A Journey to my first NIH/NCI R01 Grant

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Overview

- Brief introduction of myself and my R01 project
- Before start
- On the journey
  - Trials of failure
  - Write the application
  - Submit the application
  - Failure is the mother of sucess
- Destination is a new start

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Brief introduction of myself

- Nuclear physics and semiconductor physics background
- Graduated from a medical physics resident program when there were only handful of physics residents in the world
- Work in a semi-academic institution as a full time clinical physicist
- Like to have innovative ideals, published ~2 first-author articles per year

Brief introduction of the R01 project

- Title: A synchronized moving grid (SMOG) to improve CBCT for IGRT and ART
- Use a moving grid to address 3 major issues: scatter, image lag, and geometric variations
- Expect to substantially improve the image quality of CBCT
- Has applications in image guided radiotherapy (IGRT), adaptive radiotherapy (ART) and other feilds

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Before start – preparing for the journey

- Have been familiar or mastered the clinical part of work (passing the ABR board, understanding the capability and limitation of our field)
- Constantly generate new ideals during daily practicing and lessening to scientific and clinical presentations
- Accumulate reasonable research experience and publications by testing the new ideals
- A strong desire to explore the unknown

Preparing for the journey

- Get supports from my boss and colleagues
- Learning the potential funding resources: the NIH, DOD, private foundations, related professional societies (ASTRO, AAPM, RNSA, cancer society…)…
- Get advices from experienced and successful researchers
- Learning the basic procedures

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On the journey – the first launch

- My first try is a R21 application on combined optical and x-ray imaging to monitor patient motion during spinal radiosurgery
- Get a score of 54%--triaged
- Get some review comments, significance is low because the project only benefits for small percentage of patients
- Get familiar with the whole application procedure

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On the journey – the 2nd launch

- The second attempt was still a R21 applicatio: the SMOG CBCT project
- The project had much broader application, higher significance
- Got a score of 40%, got reviewed and some comments back
- Got to know better that the reviewers may do not have time to read and understand my writing: simplicity is the key!

On the journey: change from R21 to R01

- According to a presentation by a NIH specialist, a R01 application is better than R21 for me because R01 can take advantage of the new-investigator status
- My boss also helped me to get a strong team for a bigger project
- More preliminary results were also available

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On the journey: write the application

- The scientific part has been shorted from 21 pages to 12 + 1 pages
- Specific aim: 1 page
- Research strategy: total 12 pages, includes
  - Significance
  - Innovation
  - Approach
- Other parts of application

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Specific aims

- The most important part of the application
- The voting members of the study section may only briefly read this part
- Concisely introduce the project and the hypothesis
- Clearly state each specific aim, and the rationale and approach to achieve the aim
- Final summary of the significance and impact

Specific Aims

The development of on-board cone-beam CT (CBCT) imaging is a significant advancement in image-guided radiation therapy (IGRT) because it uses volumetric anatomical information for target localization. However, the image quality in current first generation CBCT scanners is not ideal for routine IGRT, and especially not adequate for image guided adaptive radiation therapy (ART). This is primarily due to 3 factors: scatter, image lag and gantry flex. Considering that the image volume is usually much larger than the treatment volume, imaging dose from daily IGRT also presents a concern for secondary cancer induction. Many methods have been proposed to address these issues. However, the improvement has been limited, especially with regard to the scatter problem. This is because most of these methods use scatter correction approaches, which only reduce scatter artifacts with a side effect of degrading the contrast-to-noise ratio (CNR). Recently we demonstrated that a simultaneous scatter reduction and correction method with a static grid not only removed scatter artifacts, but also improved CNR (Jin et al 2010). This technique was considered "to be promising in IGRT" (Ruhrnschopf et al 2011). However, the technique requires two rotations for data acquisition. In this study, we propose a Synchronized Moving Grid (SMOG) system to not only overcome the two-rotation problem in the static grid technique, but also comprehensively address other issues. **We hypothesize that**: **(1)** the SMOG system will mitigate all three effects (scatter, lag and flex); **(2)** optimizing the SMOG system parameters using Monte Carlo (MC) simulations and a compressed sensing algorithm will improve image quality and minimize imaging dose; **(3)** the combined benefit of these developments in the SMOG system will vastly improve CBCT image quality with reduced imaging dose for IGRT and ART applications.
The specific aims of this study are:

