that are aimed at evaluating a medical, surgical, or behavioral intervention. They are the primary way that researchers find out if a new treatment, like a new drug or diet or medical device (for example, a pacemaker) is safe and effective in people. Often a clinical trial is used to learn if a new treatment is more effective and/or has less harmful side effects than the standard treatment.”

From https://www.nia.nih.gov/health/what-are-clinical-trials-and-studies
Major Elements of Clinical Trials

- A primary clinical endpoint (e.g. “five year disease free survival”)
- Sufficiently powered sample size determined by statistical analysis
- Randomization of the intervention when applicable (esp. Phase III)
  - Institutional Review Board approval and oversight
    - Informed consent from all participants
  - Meticulous data collection and monitoring
    - Monitoring for adverse events
  - A detailed written protocol
Clinical trials look at safety and effectiveness.

How do we do this ethically?
A Little More History

- 10 principles of human research were outlined in the **Nuremberg Code** of 1947, a response to Nazi medical atrocities.

- The **Nuremberg Code** led to the **Declaration of Helsinki** in 1964.

- The **Belmont Report** was authored by a special U.S. commission for the protection of human subjects in 1979.

- The **Belmont Report** establishes three fundamental principles for ethical research: *Respect for Persons, Beneficence, and Justice*.

A Little More History

The **Belmont Report**’s principles are implemented via:

1. Informed consent
2. Detailed assessment of risks vs benefits
3. Equity in the selection of research subjects

A Little More History

- In the United States, the “Common Rule” for protection of human research subjects was passed as law (45 CFR Part 46).

- The “Common Rule” applies to all federally supported or conducted research.

Identify the hypothesis / question

Identify who will sponsor and conduct your clinical trial

Grant application or letter of intent with study design

Detailed protocol development

Approvals, approvals, approvals

Infrastructure development

Clinical Trial Development
A great deal happens before you even see the trial!

Randomized Clinical Trials

- “Randomized controlled trials (RCTs) are the gold standard for comparing treatment efficacy.”

- Regarding observational studies and RCTs: “There was no agreement beyond what is expected by chance.”

Comparison of Population-Based Observational Studies With Randomized Trials in Oncology

Payal D. Soni, MD¹; Holly E. Hartman, MS²; Robert T. Dess, MD²; Ahmed Abugharib, MD³; Steven G. Allen, PhD²; Felix Y. Feng, MD⁴; Anthony L. Zietman, MD⁵; Reshma Jagsi, MD, DPhil²; Matthew J. Schipper, PhD²; and Daniel E. Spratt, MD⁵

Journal of Clinical Oncology 2019 37:14, 1209-1216
Phases of Clinical Trials

Phase I trials test safety (e.g. maximum tolerated dose) in a small number of patients.

Phase II trials investigate preliminary evidence of efficacy.

Phase III confirms efficacy and identifies common side effects by comparing to standard-of-care.

Phase IV is voluntary and looks at effects in large populations after a drug / intervention is approved.
Preliminary Report

Extracranial Stereotactic Radioablation*: Results of a Phase I Study in Medically Inoperable Stage I Non-small Cell Lung Cancer

Timmerman, Robert MD, Papiez, Lech PhD, McGarry, Ronald MD, Likes, Laura RT, DesRosiers, Colleen MS, Frost, Stephanie MS, Williams, Mark MD

*Show more
Phase II Example in Radiation Oncology

Stereotactic body radiation therapy for inoperable early stage lung cancer

Robert Timmerman, Rebecca Paulus, James Galvin, Jeffrey Michalski, William Straube, Jeffrey Bradley, Achilles Fakiris, Andrea Bezjak, Gregory Videtic, David Johnstone, Jack Fowler, Elizabeth Gore, Hak Choy

RADIATION THERAPY ONCOLOGY GROUP

RTOG 0236

A Phase II Trial of Stereotactic Body Radiation Therapy (SBRT) in the Treatment of Patients with Medically Inoperable Stage I/II Non-Small Cell Lung Cancer
Phase III Example in Radiation Oncology

