QUANTITATIVE SUSCEPTIBILITY WEIGHTED IMAGING (SWI) IN GRADING OF INTRACRANIAL MASS LESIONS AND ASSESSMENT OF ACUTE ISCHEMIC STROKE PENUMBRA

RUPSA BHATTACHARJEE

CENTRE FOR BIOMEDICAL ENGINEERING
INDIAN INSTITUTE OF TECHNOLOGY DELHI
OCTOBER 2021

Indian Institute of Technology Delhi (IITD), New Delhi, 2021

QUANTITATIVE SUSCEPTIBILITY WEIGHTED IMAGING (SWI) IN GRADING OF INTRACRANIAL MASS LESIONS AND ASSESSMENT OF ACUTE ISCHEMIC STROKE PENUMBRA

by

RUPSA BHATTACHARJEE

CENTRE FOR BIOMEDICAL ENGINEERING

Submitted

in fulfilment of the requirements of the degree of Doctor of Philosophy

to the

INDIAN INSTITUTE OF TECHNOLOGY DELHI

OCTOBER 2021

Dedicated to,

Baba, Maa, Aju & Tarun!

CERTIFICATE

This is to certify that the thesis entitled, "**Quantitative susceptibility weighted imaging (SWI) in grading of intracranial mass lesions and assessment of acute ischemic stroke penumbra**", submitted by **Ms Rupsa Bhattacharjee (2016BMZ8112)** 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 her under my supervision and guidance. She has fulfilled the requirements for submission of this thesis, which to the best of my 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. Anup Singh)
Associate Professor
Centre for Biomedical Engineering
Indian Institute of Technology Delhi
New Delhi – 110016, India
Date:
New Delhi

Acknowledgements

I would like to take this opportunity to set aside the focus from the scope of the thesis and put the spotlight on some of those very important people. I will start by thanking my supervisor Dr Anup Singh. Sir didn't just guide me in the research by framing the critical questions or interpreting the outcome of our analysis, he rather stood beside me as a friend when I needed to hear words of encouragement, inspired us with his example, took us to tea and pizza breaks whenever we were tired of long hours in the lab. Sir always has provided me with a fresh new perspective/feedback of every piece of work and shown confidence in my capabilities, which I believe has shaped my thesis in unexpected but impactful ways. I would like to thank Kiran Maám and Vihaan for hosting us at odd hours always with the biggest smile, largest spread of snacks and nonstop hours of conversions and stories at their nest.

I would hereby extend my heartfelt thanks to the committee members. Prof. Veena Koul has always inspired us to believe we can achieve as much as women in science by working equally or doubly hard if need be, without any excuses. Prof. Kedar Khare has been the most inquisitive person on the committee with always asking questions I didn't know. It made me go back and study harder to be better prepared for the next meetings. Prof Amit Mehndiratta has constructively criticized my work in progressive years of SRC meetings to make it sounder technically and clinically, with questions and suggestions which led the overall work to a much solid outcome. I would also like to express my gratitude to all the faculty and staff members in our department.

I am especially indebted to Dr Rakesh Kumar Gupta, HOD and Director of Radiology Department in Fortis Memorial Research Institute. He has always taught me to start with the clinical idea or need/existing gaps in current research frameworks, to think about how these works can lead to outcomes that are necessary for radiologists to use and has provided me with real-time honest feedback and guidance, crucial for a novice researcher. I would be always thankful to Mr Karthick Raj, my friend and first reporting manager for the duration in Philips Healthcare, who has been extremely patient in guiding and mentoring me into understanding MRI when I first entered this domain eight years back. I am thankful to Dr Indrajit Saha, Clinical Scientist, Diagnostic Imaging, Philips India Limited and for being the toughest critic and mentor, providing wonderful suggestions both professionally and personally. His wife Dr Barnali Saha has been the elder sister for me in this city away from home, always feeding me her delicacies with immense

love. I would also like to express my gratitude to all my colleagues in Philips India Ltd., who over the past eight years have provided me with the friendliest and resourceful working environment and have honestly pat my back for every small achievement I have ever made.