Aim 1: *To conceptually prove that a SMOG device will minimize the effects of scatter, lag and flex.* The SMOG system takes multiple partial projections at each gantry position with a moving grid operating in a rapidly oscillating pattern synchronized with the gantry motion. Image data are acquired in the inter-space region, while scatter is measured in the shadow region. A full projection is obtained by merging the partial projections, and only one rotation is needed for data acquisition. The moving grid also switches between the image and shadow regions repeatedly in the imager, so that the image lag in the two regions are similar. Thus, the lag will be removed during scatter correction. Moreover, a grid with a small aperture in the septa will be used to directly detect gantry flex information and correct for it. We have used a static grid with multiple rotations to simulate the SMOG approach for evaluating scatter reduction and correction, and an image lag model to simulate lag correction. These preliminary studies have shown very promising results.

Aim 2: *To optimize the SMOG system parameters with MC simulation and compressed sensing*. The SMOG system parameters, including the grid parameters and the number of exposures (*n*) in each gantry position, greatly impact the image quality and imaging dose of the CBCT system. MC simulation is used to study the impact of the grid parameters (including thickness and width of the grid septa, septa-to-interspace ratio, and source-to-grid distance) on primary and scattered radiation, and to optimize these parameters based on the simulation results. Compressed sensing is used primarily to optimize *n* to further reduce scatter and imaging dose. This is achieved by optimizing the number of projections (*N*) in reconstruction, because the total number of exposures in a scan, $N*n$, is usually constant due to the limited frame rate of the flat panel detector.

Aim 3: *To develop and evaluate a SMOG-based CBCT prototype system for IGRT and ART.* The combined benefits of the innovative aspects of the SMOG system can only be demonstrated by developing a SMOG-based CBCT prototype system. A synchronized moving grid with optimized parameters will be fabricated, first tested on an available CBCT test bench, and finally installed in an on-board or stand-alone CBCT system. Phantoms and cadavers will be used to evaluate the improvements in image quality, imaging dose, and image accuracy for applications in IGRT and ART. Auto-segmentation, rigid and deformable image registration and dose calculation will be used as the metrics for IGRT and ART applications.

Innovation/Impact: *Using a SMOG system to simultaneously address three important issues in CBCT imaging is the major innovation of this proposal*. In each of the 3 issues, preliminary studies suggest that the SMOG device presents an appreciable improvement over previous techniques. The proposal is also *innovative in its use of MC simulation and compressed sensing to optimize system parameters to improve image quality and minimize imaging dose*. We anticipate that the combined benefits of these innovations will **vastly improve image quality with reduced patient dose**. If successful, it may lead to the development of a new generation of CBCT with image quality adequate for ART applications. This study will affect the lives of millions of patients requiring IGRT and ART who would benefit from improved radiation treatment, and also impact other fields of medicine, given the wide range of applications in which CBCT imaging is applicable.

An example of the specific aim

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Research strategy

- ❑ Significance

1-3 pages, state the importance of this project. May review what others have done, and what difference I will make

- ❑ Innovation

1-3 pages, list all the innovations for each specific aim

- ❑ Approaches

6-10 pages, detailed description of the research plan for each specific aim. Incorporate the preliminary results here!

Get comments from others

- Ask one person not in the related field to read – can it be read through? Does it make sense?
- Ask one person knowing something about the related field to review
- Ask an expert, and co-investigators to review

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Other documents

- Many documents!!!
- The good news is that the research administrators may help for some of these
- Biosketch of all co-investigators
- A statistician
- Support letters!!!
- Clinical protocols

Submission

- Be ready one weeks before deadline
- The research administrator of the institution will check the documentation and submit for the application
- Check for the accuracy of the documentation after submission (there are several days of grace period)
- Waiting for another failure and critical comments

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Resubmission

- One page of introduction to address all the concerns and questions from the reviewers' comments
- May wait for one cycle to resubmit
- The score may get worse in the resubmission
- The score may also be dramatically improved

Failure is the mother of success

Failure is the Mother of Success
(Chinese Translation)
失败是成功之母

- I finally get a 3% review score and the project finally get funded

After receiving the award

- Congratulations!!!
- Waiting for the money to moving in
- Hiring postdoc and graduate students
- Buying related equipment
- Reduced clinical coverage

Every destination is a new start

- A NIH project is not the same as just writing a paper
- Many tasks, including mechanic and electronic engineering and designs
- Have to worry about the annual report
- Have to worry about Postdocs quits the job
- Good news: have time and money to think about new interesting projects

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Enjoy a SMOG show