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In-vivo Validierung, altersabhängige Normwerte sowie Einfluss von Tageszeit und sportlicher Betätigung auf die biochemisch-sensitive Knorpelevaluation am Hüft- und Kniegelenk mittels T2*-Relaxometrie

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BEITRAGENDE ORIGINALARBEITEN

Abkürzungsverzeichnis

2D:	Zweidimensional
3D:	Dreidimensional
BMI:	*Body-Mass-Index*
DESS:	*Double-echo steady state*
dGEMRIC:	*Delayed-Gadolinium enhanced Magnetic Resonance Imaging of Cartilage*
FAI:	Femoroazetabuläres Impingement
gagCEST:	*Glycosaminoglykan Chemical Exchange Saturation Transfer*
GRE:	Gradienten-Echo
HF-Impuls:	Hochfrequenz-Impuls
ICC:	*Intraclass Correlation Coefficient*
JIF:	*Journal Impact Factor*
KI:	Konfidenzintervall
MRT:	Magnet-Resonanz-Tomographie
ms:	Millisekunden
OA:	Osteoarthrose
SE:	Spin-Echo
$T1_{Gd}$:	T1-Relaxationszeit nach Applikation eines Gadolinium-haltigen Kontrastmittels
TE:	Echozeit
vs:	versus

Übersicht der beitragenden Originalarbeiten

Hesper T, Miese FR, Hosalkar HS, Behringer M, Zilkens C, Antoch G, Krauspe R, Bittersohl B. Quantitative T2(*) assessment of knee joint cartilage after running a marathon. *Eur J Radiol.* 2015;84:284-289.

JIF: 2,593

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JIF: 2,621

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JIF: 2,621

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JIF: 2,621

Bittersohl B, Benedikter C, Franz A, **Hesper T**, Schleich C, Antoch G, Hosalkar HS, Krauspe R, Zilkens C. Elite Rowers Demonstrate Consistent Patterns of Hip Cartilage Damage Compared With Matched Controls: A T2* Mapping Study. *Clin Orthop Relat Res*. Zur Publikation angenommen am 30.10.2018. DOI 10.1097/CORR.0000000000000576.

JIF: 4,091

Zusammenfassung

Goldstandard in der Diagnostik von Knorpelveränderungen ist die Magnetresonanztomographie (MRT). Unter Verwendung unterschiedlich gewichteter Sequenzen können morphologische Knorpelveränderungen zuverlässig und reproduzierbar beurteilt werden, molekulare Kompositionsveränderungen des Knorpels, welche frühzeitig im Rahmen der Knorpeldegeneration nachweisbar sind, bleiben hierbei jedoch unentdeckt. Bei der T2*-Relaxometrie handelt es sich um ein biochemisch-sensitives MRT-Verfahren, welches sensitiv für Veränderungen des Wassergehalts und der Kollagenfaserorientierung des Gelenkknorpels ist. Gegenüber anderen etablierten Verfahren der biochemisch-sensitiven Knorpelbildgebung bietet es verschiedene Vorteile, hierzu zählen v.a. die vergleichsweise einfache Implementierbarkeit in die klinische Routine, kurze Akquisitionszeiten und eine hohe, isotrope Bildauflösung ohne die Notwendigkeit einer Kontrastmittelapplikation.

Neben Unterschieden in der molekularen Komposition von lasttragenden- und nicht-lasttragenden Knorpelregionen müssen zonale Unterschiede (z. B. höherer Wassergehalt in oberflächlichen Knorpelschichten) bei der Interpretation der T2*-Messungen berücksichtigt werden. In diesem Zusammenhang sind – insbesondere im Bereich der unteren Extremität – tageszeit- und belastungsabhängige Schwankungen des Knorpelwassergehalts von Bedeutung. Bislang propagieren viele Autoren, T2*-Messungen am Ende des MRT-Protokolls, und nur nach einer ausreichenden Zeit der Gelenkentlastung durchzuführen. Zudem liefern bislang publizierter Studien T2*-Normwerte lediglich für vergleichsweise Junge Patienten, wohingegen Patienten mittleren Alters nur unzureichend abgebildet sind.

In der hier vorgelegten Arbeit wird ausführlich der Einfluss der Messzeit und sportlicher Betätigung (Gelenkbelastung) auf die T2*-Relaxometrie am Hüft- und Kniegelenk dargelegt. Zudem werden T2*-Normwerte unterschiedlicher Altersgruppen und deren

Verteilungsmuster am Hüftgelenk präsentiert. Limitierungen der vorgestellten Studien und der Einfluss der Ergebnisse auf die klinische Anwendung der T2*-Relaxometrie werden diskutiert.