I cannot thank my friends/colleagues in IIT MedImg and Fortis enough: Prativa, Snekha, Rafeeq, Dharmesh, Sameer, Banasmita, Mamta, Anandh, Suhail, Archana, Neha, Ayan, Eshadi, Anirban, Virender, Rakshit, Sandeep, Ankit and Raufiya. I have shared many wonderful conversations, enjoyable and affectionate moments, innumerable WhatsApp chats and intense research discussions with them over a cup of tea or a slice of pizza, those have made my time in research colorful and every bit worth remembering. A special mention to Dinil, who has been a brother, a fellow friend for the last five years. We have solved problems, enjoyed paper acceptances (and rejections too), have had thoughtful discussions beyond research and progressed together. He has always been a phone call/text away whenever I needed his support for anything.

I have been encouraged, sustained, inspired, and tolerated by the greatest group of people and cheerleaders in my life than anyone ever had. My little brother, Aju, has been my arch-nemesis and my favorite person under the sky both at the same time. I have no words of gratitude for my dear husband, Tarun. I have truly been lucky to have him holding my hand in this tough PhD journey, always believing in me, in “us”, ever putting me and my priorities first, ever diluting all my problems with the poorest joke under the sun. This thesis is his as much as mine. Nupur, my best friend, has always been there putting many hats of a guide, a sister, a travel partner, a philosopher and a therapist, a teacher and whatnot. Her presence has given me the comfort of being understood, being home. My pseudo-family: Samapika, Sudipta, Saheli, Jackson, Mudasir, Peeyush and Prateek who have had more faith in my abilities than I can ever imagine. My extended family, in-laws, uncles, aunts and cousins have applauded me even for my smallest achievements.

In the end, I thank my parents, Baba, and Ma for building me up literally from ground zero into the person I am today. Baba has taught me the value of truth, integrity, kindness and stimulating conversations, that there is always room for progress at whatever I do. Ma has led me by the example of a perfect working woman balancing all the tough balls putting up the largest smile on her face. Like Sheldon Cooper would have hoped me saying, I know I haven't been the student, friend, wife or daughter you deserve. But I want you to know in my way, I love you all.

Abstract

This PhD thesis aims to explore the novel potentials of one of the advanced MRI methods known as Susceptibility Weighted Imaging (SWI), to develop quantitative biomarkers from SWI and to finally validate their implication in routine clinical setting particularly for specific disease conditions: glioma, primary cerebral nervous system lymphoma (PCNSL), and acute ischemic stroke. The scope of this thesis results in finding unmet benefits in terms of diagnostic accuracy, confidence as well as in reducing scan time and contrast dosage. It aims for better treatment prognosis, planning and management that can benefit the patients.

The second chapter of the thesis proposes a noninvasive segmentation based quantitative approach to analyze intra tumoral susceptibility signal (ITSS) from SWI and finally calculate ITSS vasculature volume (IVV) within grades of glioma. The proposed method scores over the existing semiquantitative method in terms of ITSS estimation and grading accuracy. The current study also evaluates the role of quantitative susceptibility mapping (QSM) for segmentation of ITSS into hemorrhage and vasculature; compute QSM based IVV and compare the results with R_2^* based IVV for glioma grading. A high correlation between both these methods is found. Therefore, QSM can be used interchangeably with R_2^* to calculate IVV for differentiation between grade II vs III and grade II vs IV. For grade III vs IV, R_2^* based IVV scores better. True biological classification of ITSS is necessary to understand the tumor viability, aggressiveness, and angiogenesis. This study develops a novel quantitative approach that combines SWI, R_2* relaxivity and DCE MRI parameters for segmenting ITSS and its further classification into biological behaviour-based subcategories.

The third chapter of the thesis, our findings suggest SWI to be the most useful sequence in the glioma grading as it contributes to calculating the IVV metric, which can singlehandedly improve the glioma grading much further when combined with radiomic analysis used in combination with PCA feature reduction and random forest ML classifier. In the case of patients where contrast injection is impossible due to renal impairments, non-contrast way of glioma grading based on radiomic analysis use of SWI alone can provide almost as good accuracy as using the combinational approach of FLAIR and SWI. This chapter explores the differences between

hemorrhage and vasculature ITSS masks regions within the tumor, assessed by SWI images involving radiomic features extraction and machine learning-based classification. This chapter also focuses on evaluating the performance of texture-based features of SWI in improved differentiation of PCNSL from grade IV gliomas which proves to be a better standalone classification method.

