

**SEGMENTATION AND QUANTITATIVE  
EVALUATION OF TIBIO-FEMORAL CARTILAGE  
USING MR PARAMETERS**

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**CENTRE FOR BIOMEDICAL ENGINEERING  
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EVALUATION OF TIBIO-FEMORAL CARTILAGE  
USING MR PARAMETERS**

*by*

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**CENTRE FOR BIOMEDICAL ENGINEERING**

*Submitted*

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

*to the*



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*Dedicated*

*To*

*My Family, Teachers and Almighty God*

## **CERTIFICATE**

This is to certify that the thesis entitled, “**Segmentation and Quantitative Evaluation of Tibio-Femoral Cartilage using MR Parameters**”, submitted by **Mr. Rafeek T (2016BMZ8336)** for the award of the degree of the **Doctor of Philosophy** to 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.

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## **ABSTRACT**

Osteoarthritis (OA) is one of the leading chronic disability mainly affects elder population. The degeneration of weight-bearing articular cartilage present in the hip and knee is the prime reason for OA condition. Presently, medical imaging-based screening methods are widely used for the diagnosis of OA because of its non-invasive nature. MR-imaging is considered as an important imaging technique due to its soft tissue contrast and 3D visualisation property. The recently developed advanced MRI techniques shows promising potential in OA diagnosis and grading. Both structural and molecular changes can be evaluated using MRI techniques. Despite applications of quantitative MRI in OA diagnosis, its potential use in the routine clinical practice is limited. There are some challenges in the quantitative evaluation of these advanced MRI techniques including cartilage segmentation, which should be addressed for its potential clinical applications. There is need of robust computer-aided-diagnosis (CAD) systems for automated or semi-automated evaluation of quantitative changes in knee joints cartilage and for evaluating clinical potential of quantitative MRI in OA diagnosis and grading.

In this dissertation, research studies have been carried out for addressing some of the challenges of quantitative evaluation of knee joint MRI along with evaluating its clinical potential in diagnosis and grading of OA. The main objectives of the study were to develop weight-bearing articular cartilage segmentation algorithms especially in OA patients having subchondral bone abnormality (SBA) and to develop a framework to automatize the quantitative evaluation methods of cartilage degeneration followed by grading of OA disease. Another objective of the study was to quantitatively evaluate the biochemical and morphological characteristics of cartilage corresponding to the biomechanical loading.

Subchondral bone abnormality (SBA) is considered as one of the advanced characteristics of OA. Therefore, the evaluation of characteristic changes of weight bearing cartilage area, superficial to SBA, is important in OA diagnosis. In the current study, a modified radial search approach using thresholding, connected component labelling, convex-hull operation and spline-based curve fitting was introduced for the improved segmentation of tibiofemoral cartilage especially in patients with SBA condition. Modified radial-search approach successfully performed on different MRI sequence images. Proposed approach has great potential in the quantitative evaluation of cartilage degradation studies.

Presently, the clinicians qualitatively analyse the MR-images for detecting the abnormality. The quantitative evaluation of cartilage degeneration using advanced MRI is promising; however, in general clinicians draw line segments and select different ROIs manually from slices of interest. This approach is time consuming and prone to inter-intra reader variability. To overcome this difficulty, we have developed a framework (CAD) for quantitative evaluation of cartilage degeneration followed by OA diagnosis. In the current study, the proposed framework showed promising results in differentiating healthy volunteers' group from OA patients group as well as Early-OA group from Advanced-OA group. Proposed tool and research findings can be used for screening and disease diagnosis.

MR studies with and without loads on knee joint is important for analysing the stress distribution during loading. In the current study, the changes present in the biochemical and morphological characteristics of articular cartilage corresponding to the applied load was examined with the help of an in-house developed MRI compatible loading device. The T2 relaxation time changes corresponding to the biomechanical load are quite small; therefore initially, the inter-intra day variability of MRI parameters is evaluated. For the quantitative analysis, we have evaluated the changes present in the T2 relaxation time and thickness values of cartilage in load and unload condition. In the current study, the changes due to loading effect

were more on medial compartment than lateral compartment. Also, during loading, the T2 mean values were increased in deep layer and decreased in superficial layer in medial compartment.

In brief, the thesis work is a comprehensive study of weight-bearing cartilage segmentation methods, development of a framework for quantitative evaluation of cartilage degeneration, optimisation of MR-parameters for OA classification, loading response of articular cartilage and some clinical applications of the proposed methodologies. The current research work presented in this thesis would be beneficial to clinicians for improved diagnosis and treatment planning of OA patients.

