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-

nar mammographic and histological images. Moreover, the possibility of further image post-processing, as 3D rendering and segmentation or bi-dimensional data compression, is investigated.

- Chapter 7 provocatively raises the question on whether it is worth to use synchrotron radiation for clinical/biomedical imaging tasks. The tentative answer is based on experimental results acquired with two setups featuring conventional rotating anode X-ray sources. In the first case, a state-of-the-art laboratory micro-CT setup, yielding monochromatic X-rays, is characterized and used in a PB configuration to image biological samples with dimensions of the order of few mm within laboratory-compatible times (from minutes to hours). This suggests that, to some extent and at a different scale, PB imaging can be implemented in a compact design even with high-power rotating anode sources. In the second case, imaging results obtained with a commercial breast CT scanner are compared with the synchrotron-based system at similar imaging conditions, showing the advantages provided by the synchrotron in terms of signal, noise, spatial resolution and, ultimately, detail visibility. Obviously these findings do not suggest that synchrotron machines should replace hospital CT scanners but, instead, that synchrotron-based studies can serve as benchmarks in terms of achievable image quality, possibly being the driving force for the development of more compact systems.