Objectives of the fourth chapter of the thesis are to enhance the Prominent hypo-intense vein sign (PHVS) visibility in SWI, automatically segment and quantify stroke penumbra volume from it and calculate the mismatch ratio between PHVS(SWI) and DWI. The proposed approach demonstrates a high correlation with the gold standard ASL method, suggesting that PHVS and SWI based penumbra quantification has the potential to be used as an alternative for perfusion-based methods in stroke therapy setups. It could save the scan time, does not require any contrast dose to be injected and therefore should be beneficial for acute stroke therapy management.

The author believes that the work in the thesis can help the clinicians (radiologists, neurosurgeons, and neurologists) in improved diagnosis and overall treatment planning of the patients and will also benefit the patients suffering from neuro-diseases (glioma, PCNSL, acute ischemic stroke) to be benefited from no harmful contrast dosage, lesser scan time with expected outcomes. The author sincerely hopes her work will help humanity in general.

सार

इस थीसिस का उद्देश्य विशिष्ट रोग जैसे कि ग्लिओमा, लिम्फोमा और तीव्र एक्सकेमिक स्ट्रोक के नैदानिक उपचार व्यवस्था में एसडब्लूएआई से विकसित मात्रात्मक बायोमार्कर की उपयोगिता की खोज करना है | इस थीसिस का परिणाम नैदानिक उपचार की सटीकता, स्कैन समय और कंट्रास्ट की खुराक को कम करने के सन्दर्भ में परिलक्षित होता है| यह थीसिस उपचार पूर्वानुमान , योजना और प्रबंधन में सहायक है, जो रोगियों के उपचार में अतिआवश्यक उपयोगिता को दर्शाता है|

दूतीय अध्याय, एक गैर-विभेदक विभाजन आधारित दृष्टिकोण का प्रस्ताव करता है, जिसकी सहायता से इंट्रा ट्यूमरल संवेदनशीलता संकेत (आईटीएसएस) का विश्लेषण और ग्लियोमा के ग्रेड के भीतर आईटीएसएस वास्कुलचर वॉल्यूम (आईवीवी) की गणना की गयी है| प्रस्तावित पद्धति, अनुमान और ग्रेडिंग सटीकता के संदर्भ में अन्य पद्धतियों से श्रेष्ठ है| वर्तमान अध्ययन रक्तस्राव और वाहिका में आईटीएसएस के विभाजन के लिए क्यूएसएम् की भूमिका का मूल्यांकन करता है| वर्तमान अध्ययन में रक्तस्राव और वाहिका में आईटीएसएस के विभाजन के लिए क्यूएसएम की भूमिका के मूल्यांकन के साथ-साथ, क्यूएसएम आधारित आईवीवी की गणना और ग्लियोमा ग्रेडिंग के लिए आर2* आधारित आईवीवी के साथ परिणामों की तुलना की गयी है| इन दोनों विधियों के बीच उच्च सहसंबंध पाया गया है| ग्रेड ।। बनाम ।।। और ग्रेड ।। बनाम ।V के लिए ।VV की गणना के लिए क्यूएसएम् का परस्पर उपयोग किया जा सकता है। इस अध्ययन में R_2* आधारित ।VV स्कोर ग्रेड ।।। बनाम ।V के लिए बेहतर पाया गया| ट्यूमर की व्यवहार्यता, आक्रामकता और एंजियोजेनेसिस को समझने के लिए आईटीएसएस का सही जैविक वर्गीकरण आवश्यक है। यह अध्ययन एक नया मात्रात्मक दृष्टिकोण विकसित करता है जो आईटीएसएस को विभाजित करने और जैविक व्यवहार-आधारित उपश्रेणियों में इसके आगे के वर्गीकरण के लिए एसडब्ल्यूआई, R_2*रिलैक्सीविटी और डीसीई एमआरआई मापदंडों को जोड़ता है।

थीसिस का त्रितीय अध्याय, ग्रेड ।V ग्लिओमास से पीसीएनएसएल के बेहतर विभेदीकरण में एसडब्ल्यूआई की बनावट-आधारित विशेषताओं के प्रदर्शन का मूल्यांकन करने पर केंद्रित है जो एक बेहतर स्टैंडअलोन वर्गीकरण पद्धति साबित होती है। यह अध्याय ट्यूमर के भीतर रक्तस्राव और वास्कुलचर आईटीएसएस मास्क क्षेत्रों के बीच के अंतरों की भी पड़ताल करता है, जिसका मूल्यांकन एसडब्ल्यूआई छवियों द्वारा किया जाता है जिसमें रेडियोमिक फीचर निष्कर्षण और मशीन लर्निंग आधारित वर्गीकरण शामिल है।

