## Abstract

Nowadays, medical imaging plays an essential role in the detection and diagnosis of several diseases, ranging from the extraction of anatomical and functional information to cellular and molecular expressions. However, visual inspection of biomedical images is often time-consuming, highly subjective and requires experienced operators. Computer aided diagnosis systems (CADx) have been extensively used in clinical practise to support the interpretation of medical images; however, most of the current CADx approaches still entail substantial user-dependency. On the other hand, the development of fully automated solutions is still challenging due to the heterogeneity of the analysed medical images. In fact, even if images are acquired with the same imaging device and standardized protocol, the shape, appearance, and size of internal body structures may vary for different patients (inter-subject variability) and for the same patient at different times (intra-subject variability).

The aim of this thesis work is to develop and validate a series of automated solutions applied to different medical imaging modalities and scales for the modeling and interpretation of physiopathological processes. The proposed approach aims to overcome the limitation of traditional CADx systems and become the bridge technology that enables the effective extraction of quantitative data from biomedical images.

This thesis work can be divided into two macro-sections: firstly, a novel and fully automated strategy for the detection of biological structures is presented. Secondly, six automated algorithms for the reliable quantification and characterization of biomedical images are described.

In the first part, an adaptive algorithm, named ARCO (Adaptive Rapid Curve Optimization), is proposed for the detection of relevant objects in medical images. The ARCO algorithm is the first fully automated method for a fast and accurate segmentation of biological structures in several imaging modalities, where objects exhibit different shapes, dimensions, and color appearance. The proposed technique has been used as starting point to develop more complex algorithms for the extraction of functional and anatomical information in medical imaging.

In the second part, six algorithms are proposed for the automatic and objective analysis of medical images, ranging from the microscale (optical microscopy) to in-vivo imaging (ultrasound). The first algorithm, named CARE (CARdiosphere Evaluation), is designed for the architectural modeling of cardiac stromal cells in fluorescence images. Then, three fully automated methods are proposed for the analysis of histopathological images. The MANA

(Multiscale Adaptive Nuclei Analysis) algorithm is a multi-tissue strategy for nuclei detection, while two other presented methods are for the detection of cancer tissue in prostate and breast histopathological images. Finally, two algorithms are proposed for the extraction of architectural muscle parameters in ultrasound images. The Muscle UltraSound Analysis (MUSA) algorithm is designed to measure the muscle thickness on longitudinal images while the TRAnsverse Muscle Analysis (TRAMA) algorithm is able to measure the muscle cross-sectional area (CSA) in transverse scans.

In conclusion, the proposed techniques achieve high quality results in the architectural and functional modelling of healthy and pathological structures. These algorithms can be extended in the investigation of other organs, diseases and embedded in CADx systems for obtaining a reliable and user-independent diagnosis.