Einleitung

Gelenkknorpelaufbau und Veränderungen im Rahmen der Knorpeldegeneration

Bei hyalinem Gelenkknorpel handelt es sich um eine Verbundstruktur aus Chondrozyten und der von ihnen produzierten extrazellulären Matrix, welche zu ca. 60-85% aus Wasser, 10-20% aus Kollagenfasern und zu 5-10% aus Proteoglykanen besteht[1, 2]. Der Proteoglykankomplex besteht aus einer zentralen Kohlenstoffkette, der Hyaluronsäure, welche als eine Art Rückgrat fungiert. An diese Kohlenstoffkette binden zahlreiche Glykosaminoglykan (GAG)-Seitenketten, welche hauptsächlich aus Chondroitinsulfat und Keratansulfat bestehen. Zum einen binden diese GAG-Seitenketten Kollagenfasern und vernetzen diese so untereinander. Zum anderen trägt ihre zweifach negative Ladung zu der hohen Wasserbindungskapazität des Gelenkknorpels und so zu seiner mechanischen Steifigkeit bei. Auf molekularer Ebene stehen sich im Wesentlichen der osmotische Druck – bedingt durch die negativ geladenen, hydrophilen GAG-Seitenketten und deren Anziehung von positiven Ionen und der sie umgebenden Flüssigkeit – und die Zugfestigkeit des Kollagenfasernetzwerkes gegenüber. Wird der Gelenkknorpel unter Belastung komprimiert, diffundieren Wasser und Elektrolyte solange in den Gelenkspalt, bis sich der von außen wirkende mechanische Druck und der hydrostatische Druck innerhalb des Gelenkknorpels im Gleichgewicht befinden. Lässt der mechanische Druck nach, weichen die GAG-Ketten aufgrund der zwischen ihnen herrschenden Abstoßungskraft aufgrund der negativen Ladung wieder auseinander und der Knorpel nimmt durch wiedereinströmendes Wasser sein Ursprungsvolumen wieder an.

Bedingt durch Unterschiede in der biochemischen Zusammensetzung und der Ausrichtung der Kollagenfasern lässt sich hyaliner Gelenkknorpel in vier unterschiedliche Regionen unterteilen. In der oberflächlichen bzw. Tangentialzone (10-20% der Gesamtknorpeldicke)

verlaufen die Kollagenfasern parallel zur Oberfläche. Es handelt sich um die zellreichste Zone mit einem hohen Kollagen- und Wassergehalt, wohingegen der Proteoglykangehalt in dieser Zone gering ist. Im weiteren Verlauf von der Knorpeloberfläche bis hin zum subchondralen Knochen nimmt der Kollagen- und Wassergehalt immer mehr ab und der Proteoglykangehalt zu. In der Übergangszone (ca. 60% der Knorpeldicke) zeigt sich eine gemischte Kollagenfaserorientierung mit einem zunehmend arkadenförmigen Verlauf der Fasern in tieferen Schichten. In der Radiärzone verlaufen die Kollagenfasern senkrecht zur Knorpeloberfläche und die Chondrozyten zeigen eine säulenartige Anordnung. Bei der tiefsten Schicht handelt es sich um die verkalkte Zone, die Knorpel-Knochen- Grenzfläche[1, 2]. Neben zonalen Unterschieden lassen sich auch belastungsabhängige, regionale Unterschiede innerhalb des Gelenkknorpels nachweisen[3-5]. In Knorpelbereichen, die einer hohen Druckbelastung ausgesetzt sind (z.B. Hauptbelastungszonen der großen Gelenke der unteren Extremitäten), findet sich ein höherer Anteil von GAG-Ketten, eine dickere Radiärzone und eine dünnere Übergangszone als in weniger stark belasteten Knorpelregionen.

Bei fortschreitendem Gelenkknorpelverschleiß / Osteoarthrose (OA) lassen sich auf mikro- und makroskopischer Ebene verschiedene Zusammensetzungs- und Strukturveränderungen des Gelenkknorpels beobachten, welche während der verschiedenen Phasen der Degeneration im gleichen Gelenk koexistieren können[2, 6-8]. Diese Veränderungen können mitunter sehr vielfältig sein: Im Rahmen einer beginnenden OA zeigt sich meist zunächst ein Ausfransen oder Fibrillieren der oberflächlichen Zone. Im weiteren Verlauf werden dann intrachondrale Risse, die bis zum subchondralen Knochen reichen können, beobachtet. Häufig kommt es auch zu – aus dem Knorpelverbund gelösten – fibrillierten Knorpeltrümmern, einer zunehmenden Abnahme der Knorpeldicke (Knorpelabrasion) bis hin zum vollständigen Knorpelverlust[2]. Betrachtet man die im Rahmen der OA

einhergehenden Veränderungen auf molekularer Ebene, zeigt sich zunächst ein Abbau der Kollagen-Proteoglykan-Verbindungen, woraus eine zunehmende Desorganisation des Kollagenfasernetzwerkes, ein Kollagenabbau, eine Proteoglykanmatrix-Aufspaltung und schließlich ein Proteoglykanverlust resultiert[6, 8]. In den Frühstadien der OA wird häufig zunächst ein Anstieg des Knorpelwassergehalts beobachtet. Dieses lässt sich im Wesentlichen auf folgende Umstände zurückführen:

1. Es kommt zu einer Freilegung der negativ geladenen Wasserbindungsmoleküle an den Kollagenfibrillen;
2. Durch die Proteoglykanaufspaltung kommt es zu einem höheren Anteil von nicht-aggregierten Proteoglykankomplexen, was zu einer erhöhten Penetrierbarkeit der extrazellulären Matrix führt;
3. Es resultiert eine verminderte Zugsteifigkeit des Knorpels, welche dem osmotischen Gradienten gegenübersteht;
4. Möglicherweise ein vorübergehender reaktiver Anstieg in der Netto-Syntheserate von Proteoglykanen.

Der fortschreitende Verlust der mikro- und makro-Architektur in späteren Stadien der OA geht schließlich regelhaft mit einer Abnahme des Knorpelwassergehalts einher[8].