कुल मिलाकर, हमारे निष्कर्ष एसडब्ल्यूआई को ग्लियोमा ग्रेडिंग में सबसे उपयोगी और अपरिहार्य अनुक्रम होने का सुझाव देते हैं क्योंकि यह आईवीवी मीट्रिक की गणना करने में योगदान देता है| आईवीवी मीट्रिक और रेडिओमिक्स फीचर का संयुक्त विश्लेषण ग्लिओमा ग्रेडिंग को सुधार सकता है| वर्गीकरण के पहले रेडिओमिक्स फीचर का चुनाव पीसीए विधि का उपयोग करके किया गया| वर्गीकरण, रैंडम फारेस्ट विधि का उपयोग करके किया गया| उन रोगियों के मामले में जहां गुर्दे की खराबी के कारण कंट्रास्ट इंजेक्शन असंभव है, अकेले एसडब्ल्यूआई के रेडियोमिक विश्लेषण के आधार पर ग्लियोमा ग्रेडिंग का गैर-विपरीत तरीका (फ्लेयर और एसडब्ल्यूआई का संयोजन) लगभग अच्छी सटीकता प्रदान कर सकता है।

थीसिस के चौथे अध्याय का उद्देश्य एसडब्ल्यूआई में पीएचवीएस दृश्यता को बढ़ाना, स्वचालित विभाजन, स्ट्रोक पेनम्ब्रा वॉल्यूम का मापन और पीएचवीएस (एसडब्ल्यूआई) और डीडब्ल्यूआई के बीच बेमेल अनुपात की गणना करना है। प्रस्तावित दृष्टिकोण स्टैण्डर्ड मानक एएसएल पद्धति के साथ उच्च सहसंबंध को प्रदर्शित करता है और यह सुझाव देता है कि पीएचवीएस और एसडब्ल्यूआई आधारित मात्रात्मक पेनम्ब्रा विधि, स्ट्रोक थेरेपी सेटअप में छिड़काव-आधारित विधियों के विकल्प के रूप में उपयोग की जा सकती है| इस विधि से स्कैन समय बचाया जा सकता है| इस विधि में कंट्रास्ट इंजेक्शन खुराक की आवश्यकता नहीं होती है और इसलिए यह विधि तीव्र स्ट्रोक थेरेपी प्रबंधन के लिए फायदेमंद है|

शोधकर्ता का मानना है कि थीसिस कार्य रोगियों के बेहतर निदान और समग्र उपचार योजना में चिकित्सकों (रेडियोलॉजिस्ट, न्यूरो-सर्जन और न्यूरोलॉजिस्ट) की मदद कर सकता है| थीसिस कार्य, न्यूरो-रोगों (ग्लियोमा, लिम्फोमा, तीव्र इस्केमिक) से पीड़ित रोगियों को भी लाभान्वित करेगा। शोधकर्ता को पूरा विश्वास है कि उसका कार्य सामान्य रूप से मानवता की मदद में सहायक होगा |

Content

List of Figures

List of Tables

List of Abbreviations

EEG = Electro Encephalography

PET = Positron Emission Tomography

CT = Computed Tomography

MRI = Magnetic Resonance Imaging

SWI = Susceptibility Weighted Imaging

DWI = Diffusion Weighted Imaging

ADC = Apparent Diffusion Coefficient

EES = Extracellular Extravascular Space

HCT = Hematocrit

CNR = Contrast to Noise Ratio

SNR = Signal to Noise Ratio

FFE = Fast Field Echo

PADRE = Phase difference-enhanced imaging

EPI = Echo Planar Imaging

FLAIR = Fluid Attenuated Inversion Recovery

MRA = Magnetic Resonance Angiography

ITSS = Intra tumoral susceptibility signal

IVV = ITSS vasculature volume

TIV = Total ITSS volume

VEGF = Vascular endothelial growth factor

DSC = Dynamic Susceptibility Contrast

DCE = Dynamic contrast enhanced

ROI = Region of Interest

ROC = Receiver operator characteristic

AUC = Area under the curve

QSM = Quantitative susceptibility mapping

CBF = Cerebral blood flow