Preface to the second edition

It seems like only yesterday that I was sending the “camera ready” pdf file of this book off to Prentice Hall. Despite a very positive response from the mathematics and engineering communities, Pearson decided, last year, to let the book go out of print. I would like to thank George Lobell, my editor at Prentice Hall, for making it so easy to reacquire the publication rights. Secondly I would like to thank SIAM, and my editors Sarah Granlund and Ann Manning Allen, for making it so easy to prepare this second edition. I would be very remiss if I did not thank Sergei Gelfand, editor at the AMS, who prodded me to get the rights back, so I could prepare a second edition.

The main differences between this edition and the Prentice Hall edition are: 1. A revised section on the relationship between the continuum and discrete Fourier transforms, Section 10.2.2 (reflecting my improved understanding of this problem); 2. A short section on Grangreat’s formula, Section 10.2.2, which forms the basis of most of the recent work on cone-beam reconstruction algorithms; 3. A better description of the gridding method, Section 11.8 (many thanks to Leslie Greengard and Jeremy Magland for helping me to understand this properly); 4. A chapter on magnetic resonance imaging, Chapter 14; 5. A short section on noise analysis in MR-imaging, Section 16.3. For the last two items I would like to express my deep gratitude to Felix Wehrli, for allowing me to adapt an article we wrote together for the Elsevier Encyclopedia on Mathematical Physics, and for his enormous hospitality, welcoming me into his research group, the Laboratory for Structural NMR Imaging, at the Hospital of the University of Pennsylvania.

With a bit more experience teaching the course and using the book, I now feel that it is essential for students to have taken at least one semester of undergraduate analysis, beyond calculus, and a semester of linear algebra. Without this level of sophistication, it is difficult to appreciate what all the fuss is about.

I have received a lot of encouragement to prepare this second edition from the many people who used the book, either as a course textbook or for self study. I would like to thank Rafe Mazzeo, Petra Bonfert-Taylor, Ed Taylor, Doug Cochran, John Schotland, Larry Shepp, and Leslie Greengard for their kind words and advice. Finally, I thank my wife, Jane, and our children, Leo and Sylvia, for their forebearance during the endless preparation of the first edition, and their encouragement to produce this second edition.

Charles L. Epstein
May 16, 2007

Preface

Over the past several decades, advanced mathematics has quietly insinuated itself into many facets of our day-to-day life. Mathematics is at the heart of technologies from cellular telephones and satellite positioning systems to online banking and metal detectors. Arguably no technology has had a more positive and profound effect on our lives than medical imaging, and in no technology is the role of mathematics more pronounced or less appreciated. X-ray tomography, ultrasound, positron emission tomography, and magnetic resonance imaging have fundamentally altered the practice of medicine. At the core of each modality is a mathematical model to interpret the measurements and a numerical algorithm to reconstruct an image. While each modality operates on a different physical principle and probes a different aspect of our anatomy or physiology, there is a large overlap in the mathematics used to model the measurements, design reconstruction algorithms, and analyze the effects of noise. In this text we provide a tool kit, with detailed operating instructions, to work on the sorts of mathematical problems that arise in medical imaging. Our treatment steers a course midway between a complete, rigorous mathematical discussion and a cookbook engineering approach.

The target audience for this book is junior or senior math undergraduates with a firm command of multi-variable calculus, linear algebra over the real and complex numbers, and the basic facts of mathematical analysis. Some familiarity with basic physics would also be useful. The book is written in the language of mathematics, which, as I have learned, is quite distinct from the language of physics or the language of engineering. Nonetheless, the discussion of every topic begins at an elementary level and the book should, with a little translation, be usable by advanced science and engineering students with some mathematical sophistication. A large part of the mathematical background material is provided in two appendices.

X-ray tomography is employed as a *pedagogical machine*, similar in spirit to the elaborate devices used to illustrate the principles of Newtonian mechanics. The *physical principles* used in x-ray tomography are simple to describe and require little formal background in physics to understand. This is not the case in any of the other modalities listed nor in less developed modalities like infrared imaging or impedance tomography. The *mathematical* problems that arise in x-ray tomography and the tools used to solve them have a great deal in common with those used in the other imaging modalities. This is why our title is *Introduction to the Mathematics of Medical Imaging* instead of *Introduction to the Mathematics of X-Ray Tomography.* A student with a thorough understanding of the material in this book should be mathematically prepared for further investigations in most subfields of medical imaging.

Very good treatments of the physical principles underlying the other modalities can be found in *Radiological Imaging* by Harrison H. Barrett and William Swindell, [6], *Principles of Computerized Tomographic Imaging* by Avinash C. Kak and Malcolm Slaney, [76], *Foundations of Medical Imaging* by Cho, Jones, Singh, [22], *Image Reconstruction from Projections* by Gabor T. Herman, [52], and *Magnetic Resonance Imaging* by E. Mark Haacke, Robert W. Brown, Michael R. Thompson, Ramesh Venkatesan, [50]. Indeed these books were invaluable sources as I learned the subject myself. My treatment of many topics owes a great deal to these books as well as to the papers of Larry Shepp and Peter Joseph and their collaborators. More advanced treatments of the mathematics and algorithms introduced here can be found in *The Mathematics of Computerized Tomography* by Frank Natterer, [95], and *Mathematical Methods in Image Reconstruction* by Frank Natterer and Frank Wübbelling, [96].

