Strategizing for Submission of Original and Revised NIH Grant Proposals

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Disclosures

Research Support and Funding from

- National Institutes of Health (R01 CA169102, R01 CA202761)
- Varian Medical Systems
- Vision RT Ltd.

Professional Background

- Medical Physicist with >80% FTE research
- Research Interests: Imaging, IGRT, Motion Management, Functionally-Guided RT, Pre-clinical (small animal) IGRT
- Principal Investigator on several extramural grants including two active NIH R01 awards

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Purpose and Scope

- Share experience on good grant writing practices
  - Emphasis on Medical Physics-centered applications
- Several resources for general grant writing are available
  - Your own institution
  - NIH web site has examples of complete packages, including summary statements and reviews, of successful applications
  - NIH RePorter https://projectreporter.nih.gov/reporter.cfm
- We will focus on NIH R01 grants
  - Regarded as a "rite-of-passage" for junior and mid-career faculty
  - R01 or "equivalent" is a major factor in deciding tenure at academic institutions

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BEFORE YOU START WRITING

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Talk to your doctor(s)!

Identify Unmet Clinical Needs

- Physicists:
  - Develop good professional relationships with your physicians
    - Not just top-down
  - Attend "clinical" talks, patient treatments with new procedures
  - Be aware of ongoing and completed clinical trials
  - Be aware of controversial issues/studies
  - Discuss/initiate "physics-driven" solutions and clinical studies

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Understand Your Own Research

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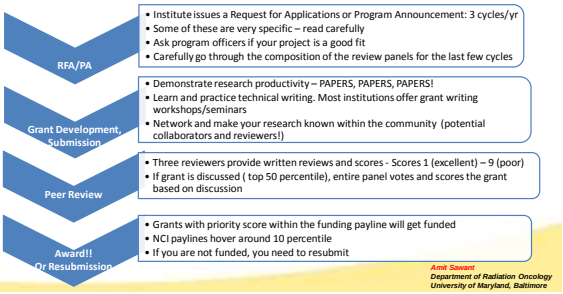
Understand The Process



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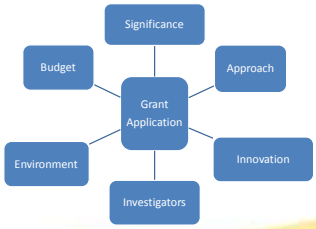
Understand The Review Criteria

These form the building blocks of your grant



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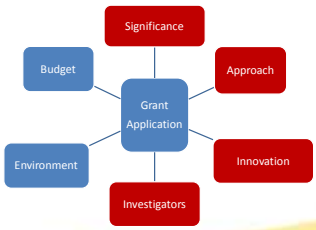

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WRITING

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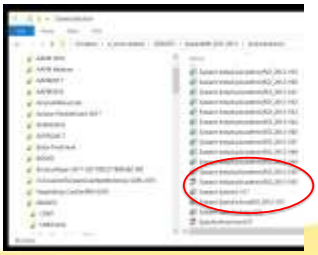
START EARLY!

- Good writing takes time and several iterations



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START EARLY!

- Most common PI mistake – underestimating the time required
  - If you submit hastily put-together applications, you will get a reputation for submitting junk
- New PIs – Start writing 6-8 months before submission deadline
  - Involve collaborators from the beginning. Especially important for multidisciplinary projects (e.g., physicist + clinican, physicist + radiobiologist)
  - Aim to send the first draft to co-Is and senior colleagues at least 2 months before deadline

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Science Section - 1 + 12 pages

- Suggested allocation – will vary from grant-to-grant
  - Specific Aims: 1 page (hard limit)
  - Significance: 1.5 pages
  - Innovation: ½ page
  - Approach: 10 pages

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Specific Aims

- Spend a lot of time on this section
- Send this to senior colleagues. Ask them to be very critical!
- "Mini-grant" – experienced reviewers will use this section to triage applications
- One-page limit – use your real estate wisely
  - Physicists: avoid the temptation to include complicated formulas, flowcharts and figures

- Develop your budget in parallel with your SA
  - Will help you determine the scope of your research plan

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Specific Aims

- Elevator pitch
- Significance, previous work/expertise, potential impact
- Central Hypothesis/Goal
- Aims
  - Hypothesis or goals
- Research Team

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Significance

- Foundational section
  - Is your work clinically important? Does it address a gap in the field or an unmet clinical need?
  - If successful, will it make a significant, impactful difference?

