Planning and Executing a Research Project

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Overall Learning Objectives

- ★ Identify common study designs used in medical imaging research
- ★ Form a testable hypothesis from a clinical problem or question
- ★ Perform a literature review
- ★ List the steps required to plan a research project
- ▶ **Locate funding opportunities on the web**
- ▶ **Identify the safeguards for performing ethical human research**
- ▶ **List the steps required to submit a grant proposal**
- ▶ **List the steps required to execute a research study**
- ▶ **List the steps required to publish medical manuscripts**

Outline

- Finding funding and writing a grant
- Writing a protocol
- Ethical considerations and working with COMIRB
- Running the study
- Publishing the results
- Break
- Group brainstorming for the mentored scholarly activity

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Funding Basics

- Find a funding announcement that is relevant to your scientific field, research goal, and is appropriate to your level of training
- Determine the application submission date
- Determine the application requirements
- Write the grant
- Route through the Office of Grants and Contracts
- Submit the grant

University funding sources

- Department of Radiology
  - Faculty development grants
  - Pilot grants
- Colorado Clinical and Translational Science Institute (CCTSI)
- Colorado Translational Research Imaging Center (CTRIC)
- University of Colorado Cancer Center

External funding sources

- National Institutes of Health
  - http://grants.nih.gov/grants/guide/index.html
- Radiological Society of North America (RSNA)
- ACGME Holman pathway
- National societies such as American Cancer Society, Alfred P. Sloan, and many others
  - http://www.ucdenver.edu/academics/colleges/medicalschool/research/Pages/FundingOpps.aspx
- Office of Research Development and Education
  - http://www.ucdenver.edu/academics/research/AboutUs/ORDE/Pages/orde.aspx

Anatomy of a grant application

- Cover letter
- Project summary or abstract
- Project narrative
- References
- Facilities and other resources
- Biographical sketches and other support
- Research plan: specific aims page
- Research plan: strategy
- Budget

Research Plan: Significance

- Explain the importance of the problem or critical barrier to progress in the field that the proposed project addresses.
- Explain how the proposed project will improve scientific knowledge, technical capability, and/or clinical practice in one or more broad fields.
- Describe how the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field will be changed if the proposed aims are achieved.

Research plan: Innovation

- Explain how the application challenges and seeks to shift current research or clinical practice paradigms.
- Describe any novel theoretical concepts, approaches or methodologies, instrumentation or intervention(s) to be developed or used, and any advantage over existing methodologies, instrumentation or intervention(s).
- Explain any refinements, improvements, or new applications of theoretical concepts, approaches or methodologies, instrumentation or interventions.

Research plan: Approach

- Describe the overall strategy, methodology, and analyses to be used to accomplish the specific aims of the project. Unless addressed separately in the Resource Sharing Plan, include how the data will be collected, analyzed, and interpreted as well as any resource sharing plans as appropriate.
- Discuss potential problems, alternative strategies, and benchmarks for success anticipated to achieve the aims.
- If the project is in the early stages of development, describe any strategy to establish feasibility, and address the management of any high risk aspects of the proposed work.
- Point out any procedures, situations, or materials that may be hazardous to personnel and precautions to be exercised. A full discussion on the use of Select Agents should appear in 5.5.11 below.
- If research on Human Embryonic Stem Cells (hESCs) is proposed but an approved cell line from the NIH hESC Registry cannot be identified, provide a strong justification for why an appropriate cell line cannot be chosen from the Registry at this time.

Writing tips from NIH

- Convey the value of the research in plain language – clear, succinct, and professional
- Be comprehensible to both scientists and the public
- Relay the potential impact of the research on health
- Leave time for proofreading!

Budgeting

- Specific budget details depend on the sponsor requirements and research requirements
- Common budget items
  - Personnel and consultants
  - Equipment
  - Supplies
  - Travel
  - Publishing costs
  - Indirect costs: facilities, utilities, office supplies, etc.

