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Luca Brombal

X-Ray Phase-Contrast Tomography

Underlying Physics and Developments for Breast Imaging

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X-Ray Phase-Contrast Tomography

Underlying Physics and Developments for Breast Imaging

Doctoral Thesis accepted by
University of Trieste, Trieste, Italy

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Author
Dr. Luca Brombal
Department of Physics
University of Trieste
Trieste, Italy

Supervisor
Prof. Renata Longo
Department of Physics
University of Trieste
Trieste, Italy

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Supervisor's Foreword

Modern physics contributes significantly to diagnostics and therapy in medicine: X-ray computed tomography, positron emission tomography, nuclear magnetic resonance, and particle therapy are very well-known examples. The scientific interest and the strong impact of applied physics motivate a new generation of brilliant young physicists in investigating medical applications of emerging techniques. One of them is X-ray phase-contrast imaging, which aims at exploiting the X-ray refraction by converting the phase shift into an intensity modulation to obtain an additional contrast mechanism in the recorded image. The ultimate promise of this technique is to detect low contrast details which are presently invisible to state-of-the-art clinical radiology systems. Synchrotron radiation laboratories are the headquarters of these researches, whose final goal is the translation toward compact sources.

Luca Brombal is one of the brilliant young physicists enthusiastic about medical applications; his Ph.D. research project is about X-ray phase-contrast physics and its application to improve medical imaging. This book is the scientific report of his 3 years of Ph.D. studies. The goal of the thesis is ambitious and compelling, contributing to the breast cancer diagnosis with state-of-the-art X-ray imaging techniques. The project has been developed in a European laboratory, the synchrotron radiation facility ELETTRA in Trieste (Italy), where X-ray phase-contrast imaging techniques have been developed and applied to biomedical imaging. Dr. Luca Brombal, after joining my group, quickly gained a reputation among colleagues as a brilliant physicist, equally skilled for the experimental work and the data analysis, including formal models and numerical simulations, and as a good scientific communicator. These qualities are, I believe, well represented in this Ph.D. thesis. He presents the underlying physics of X-ray phase-contrast tomography in a very plain style. However, such simplicity is the result of a deep understanding of the results published by different authors with different notations that he reported in a unified formalism. The most recent phase-contrast image formation models are explored and extended. The original results obtained during the Ph.D. project are reported in a very effective way that lets the reader understand various aspects of the interdisciplinary research. Moreover, the thesis provides the reader with practical and numerical methods to overcome the difficulties encountered in the implementation of X-ray phase-contrast imaging.

Medical Physics is often in equilibrium between basic science and public commitment, and a good project in Medical Physics should be developed in an interdisciplinary environment. This thesis well represents all these elements and I hope the reader is going to increase his/her knowledge of the exciting and challenging field of X-ray diagnostic imaging.

Trieste, Italy
June 2020

Prof. Renata Longo

Abstract

X-ray phase-contrast tomography is a powerful tool to dramatically increase the visibility of features exhibiting a faint attenuation contrast within bulk samples, as is generally the case of light (low-Z) materials. For this reason, the application to clinical tasks aiming at imaging soft tissues, as, for example, breast imaging, has always been a driving force in the development of this field. In this context, the SYRMA-3D project, which constitutes the framework of the present work, aims to develop and implement the first breast computed tomography system relying on the propagation-based phase-contrast technique at the Elettra Synchrotron facility (Trieste, Italy). This thesis finds itself in the 'last mile' towards the in-vivo application, and the obtained results add some of the missing pieces in the realization of the project, which requires multifaceted issues ranging from physical modelling to data processing and quantitative assessment of image quality to be addressed. The first part of the work introduces a homogeneous mathematical framework describing propagation-based phase contrast from the sample-induced X-ray refraction, to detection, processing and tomographic reconstruction. The original results reported in the following chapters include the implementation of a pre-processing procedure dedicated to a novel photon-counting CdTe detector; a study, supported by a rigorous theoretical model, on signal and noise dependence on physical parameters such as propagation distance and detector pixel size; hardware and software developments for improving signal-to-noise ratio and reducing the scan time; and, finally, a clinically-oriented study based on comparisons with clinical mammographic and histological images. The last part of the thesis has a wider experimental horizon, and results obtained with conventional X-ray sources are presented: a first-of-its-kind quantitative image comparison of the synchrotron-based setup against a clinically available breast-CT scanner is reported and a practical laboratory implementation of monochromatic propagation-based micro-tomography, making use of a high-power rotating anode source, is detailed.

The achieved advancements in terms of software and hardware have been significant steps towards the final goal of performing the clinical examination as effectively as possible. On the other hand, the theoretical modelling and data analysis, despite being finalized to the breast computed tomography, have a rather general validity and they can be easily extended to other propagation-based setups. The direct comparison with an existing clinical system provided further justification for the realization of the SYRMA-3D project, also suggesting the importance of synchrotron-based clinical programmes which have the potential to trigger the transition of phase-contrast imaging from synchrotrons to hospitals.