The standard of care for stage I non-small cell lung cancer has historically been surgical resection in patients who are medically fit to tolerate an operation. Recent data now suggests that stereotactic radiotherapy may be a suitable alternative. This includes the results from a pooled analysis of two incomplete phase III studies that reported a 15% overall survival advantage with stereotactic radiotherapy at 3 years. While these data are promising, the median follow-up period was short, the results underpowered, and the findings were in contradiction to multiple retrospective studies that demonstrate the outcomes with surgery are likely equal or superior. Therefore, the herein trial aims to evaluate these two treatments in a prospective randomized fashion with a goal to compare the overall survival beyond 5 years. It has been designed to enroll patients who have a long life-expectancy, and are fit enough to tolerate an anatomic pulmonary resection with

*Medical Physics Navigator for Clinical Trials*
The Protocol

Written Protocol

- Background and Study Objectives
- Data collection, analysis, management, and protection
- Safety and Adverse Events
- Human Subjects Protection and Informed Consent
- Study Endpoints
- Study Population and Design

Medical Physics Navigator for Clinical Trials
Equipoise and the ethics of clinical research

B Freedman

PMID: 3600702 DOI: 10.1056/NEJM198707163170304

Abstract

The ethics of clinical research requires equipoise--a state of genuine uncertainty on the part of the clinical investigator regarding the comparative therapeutic merits of each arm in a trial. Should the investigator discover that one treatment is of superior therapeutic merit, he or she is ethically obliged to offer that treatment. The current understanding of this requirement, which entails that the investigator have no "treatment preference" throughout the course of the trial, presents nearly insuperable obstacles to the ethical commencement or completion of a controlled trial and may also contribute to the termination of trials because of the failure to enroll enough patients. I suggest an alternative concept of equipoise, which would be based on present or imminent controversy in the clinical community over the preferred treatment. According to this concept of "clinical equipoise," the requirement is satisfied if there is genuine uncertainty within the expert medical community--not necessarily on the part of the individual investigator--about the preferred treatment.
More Terms

Data Monitoring Committee

An independent panel that protects trial participants by monitoring and acting upon ongoing trial results.

From: https://www.nih.gov/health-information/nih-clinical-research-trials-you/basics
Case report forms are used to collect the data from clinical trials. They are carefully designed and each data element is tied to a source document.
Study Principal Investigator

The study Principal Investigator is responsible for all aspects of the trial such as: screening, enrollment, treatment, compliance with federal regulations, ensuring proper IRB oversight, data collection, data monitoring, data reporting, financial aspects, patient welfare, the conduct of other co-investigators and staff....

AN ENORMOUS RESPONSIBILITY!
Clinical trials that involve radiation therapy, advanced imaging, or novel uses of ionizing radiation may include a Medical Physics Co-Chair. She/he reports to the principal investigator and manages medical physics aspects of the trial.
Site (Principal) Investigator

Applies to a multi-center clinical trial: A site PI will oversee, and be responsible for, the conduct of the trial at each participating site.
Site Clinical Research Coordinator

Applies to a multi-center clinical trial: Each site will typically have a clinical research coordinator that is assigned the specific study and works under the direction of the site PI. They are a clinical trial professional that manages many of the day-to-day study operations at the local level.
One Last Definition

“In virtually every research study departures occur from the procedures set forth in the IRB-approved protocol. Various terms are used to describe these departures, including “protocol deviations,” “protocol violations,” “protocol variances,” and “non-compliance.” For the purposes of this recommendation, such departures shall be herein referred to as “protocol deviations.”

From: https://www.hhs.gov/ohrp/sachrp-committee/recommendations/2012-march-30-letter-attachment-c/index.html
Has This Happened to You?

“I’m checking a prostate plan and I see that the proximal seminal vesicle structure doesn’t match our standard clinical approach. There is a note about following protocol XYZ. Are we currently enrolling patients on this protocol?”
RO Clinical Trials

Question: What can a Medical Physicist do to ensure the success of a Radiation Oncology clinical trial?