Submitting the grant

- Grants are processed by the Office of Grants and Contracts (OGC) http://www.ucdenver.edu/academics/research/AboutUs/GrantsContractsOffice/Pages/default.aspx
- Basic process
  1. Principal investigator creates a Grant Application for sponsored research
  2. PI / department "routes" the application to OGC
  3. OGC reviews the application for policy and legal issues
  4. OGC provides Institutional Endorsement of the application, and returns it to the PI or department
  5. PI or department submits the application to the funding agency

Grant process summary

- Find funding announcement
- Determine submission deadlines
- Write the grant application per the announcement instructions
- Route the application to the Office of Grants and Contracts
- Submit the application to the funding agency
- For questions, contact Patty Nash, PATRICIA.NASH@UCDENVER.EDU

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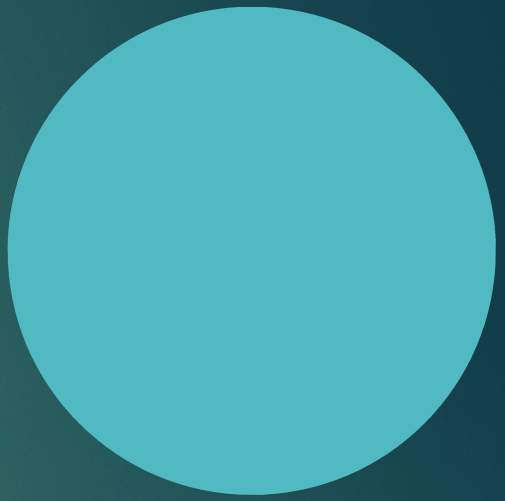

Writing an IRB protocol: Background

- Hypothesis and specific aims
  - What are the main goals of the research and what will you test?
- Background and significance
  - What previous work has been done?
  - Why do I care?
- Preliminary studies
  - What other work have **you and your group** conducted in this area?

Writing an IRB protocol: Methods

- Research Methods
  - Outcome measures
  - Population of interest
  - Study design and research methods
    - Enrollment and consent process
    - Randomization scheme (if applicable)
    - Interventions and treatments
    - Planned visits and follow-ups
    - Data collection plan

Writing an IRB protocol: Risks

- Description, risks, and justification of procedures and data collection
  - Details each intervention and procedure used
  - Describe the risks
  - State why the procedure is necessary to achieve the study aims
- Potential scientific problems
- Data safety monitoring plan for research involving more than minimal risk

Writing an IRB protocol: Analysis plan

- Call the biostatisticians
- For quantitative analysis
  - Describe the statistical tests for each outcome measure
  - Provide a justification for the proposed sample size
- For qualitative analysis
  - Describe and justify the qualitative methods used

Writing an IRB protocol: Wrapping it up

- Summarize the knowledge to be gained
- Provide references

- If you get stuck…
  - Contact the clinical research coordinator
    - Michelle Carr, MICHELLE.L2.CARR@UCDENVER.EDU
  - Contact the biostatisticians
    - Sarah Kreidler, SARAH.KREIDLER@UCDENVER.EDU

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Ethics in Human Research

- Basic Ethical Principles
  - Respect for Persons
  - Beneficence
  - Justice
- Applications
  - Informed consent
  - Assessment of risk and benefits
  - Selection of subjects
    - The phrase “human research participants” is now preferred over “subjects”

Institutional Review Board Basics

- The **Colorado Multiple Institutional Review Board (COMIRB)** is an administrative body established to protect the rights and welfare of human research participants recruited to participate in research activities
  - http://www.ucdenver.edu/academics/research/AboutUs/comirb/Pages/comirb-home.aspx
- Types of submissions
  - Non-human subject research determination
  - Exempt review
  - Expedited review
  - Full Board review
  - Submissions for special cases
- New researchers must complete CITI/HIPAA training
- For questions, contact Michelle Carr, MICHELLE.L2.CARR@UCDENVER.EDU

Quality Improvement vs. Research

- Quality improvement (QI): a project designed to improve practice or process within a particular institution or ensure it confirms with expected norms
  - Does not need to be submitted to COMIRB
  - Dissemination of information typically within the organization
- Research: a project designed to develop or contribute to generalizable knowledge.
  - Must submit to COMIRB
  - Published in medical journals, presented at conferences, etc.

