

QUANTITATIVE ANALYSIS OF MR IMAGES FOR CHARACTERIZATION AND DIAGNOSTIC ASSESSMENT OF PROSTATE CANCER

DHARMESH SINGH



CENTRE FOR BIOMEDICAL ENGINEERING

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by

DHARMESH SINGH
CENTRE FOR BIOMEDICAL ENGINEERING

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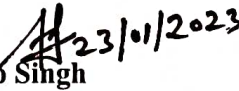
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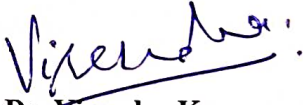


CERTIFICATE

This is to certify that the thesis entitled, “Quantitative analysis of MR images for characterization and diagnostic assessment of prostate cancer”, submitted by Mr Dharmesh Singh (2017BMZ8359) for the award of the degree of the Doctor of Philosophy, to the Centre for Biomedical Engineering, Indian Institute of Technology Delhi, is a record of the bonafide research work carried out by him under our supervision and guidance. He has fulfilled the requirements for submission of this thesis, which to the best of our knowledge, has reached the requisite standard. The contents of this thesis have not been submitted in part or full to any other university or institute for the award of any other degree or diploma.


Dr. Amit Mehndiratta
Associate Professor
Centre for Biomedical Engineering
Indian Institute of Technology Delhi
New Delhi - 110016, India


Dr. Anup Singh
Associate Professor
Centre for Biomedical Engineering
Indian Institute of Technology Delhi
New Delhi - 110016, India


Dr. Virendra Kumar
Professor
Department of NMR
All India Institute of Medical
Sciences Delhi
New Delhi - 110029, India

Date: 23/01/2023
New Delhi

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Abstract

Prostate cancer (PCa) is the most commonly diagnosed cancer among men and remains a second leading cause of deaths in men globally. The risk of developing PCa is related to advancing age, family history and might be influenced by diet and other factors. Transrectal ultrasound (TRUS) guided systematic 12-core biopsy is the standard-of-care method for the diagnosis of PCa. TRUS guided biopsy is recommended in men with raised serum prostate-specific antigen (PSA) levels and/or abnormal digital rectal examination. However, accurate diagnosis of PCa remains challenging due to the high false negative rate of TRUS guided biopsy and low specificity of PSA. In this context, magnetic resonance imaging (MRI) has shown a promising role in the evaluation of PCa over the last decade. Consequently, clinical applications of prostate MRI have expanded to include tumor detection, localization, characterization, assessment of suspected recurrence, image guidance for biopsy and prediction of the location of the PCa. According to latest guidelines of Prostate Imaging Reporting and Data System version 2 (PI-RADS v2), advances in MRI technology have led to the development of multiparametric MRI (mpMRI), which combines anatomic T2 weighted imaging (T2WI), diffusion-weighted imaging (DWI) and its derivative apparent-diffusion coefficient (ADC) maps.

MpMRI can be used for screening at large and might allow to avoid unnecessary biopsies and improve diagnostic accuracy. These technological advances, combined with a growing interpreter experience with mpMRI, have substantially improved diagnostic capabilities for addressing the central challenges in PCa care: 1) improving detection of cancer, which is critical for reducing mortality, and 2) increasing confidence in the detection of other diseases affecting prostate such as benign prostatic hyperplasia and/or prostatitis, which are less likely to cause severe morbidity, in order to reduce unnecessary biopsies and treatment.

One of the key challenges in PCa treatment selection is predicting which patients do or do not need treatment. Computer-aided diagnosis (CAD) models may have a role in addressing this challenge as these models have shown to improve the diagnostic accuracy of PI-RADS scoring when combining the system score with a radiologist score. The aim of this thesis is to develop a CAD model for PCa using MRI, which could increase the objectivity in the diagnosis and assessment of lesion aggressiveness and as a result, reduction of unnecessary biopsies which could prevent overdiagnosis and overtreatment, all in all leading to an increase in quality of life for the patient.

The purpose of the first study of this thesis is to develop an automated framework to segment prostate gland and its zones simultaneously using DWI, which is an essential preprocessing step for any CAD system for PCa. This study consisted of four main parts, prostate gland segmentation, atlas construction, prostate zonal segmentation and partial volume correction. The objective of the second study of this is to explore the role of texture features and machine learning methods for classification of the PI-RADS v2 scores into low vs. intermediate vs. high score as well as score 4 vs. score 5. Lesion ROI marking, texture feature extraction methods, feature selection and classifiers were assessed for characterization of prostate lesions. This chapter also examines the best combination of texture features of DWI, ADC and T2WI for PCa characterization. The third work in this thesis attempts to develop a 2D and 3D tumor measurement algorithms. Another goal of this work was to develop a semi-automated framework for PI-RADS v2 assessment in order to speed up and simplify the reporting process and analyzes the diagnostic performance of the proposed framework by classifying PI-RADS scores using machine learning methods. A new scoring system for the detection of clinically significant cancer was proposed in the final study, which could help to reduce the number of unnecessary biopsies, or overtreatment.