Grundlagen der Magnet-Resonanz-Tomographie und der Gelenkknorpelrelaxometrie

Wesentliches Merkmal der MRT sind die physikalischen Eigenschaften der Protonenrelaxation. Während der MRT kreiseln (präzedieren) Protonen um ein angelegtes statisches Magnetfeld B_0. Durch einen zur Magnetfeldrichtung von B_0 90° gerichteten Hochfrequenz (HF)-Impuls werden die kreiselnden Kerne senkrecht zu B_0 „gekippt“ und synchronisiert (sog. In-Phase Präzession bzw. transversale Magnetisierung). Diese

transversale- oder auch Quermagnetisierung bewirkt einen HF-Impuls, der eine Spannung (und damit ein messbares MR-Signal) in der jeweiligen Empfängerspule erzeugt. Unmittelbar im Anschluss an die Quermagnetisierung der Protonen kehren diese in ihren Ausgangszustand zurück, wobei ein Energieaustausch zum einen zwischen den jeweiligen Kernen und deren Umgebung (Spin-Gitter bzw. T1-Relaxation), zum anderen durch Wechselwirkungen zwischen benachbarten Kernen aufgrund von Variationen in den präzessierenden Eigenfrequenzen der Kerne (Spin-Spin bzw. T2-Relaxation), beobachtet wird.

Diese Mechanismen der Bilderzeugung können unterschiedlich gewichtet werden. In einer T2-gewichteten Sequenz ist das Bild vornehmlich von der transversalen Relaxation (Spin-Spin) bestimmt. Eine T1-Wichtung stellt überwiegend die longitudinale Relaxation dar, also die Zeit, in der sich die Längsmagnetisierung durch Energieabgabe der Spins an die Umgebung (Spin-Gitter-Relaxation) wiederaufbaut.

Grundsätzlich können zwei- und dreidimensionale (3D) MR-Messungen durchgeführt werden. Der Unterschied besteht darin, dass im Gegensatz zur Schicht-selektiven Anregung bei der 2D-Messung bei der 3D-Messung Volumen-selektiv das gesamte zu untersuchende Volumen angeregt wird. 3D-Messungen bieten verschiedene Vorteile, u.a. eine geringere Schichtdicke, kleine Abstände zwischen den zu untersuchenden Schichten (= slice gap) sowie eine hohe Ortsauflösung. Um eine isotrope 3D MRT-Karte der gemessenen Relaxationszeiten zu generieren, sind verschiedene, aufeinanderfolgende Bilder mit unterschiedlichen Echozeiten (TE) notwendig. Dieses gelingt durch die Verwendung sog. Multi-Echo-Sequenzen. Die TE werden hierbei so gewählt, dass sie das zu erwartende Signalverhalten des zu untersuchenden Gewebes beinhalten. Anhand des gemessenen Signalabfalls zu unterschiedlichen TE kann die Relaxationszeit mittels einer Exponentialfunktion berechnet werden, die als Abfall des Signals um 1/e (37%) definiert ist.

Üblicherweise werden die MRT-Datensätze im Anschluss an eine Workstation mit entsprechender Bildbearbeitungs-Software übertragen und die gemessenen Relaxationszeiten können sodann in grau- bzw. farbskalierten MRT-Karten dargestellt werden. Die Analyse erfolgt entweder in frontal-, sagittal- oder axialen Schichten oder anhand standardisierter, aus dem 3D-Datensatz unter Verwendung einer sog. MPR (*multiplanar reconstruction*) - Software rekonstruierter Schichten (z.B. radiäre Schichten entlang des Schenkelhalses zur Knorpelevaluation am Hüftgelenk). Für die Gelenkknorpelevaluation hat sich in der Vergangenheit die Auswertung mittels *Region of Interest* (ROI)-Analyse bewährt. Hierbei werden in die MRT-Karten (und ggf. korrespondierenden morphologischen Sequenzen, welche die anatomischen Gewebegrenzen genauer darstellen) verschiedene Markerpunkte eingezeichnet, die die zu evaluierende Geweberegion umschließen.

Biochemisch-sensitive MRT-Verfahren

T2 / T2*-Mapping

Die physikalischen Grundlagen der Bildentstehung entsprechen beim T2-Mapping den oben aufgeführten Prinzipien. Diese sogenannte Spin-Echo-(SE)-Technik beruht auf der Applikation eines 180°-Refokussierungsimpulses im Intervall zwischen 90°-Anregung und Detektion des MR-Signals, um störende Einflüsse äußerer Magnetfelder auf die präzisierenden Spins zu verhindern. Hierdurch kommt es zu einer Verlangsamung der Querrelaxation, welche nun nicht mehr mit der Zeitkonstanten T2*, sondern langsamer mit der gewebsspezifischen Konstante T2 erfolgt. Im Gegensatz hierzu beruht die T2*-Mapping-Technik auf einer Gradienten-Echo (GRE)-Sequenz. Charakteristisches Merkmal aller GRE-Sequenzen ist der Verzicht auf den 180°-Refokussierungsimpuls. Hierdurch tragen weitere Dephasierung-Effekte zum T2-Signal bei, was im Allgemeinen als T2*-

Relaxation bezeichnet wird[9]. Zu diesen Dephasierungs-Effekten zählen vor allem *chemical-shifts* (sog. chemische Verschiebungen: Bedingt durch unterschiedliche Präzessionsfrequenzen von an Wasser- und Fett gebundenen Protonen), Unterschiede in der magnetischen Suszeptibilität (Magnetisierbarkeit) verschiedener Gewebearten und Hauptmagnetfeld-Inhomogenitäten. Das Verhältnis von T2 zu T2* verhält sich wie folgt: $1/T2^* = 1/T2 + \gamma\Delta B_{inhom}$; γ = gyromagnetisches Verhältnis, ΔB_{inhom} = Magnetfeld-Inhomogenität in einem Voxel[9].