Answer: Prepare in advance, be an expert on the clinical aspects of the protocol, develop a working relationship with the key players, adapt your clinical processes as needed, and implements methods to ensure trial compliance.
Preparation for Clinical Trials

1. Know the Protocol

- Identify where your standard processes differ from the protocol.

- Does your hardware and software meet protocol standards?

  Example: Your TPS algorithm

- Step up and lead the way.
Preparation for Clinical Trials

Do you use the same target and OAR nomenclature found in the protocol?

Here are target names from S1914.

Follow the protocol!
Preparation for Clinical Trials

Target and OAR structure definitions are critical

Organ at risk delineation for radiation therapy clinical trials: Global Harmonization Group consensus guidelines

Romaana Mir 1, Sarah M Kelly 2, Ying Xiao 3, Alisha Moore 4, Catharine H Clark 5, Enrico Clementel 6, Coreen Conning 6, Martin Ebert 7, Peter Hoskin 8, Coen W Hurkmans 9, Jørgen Kristensen 11, Stephen F Kry 12, Joerg Lehmann 13, Jeff M Michalski 14,
Preparation for Clinical Trials

Rigid and Deformable Image Registration for Radiation Therapy: A Self-Study Evaluation Guide in YYYY Clinical Trial Participation

Yi Rong 1, Mihaela Rosu-Bubulac 2, Stanley H Benedict 3, Yunfeng Cui 4, Russell Ruo 5, Tanner Connell 5, Rojano Kashani 6, Kujtim Latifi 7, Quan Chen 8, Huaizhi Geng 9, Jason Sohn 10, Ying Xiao 9

Affiliations + expand
PMID: 33662576 DOI: 10.1016/j.prro.2021.02.007
2. Know The People

- You should know your site principal investigator and, if possible, develop a strong working relationship with them.
  - Work closely with the site clinical study coordinator on documentation, data collection, and data submission. They will keep you up-to-date on enrollments, randomizations, and training.
- If you have questions about the protocol reach out to your local team first, then Medical Physics co-chair or Study PI if needed.
Preparation for Clinical Trials

3. Modify Local Processes / Procedures If Required

- In some cases local processes and procedures could lead to a protocol deviation. You may need to modify existing methods and/or possibly develop new ones and then train staff.

Simple example: The trial protocol requires a 2 mm or smaller slice thickness when performing a CT simulation scan. Your current clinical simulation method uses a 2.5 mm slice thickness.
Preparation for Clinical Trials

4. Implement Protocol-Specific Compliance Tools and Templates

- If you can’t meet a trial constraint you should know before you approve the plan!

  Are there any major violation?
  What are acceptable deviations?
  Are the margins and dose coverage per protocol?
  Are unique structure name and contour requirements followed?
Preparation for Clinical Trials

4. Implement Protocol-Specific Compliance Tools and Templates

PTV Name: 

PTV Margin: CTV + mm axial and mm craniocaudal expansion
- Acceptable (5 mm to 7 mm)
- Deviation (< 5 mm or > 7 mm)

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<tr>
<th>Parameter</th>
<th>Result</th>
<th>Protocol Score</th>
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<tbody>
<tr>
<td>1. Lung V20 (%)</td>
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</tr>
<tr>
<td>2. Spinal Cord Dose to vol (Gy)</td>
<td>10.7</td>
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<tr>
<td>3. Spinal Cord Dmax (Gy)</td>
<td>12.4</td>
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<td>4. Esophagus Dose to vol (Gy)</td>
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<td>6. Brachial Plexus Dmax (Gy)</td>
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<tr>
<td>7. Heart Dose to vol (Gy)</td>
<td>9.1</td>
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</tr>
<tr>
<td>8. Heart Dmax (Gy)</td>
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<tr>
<td>9. Great Vessel Dose to vol (Gy)</td>
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<td>10. Great Vessel Dmax (Gy)</td>
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<td>15. Rib Dose to vol (Gy)</td>
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<td>16. Rib Dmax (Gy)</td>
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</table>

Medical Physics Navigator for Clinical Trials
Preparation for Clinical Trials

Medical Physics Navigator for Clinical Trials

Scripting and Automation Applications in Photo/Proton Clinics and Clinical Trials

Taoran Li, Ph.D., DABR
Assistant Professor
Perelman School of Medicine, University of Pennsylvania
Preparation for Clinical Trials

Know How to Prepare Trial Data

- Many clinical trials require the submission of RT treatment plans and treatment records.
- The Medical Physicist often oversees the data preparation and submission. Follow the instructions referenced in the protocol.

