

Clinical Trials 101

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&

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Overview

- **What are Clinical Trials?**
- **How to review a Clinical Trial Protocol**
- **How to review a Consent Form**

What are Clinical Trials

- **Definition**
- **Why they are Important**
- **Phases of Clinical Trials**
- **Barriers**
- **Benefits**
- **Risks**
- **Protections**
- **Resources**

What are Cancer Clinical Trials?

- Research studies involving people
- They try to answer scientific questions and find better ways to **prevent, diagnose, or treat** cancer



Why Are Cancer Clinical Trials Important?

- **Cancer affects all of us**
- **Each year in the U.S.A:**
 - **1,500 people die each day**
 - **1 of 4 deaths is from cancer**
 - **The more people that take part, the faster we can:**
 - Answer critical research questions
 - Find better treatments and ways to prevent cancer



Clinical Trial Phases

■ Phase I

- What dose is safe
- A few people in one or two centers

■ Phase II

- safety and effectiveness
- <100 people in a few centers

■ Phase III

- Compare it against standard of care
- Large numbers of people, around the Country

■ Phase IV

- After drug is approved, further safety and effectiveness

Barriers to Participation in Clinical Trials

- **Physicians & other providers may:**
 - **Be unwilling to lose control of patient's care**
 - **Believe that standard therapy is best**
 - **Believe that clinical trials are more work**
 - **Worry about the patient's care or how the person will react to suggestion of clinical trial participation**

Barriers to Participation in Clinical Trials

■ Patients may:

- Be unaware of clinical trials
- Lack access to trials
- Fear or be suspicious of research
- Have practical or personal obstacles
- Face insurance or cost problems
- Be unwilling to go against their physicians' wishes

Benefits of Participation

■ Possible benefits:

- Subjects may receive, at a minimum, the best standard treatment
- If the new treatment or intervention is proven to work, subjects may be among the first to benefit
- Subjects have a chance to help others and improve cancer care

Risks of Participation

■ Possible risks:

- New treatments or interventions under study are not always better than, or even as good as, standard care
- Even if a new treatment has benefits, it may not work for every subject
- Health insurance and managed care providers do not always cover clinical trials

Protection of Participants

- Nuremberg
- National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research
- Belmont Report
- National Research Act

Protecting Participants Before a Trial

- **Scientific review by sponsoring organization**
- **Institutional review board approval**
- **Informed consent**

Protecting Participants During a Clinical Trial

- **Institutional review boards (IRBs)**
- **Data & safety monitoring boards (DSMBs)**
 - Minimize risks
 - Ensure integrity of data
 - Can stop study if necessary

Questions: Ask & Answered

- **What is the study about?**
- **Who put the study together?**
- **Where is the trial being conducted?**
- **What will the I get out of the study?**
- **What are the risks?**
- **How long will the study last?**
- **What tests are involved?**

More Questions: Ask & Answered

- **How will I be protected from harm?**
- **Do I have to pay for any part of the trial?**
- **Who should be contacted for problems or questions?**
- **What do I have to do in this study?**
- **What are my other options?**

Subject's Decision & Rights

- The decision to participate is the subject's
- Informed Consent is more than a signature
 - **it is a process**
 - All the facts about a study must be given before the patient decides to participate
 - Including details about all treatments and test(s) and the benefits and risks
 - Rights should be fully explained

How to Find Clinical Trials

■ The Internet

➤ National Library of Medicine

- <http://www.ClinicalTrials.gov>

➤ Centerwatch Clinical Trials

- <http://www.centerwatch.com>

➤ NCI/CancerNet

- <http://cnetdb.nci.nih.gov/trials.html>

- www.cancer.gov

■ Your healthcare provider

- **1-800-4-CANCER (1-800-422-6237)**

A photograph of a person walking away from the camera on a sandy beach towards the ocean. The person is silhouetted against the bright, sunlit water and sky. The ocean has gentle waves breaking on the shore. The sky is blue with scattered white clouds. The overall mood is serene and contemplative.