Vereinfacht dargestellt spiegeln die gemessenen T2- und T2*-Werte den Knorpelwassergehalt sowie die Wechselwirkungen zwischen den Wassermolekülen und dem Kollagenfasernetzwerk wieder[9, 10, 11], wobei hohe Werte einem hohen Wassergehalt und einer großen Wassermolekülmobilität entsprechen. Im gesunden Gelenkknorpel zeigt sich daher eine physiologische Abnahme der T2 / T2*-Relaxationszeiten in tieferen Knorpelschichten, in denen die senkrecht zur Knorpeloberfläche verlaufenden Kollagenfasern und der hohe Proteoglykangehalt die Anzahl an Wassermolekülen und deren Mobilität beschränken[12, 13].

Auch wenn einige Studien eine Korrelation zwischen T2- und T2*-Relaxationszeiten beschreiben [14, 15, 16, 17], müssen aufgrund der methodischen Unterschiede im Sequenzdesign wichtige Unterschiede zwischen T2- und T2*-Mapping berücksichtigt werden, die zu divergierenden Ergebnissen in unterschiedlichen Stadien der Knorpeldegeneration führten [18, 19, 20, 21, 22, 23, 24, 25]. Wie oben dargelegt, ergeben sich T2*-Werte aus der Gewebe-T2-Relaxation sowie eben jenen zusätzlichen Dephasierungs-Effekten, die zu einer schnelleren Rückkehr der Protonen in ihren Ausgangszustand führen. Hieraus ergeben sich charakteristischer Weise niedrigere Gewebe-T2*-Werte. Durch den fehlenden 180°-Refokussierungsimpuls ist T2*-Mapping zudem weniger empfänglich gegenüber Störfaktoren, wie stimulierten Echos und Magnetisierungstransfer zwischen benachbarten

Protonen [16, 26]. Im Gegensatz müssen Suszeptibilitätsartefakte, die an Gewebe-Grenzflächen auftreten und durch Fremdmaterial verursacht werden können, berücksichtigt werden[9]. Zudem werden in SE-basierten T2-Mapping-Sequenzen TE von ca. 10 bis 100 ms verwendet, was zu einer geringen Sensitivität gegenüber T2-Signalen mit kürzerer Relaxationszeit (<10 ms) führt[27, 28]. T2-Relaxationszeiten reflektieren daher überwiegend nicht-gebundene Wassermoleküle, wohingegen die T2*-Mapping-Technik (die kürzere TE beinhaltet) einen breiteren Bereich der Signale widerspiegelt, die im Knorpelgewebe auftreten.

Für beide Anwendungen muss der sog. Magic Angle Effekt berücksichtigt werden[29]. Dieser beschreibt einen Anstieg der T2 / T2*-Werte, wenn die zu untersuchende Knorpelregion ca. 55° zum Hauptmagnetfeld B_0 ausgerichtet ist. Grund dafür sind geringere Spin-Spin-Wechselwirkungen zwischen benachbarten Wassermolekülen in dieser Ausrichtung. Insbesondere in Körperregionen mit gewölbter Knorpelfläche, wie z.B. dem Hüftgelenk, ist dieses Phänomen von Bedeutung und muss bei der Interpretation der gemessenen Relaxationszeiten berücksichtigt werden.

Weitere biochemisch-sensitive MRT-Sequenzen

Neben T2 / T2*-Mapping stellt das sog. *Delayed gadolinium-enhanced magnetic resonance imaging of cartilage* (dGEMRIC) ein etabliertes Verfahren zur Knorpelevaluation dar, dessen Validität und Reproduzierbarkeit in zahlreichen in-vivo- und in-vitro Studien belegt wurde. Hierbei werden Veränderungen in den negativ geladenen GAG-Seitenketten der extrazellulären Knorpelmatrix detektiert. Nach intravenöser Applikation eines negativ-geladenen Gadolinium-haltigen Kontrastmittels (dessen Notwendigkeit einen wesentlichen Nachteil dieses Verfahrens darstellt) penetriert dieses über einen definierten Zeitraum in den Gelenkknorpel und reichert sich in GAG-depletierten Knorpelregionen an. Knorpelregionen

mit hohem GAG-Verlust nehmen so größere Mengen an Kontrastmittel auf und umgekehrt[12]. Das aufgenommene Kontrastmittel führt zu einer verkürzten T1-Relaxationszeit ($T1_{Gd}$). Niedrige T1-Werte werden so in GAG-depletierten Knorpelregionen gemessen.

Weitere etablierte biochemisch-sensitive MRT-Verfahren zur Knorpelbildgebung umfassen die Technik der $T1_{rho}$-Bildgebung[30, 31], Natrium-Bildgebung[31], Diffusions-Bildgebung[32] sowie die Technik des *glykosaminoglycan-chemical-exchange-saturation-transfer* (gagCEST)[33]. Alle diese Verfahren reflektieren unterschiedliche Veränderungen auf molekularer Ebene im Gelenkknorpel. Da diese Techniken nicht Gegenstand der vorliegenden Arbeit sind, wird an dieser Stelle nicht näher auf die einzelnen Techniken eingegangen. Eine Übersicht über die jeweilige molekulare Zielstruktur sowie die verschiedenen Vor- und Nachteile der verfügbaren biochemisch-sensitiven MRT-Sequenzen gibt Tabelle 1.