TRIAD securely moves DICOM images, structured and unstructured reports, and DICOM RT objects across the Internet.

https://triadhelp.acr.org/
If you are going to become involved in a trial, then you should strive to be the site expert on implementing the protocol in your clinic!
Preparation for Clinical Trials

Your homework: Read and Follow the AAPM Task Group Report

Guidance for the Physics Aspects of Clinical Trials

The Report of AAPM Task Group 113

January 2018
Preparation for Clinical Trials

FLASHBACK: BEFORE YOU ENROLL PATIENTS

Credentialing

Paige Taylor from IROC @ MD Anderson will tell you everything you need to know about credentialing and will also discuss key organizations and resources for aspiring trial physicists.
Introduction

- Paige Taylor, MS, DABR
- Medical Physicist at IROC’s Houston Office
- Focus: radiation therapy

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Session Learning Objectives

• Distinguish the different types of clinical trials, identify their important elements, and identify key personnel involved in trial success.

• Understand the steps involved in clinical trial credentialing.

• Identify how medical physicists can contribute to clinical trials.
So. Many. Acronyms.

Let’s start with some basic org charts and common acronyms you’ll hear in the clinical trials space.

https://makeameme.org/meme/acronyms-acronyms-everywhere-5981993604
NCI Trial Organizations

- National Cancer Institute (NCI)
  - Division of Cancer Prevention (DCP)
  - Cancer Therapy Evaluation Program (CTEP)
    - NCI Community Oncology Research Program (NCORP)
    - National Clinical Trial Network (NCTN)
    - Experimental Therapeutics Clinical Trial Network (ETCTN)

- Alliance
- ECOG-ACRIN
- NRG Oncology
- SWOG
- Children’s Oncology Group (COG)

AAPM Work Group on Clinical Trials
Key Organizations: NCTN

LEGEND:
- Central Functions:
  - CIRB
  - CTSU
  - IROC
  - Common Data System/Hosting
  - Network Accrual Team
- 30 LAPS
- Tumor Banks
- Operations Centers
- Member Sites
- Statistics/Data Ctrs

Medical Physics Navigator for Clinical Trials
Key Organizations: International Trial Groups

- Canadian Cancer Trials Group (CCTG)
- European Organisation for Research and Treatment of Cancer (EORTC)
- Japan Clinical Oncology Group (JCOG)
- UK’s National Institute for Health Research (NIHR)
- Trans-Tasman Radiation Oncology Group (TROG)
Key Organizations: IROC

NCI Clinical Trial Support

1. Site Qualification
2. Trial Design Support
3. Credentialing
4. Data Management
5. Case Review
Clinical Trial Group Membership
Membership: NCTN

- Each clinical trial group within the NCTN has its own membership process
  - Alliance: https://www.allianceforclinicaltrialsinoncology.org/main/public/standard.xhtml?path=%2FPublic%2FBecome-Member
  - COG: https://childrensoncologygroup.org/index.php/joiningcog
  - ECOG-ACRIN: https://ecog-acrin.org/about-us/membership
  - NRG: https://www.nrgoncology.org/About-Us/Membership
  - SWOG: https://www.swog.org/about/join-swog-cancer-research-network
  - CCTG: https://www.ctg.queensu.ca/public/become-member
Membership: NCTN

- Various Membership Types: Lead, Affiliate, International, etc.
- Reciprocity between NCTN groups

NCTN Group Membership

State Dept. Clearance
- ONLY for international members outside North America, US State Department clearance is required