**Today's Standard Treatment
Was Yesterday's Clinical Trial**

How to Review a Clinical Trial Protocol

- Use ACRIN's project IMPACT template
- Why our review is important
- Basic

Project IMPACT

- www.ACRIN.org / project IMPACT
- A template designed by advocates **FOR** advocates

Why our Review is Important

- **Scientists focus on what they care about**
- **We provide a reality check: what is do able**
- **Paper Trail:**
 - **Comments on conference calls may not be captured**
 - **No record of advocate concerns/support**
 - **No way to track if our concerns where incorporated into protocol**
 - **No way to capture our accountability to process**

Structure of all Protocols

- **Background / Introduction**
- **Study Hypothesis**
- **Study Design**
- **Rationale / Objective**
- **Eligibility**
- **Statistical Design**
- **Schema / Flowchart**
- **Informed Consent Process**
- **Accrual / Communication Plan**

Background / Introduction

- **What is the question?**
- **What is the value to patients?**
- **Will the study help patients live longer?**
- **How long will it take to complete the trial?**
- **Will the answer be relevant when the trial is over?**

Study Hypothesis

- Define the Hypothesis: **so you understand it**
- Indicate what kind of study it is
 - Treatment
 - QOL
 - Surgery
 - Imaging
 - Prevention
 - New dosing
 - New order drugs are given

Study Design

- How does the study design compare to standard of care
- Do you feel that demands on patients are reasonable compared to standard of care? (Yes/No)
- Are correlative studies included? Encourage
- Will this study be conducted in the community? (Yes/No)

Rationale / Study Objective

- **What are the formal trial endpoints?**
- **Do they compare to the hypothesis goals?**
 - **For example, if the hypothesis states that the trial will increase survival, but the endpoints don't measure survival, why not?**

Eligibility

- Who's included - excluded
- Do you think that the trial population is representative of the patient population?
- Will the study be open in sites with diverse populations?

Preliminary Statistical Design

- If the trial examines more than one treatment, are participants randomized to a single treatment
- Is crossover allowed whereby participants may receive some or all of the treatments being studied?
 - Why or why not
 - Do you agree with the trial design?

Feasibility

- Do you think patients will be interested in enrolling? (Yes/No)
- Do you think the numbers expected to enroll are reasonable? (Yes/No)
- Are there aspects of the trial that you think will make accrual more difficult? (Yes/No)
- Diversity:
 - Is there a plan to include a diverse population? (Yes/No)
 - Will the trial be at sites with diverse populations? (Yes/No)

Schema / Flowchart

- Is the schema designed in a patient-friendly form? (Yes/No)
- Reading left to right, not top to bottom? (Yes/No)
- Other specific comments on how to make it as patient-friendly as possible?

Informed Consent Process

- Does the protocol describe the informed consent process (Yes/No)
 - Are there Follow-up materials? (Yes/No)
- Is the informed consent based on the new NCI template? (Yes/No)
- What happens in the event of an injury:
- Any correlative studies (i.e. tissue)
 - Use patient's tissue for future studies? (Yes/No)

How to review a Consent Form

- From an Advocate Perspective

The Consent Form

- **6-8 Grade Reading Level**
- **Formatting**
- **Study Requirements clear**
- **Other Options Clear**

The Consent Form: Readability

- **6th-8th Grade level: 14-17 words/sentence; 139-147 syllables/100 words**
- **Does “readability” = “understanding”¹**
 - Concept words; category words; value judgment word
- **Clear Writing Tips ²**
- **Word Substitution Lists ³**

¹ Hochhauser, M., IRB: Ethics & Human Research 25, no. 5 (2003):7-10

² Kripalani, S., Texas Medicine, 91(8), 40-45

³ Hilts, L. & Krilyk B. J. (1991). Write readable information to educate.

The Consent Form: Formatting ¹

■ Techniques to use:

- **Use font size of 12 or greater**
- **Use fonts with “tails”, like GRAMMOND, CENTURY or COPPER PLATE LIGHT**
- **Bullet all:**
 - **study requirements ,headings and risks**
- **Use short paragraphs**
- **Lots of white space**

¹ courtesy of Ralph Kennedy

The Consent Form: What is required

- **Techniques to use:**
 - **List all Treatments**
 - **List all Tests**
 - **List extra visits**
 - **How does that fit into daily life**
 - **Graphic flowchart ¹**

¹ CISN

The Consent Form: Options Are Clear

■ Techniques to use

- List other options**
- Not just standard of care**
- Compare clinical trial & standard of care ¹**
- Better distinction between risks and benefits**
 - side by side comparison chart ²**

¹ Hochhauser, M., "The Informed Consent Form: Document Development", Drug Information Journal, 34 (4) 1309-1317 (2000)

² CISN

Need: Educational Materials

- **Too many elements to process** ¹
 - **14** required, **6** optional + **5** HIPPA
 - Decision to participate may be based on what patient is able to process and understand
- **Omission neglect: You can't use what you don't see** ^{1, 2}
 - **Compare standard vs. study**

¹ **Hochhauser, M.**, "Applying Consumer Psychology to Subject Recruitment", actmagazine.com

² **F.R. Kardes and D.M. Sanbonmatsu**, "Omission Neglect, the importance of Missing Information," *Skeptical Inquirer*, 27 (2) 42-46 (2003)