MRT-Technik	Biochemische Zielstruktur	Vorteile	Nachteile
T2-Mapping	Knorpel-Wassergehalt; Kollagenfaser-Netzwerk; →Zonale Variation entsprechend Knorpelzusammensetzung	Vielzahl publizierter Studien zur T2-Knorpelevaluation; Kommerziell verfügbar auf klinischen MR-Scannern	Relativ lange Akquisitionszeit; geringe Sensitivität in frühen Stadien der Knorpeldegeneration; T2-Variationen in Abhängigkeit der Tageszeit und Sequenzeinstellungen; Magic Angle Effekt
T2*-Mapping	Knorpel-Wassergehalt; Kollagenfaser-Netzwerk; →Zonale Variation entsprechend Knorpelzusammensetzung	Hohe Bildauflösung; kurze Akquisitionszeit; 3D-Knorpelevaluation; UTE-T2*-Mapping; Hohe Sensitivität gegenüber Knorpelveränderungen in tiefen Knorpelschichten	Anfällig für Suszeptibilitätsartefakte (z.B. postop. Debris, Gewebegrenzflächen); Magic Angle Effekt
dGEMRIC	Knorpel GAG-Gehalt; Knorpel-Ladungsdichte	Vielzahl publizierter Studien; Spezifisch für Knorpel GAG-Gehalt; 3D-Knorpelevaluation und kurze Akquisitionszeit möglich	KM-Applikation notwendig; KM-Aufnahme verlängert Untersuchungsdauer; KM-Aufnahme abhängig von Patientenfaktoren (z.B. BMI); benötigt standardisiertes Protokoll
T1rho-Bildgebung	Knorpel-Wassergehalt; Knorpel GAG-Gehalt	Sensitiv für frühe Knorpelveränderungen; Korrelation mit röntgenologischen Zeichen der Knorpeldegeneration, Gelenkschmerzen und Funktionseinschränkungen	Schwierig in die klinische/wissenschaftliche Routine zu implementieren; Benötigt hohe Feldstärken und hohe RF-Impulse; Beeinflusst durch die Orientierung des Knorpels innerhalb des Hauptmagnetfeldes
Natrium-Bildgebung	Knorpel GAG-Gehalt	Spezifisch für Knorpel GAG-Gehalt	Technisch anspruchsvoll; Benötigt hohe Feldstärken (≥3 Tesla), hohe Gradienten und spezielle RF-Spulen; geringes Signal-Rausch-Verhältnis
gagCEST	Knorpel GAG-Gehalt	Potentiell spezifisch für Knorpel GAG-Gehalt	Robuste gagCEST-Sequenzen wurden bislang nicht in die klinische Routine implementiert;
Diffusions-Bildgebung	Wassermolekül-Mobilität	Bislang publizierte Ergebnisse: Homogene Ergebnisse nach gelenkerhaltenden Operationen	Technisch anspruchsvoll; Geringes Signal-Rausch-Verhältnis und Ortsauflösung

Tab. 1: Übersicht biochemisch-sensitiver MRT-Sequenzen[34]

Femoroazetabuläres Impingement

Beim femoroazetabulären Impingement (FAI) führen eine Entrundung des Hüftkopfes (CAM-FAI), eine vermehrte Überdachung des Azetabulums (Pincer-FAI) oder eine Kombination aus beidem (gemischtes-FAI) zu einem mechanischen Anschlagen zwischen Schenkelhals und Azetabulumrand. Während CAM-FAI überwiegend bei jungen, männlichen Patienten symptomatisch wird, ist ein Pincer-FAI häufiger bei Frauen mittleren Alters. Typischerweise werden Knorpel- sowie Labrumschäden beim CAM-FAI in der anterioren bis superioren (3 bis 12 Uhr) Gelenkregion beobachtet, wenn die Asphärizität *(„Bump“)* des Schenkelhals-Kopfüberganges, insbesondere bei Hüftbeugung und Innenrotation, Scherkräfte auf die Gelenklippe (=Labrum azetabulare) und den azetabulären Knorpel in dieser Region ausübt[35, 36]. Insbesondere hierbei kann es zu einem sog. Teppich-Phänomen kommen, bei dem der azetabuläre Knorpelbelag wie ein Teppich von dem subchondralen Knochen abgeschoben wird. Häufig erschwert dieses aufgrund der noch intakten Knorpeloberfläche die Diagnostik mittels MRT oder MR-Arthrographie. Gelegentlich wird eine sog. Contre-coup-Läsion beim Pincer-FAI beobachtet[36]. Hierbei kommt es zu einem pathologischen Hebel-Mechanismus am anterioren Pfannenrand während der Hüftbeugung, was zu einem Anschlagen des Femurkopfes im Bereich der posterior-inferioren Azetabulumwand führen und so Knorpelschäden in dieser Region verursachen kann. Symptomatisches FAI, sofern unbehandelt, stellt eine präarthrotische Deformität dar[37, 38]. Bislang ist dabei nicht vollständig geklärt, welche der FAI-assoziierten Schäden im Bereich des Hüftgelenkes (Knorpelschäden, Labrumrupturen, Synovitis) primär zu Symptomen führen. Weiterhin unklar ist auch, warum dieses bei einigen Patienten zu Symptomen führt, wohingegen andere mit gleicher Hüftgelenkmorphologie keine Beschwerden haben, da die Prävalenz asymptomatischer Patienten mit CAM- und / oder Pincer-Deformitäten in der Literatur zwischen 37- 68% angegeben wird[39].

Eigene Studien und Ergebnisse

Verteilung altersabhängiger Normwerte und in-vivo Validierung der T2*-Relaxometrie am Hüftgelenk

Hesper T, Schleich C, Buchwald A, Hosalkar HS, Antoch G, Krauspe R, Zilkens C, Bittersohl B. T2* Mapping of the Hip in Asymptomatic Volunteers with Normal Cartilage Morphology: An Analysis of Regional and Age-Dependent Distribution. *Cartilage.* 2018;9:30-37.

Hesper T, Neugroda C, Schleich C, Antoch G, Hosalkar H, Krauspe R, Zilkens C, Bittersohl B. T2*-Mapping of Acetabular Cartilage in Patients With Femoroacetabular Impingement at 3 Tesla: Comparative Analysis with Arthroscopic Findings. *Cartilage.* 2017:1947603517741168.