Join NCTN Roster
- Complete New Participant Demographics Form or QUIC Imaging Survey

IROC

Medical Physics Navigator for Clinical Trials
Membership: NCTN Roster

• IROC, CTEP and CTSU are creating a new NCTN Member Roster for Imaging and Radiation Therapy Facilities participating in Network trials

• Roster includes Imaging and Radiation Therapy Facilities at non-enrolling sites as well as those at enrolling site institutions
Membership: NCTN Roster

quic.acr.org

irochouston.mdanderson.org
Clinical Trial Resources
Resources:

CTSU

CTSU Website: www.ctsu.org

- **Protocol and protocol-related documents**
  - Funding information for studies under the NCI National Clinical Trials Network (NCTN)
  - NCI Central Institutional Review Board (CIRB) documents for sites participating in the CIRB initiative
  - Links to Medidata Rave® and the Oncology Patient Enrollment Network (OPEN)
  - Access to the Data Quality Portal, Site Audit Portal, and accrual information
  - Information on regulatory submissions
  - Educational materials
  - E-mail notification on protocol updates
Resources: CTSU

In order to get access to CTSU website, need to register for CTEP IAM account:
https://ctepcore.nci.nih.gov/iam
Resources: TRIAD

- TRIAD is the American College of Radiology’s (ACR) image exchange application
- New NCTN trials use TRIAD for dosimetry digital treatment data submission

Need help with TRIAD?

https://triadhelp.acr.org
703-390-9858
Triad-Support@acr.org
NCTN has contouring atlases for:

- Brain
- Breast
- Extremity Soft Tissue Sarcoma
- GI
- GU
- GYN
- H&N
- Lung
- Male Normal Pelvis
- Upper abdomen

Resources: Physics Committees

Many clinical trial groups have medical physics committees. These are a great resource for trial information

• NRG Oncology Medical Physics Subcommittee
• COG Medical Physics Committee
• AAPM Work Group on Clinical Trials (us!)
Clinical Trial Credentialing
Importance of Credentialing

Goal of credentialing: ensure comparability and consistency across centers participating in trials

Peters, et al. found that noncompliant RT resulted in a 40% decrease in Overall Survival
Importance of Credentialing

Weber, *et al.* found that a majority of RT trials had a primary end-point negatively impacted by protocol deviations.

Clinical trial credentialing helps minimize uncertainty and reduce these deviations.
Importance of Credentialing

• Credentialing is very important in the context of new technologies in clinical trials
  – Proton therapy
  – Adaptive RT
  – MR-linacs
  – Targeted radionuclide therapy

• If our goal is comparability and consistency, credentialing is a great way to verify that for new techniques

Image from https://www.pennmedicine.org/cancer/navigating-cancer-care/programs-and-centers/roberts-proton-therapy-center
What does credentialing involve?
Creditialing

IROC is the main credentialing body for the NCI

1. Site Qualification
   FQs, ongoing QA, proton approval

2. Trial Design Support/Assistance
   protocol review, help desk

3. Credentialing
   phantoms, IGRT, knowledge assessments, benchmarks

4. Data Management
   pre-review, use of TRIAD, post-review for analysis

5. Case Review
   pre-, on-, post-treatment clinical reviews
Credentialing

• Types of credentialing:
  – Phantoms
  – IGRT
  – Scanner qualification
  – Knowledge assessments
  – Benchmarks
  – pre-, on-, post-treatment clinical reviews
Credentialing

Where can you find credentialing information?

The protocol
(check [www.ctsu.org](http://www.ctsu.org))
Credentialing

Where can you find credentialing information?

IROC website
(www.irochouston.mdanderson.org)
Credentialing

Here’s a little cheat sheet for figuring out credentialing for your center for a clinical trial

Best place to start: Credentialing Status Inquiry Form (CSI)

On IROC website
Credentialing: Phantoms

Phantoms are an effective end-to-end test of an institution’s RT treatment abilities.

Phantom are used for credentialing in a majority of NCTN RT trials.

