UNIVERSITY of MARYLAND SCHOOL OF MEDICINE

Strategizing for Submission of Original and Revised NIH Grant Proposals

Amit Sawant, PhD.
Department of Radiation Oncology
University of Maryland, Baltimore

Disclosures

Research Support and Funding from

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

Personal Background

[redacted]

TRUST ME – I'M NOT AN EXPERT!

Purpose and Scope

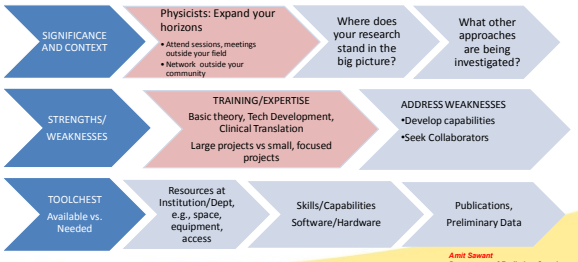
https://projectreporter.nih.gov/reporter.cfm

Amit Sawant
Department of Radiation Oncology
University of Maryland, Baltimore

BEFORE YOU START WRITING

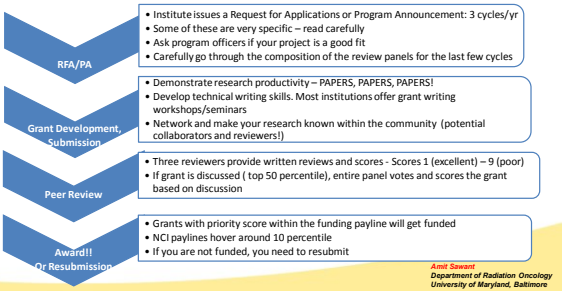
Amit Sawant
Department of Radiation Oncology
University of Maryland, Baltimore

Understand Your Research



Amit Sawant
Department of Radiation Oncology
University of Maryland, Baltimore

Understand The Process



Amit Sawant
Department of Radiation Oncology
University of Maryland, Baltimore

Understand The Review Criteria

These form the building blocks of your grant

Amit Sawant
Department of Radiation Oncology
University of Maryland, Baltimore

WRITING

Amit Sawant
Department of Radiation Oncology
University of Maryland, Baltimore

START EARLY!

- Good writing takes time and several iterations
- 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
  - Aim to send the first draft to co-Is and senior colleagues at least 2 months before deadline

Amit Sawant
Department of Radiation Oncology
University of Maryland, Baltimore

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

Amit Sawant
Department of Radiation Oncology
University of Maryland, Baltimore

Specific Aims

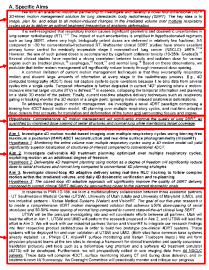
- Spend a lot of time on this section!
- Seek feedback from senior colleagues, mentors
- "Mini-grant" – experienced reviewers will use this section to triage applications
- One-page limit – use your real estate wisely
  - Physicists: avoid the temptation to include complicated formulas, flowcharts and figures

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

Amit Sawant
Department of Radiation Oncology
University of Maryland, Baltimore

Specific Aims

- Elevator pitch
- Significance, potential impact
- Hypothesis
- Aims
  - Hypothesis or goals
- Team



A. Specific Aims

Amit Sawant
Department of Radiation Oncology
University of Maryland, Baltimore

Significance

- Foundational section
  - Is your work clinically important? Does it address a gap in the field?
  - If successful, will it make a significant, impactful difference?
- Physicists: Talk to your doctor(s)!
  - Develop good professional relationships with your physicians
  - Attend "clinical" talks
  - Be aware of the latest findings from single- and multi-center trials
  - Be aware of controversial issues
  - Cite these when you make your Significance argument

Amit Sawant
Department of Radiation Oncology
University of Maryland, Baltimore

Significance

- Physicists – Cast your arguments to demonstrate 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

Amit Sawant
Department of Radiation Oncology
University of Maryland, Baltimore

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!
  - Add a statistician to your team
  - Good idea to have a hypothesis for each aim as well – shows good organization. These also need to be testable
- Add a Statistics section in your Approach to test each sub-hypothesis and the overall hypothesis

Amit Sawant
Department of Radiation Oncology
University of Maryland, Baltimore

To Hypothesize or Not?