Zur Differenzierung von „gesund“ und „krank“ sind für den klinischen Alltag T2*-Normwerte wünschenswert. Normwerte für das Hüftgelenk sind nur aus vergleichsweise kleinen Kontrollgruppen (asymptomatische Probanden) bekannt[15, 24, 40]. Zudem lassen sich, wie oben beschrieben, sowohl zonale (unterschiedliche T2*-Relaxationszeiten bedingt durch Unterschiede im Wassergehalt und der Kollagenfaserstruktur in oberflächlichen und tiefen Knorpelschichten) als auch regionale (Magic Angle Effekt) Unterschiede im T2*-Verteilungsmuster am Hüftgelenk feststellen. Veränderungen während der (z.T. physiologischen) Knorpeldegenerationen im Laufe des Älterwerdens können ferner die T2*-Relaxation beeinflussen. Zur Evaluation zonaler (peripherer versus zentraler Knorpel) und regionaler (anterior bis posterior) Unterschiede sowie eines Altersgruppen-abhängigen Verteilungsmusters von T2*-Werten am Hüftgelenk publizierten wir 2018[41] eine Studie, in die 47 gesunde, asymptomatische Probanden eingeschlossen wurden. Diese wurden in 3

verschiedene Altersgruppen unterteilt. Gruppe 1: Alter 20-30 Jahre, 15 Probanden, mittleres Patientenalter 25,9 ± 2,3 Jahre, 8 Frauen, 7 Männer, 8 linke Hüften, 7 rechte Hüften. Gruppe 2: Alter 30-40 Jahre, 17 Probanden, mittleres Patientenalter 34,1 ± 3,3 Jahre, 8 Frauen, 9 Männer, 8 linke Hüften, 9 rechte Hüften. Gruppe 3: Alter 40-50 Jahre, 15 Probanden, mittleres Patientenalter 44,7 ± 3,5 Jahre, 8 Frauen, 7 Männer, 8 linke Hüften, 7 rechte Hüften.

Aus Gründen der Vergleichbarkeit wurden alle MRTs zur gleichen Tageszeit durchgeführt und alle Probanden wurden angehalten gelenkbelastende Aktivitäten im Vorfeld der MRT-Untersuchung auf ein Minimum zu reduzieren. T2*-Werte wurden in azetabulärem und femoralem Knorpel in radiären Schichten von anterior (3 Uhr) über superior (12 Uhr) nach posterior (9 Uhr) erhoben.

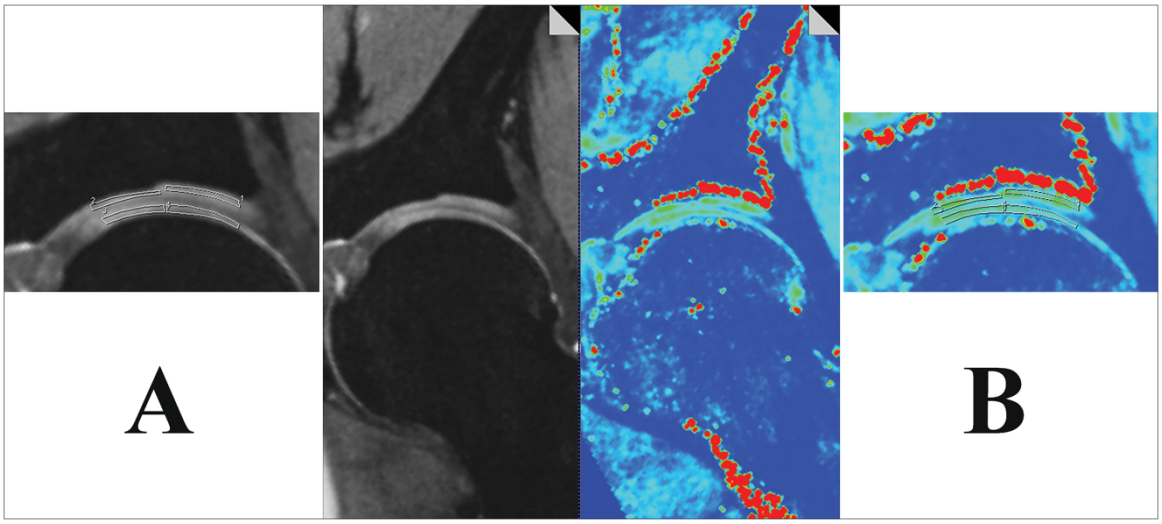

Abb. 1: T2*-Relaxometrie am Hüftgelenk in azetabulärem und femoralem Knorpel. In sieben radiären Schichten (von 3 Uhr bis 9 Uhr) wurden T2*-Werte **(B)** in peripherem und zentralem Knorpel des Femurkopfes und des Azetabulums ermittelt. Eine korrespondierende *Double-echo steady state* Sequenz (DESS, **A**) diente als morphologische Referenz, um ein Einzeichnen der ROI innerhalb der Knorpelgrenzen zu gewährleisten. Nachdruck mit freundlicher Genehmigung[41].

Über alle Altersgruppen verteilt zeigten sich T2*-Mittelwerte in femoralem Knorpel zwischen 23,60 ± 4,35 ms bis 29,64 ± 4,76 ms sowie in azetabulärem Knorpel zwischen 23,03 ± 3,31 ms und 27,18 ± 5,14 ms. Weder für azetabulären Knorpel (Gruppe 1: 24,65 ± 6,56 ms, Gruppe 2: 24,70 ± 4,83 ms, Gruppe 3: 25,81 ± 5,10 ms) noch für femoralen Knorpel (Gruppe 1: 27,08 ± 8,24 ms, Gruppe 2: 25,90 ± 7,83 ms, Gruppe 3: 26,50 ± 5,61 ms) zeigten sich signifikante Unterschiede (azetabulär: P = 0,10; femoral: P = 0,34) in den T2*-Mittelwerten.