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I sincerely acknowledge all the members of the SYRMA-3D collaboration and the SYRMEP group for their constant support in these fruitful years. I wholeheartedly thank my supervisor, Prof. Renata Longo, for the relentless support and trust accorded to me since the beginning of the Ph.D. I thank Prof. Luigi Rigon for having introduced me to this research field many years ago, and for the precious and insightful scientific discussions. I also thank Dr. Sandro Donato, with whom I worked countless days back-to-back acquiring, analyzing and fighting over data interpretation. Finally, I warmly thank Dr. Marco Endrizzi and Prof. Alessandro Olivo from University College London for having welcomed me into their group, giving me the possibility to understand things deeply and to work intensely from day one.

Contents

Chapter 1
Introduction

Conventional X-ray computed tomography (CT) enables the reconstruction of three-dimensional maps of X-ray attenuation properties within an investigated object, being one of the finest tools in the realm of diagnostic radiology. Anyway, when imaging low-Z samples, as soft tissues, the attenuation contrast between different materials can become faint to a point where they are no longer visible unless a large amount of radiation dose is delivered, which is unacceptable in medical diagnostic applications. This limitation has prevented a wide diffusion of breast CT imaging, where the need for high spatial and contrast resolutions required to differentiate the tissues composing the breast is hard to reconcile with a low-dose delivery, which is mandatory due to breast radiosensitivity. On the other hand, the availability of three-dimensional imaging of the breast, allowing to avoid superposition effects inherent to planar techniques (i.e. mammography), is regarded as key to improve early detection of breast cancer and/or follow-up and treatment planning stages; considering that breast cancer is one of the leading causes of death for women worldwide, this would bring to obvious clinical benefits. In this context, the use of X-ray phase-contrast imaging (XPCI) techniques can provide a major advantage over conventional attenuation-based X-ray imaging. In fact, XPCI enables to convert phase distortions (i.e. phase shift) occurring to X-ray waves travelling through a sample due to its refractive properties into detectable intensity modulations. These phase effects, which do not contribute to the image formation in conventional techniques, are in principle much stronger than attenuation, thus providing another pool of image contrast (i.e. phase contrast) and largely improving tissues visibility.

This thesis provides a detailed description of the physics underlying propagation-based phase-contrast tomography and presents several developments in terms of experimental setup, data processing and theoretical modelling towards its implementation in the field of breast imaging. The phase-contrast technique used throughout this work, namely propagation-based (PB) imaging, is arguably the simplest

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XPCI configuration to implement experimentally, as it only requires to insert some (propagation) distance between the scanned sample and the imaging detector. On the contrary, differently from other XPCI techniques featuring more complex setups, PB imaging relies on the presence of a highly-coherent X-ray source, thus making synchrotron facilities the most suited environment for its implementation. All the experimental work has been carried out within the framework of the SYRMA-3D project, willing to perform the first synchrotron radiation-based phase-contrast breast CT at the Elettra synchrotron facility (Trieste, Italy). The main body of the thesis is organized in six chapters, whose content is summarized in the following.

- Chapter 2 is devoted at establishing the physical principles of PB imaging, from the interaction between X-ray waves and refractive objects to the phase-contrast image formation and processing, including the application of phase-retrieval algorithms and tomographic reconstruction.
- In Chap. 3 the specific challenges related to breast CT imaging are introduced and a general overview on the experimental setup is provided. In particular, many features relevant to the clinical implementation of breast CT at the SYRMEP beamline are detailed along with the specific tasks and objectives of the SYRMA-3D project.
- The main focus of Chap. 4 is the large-area CdTe photon-counting imaging detector (Pixirad-8). This detector, as many high-Z photon-counting devices, offers remarkable advantages over conventional indirect-detection charge-integration systems as high-efficiency, minimum electronic noise and spectral capabilities. Anyway, the data processing for these novel devices is still challenging mainly due to their multi-module architecture and to the presence of impurities in the sensor crystalline structure causing charge trapping. To tackle these issues an ad-hoc pre-processing software has been implemented and successfully applied to tomographic images of breast specimens.
- In Chap. 5 a theoretical model describing the effects of several physical parameters, as the propagation distance and the detector pixel size, on image noise, signal and spatial resolution is introduced and tested against experimental images. Among the results of the chapter, it is experimentally demonstrated on breast specimens that a dramatic increase in terms of signal-to-noise ratio can be achieved at a constant spatial resolution at large propagation distances, leading to the design of an extension of the beamline. At the same time, the crucial role of pixel size in determining the effectiveness of the phase retrieval, which strongly mitigates the dependence of noise on the pixel size in CT images, is quantitatively shown. Additionally, post-reconstruction phase-retrieval pipeline is introduced demonstrating that, despite the theoretical equivalence with its standard pre-reconstruction application, the proposed approach allows to eliminate artifacts in the reconstructed volume in case of acquisitions requiring multiple vertical translations.
- Chapter 6 provides a more clinically oriented focus on the imaging capabilities of the PB breast CT experimental setup. The first fully three-dimensional scans of large mastectomy samples acquired at a clinically compatible dose levels (5 mGy) and scan times (10 min) are reported and compared with conventional pla-