IRB Exempt

- **Minimal Risk**
- Research on standard educational methods or techniques
- Research using surveys, interviews, educational tests or observation of public behavior
- Use of data, records, or documents that are **already in existence** at the time of research application.
- Research endorsed by DHHS examining public benefit or service programs
- Food taste/quality/consumer acceptance studies

IRB Expedited

- Research on drugs or devices for which no IND or IDE from the FDA are required
- Blood draws of limited volume and frequency
- Collection of biological samples, where the collection methods are minimal risk
- Non-invasive procedures to collect data (specifically excludes radiation/X-rays)
- Use of data or records, or use of samples collected for purposes other than research
- Data collected by photograph, digital image, or digital recording
- Use of questionnaires, interviews, psychological tests, or educational tests

IRB Full Board Review

- Greater than minimal risk
- Involves vulnerable populations (children, pregnant women, prisoners, persons who are challenged in decision making)
- Does not meet expedited categories

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Running the Study

- Work with the clinical research coordinator
- Follow the IRB-approved protocol
- Report adverse events to COMIRB within 5 days or according to the Data Safety and Monitoring Plan
- Submit Continuing Review Form to COMIRB annually
  - For multi-year trials only
- Keep research records for a minimum of 5 years after study completion
  - HIPAA related information a minimum of 7 years

Data Collection Tips

- Write a data dictionary describing each field in the database
- Use key files to separate PHI from research data
- Use redcap.ucdenver.edu to simplify data collection
- Add more columns, rather than using complex text fields

Tumor type	Tumor size
High grade glioblastoma	5x6x9
Low grade astrocytoma	5 by 7 by 1

Grade	Type	Length	Width	Height
High	Glioblastoma	5	6	9
Low	Astrocytoma	5	7	1

Summarizing the results

- Follow statistical analysis plan in the protocol
  - Call the biostatisticians if you need help
- Make sure your conclusions are supported by the results

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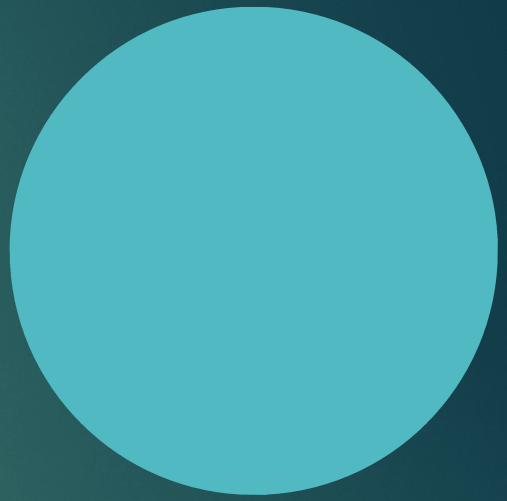
Publishing Basics

- Pick a target journal
- Determine coauthorship
- Write the manuscript
- Obtain coauthor approval
- Submit to the journal
- Respond to reviewers
- Obtain coauthor approval
- Repeat until manuscript acceptance