## सार

ऑस्टियोआर्थराइटिस (ओ.ए) एक प्रमुख पुरानी विकलांगता है जो मुख्य रूप से बड़ी आबादी को प्रभावित करती है। कूल्हे और घुटने में मौजूद भारोत्तोलन आर्टिकुलर कार्टिलेज का अधः पतन ओ.ए स्थिति का प्रमुख कारण है। वर्तमान में, ओ.ए के निदान के लिए इमेजिंग-आधारित स्क्रीनिंग विधियों का व्यापक रूप उपयोग किया जाता है क्योंकि इसकी प्रकृति गैर-आक्रामक है। एम.आर.इमेजिंग को इसके सॉफ्ट टिशू कंट्रास्ट और 3डी विजुअलाइज़ेशन गुण के कारण एक महत्वपूर्ण इमेजिंग तकनीक माना जाता है। हाल ही में विकसित उन्नत एमआरआई तकनीक OA निदान और ग्रेडिंग में आशाजनक क्षमता दिखाती है। एमआरआई तकनीकों का उपयोग करके संरचनात्मक और आणविक दोनों परिवर्तनों का मूल्यांकन किया जा सकता है। ओ.ए निदान में मात्रात्मक एमआरआई के अनुप्रयोगों के बावजूद, नियमित नैदानिक अभ्यास में इसका संभावित उपयोग सीमित है। उपास्थि विभाजन सहित इन उन्नत एम.आर.आई. तकनीकों के मात्रात्मक मूल्यांकन में कुछ चुनौतियां हैं, जिन्हें इसके संभावित नैदानिक अनुप्रयोगों के लिए संबोधित किया जाना चाहिए। घुटने के जोड़ों के कार्टिलेज में मात्रात्मक परिवर्तनों के स्वचालित या अर्ध-स्वचालित मूल्यांकन के लिए और ओ.ए. निदान और ग्रेडिंग में मात्रात्मक एम.आर.आई. की नैदानिक क्षमता के मूल्यांकन के लिए शक्तिशाली कंप्यूटर एडेड-डायग्नोसिस (सी.ए.डी.) सिस्टम की आवश्यकता है।

इस शोध प्रबंध में ओ.ए के निदान और ग्रेडिंग में इसकी नैदानिक क्षमता के मूल्यांकन के साथ-साथ घुटने के जोड़ एम.आर.आई. के मात्रात्मक मूल्यांकन की कुछ चुनौतियों का समाधान करने के लिए शोध अध्ययन किए गए हैं। अध्ययन का मुख्य उद्देश्य भारोत्तोलन आर्टिकुलर कार्टिलेज सेगमेंटेशन एल्गोरिदम विकसित करना था, विशेष रूप से ओए रोगियों में उपचंद्रल अस्थि असामान्यता (एस.बी.ए.) और ओ.ए. रोग की ग्रेडिंग के बाद कार्टिलेज डिजनरेशन के मात्रात्मक मूल्यांकन विधियों को स्वचालित

करने के लिए एक रूपरेखा विकसित करना। अध्ययन का एक अन्य उद्देश्य बायोमेकेनिकल लोडिंग के अनुरूप कार्टिलेज की जैव रासायनिक और रूपात्मक विशेषताओं का मात्रात्मक मूल्यांकन करना था।

उपचंद्रल अस्थि असामान्यता (एस.बी.ए.) को ओ.ए. की उन्नत विशेषताओं में से एक माना जाता है। इसलिए, वजन असर उपास्थि क्षेत्र के विशिष्ट परिवर्तनों का मूल्यांकन, एसबीए के लिए सतही, ओ.ए. निदान में महत्वपूर्ण है। वर्तमान अध्ययन में, विशेष रूप से एस.बी.ए. स्थिति वाले रोगियों में टिबायोफेमोरल कार्टिलेज के बेहतर विभाजन के लिए थ्रेशोल्डिंग, कनेक्टेड कंपोनेंट लेबलिंग, उत्तल-पतवार ऑपरेशन और स्पलाइन-आधारित वक्र फिटिंग का उपयोग करते हुए एक संशोधित रेडियल खोज दृष्टिकोण पेश किया गया था। संशोधित रेडियल-खोज दृष्टिकोण ने विभिन्न एम.आर.आई. अनुक्रम छवियों पर सफलतापूर्वक प्रदर्शन किया। उपास्थि क्षरण अध्ययन के मात्रात्मक मूल्यांकन में प्रस्तावित दृष्टिकोण में काफी संभावनाएं हैं।