Unterschiede ließen sich hinsichtlich des zonalen T2*-Verteilungsmusters beobachten. Insgesamt zeigten sich höhere T2*-Werte in zentralem azetabulären Knorpel im Vergleich zu peripherem azetabulärem Knorpel (25,90 ± 4,80 ms versus 24,21 ± 4,05 ms, P < 0,0001). Für femoralen Knorpel ließen sich keine signifikanten zonalen Unterschiede beobachten (26,62 ± 5,74 ms vs. 26,37 ± 5,89 ms, P = 0,44).

Die Analyse regionaler Unterschiede im T2*-Verteilungsmuster zeigte höhere Werte für azetabulären sowie femoralen Knorpel von anterior (3 Uhr) bis superior-anterior (1 Uhr). Zudem wurden posterior-superior (11 Uhr) für beide Gelenkpartner signifikant höhere Werte im Vergleich zu den benachbarten Regionen beobachtet. Eine Übersicht über das zonale und regionale T2*-Verteilungsmuster am Hüftgelenk zeigt Abbildung 2.

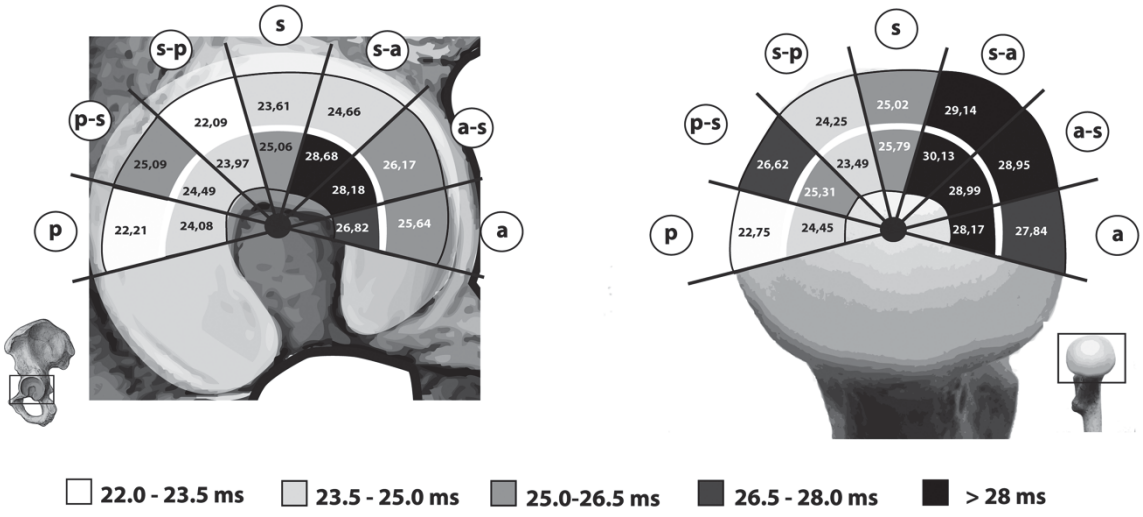

Abb. 2: Regionale und zonale Verteilung der T2*-Mittelwerte in azetabulärem (links) und femoralem (rechts) Knorpel. Höhere Werte zeigten sich v.a. anterior, anterior-superior und superior-anterior. a = anterior; a-s = anterior-superior; s-a = superior-anterior; s = superior; s-p = superior-posterior; p-s = posterior-superior; p = posterior. Nachdruck mit freundlicher Genehmigung[41].

Geschlechterabhängige Unterschiede hinsichtlich der T2*-Mittelwerte für azetabulären (Frauen: 25,21 ± 4,29 ms vs. Männer: 25,28 ± 4,32 ms, P = 0,68) oder femoralen (Frauen: 26,95 ± 4,85 ms vs. Männer: 26,37 ± 4,59 ms, P = 0,15) Knorpel zeigten sich in der Studie nicht. Eine Intra-Klassen-Korrelationsanalyse (ICC) ergab eine hohe Interobserver-Reproduzierbarkeit in dieser Studie (ICC = 0,74, P < 0,0001 für azetabuläre Messwerte, ICC = 0,85, P < 0,001 für femorale Messwerte).

Zur Validierung biochemisch-sensitiver MRT-Sequenzen dienen als Goldstandard sowohl in-vitro-Vergleiche mit der Histologie als auch in-vivo-Korrelationen mit dem intraoperativen Knorpelstatus. Eine in-vitro-Validierung der T2*-Relaxometrie für das Hüft-[23], Knie-[42] und Schultergelenk[43] erfolgte bereits in Vorarbeiten, während eine in-vivo-Validierung bislang noch ausstand. Erwähnenswert in diesem Zusammenhang ist das MRT-

Sequenzdesign dieser Vorstudien: Zur Analyse histologischer Gewebeblöcke sind Sequenzeinstellungen mit vergleichsweise sehr langen Akquisitionszeiten (≈ 30 Minuten für die T2*-Karten) notwendig. Insbesondere vor dem Hintergrund der Praktikabilität und Integrierbarkeit in die klinische Routine sind deutlich kürzere Akquisitionszeiten notwendig. In-vivo (einschließlich der im Rahmen dieser Arbeit vorgestellten Studien) können erheblich kürzere Akquisitionszeiten (≈ 14 Minuten) erreicht werden.

