Summary of the proposal

An effective way to control a chronic disease is screening examination when it is available, such as mammography, that exams seemingly healthy individual to detect the disease before the clinical symptoms showing. The optimal schedule for screening examinations for breast cancer in terms of examination frequency and ages of examination is of interest. A tangible procedure for obtaining optimal scheduling that is useful in practice is desired, and this research project is to develop such a procedure. We plan to address fundamentally important issues by establishing a mathematical model of the costs and benefits of a screening program in order to assist in identifying a true optimal screening schedule that balances the goals of reducing morbidity and mortality against the associated burden to individuals in the screening population and the cost to the health care systems.

Description of grant-supported activity

During the summary of 2009, I travelled to Houston as a visiting scholar at the Biostatistics Department, the M.D. Anderson Cancer Center, which is an institute in the University of Texas system. During the one-month visiting period, I worked on the project with my collaborators Dr. Yu Shen at M.D. Anderson Cancer Center and Dr. Charlotte Hsieh Ahern at Baylor College of Medicine. We studied the existing literature in the scheduling of screening examinations for breast cancer and some sensitive issues in this regard. We collected large pool of data from the current screen scheduling and categorized data by age and location. We recognized the areas of inadequacy of the mathematical models in the current literature and began with new models aimed at improving the current models. As our studies went deep and broad, we considered several new models in more innovative ways.

Early detection programs often involve huge costs and a long-term commitment. Therefore, it is important to evaluate the magnitude of survival benefit and to understand the trade-off between costs of examination and gains in survival. We established a stable disease model to the general non-stable disease model, and from a fixed cost, that is, the number of examinations, to a utility function that includes a non-fixed cost/number of exams. In particular, we investigated optimal scheduling programs by taking into consideration age-dependent preclinical incidence of disease as well as the costs of screening exams and the dollar value of benefit. The number of examinations may or may not be fixed for a given screening horizon. We explored two distinct frameworks for the utility function given the estimated age-dependent preclinical incidence, screening sensitivity, and sojourn time distribution. Because an equal screening interval has implementation advantages at the population level, one of our focuses was to search for the optimal equal interval within a specified screening horizon under the non-stable disease model with a screening sensitivity that may not be perfect. We further derived the optimal ages for examinations within a specified screening horizon given the number of examinations, or a fixed budget, for which the optimal screening program may not have equal screening intervals. We proved the optimality of our proposed scheduling with mathematical rigor.
• Completion of the project? Description of the difficulty experienced

The proposed project was completed, though it was not complete in the summer of 2009. The research took extended time until the spring of 2010 because the challenging part of mathematical proofs in dealing with large number of equations and parameters. The simulations in the validation of the methods also encountered substantial difficulty in coding and in computational time in process of searching optimal settings.

Although the project was completed, we recognize that our models have the certain limitations. The assumptions of a linear age-dependent incidence model and an exponential preclinical sojourn time distribution allow for a feasible mathematical proof for the existence of the optimal solution under the first framework, even though the model assumptions may not be ideal. However, any smooth function can be approximated by a linear function via the Taylor series expansion, and a linear age-specific incidence model should be a reasonable choice. While the assumption that the sojourn time in the preclinical state is exponentially distributed may not necessarily be the best fit, it is practically the only parametric model satisfactorily used in the literature. Alternative models for the preclinical incidence and distributions for the sojourn time may be further explored in future work. Moreover, we have not explicitly accounted for the cost of false-positive exams in the utility functions or included a component for competing risks for death, which opens various projects for the future research.

• The result in a product -- a manuscript

Our result has been written in a manuscript titled Optimal Cancer Screening Schedules Under the Non-Stable Disease Model. We are polishing the writing and presentation of the numerical results at this time and plan to submit it for publication soon.

• Acknowledgement

I am grateful to the Department of Mathematical Sciences, the College of Liberal Arts and Sciences, the Office of Research, the Senate Research and Development Committee, and the Office of Academic Affairs at IUSB for the support and encouragement that I have received. I am also thankful to the Indiana University for making the funds available. Such a support was critically important to the success of the project, which I deeply appreciate.