The order and presentation of topics is somewhat nonstandard. The organizing principle of this book is the evolutionary development of an accurate and complete model for x-ray tomography. We start with a highly idealized mathematical model for x-ray tomography and work toward more realistic models of the actual data collected and the algorithms used to reconstruct images. After some preliminary material we describe a continuum, complete data model phrased in terms of the Radon transform. The Fourier transform is introduced as a tool, first to invert the Radon transform and subsequently for image processing. The first refinement of this model is to take account of the fact that real data are always sampled. This entails the introduction of Fourier series, sampling theory, and the finite Fourier transform. After introducing terminology and concepts from filtering theory, we give a detailed synthesis of the foregoing ideas by describing how continuum, shift invariant, linear filters are approximately implemented on finitely sampled data. With these preliminaries in hand, we return to the study of x-ray tomography, per se. Several designs for x-ray computed tomography machines are described, after which we derive the corresponding implementations of the filtered back-projection algorithm. At first we assume that the x-ray beam is one dimensional and monochromatic. Subsequently we analyze the effects of a finite width beam and various sorts of measurement and modeling errors. The last part of the book is concerned with noise analysis. The basic concepts of probability theory are reviewed and applied to problems in imaging. The notion of signal-to-noise ratio (SNR) is introduced and used to analyze the effects of quantum noise on images reconstructed using filtered back-projection. A maximum likelihood algorithm for image reconstruction in positron emission tomography is described. The final chapter introduces the idea of a random process. We describe the random processes commonly encountered in imaging and an elementary example of an optimal filter. We conclude with a brief analysis of noise in the continuum model of filtered back-projection.

The book begins with an introduction to the idea of using a mathematical model as a tool to extract the physical state of system from feasible measurements. In medical imaging, the "state of the system" in question is the anatomy and physiology of a *living* human being. To probe it nondestructively requires considerable ingenuity and sophisticated mathematics. After considering a variety of examples, each a toy problem for some aspect of medical imaging, we turn to a description of x-ray tomography. This leads us to our first mathematical topic, *integral transforms*. The transform of immediate interest is the Radon transform, though we are quickly led to the Abel transform, Hilbert transform, and Fourier transform. Our study of the Fourier transform is dictated by the applications we have in mind, with a strong emphasis on the connection between the smoothness of a function and the decay of its Fourier transform and vice versa. Many of the basic ideas of functional analysis appear as we consider these examples. The concept of a weak derivative, which is ubiquitous in the engineering literature and essential to a precise understanding of the Radon inversion formula, is introduced. This part of the book culminates in a study of the Radon inversion formula. A theme in these chapters is the difference between finite- and infinite-dimensional linear algebra.

The next topics we consider are Fourier series, sampling, and filtering theory. These form the basis for applying the mathematics of the Fourier transform to real-world problems. Chapter 8 is on sampling theory; we discuss the Nyquist theorem, the Shannon–Whittaker interpolation formula, the Poisson summation formula, and the consequences of undersampling. In Chapter 9, on filtering theory, we recast Fourier analysis as a tool for image and signal processing. The chapter concludes with an overview of image processing and a linear systems analysis of some basic imaging hardware. We then discuss the mathematics of approximating continuous time, linear shift invariant filters on finitely sampled data, using the finite Fourier transform.

In Chapters 11 and 12 the mathematical tools are applied to the problem of image reconstruction in x-ray tomography. These chapters are largely devoted to the filtered back-projection algorithm, though other methods are briefly considered. After deriving the reconstruction algorithms, we analyze the point spread function and modulation transfer function of the full measurement and reconstruction process. We use this formalism to analyze a variety of imaging artifacts. Chapter 13 contains a brief description of "algebraic reconstruction techniques," which are essentially methods for solving large, sparse systems of linear equations.

The final topic is noise in the filtered back-projection algorithm. This part of the book begins with an introduction to probability theory. Our presentation uses the language and ideas of measure theory, in a metaphoric rather than a technical way. Chapter 15 concludes with a study of specific probability distributions that are important in imaging. In Chapter 16 we apply probability theory to a variety of problems in medical imaging. This chapter includes the famous resolution-dosage fourth power relation, which shows that to double the resolution in a CT image, keeping the SNR constant, the radiation dosage must be increased by a factor of 16! The chapter ends with an introduction to positron emission tomography and the maximum likelihood algorithm. Chapter 17 introduces the ideas of random processes and their role in signal and image processing. Again the focus is on those processes needed to analyze noise in x-ray imaging. A student with a good grasp of Riemann integration should not have difficulty with the material in these chapters.