सार

प्रोस्टेट कैंसर (पीसीए) पुरुषों में सबसे अधिक पाया जाने वाला कैंसर है और विश्व स्तर पर पुरुषों में मृत्यु का दूसरा प्रमुख कारण बना हुआ है। पीसीए विकसित होने का जोखिम बढ़ती उम्र, पारिवारिक इतिहास से संबंधित है और यह आहार और अन्य कारकों से प्रभावित हो सकता है। ट्रांसरेक्टल अल्ट्रासाउंड (TRUS) निर्देशित व्यवस्थित 12-कोर बायोप्सी पीसीए के निदान के लिए मानक देखभाल विधि है। TRUS निर्देशित बायोप्सी की सिफारिश उन पुरुषों में की जाती है, जिनके सीरम प्रोस्टेट-विशिष्ट एंटीजन (PSA) स्तर और/या असामान्य डिजिटल रेक्टल परीक्षा होती है। हालांकि, TRUS निर्देशित बायोप्सी की उच्च झूठी नकारात्मक दर और PSA की कम विशिष्टता के कारण पीसीए का सटीक निदान चुनौतीपूर्ण बना हुआ है। इस संदर्भ में, चुंबकीय अनुनाद इमेजिंग (एमआरआई) ने पिछले एक दशक में पीसीए के मूल्यांकन में एक आशाजनक भूमिका दिखाई है। नतीजतन, प्रोस्टेट एमआरआई के नैदानिक अनुप्रयोगों में ट्यूमर का पता लगाने, स्थानीयकरण, लक्षण वर्णन, संदिग्ध पुनरावृत्ति का आकलन, बायोप्सी के लिए छवि मार्गदर्शन और पीसीए के स्थान की भविष्यवाणी शामिल है। प्रोस्टेट इमेजिंग रिपोर्टिंग और डेटा सिस्टम संस्करण 2 (PI-RADS v2) के नवीनतम दिशानिर्देशों के अनुसार, एमआरआई तकनीक में प्रगति ने मल्टीपैरामेट्रिक एमआरआई (एमपीएमआरआई) का विकास किया है, जो एनाटॉमिक T2 वेटेड इमेजिंग (T2WI), डिफ्यूजन-वेटेड इमेजिंग को जोड़ती है। (DWI) और इसके व्युत्पन्न स्पष्ट-प्रसार गुणांक (ADC) मैप्स।

एमपीएमआरआई का उपयोग बड़े पैमाने पर स्क्रीनिंग के लिए किया जा सकता है और अनावश्यक बायोप्सी से बचने और नैदानिक सटीकता में सुधार करने की अनुमति दे सकता है। एमपीएमआरआई के साथ बढ़ते दुर्भाषिया अनुभव के साथ इन तकनीकी विकासों ने पीसीए देखभाल में केंद्रीय चुनौतियों का समाधान करने के लिए नैदानिक क्षमताओं में काफी सुधार किया है: 1) कैंसर का पता लगाने में सुधार, जो मृत्यु दर को कम करने के लिए महत्वपूर्ण है, और 2) प्रोस्टेट को प्रभावित करने वाले अन्य रोग जैसे कि सौम्य प्रोस्टेटिक हाइपरप्लासिया (BPH) और/या प्रोस्टेटाइटिस का पता लगाने में आत्मविश्वास बढ़ाना, जिससे अनावश्यक बायोप्सी और उपचार को कम करने के लिए गंभीर रुग्णता होने की संभावना कम होती है।

पीसीए उपचार चयन में प्रमुख चुनौतियों में से एक यह भविष्यवाणी करना है कि कौन से रोगियों को उपचार की आवश्यकता है या नहीं। इस चुनौती को संबोधित करने में कंप्यूटर एडेड डायग्नोसिस (सीएडी) मॉडल की भूमिका हो सकती

है क्योंकि इन मॉडलों ने रेडियोलॉजिस्ट स्कोर के साथ सिस्टम स्कोर को मिलाकर पीआई-आरएडीएस स्कोरिंग की नैदानिक सटीकता में सुधार दिखाया है। इस थीसिस का उद्देश्य एमआरआई का उपयोग करते हुए पीसीए के लिए एक सीएडी मॉडल विकसित करना है, जो घाव की आक्रामकता के निदान और मूल्यांकन में निष्पक्षता को बढ़ा सकता है और इसके परिणामस्वरूप अनावश्यक बायोप्सी की कमी हो सकती हैं, जो अति निदान और अति-उपचार को रोक सकती है। इससे रोगी के जीवन की गुणवत्ता में वृद्धि हो सकती है।