Need: Educational Materials

- **Learning Styles Matter ¹**
- **Patients learn best when there is a match between their preferred learning style and the presentation style:**
 - **Visual Learner**
 - **Auditory Learner**
 - **Sensory Learner**
 - **Kinesesthetic Learner**

¹ Adapted from: Teachers Make The Difference by Susan Kovalik

Need: Educational Materials

- **Study Schema (graphic) ^{1, 2}**

- Calendar Format
- Clear / color coded

- **Study Brochure ^{2, 3}**

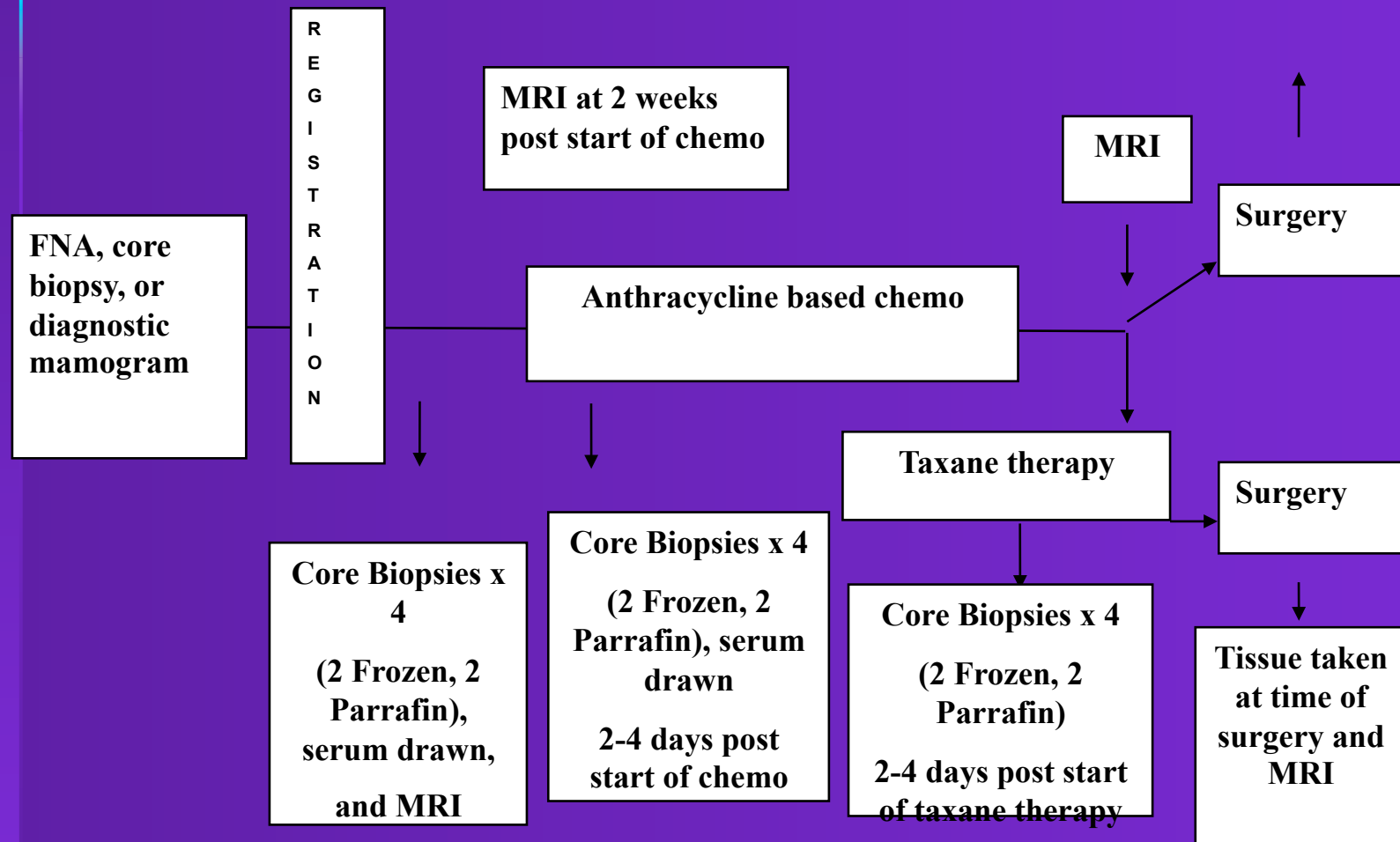
- Address possible hurdles
 - Randomization
 - Placebo