AAPM Work Group on Clinical Trials
Credentialing: Phantoms

- Improve Phantom Irradiation Performance
- Improve RT Comparability and Consistency
- High Quality Trial Data
Credentialing: Phantoms

IROC SRS Phantom

• Simulates 1.9 cm brain lesion
• Rx: 30 Gy
• Acceptance Criteria: ±5% TLD, 5%/3mm film
Credentialing: Phantoms

SRS Phantom TLD: TPS vs Irradiation Date

- Significant improvement with time ($p<<0.01$)
  - Improved small field dosimetry
  - Improved beam modeling in TPS
- 2012, average TLD ratio: 0.972
- Present, average TLD ratio: 0.987
- Before the end of 2023, average TLD ratio will reach 1.000!

Slide courtesy of Stephen Kry
Credentialing: Phantoms

Sources of SRS Phantom Errors:

- Incorrect Cone factors/output factors
  - TRS-483 is great for improving measurement
  - Modeling can be a separate issue
- Incorrect TMR in TPS
- Incorrect HU-electron density conversion
- Incorrect reference specification in TPS
- Incorrect manual adjustment of output factors

- Minimize errors by following best clinical practice
 Credentialing: Phantoms

SRS Phantom Resources

The Radiological Physics Center’s standard dataset for small field size output factors

David S. Followill,1,a Stephen F. Kry,1 Lihong Qin,2 Jessica Leif,1 Andrea Molineu,1 Paola Alvarez,1 Jose Francisco Aguirre,1 and Geoffrey S. Ibbott1

Department of Radiation Physics,1 Radiological Physics Center, The University of Texas M. D. Anderson Cancer Center, Houston, Texas, USA; Department of Therapeutic Radiology,2 University of Minnesota, Minneapolis, MN, USA
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Received 4 March, 2012; accepted 30 May, 2012
Credentialing: Phantoms

IROC H&N Phantom

• Simulates nasopharyngeal lesion with nodal involvement

• Acceptance Criteria: ±7% TLD, 7%/4mm film
Credentiaing Phantoms

Main sources of H&N phantom errors:

- **Systematic dose**
- Setup
- Local
- Global
Credentialing Phantoms

69% of H&N phantoms failures were due to:

Systematic errors in the TPS dose calculation

Credentialing Phantoms

Phantoms with motion: lung & liver

Can you guess the number one source of error in these phantoms??

Lung Phantom

Liver Phantom
Credentialing Phantoms

Top error in lung and liver phantoms:

Localization error in the direction of motion
Credentialing Phantoms
Credentialing Phantoms

Second most common error in lung phantoms:

**Systematic dose error**

Typically a result of less sophisticated algorithms
Pencil beam algorithms not allowed for photons or protons on NCTN lung protocols anymore
Credentialing: IGRT

IGRT Credentialing
• Typically required for trials that allow reduced treatment margins (<5 mm)

2 Types
• Boney
  H&N/brain + pelvis
• Soft Tissue
  Lung/liver/pancreas + pelvis

Submission Requirements
• Planning CT (DICOM) for 1 patient
• DICOM RT Structures
• DICOM RT Plan
• DICOM RT Dose
• DICOM localization images (e.g. CBCT or MRI) for 2 fx
• DICOM spatial registration file
• Completed DDSI
• Completed Online IGRT Questionnaire
 Credentialing: IGRT

Potential pitfall: inconsistent bladder filling

Slide courtesy of Andrea Molineu
Credentialing: Imaging Scanners

- Credentialing required for some imaging modalities, like PET/CT
- Might be required multiple times during protocol, e.g. PET credentialing required annually for NRG GY006 protocol
Credentialing: Benchmarks

- Benchmark plans provide single data set for every institution to practice on
- Credentialing reviews:
  - Contouring
  - Planning
  - Both

Slide courtesy of Jessica Lowenstein
Credentialing: Patient Plan Reviews

• Pre-treatment
  – Must be reviewed rapidly before patient is treated
  – Biggest impact, but lots of pressure