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Significance

- Physicists – Articulate the clinical relevance
  - If successful, what will be the impact on patient-care, outcomes?
  - How many patients will this potentially help?
- For example,
  - "Physics" argument – Better motion management will lead to improved geometric and dosimetric accuracy, reducing dose to OARs
  - "Clinical" argument – Improved margin reduction and OAR sparing through better motion management may enable the inclusion of lung cancer patients with larger and/or more central tumors who are currently ineligible for lung SBRT
- Caveat: Don't overreach. Craft your language carefully

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To Hypothesize or Not?

- Physicists – Sometimes your research may not be amenable to a hypothesis.
  - E.g., device or algorithm development, shared data or QA framework
- In these cases, have clear, quantifiable, and testable goals
- If you propose a hypothesis, it should be statistically testable!
  - Do: Add a biostatistician to your team
  - Don't: Try to add them at the last minute – you may get a letter of support, but a poor statistical design
- Add a Statistics section in your Approach to test each sub-hypothesis and the overall hypothesis

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To Hypothesize or Not?

- Physicists: DON'T force a hypothesis

Forced hypothesis:

We hypothesize that we will successfully develop a photon-counting flat panel imager

Poorly constructed hypothesis:

4π RT is important in reducing toxicity in GBM patients

Testable hypothesis:

4π RT yields significant normal tissue dose reduction compared to VMAT in GBM patients

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Approach (Research Plan)

- Present your preliminary data
- Clearly define the scope of your proposed work
- Your Approach should test your overall hypothesis or articulate how you will achieve your stated goals
- Each aim should contain the following parts, explicitly or implicitly:
  - Proposed work and expected results – Be specific. Don't go fishing!
    - Fishing example: we will evaluate several deformable image registration algorithms and use the best performing DIR.
  - Validation – independent ground truth, gold standard, clinical consensus
  - Challenges and alternate approaches

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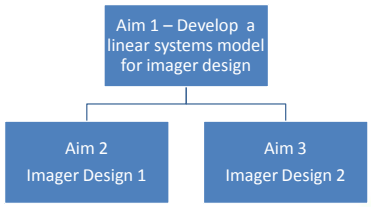
Approach: Connect your specific aims



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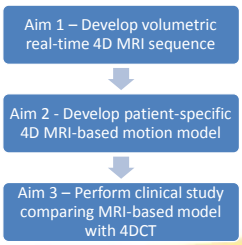
Approach: Connect your specific aims



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Approach: Fallback and alternate strategies

- Aims should be connected but not completely dependent, i.e., is Aim (n+1) possible if Aim n fails
- Say, proposed rapid 4D MRI in Aim 1 is not successful
  - Use the simplistic model demonstrated in your preliminary data
    - lower performing but allows you to proceed with Aims 2 and 3
  - Develop a model using repeat 4DCTs and 2D+t MRI (assuming both are available)
    - comparable performance to originally proposed model but higher imaging dose
    - Allows you to proceed with Aims 2 and 3

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Innovation

- Every RFA/PA clearly articulates how they define innovation specific to that mechanism – read carefully
- Explain why your proposed work is innovative according to the criteria defined in the announcement
- E.g.,
  - Basic science grants – innovation is novel discoveries, methods, technical development
  - Academic Industrial Partnerships – innovation is development and end-user testing of a new prototype
- Explain the potential short- and long-term impact on research within the community if your work is successful

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Environment

- List and describe the equipment, resources available at your institution
- Tie each to one or more Specific Aims if possible
- Include pictures – makes things look real
- No page limits in this section. But do not irritate the reviewers by doing a data dump!

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Budget and Justification

- Develop your budget when you develop your Specific Aims
  - Ensures that you don't overshoot or undershoot in terms of resources
- Don't try to "pad" the budget – irritates reviewers and harms your credibility
- Don't try to under-budget either. Reviewers need to know: Will you have adequate resources to perform the work proposed.
- Justify, Justify Justify!
- Tie your personnel and equipment justifications to your Specific Aims
  - E.g., we need a high-performance GPU workstation for real-time sparse image reconstruction proposed in Aim 1

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Investigators

- For new PIs - Delicate balance between getting senior and junior co-Is
- Make sure that each Biosketch and letter of support is carefully crafted
- The Biosketch paragraph and listed publications should contain general expertise and expertise specific to the grant
- Letters of support should include the specific responsibilities of each co-I

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Do's and Don'ts

- New PIs – Don't be over ambitious in terms of scope or impact. Stick to what you can test, validate.
- Stay on message! Be logically consistent across the grant (Approach, Budget, LoS, Environment).
- Include pictures of critical prototypes, experimental setups, etc. in the main body of the research plan
- Errors and sloppiness can be deadly!
  - Proof read thoroughly
  - Ask friends, colleagues to proof read – Most physicists work for beer!