¹ CISN

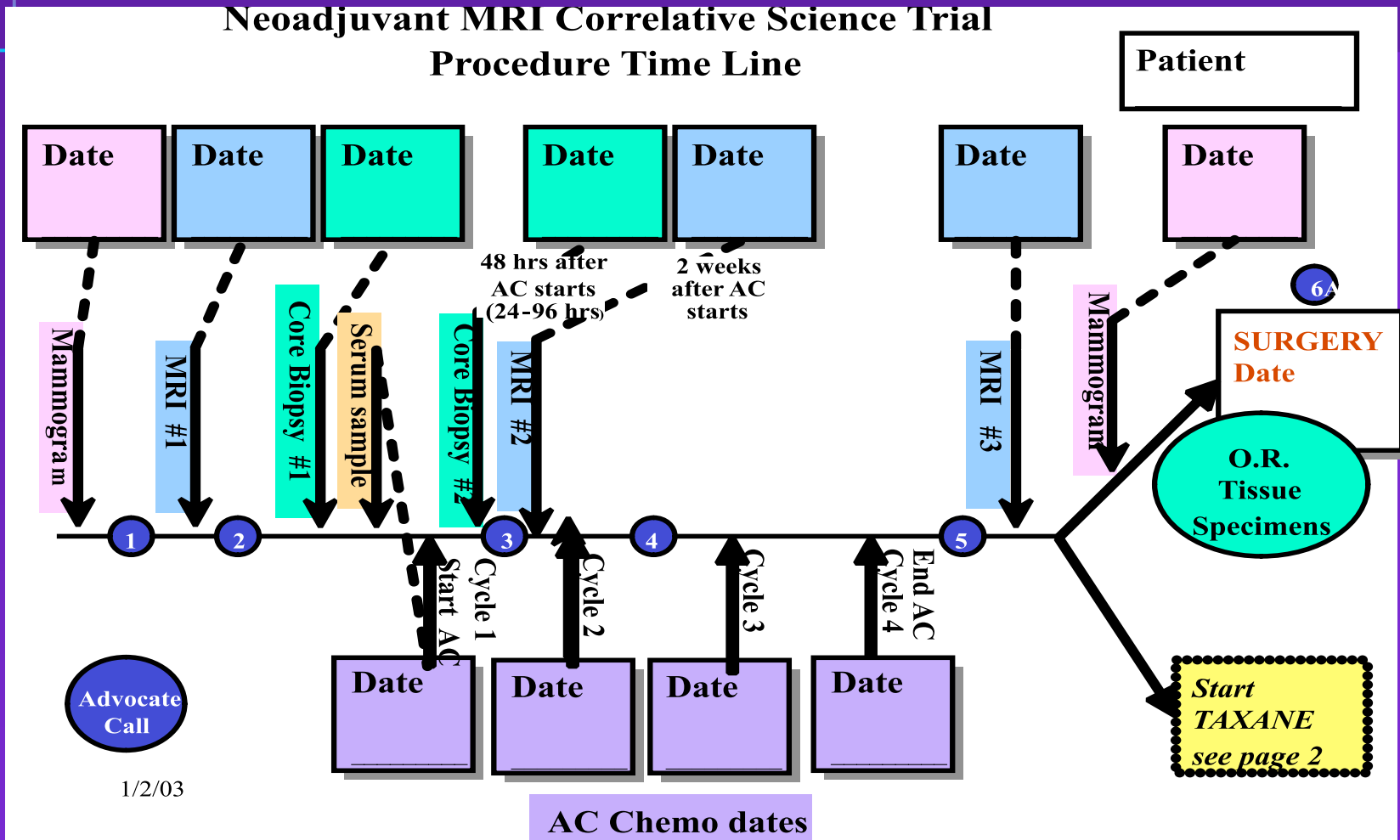
² Hochhauser, M., "Applying Consumer Psychology to Subject Recruitment", actmagazine.com

³ Doak, L. G., Doak C. C. & Meade, C. D. (1996). Strategies to improve cancer education materials. Oncology Nursing Forum, 23(8)

Original Co-operative group Schema



CISN Version of Study Schema



Study timeline developed for UCSF by Peggy Devine

ACRIN Advocate Help

MRI of the Contralateral Breast

ACRIN Research Study 6667

An ACRIN Research
Study for Women
with a
Recent Diagnosis of
Breast Cancer

*Information for
Participants*

acrin American College of Radiology
Imaging Network



Breast MRI Study

Imaging your cancer-free breast



Are you a breast cancer
patient with concerns
about your healthy breast?

acrin American College of Radiology
Imaging Network

Summary

- **Advocates Can Make a Difference**
 - **When reviewing protocols**
 - **Helping write the consent form**

Thank You

- **Summit Series on Clinic Trials**
- **Coalition of Cancer Cooperative Groups**
- **Funders**
- **ACOSOG and ACRIN**
- **CISN**