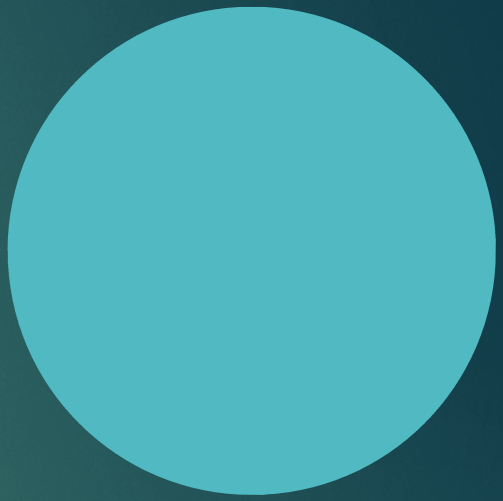


Anatomy of a manuscript

- Title page
- Acknowledgements and disclosures
- Abstract, including key words
- Body of the manuscript
- References
- Tables
- Figures

Manuscript body

- Introduction
  - What is the context?
  - What is the problem and why do I care?
  - What is the solution we propose?
  - What is the motivating example?
  - What did everyone else do?
  - What is the organizational structure of the paper?



Manuscript body

- Methods
  - Who are the participants?
  - What instruments were used?
  - What clinical procedures were used?
  - How was the statistical analysis performed?
- Results
  - Summarize the important results of the experiment
  - Tell the story, support with statistical results

Manuscript body

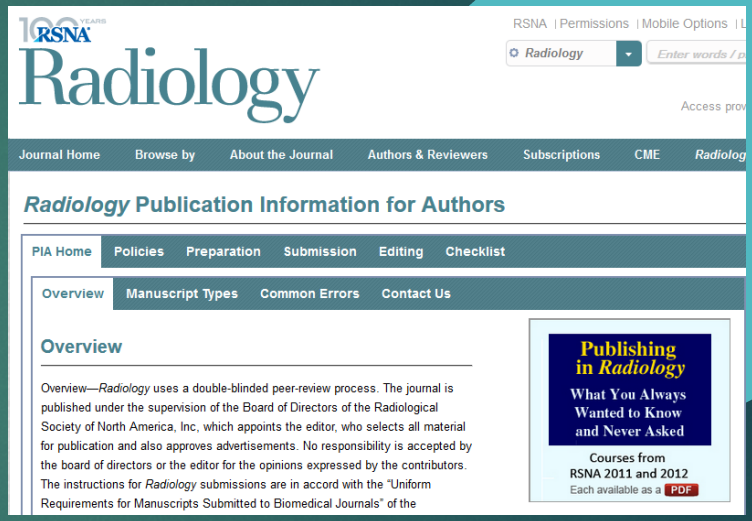
- Discussion
  - Interpret the results in the context of the clinical problem
  - Describe the limitations of the experiment
  - Describe how your findings relate to previously reported results
  - Describe how the work contributes to medical science
  - Suggest to readers how the work may be used in clinical practice

Communicating with coauthors

- Individuals who make an intellectual contribution to the project should be coauthors
- Obtain coauthor approval of the work prior to submitting or resubmitting to a journal or meeting
  - This applies to both abstracts and manuscripts

Journal submission

- Read the instructions for authors
- Note any page, word count or other length restrictions
- Format text, tables, and figures
- Submit all required documents
- The journal will typically assign a manuscript ID for correspondence



Journal response

- After review, the journal editor will determine if the manuscript is
  - Accepted
  - Rejected
  - Invited to resubmit with revisions
- The corresponding author will receive reviewer comments on the work

Response to Reviewers

- The authors must address all comments from the reviewers
- Create a separate document including reviewer comments
- Respond to each comment
  - Briefly describe changes made to the manuscript, or
  - Provide justification as to why no change was made
- Obtain coauthor approval for the updated manuscript and response to reviewers document
- Resubmit to the journal

A note about rejection

- A large proportion of manuscripts are rejected on the first try
- A rejection decision does not necessarily indicate that the work is not scientifically useful
- Often another journal may be a better venue
- Work with your coauthors to determine the best strategy
- Sho Kashima: "The pursuit of perfection is nothing without an appetite for failure"

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Mentored Scholarly Activity

- Specific Aims
- Significance and Innovation
- Materials and Methods
- Data collection plan
- Sample size selection
- Analysis plan

Question?