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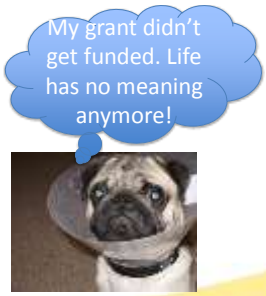
RESUBMISSION



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RESUBMISSION

- Most applicants don't get funded in the first submission. Don't take it personally.
- If your grant did not get discussed, the reviewers found serious flaws
  - You may need to seriously reconsider your research question, redefine your focus
- If you received a score but were not funded, there are issues, but very likely, fixable
  - Wait until you receive the Summary Statement
  - Talk to your program officer. If they were in the room during the discussion, they may have some additional insight
  - Do NOT try to contact the reviewers yourself. Even if you know them.

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RESUBMISSION

- You get 1 page for a rebuttal
- As for Specific Aims, real estate is important
- First – Thank the reviewers for their time and effort in critiquing your grant.
- Focus on the positives expressed in the Summary Discussion
- Paraphrase or quote the concerns expressed by the committee
- Summarize how you have addressed these in your resubmission, making it a significantly improved application. E.g.,
  - Publications: Developed and published a feasibility study on real-time 4DMRI
  - Preliminary Data: Analyzed and included retrospective motion error data from 20 patients
  - Expertise: Added Dr. Smith to the team. Dr. Smith is a world expert on sparse sampling and reconstruction in MR imaging

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RESUBMISSION

- Consolidate the critiques from individual reviewers. Create a key (SS – Summary St., R1, R2, R3)
- Make sure you address each major critique. Often, a reviewer is part a standing study section and serves on multiple cycles.
- New PIs - Be very conscious of your "tone"
  - Do not be dismissive or irritable. Even if you think the reviewer is being unfair. Try to understand where the reviewer is coming from

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2. Investigator(s):

Strengths

- Multi-investigator team brings significant expertise and experience to bear on the proposed aims
- Positions are filled with named individuals

Weaknesses

- An AIP with as many academic and industrial partners may not be the best platform for a new investigator to begin to establish an independent identity given the complexity of the additional relationships that have to be managed and led
- Accordingly, the number of first-author or senior-author peer-reviewed papers is relatively modest and, if continued, is likely to undermine the career development of the applicant

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RESUBMISSION

- Two ways to go – agree with the reviewer and make required changes; or disagree with the reviewer and explain why

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RESUBMISSION

- If you agree, all you require is a one sentence response
  - Agreed. We have included a rigorous experimental technique to validate the geometric fidelity of 4D MRI (Sec. C.2.2)
- If you disagree, do so respectfully and politely. Do this very rarely!
  - First find some common ground
  - Then politely point out why the reviewer's understanding, interpretation, concern is incorrect. Best way to do so is to provide supporting data and/or citations
  - E.g., *Rapid 4D MRI of the lung may produce severe geometric distortions due to susceptibility artifacts making it unsuitable for RT image guidance (R1)* –

We agree that geometric fidelity is critical for RT guidance. However, recent studies (Refs 1-5) suggest that such artifacts are minimal at 1.5 T, the field strength proposed in our study. Furthermore, in order to address the reviewer's concern, we present recently acquired data from a lung MRI phantom using the sequences proposed in this application. Our analysis determined that the mean geometric distortions along three dimensions were 0.3 mm (AP), 1.1 mm (SI) and 0.8 mm (LR), suggesting that the field strength and the selected imaging sequences proposed will yield images suitable for RT guidance.

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Summary and Conclusion

- Putting together a competitive R01 is a lot of work
- There is no box of magic tricks. It takes practice, persistence and more practice
- Science section is only a part of the application. Other parts, e.g., budget, letters of support, environment, are also very important
- Getting funded is a very intellectually rewarding experience
- New PIs – get writing!

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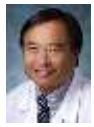

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