Acknowledgments

Perhaps the best reward for writing a book of this type is the opportunity it affords for thanking the many people who contributed to it in one way or another. There are a lot of people to thank, and I address them in roughly chronological order.

First I would like to thank my parents, Jean and Herbert Epstein, for their encouragement to follow my dreams and the very high standards they set for me from earliest childhood. I would also like to thank my father and Robert M. Goodman for imparting the idea that observation and careful thought go a long way toward understanding the world in which we live. Both emphasized the importance of expressing ideas simply but carefully.

My years as an undergraduate at the Massachusetts Institute of Technology not only provided me with a solid background in mathematics, physics, and engineering but also a belief in the unity of scientific enquiry. I am especially grateful for the time and attention Jerry Lettvin lavished on me. My interest in the intricacies of physical measurement surely grew out of our many conversations. I was fortunate to be a graduate student at the Courant Institute, one of the few places where "pure" and "applied" mathematics lived together in harmony. In both word and deed, my thesis advisor, Peter Lax, placed mathematics and its applications on an absolutely equal footing. It was a privilege to be his student. I am very grateful for the enthusiasm that he and his late wife, Anneli, showed for turning my lecture notes into a book.

I would like to acknowledge my friends and earliest collaborators in the enterprise of becoming a scientist—Robert Indik and Carlos Tomei. I would also thank my friends and current collaborators, Gennadi Henkin and Richard Melrose, for the vast wealth of culture and knowledge they have shared with me and their forbearance, while I have been "missing in action."

Coming closer to the present day, I would like to thank Dennis Deturck for his unflagging support, both material and emotional, for the development of my course on medical imaging and this book. Without the financial support he and Jim Gee provided for the spring of 2002, I could not have finished the manuscript. The development of the original course was supported in part by National Science Foundation grant DUE95-52464. I would like to thank Dr. Ben Mann, my program director at the National Science Foundation, for providing both moral and financial support. I am very grateful to Hyunsuk Kang, who transcribed the first version of these notes from my lectures in the spring of 1999. Her hard work provided the solid foundation on which the rest was built. I would also like to thank the students who attended Math 584 in 1999, 2000, 2001, and 2002 for their invaluable input on the content of the course and their numerous corrections to earlier versions of this book. I would also like to thank Paula Airey for flawlessly producing what must have seemed like endless copies of preliminary versions of the book.

John D'Angelo read the entire text and provided me with an extremely useful critique as well as a lot of encouragement. Chris Croke, my colleague at the University of Pennsylvania, also carefully read much of the manuscript while teaching the course and provided many corrections. I would like to thank Phil Nelson for his help with typesetting, publishing, and the writing process and Fred Villars for sharing with me his insights on medicine, imaging, and a host of other topics.

The confidence my editor, George Lobell, expressed in the importance of this project was a strong impetus for me to write this book. Jeanne Audino, my production editor, and Patricia M. Daly, my copy editor, provided the endless lists of corrections that carried my manuscript from its larval state as lecture notes to the polished book that lies before you. I am most appreciative of their efforts

I am grateful to my colleagues in the Radiology Department—Dr. Gabor Herman, Dr. Peter Joseph, Dr. David Hackney, Dr. Felix Wehrli, Dr. Jim Gee, and Brian Avants—for sharing with me their profound, first-hand knowledge of medical imaging. Gabor Herman's computer program, *SNARK93*®, introduced me to the practical side of image reconstruction and was used to make some of the images in the book. I used Dr. Kevin Rosenberg's program *ctsim* to make many other images. I am very grateful for the effort he expended to produce a version of his marvelous program that would run on my computer. David Hackney provided beautiful, state-of-the-art images of brain sections. Felix Wehrli provided the image illustrating aliasing in magnetic resonance imaging and the x-ray CT micrograph of trabecular bone. I am very grateful to Peter Joseph for sharing his encyclopedic first-hand knowledge of x-ray tomography and its development as well as his treasure trove of old, artifact-ridden CT images. Jim Gee and Brian Avants showed me how to use MATLAB® for image processing. Rob Lewitt provided some very useful suggestions and references to the literature.

I would also like the acknowledge my World Wide Web colleagues. I am most appreciative for the x-ray spectrum provided by Dr. Andrew Karellas of the University of Massachusetts, the chest x-ray provided by Drs. David S. Feigen and James Smirniotopoulos of the Uniformed Services University, and the nuclear magnatic resonance spectrum (NMR) provided by Dr. Walter Bauer of the Erlangen-Nürnberg Univerisity. Dr. Bergman of the Virtual Hospital at the University of Iowa (www.vh.org) provided an image of an anatomical section of the brain. The World Wide Web is a resource for imaging science of unparalleled depth, breadth, and openness.

Finally and most of all I would like to thank my wife, Jane, and our children, Leo and Sylvia, for their love, constant support, and daily encouragement through the many, many, moody months.

Charles L. Epstein
Philadelphia, PA
January 8, 2003