वर्तमान में, चिकित्सक असामान्यता का पता लगाने के लिए एम.आर. छवियों का गुणात्मक विश्लेषण करते हैं। उन्नत एम.आर.आई. का उपयोग करके उपास्थि अधः पतन का मात्रात्मक मूल्यांकन आशाजनक है, हालांकि, सामान्य तौर पर चिकित्सक लाइन सेगमेंट बनाते हैं और आवश्यक छवि से मैनुअल रूप से विभिन्न आर.ओ.आई. का चयन करते हैं। यह दृष्टिकोण समय लेने वाला है और अंतर-पाठक परिवर्तनशीलता के लिए प्रवण है। इस कठिनाई को दूर करने के लिए, हमने ओ.ए. निदान के बाद उपास्थि अधः पतन के मात्रात्मक मूल्यांकन के लिए एक रूपरेखा (सी.ए.डी.) विकसित की है। वर्तमान अध्ययन में, प्रस्तावित ढांचे ने स्वस्थ स्वयंसेवकों के समूह को ओ.ए. रोगियों के समूह के साथ-साथ प्रारंभिक ओ.ए. समूह को उन्नत ओ.ए. समूह से अलग करने में आशाजनक परिणाम दिखाए। प्रस्तावित उपकरण और शोध निष्कर्षों का उपयोग स्क्रीनिंग और रोग निदान के लिए किया जा सकता है।

घुटने के जोड़ पर भार के साथ और बिना के साथ एम.आर. अध्ययन लोडिंग के दौरान तनाव वितरण का विश्लेषण करने के लिए महत्वपूर्ण है। वर्तमान अध्ययन में, आंतरिक रूप से विकसित

एम.आर.आई. संगत लोडिंग डिवाइस की मदद से लागू भार के अनुरूप आर्टिकुलर कार्टिलेज की जैव रासायनिक और रूपात्मक विशेषताओं में मौजूद परिवर्तनों की जांच की गई। बायोमेकेनिकल लोड के अनुरूप T2 विश्राम समय में परिवर्तन काफी छोटा है; इसलिए शुरू में, एम.आर.आई. मापदंडों की अंतर-अंतरा दिन परिवर्तनशीलता का मूल्यांकन किया जाता है। मात्रात्मक विश्लेषण के लिए, हमने लोड और अनलोड स्थिति में T2 विश्राम समय और उपास्थि के मोटाई मूल्यों में मौजूद परिवर्तनों का मूल्यांकन किया है। वर्तमान अध्ययन में, लोडिंग प्रभाव के कारण होने वाले पार्श्व परिवर्तन की तुलना में औसत दर्जे हिस्से पर अधिक थे। इसके अलावा, लोडिंग के दौरान, T2 माध्य मानों को गहरी परत में बढ़ाया गया था और औसत दर्जे के हिस्से में सतही परत में कमी आई थी।

संक्षेप में, थीसिस कार्य भारोत्तोलन उपास्थि विभाजन विधियों का एक व्यापक अध्ययन है, उपास्थि अधः पतन के मात्रात्मक मूल्यांकन के लिए एक रूपरेखा का विकास, ओ.ए. वर्गीकरण के लिए एम.आर. परिमाणों का अनुकूलन और आर्टिकुलर कार्टिलेज की लोडिंग प्रतिक्रिया आदि कुछ प्रस्तावित नैदानिक अनुप्रयोग हैं। इस थीसिस में प्रस्तुत वर्तमान शोध कार्य ओ.ए. रोगियों के बेहतर निदान और उपचार योजना के लिए चिकित्सकों के लिए फायदेमंद होगा।

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## LIST OF ABBREVIATIONS

OA	Osteoarthritis
NHP	National Health Portal
WHO	World Health Organisation
MRI	Magnetic Resonance Imaging
JSW	Joint Space Width
KL	Kellgren Lawrence
SNR	Signal to Noise Ratio
NMR	Nuclear Magnetic Resonance
EPI	Echo-Planar Imaging
RF	Radio Frequency
FID	Free Induction Decay
SE	Spin Echo
TE	Echo Time
TR	Repetition Time
GRE	Gradient Recalled Echo
FSE	Fast Spin Echo
PD	Proton Density
SPGR	Spoiled Gradient Recalled Echo
ECM	Extracellular Matrix
SL	Spin Lattice
dGEMRIC	delayed Gadolinium Enhanced MRI of Cartilage
GAG	Glycosaminoglycans
CEST	Chemical Exchange Saturation Transfer
BCI	Bone Cartilage Interface
ML	Machine Learning
qMRI	quantitative MRI
ACL	Arterial Cruciate Ligament
SBA	Subchondral Bone Abnormalities
AS	Asymptomatic
BME	Bone Marrow Oedema

DC	Dice Coefficient
JC	Jaccard Coefficient
SI	Sensitivity Index
CV	Coefficient of Variation
MOBC	Modified Outerbridge Classification
WORMS	Whole Organ Magnetic Resonance Imaging Scoring
ROIs	Region of Interests
SRA	Sub-Region Analysis
SL	Sub-Region Length
ANOVA	Analysis of Variance
HSD	Honestly Significant Difference
ICC	Intraclass Correlation Coefficient
ROC	Receiver Operator Characteristics
AUC	Area Under the Curve