• On-treatment
  – Relieves some of the time pressure, but allows PIs insight into common planning deviations
  – Opportunity to discuss with co-investigators while the trial is accruing

• Post-treatment
  – Done for most trials to check if trial constraints were met
Credentialing: Knowledge Based Planning

• Becoming more popular for clinical use

• Also employed in a few clinical trials (e.g. NRG GY006)
  – Institution’s plan run through KBP program
  – Recommendations to institution about possible ways to improve their plan
## Credentialing: Patient Plan Reviews

<table>
<thead>
<tr>
<th>Review Type</th>
<th>Major Deviation Rate 2018</th>
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<tr>
<td>Benchmark</td>
<td>16%</td>
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<tr>
<td>Pre-treatment</td>
<td>21%</td>
</tr>
<tr>
<td>Post-treatment</td>
<td>9%</td>
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Slide courtesy of Jessica Lowenstein

Medical Physics Navigator for Clinical Trials
Credentialing

• Credentialing → reduce deviations
• We hope you can use some of these tips and tricks to help you on your own credentialing journey
• Don’t hesitate to reach out if you ever have questions!

credentialingtips@mdanderson.org

@mpPaigeTaylor
And once all the credentialing is done...

You can pass the torch to your physician colleagues!

Now for the clinician perspective on clinical trials, from Shruti Jolly, M.D.

Professor and Associate Medical Director of Strategic Planning & Business Development, University of Michigan
The Physician’s Perspective

Shruti Jolly MD
Professor, Department of Radiation Oncology
University of Michigan, Ann Arbor, MI
Outline

• Clinical Research Overview
• Radiation Oncologist’s Role
• Role in trial development and leadership
• Recruitment strategies
• Case scenarios
Defining clinical research

• The study of human beings in a systematic investigation of human biology, health, or illness, designed to develop or contribute to generalizable knowledge

• Inclusive of a set of activities that are meant to test a hypothesis, formed on particular treatments/diagnostics/medical devices...

• The conclusions drawn from such research, thereby contribute to generalizable knowledge which will be used to improve medical care or the public health and thus serve the common or collective good.
Defining physician’s role

- Investigator in clinical trials
  - Enroll patients of clinical practice into clinical trials
- Tailor studies independently
  - Helps in understanding and revising the modes of practice
- Industry
  - Medical monitor, clinical administrator, medical advisor, CMO
Role in trial development & leadership

• Designing of investigator initiated trial
  • Clinical
  • Biomarker driven
  • Drug design
• Multi-institutional collaborative clinical trial
  • NRG, SWOG
  • Various subcommittees and trials of NRG led by physicists
• Prospective registry data
• NIH, Industry
Clinical Trial Recruitment

• Recruitment strategies
  • Sharing with other health care providers (locally and nationally)
  • Connecting with patient advocates
  • Recruitment campaigns (social media)
  • Screening for multiple trials at a time
  • Patient convenience
  • Incentives
Case scenario 1
Case scenario 2

- UM IIT study (UMCC 2015.035) Individualization of Lung cancer Treatment – using radiographic and biological biomarkers
  - PO1 funding, clinical protocol design
  - Frequent research team meetings to evaluate accrual, adverse events and logistical issues
    - Evaluate lung toxicity, and tumor failures
  - Trial analyses, abstracts/manuscripts
  - Decide on next steps and ways to obtain additional funding to continue building upon work
Case scenario 3

- **SPRINT study** (Merck sponsored multisite study, Ohri et al.) —
  - Locally Advanced NSCLC patients with high PDL1 undergo 3 cycles of Pembrolizumab then PET adaptive radiation (no chemo)
  - 1 year later, patient presented with hemoptysis and was found to have local recurrence. Restaging scans were otherwise negative.
AAPM Work Group on Clinical Trials

2.4 Gy in 20 fx to 48 Gy per protocol

Local Recurrence treated in 15 fractions

Medical Physics Navigator for Clinical Trials
Conclusions

• Partnership of radiation oncologist with medical physicist is vital to the success of clinical trials in the radiation oncology clinic