- Physicists: DON'T force a hypothesis

Forced hypothesis:

We hypothesize that we will successfully develop a high-performance breast CT system using a x-ray photon counting imager

Poorly constructed hypothesis:

4π RT is important in reducing toxicity in GBM patients

Testable hypothesis:

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

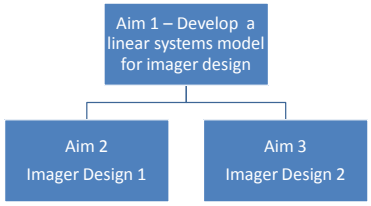
Amit Sawant
Department of Radiation Oncology
University of Maryland, Baltimore

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 or gold standard
  - Challenges and alternate approaches

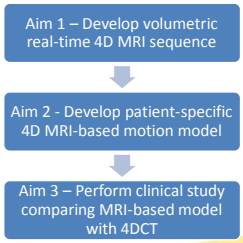
Amit Sawant
Department of Radiation Oncology
University of Maryland, Baltimore

Approach: Connect your specific aims



Amit Sawant
Department of Radiation Oncology
University of Maryland, Baltimore

Approach: Connect your specific aims



Amit Sawant
Department of Radiation Oncology
University of Maryland, Baltimore

Approach: Fallback and alternate strategies

- One concern for connected aims is dependency, i.e., is Aim (n+1) possible if Aim n fails
- Say, proposed 4D MRI sequence 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

Amit Sawant
Department of Radiation Oncology
University of Maryland, Baltimore

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

Amit Sawant
Department of Radiation Oncology
University of Maryland, Baltimore

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!

Amit Sawant
Department of Radiation Oncology
University of Maryland, Baltimore

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
- Justify, Justify Justify! Remember that, in a sense, the entire grant is a budget justification
- Tie your personnel and equipment justifications to your Specific Aims

Amit Sawant
Department of Radiation Oncology
University of Maryland, Baltimore

Investigators

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

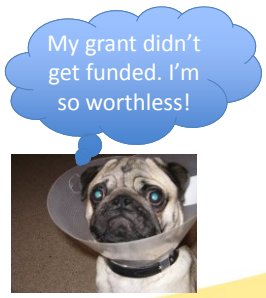
Amit Sawant
Department of Radiation Oncology
University of Maryland, Baltimore

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!

Amit Sawant
Department of Radiation Oncology
University of Maryland, Baltimore

RESUBMISSION



Amit Sawant
Department of Radiation Oncology
University of Maryland, Baltimore

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.

Amit Sawant
Department of Radiation Oncology
University of Maryland, Baltimore

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 significantly improved application. E.g.,
  - In response to the critiques we have
    - Developed and published a feasibility study on real-time 4DMRI
    - Analyzed and included retrospective motion error data from 20 patients
    - Added Dr. Smith to the team. Dr. Smith is a world expert on sparse sampling and reconstruction in MR imaging

Amit Sawant
Department of Radiation Oncology
University of Maryland, Baltimore

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 cycle.
- New PIs - Be very conscious of your "tone"
  - Do not be dismissive or irritable. Even if you think the reviewer is being unfair
- Two ways to go – agree with the reviewer and make required changes; or disagree with the reviewer and explain why

Amit Sawant
Department of Radiation Oncology
University of Maryland, Baltimore

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.

Amit Sawant
Department of Radiation Oncology
University of Maryland, Baltimore

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!

Amit Sawant
Department of Radiation Oncology
University of Maryland, Baltimore

Acknowledgements


Larry Antonuk
University of Michigan


Paul Keall
University of Sydney


John Wong
Johns Hopkins University

Amit Sawant
Department of Radiation Oncology
University of Maryland, Baltimore