इस थीसिस के पहले अध्ययन का उद्देश्य DWI का उपयोग करके प्रोस्टेट ग्रंथि और उसके क्षेत्रों को एक साथ खंडित करने के लिए एक स्वचालित ढांचा विकसित करना है, जो पीसीए के लिए किसी भी सीएडी सिस्टम के लिए एक आवश्यक प्रीप्रोसेसिंग कदम है। इस अध्ययन में चार मुख्य भाग शामिल थे, प्रोस्टेट ग्रंथि विभाजन, एटलस निर्माण, प्रोस्टेट जोनल विभाजन और आंशिक मात्रा सुधार। इसके दूसरे अध्ययन का उद्देश्य PI-RADS v2 स्कोर को निम्न बनाम मध्यवर्ती बनाम उच्च स्कोर के साथ-साथ स्कोर 4 बनाम स्कोर 5 में वर्गीकृत करने के लिए बनावट सुविधाओं और मशीन सीखने के तरीकों की भूमिका का पता लगाना है। लीजन आरओआई प्रोस्टेट घावों के लक्षण वर्णन के लिए अंकन, बनावट सुविधा निष्कर्षण विधियों, फीचर चयन और क्लासिफायर का मूल्यांकन किया गया था। यह अध्याय पीसीए लक्षण वर्णन के लिए DWI, ADC और T2WI की बनावट सुविधाओं के सर्वोत्तम संयोजन की भी जाँच करता है। इस थीसिस में तीसरा काम 2डी और 3डी ट्यूमर मापन एल्गोरिदम विकसित करने का प्रयास करता है। इस कार्य का एक अन्य लक्ष्य PI-RADS v2 मूल्यांकन के लिए एक अर्ध-स्वचालित ढांचा विकसित करना था ताकि रिपोर्टिंग प्रक्रिया को तेज और सरल बनाया जा सके और मशीन सीखने के तरीकों का उपयोग करके PI-RADS स्कोर को वर्गीकृत करके प्रस्तावित ढांचे के नैदानिक प्रदर्शन का विश्लेषण किया जा सके। अंतिम अध्ययन में चिकित्सकीय रूप से महत्वपूर्ण कैंसर का पता लगाने के लिए एक नई स्कोरिंग प्रणाली प्रस्तावित की गई थी, जो अनावश्यक बायोप्सी, या अति-उपचार की संख्या को कम करने में मदद कर सकती है।

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List of Abbreviations

ADC= Apparent Diffusion Coefficient

AI= Artificial Intelligence

ASM= Angular Second Moment

AUC= Area under the Curve

BPH= Benign Prostate Hyperplasia

CAD= Computer Aided Diagnosis

CFS= Correlation-based Feature Selection

CNN= Convolution Neural Network

CPCS= Comprehensive Prostate Cancer Scoring

CV= Cross-Validation

CsPCa= Clinically Significant Prostate Cancer

CZ= Central Zone

DCE= Dynamic Contrast Enhanced

DL= Deep Learning

DRE= Digital Rectal Examination

DSC= Dice Similarity Coefficient

DWI = Diffusion Weighted Imaging

EE= Edge-Edge

ES= Edge-Spot

ESUR= European Society of Urogenital Radiology

FID= Free Induction Decay

FOS= First-Order Statistics

FOV= Field of View

GG = Grade Group

GLCM= Gray Level Co-Occurrence Matrix

GLN= Gray Level Non-Uniformity
GLRLM= Gray Level Run Length Matrix
GS= Gleason Score
HG= High Grade
HGRE= High Gray Level Runs Emphasis
IG= Intermediate Grade
JC= Jaccard Coefficient
KNN= K-Nearest Neighbour
NMR= Nuclear Magnetic Resonance
MpMRI= Multi-parametric MRI
ML= Machine Learning
MRI= Magnetic Resonance Imaging
LDA= Linear Discriminant Analysis
LE= Level-Edge
LG= Low Grade
LS= Likert Scale
LL= Level-Level
LRE= Long Runs Emphasis
LRHGE= Long-Run High Gray Level Emphasis
LRLGE= Long-Run Low Gray Level Emphasis
LGRE= Low Gray Level Runs Emphasis
LS= Level-Spot
LTEM= Law's Texture Energy Measures
PCa= Prostate Cancer
PET= Positron Emission Tomography
PI-RADS v2= Prostate Imaging Reporting and Data System Version 2
PSA= Prostate Specific Antigen
PSAd= Prostate Specific Antigen Density

PV= Partial Volume
PZ= Peripheral Zone
RF= Random Forest
RLN= Run-Length Non-Uniformity
ROI= Region of Interest
ROC= Receiver-Operating Characteristic
SD= Standard Deviation
SFM= Statistical Features Matrix
SI= Signal Intensity
SNR= Signal-to-Noise Ratio
SRE= Short Runs Emphasis
SRHGE= Short-Run High Gray Level Emphasis
SRLGE= Short-Run Low Gray Level Emphasis
SVM= Support Vector Machine
T2WI= T2-Weighted Imaging
TE= Echo Time
TMD= Tumor Maximum Diameter
TR= Repetition Time
TRUS= Transrectal Ultrasound
TV= Tumor Volume
TZ= Transition Zone
2D= Two Dimensional
3D= Three Dimensional

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