Zur in-vivo-Validierung der T2*-Relaxometrie am Hüftgelenk wurden in einer Studie der hier vorgelegten Arbeit 29 FAI-Patienten (17 Frauen, 12 Männer, Durchschnittsalter 35,6 ± 12,8 Jahre) eingeschlossen, die zwischen 2010 und 2016 eine Hüftarthroskopie sowie ein präoperatives MRT inklusive T2*-Mapping der betroffenen Hüfte erhielten[44]. Retrospektiv wurden alle intraoperativen Bilder, Videosequenzen sowie Befundberichte aus dem OP-Bericht analysiert. Hiervon abgeleitet wurden zentraler und peripherer Knorpel des Azetabulums von 3 Uhr (anterior) über 12 Uhr (superior) nach 9 Uhr (posterior) evaluiert. Der Knorpelstatus wurde anhand einer modifizierten *Outerbridge*-Klassifikation[45] eingeteilt (Grad 0 = normaler Knorpel, Grad 1 = Knorpelerweichung, Grad 2 = Knorpelabrasion, Grad 3 = Knorpelverlust). Bei mehreren Knorpeldefekten innerhalb einer Region wurde der jeweils höchste Defektgrad gewählt. Aus den präoperativen MRT-Datensätzen wurden azetabuläre T2*-Werte in rekonstruierten, radiären Schichten von anterior (3 Uhr) über superior (12 Uhr) nach posterior (9 Uhr) erhoben.

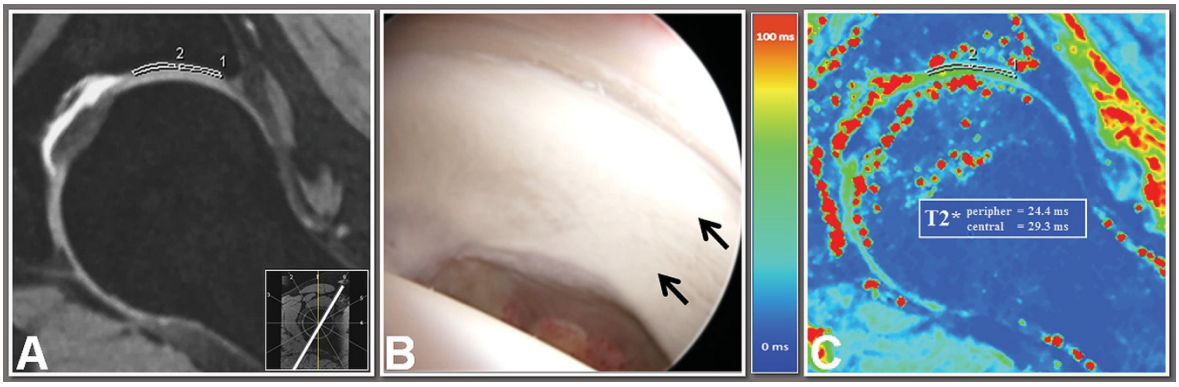

Abb. 3: MRT- und intraoperativer Knorpelbefund bei einem FAI-Patienten posterior-superior. Eine DESS- (A) Reformatierung der posterior-superioren (10 Uhr) Gelenkregion, der intraoperative Befund (B, Pfeile) und eine T2*-Karte (C) der korrespondierenden Region eines 15-jährigen Patienten mit FAI. In dieser Region zeigten sich weder intraoperativ noch im MRT eine Knorpeldegeneration. Nachdruck mit freundlicher Genehmigung[44].

Die Korrelation zwischen T2* und dem intraoperativen Befund wurde mittels Korrelationsanalyse (Spearman) berechnet. Eine ICC-Analyse (paarweiser-Vergleich, absolute Übereinstimmung) untersuchte die Intra- und Inter-Reader Reliabilität. Für jede der Knorpelregionen wurde der Knorpel anschließend anhand der intraoperativen Daten in „gesund“ (Outerbridge Grad 0) und krank (Outerbridge Grad 1 und 2) und die korrespondierenden T2*-Werte in „normal“ und „erniedrigt“ eingeteilt. Zur Differenzierung wurden hierfür die Daten aus der zuvor beschriebenen Studie asymptomatischer Probanden (s.o.) herangezogen. Die gemessenen T2*-Werte wurden als „erniedrigt“ gewertet, wenn sie unterhalb des 95% Konfidenzintervalls (KI) der T2*-Mittelwerte der altersgematchten Kontrollgruppe lagen. Für jeden FAI-Patienten wurde dabei die korrespondierende Gelenkregion aus der Gruppe der asymptomatischen Probanden gewählt, um die regionale T2*-Heterogenität zu berücksichtigen. Mittels Vierfeldertafel wurden anschließend Sensitivität, Spezifität, positiver prädiktiver Wert (PPW) und negativer prädiktiver Wert (NPW) errechnet.

Unsere Ergebnisse zeigten signifikant höhere T2*-Werte in arthroskopisch normal evaluiertem Knorpel gegenüber Regionen mit Knorpeldegeneration (T2*-Durchschnittswerte 25,6 ± 4,7 ms vs. 19,9 ± 4,5 ms, $P < 0{,}001$). Den intraoperativen Befund als Referenz zu Grunde legend betrugen Sensitivität, Spezifität, NPW und PPW 83,5%, 67,7%, 78,4% und 74,4%. Die Korrelation zwischen T2*-Mapping und dem intraoperativen Befund erwies sich als moderat ($\varrho = -0{,}557$, $P < 0{,}001$). Eine Subgruppenanalyse der verschiedenen Regionen zeigte eine vergleichsweise gute Korrelation anterior und anterior-superior ($\varrho = -0{,}750$, $P < 0{,}001$) verglichen mit den übrigen Gelenkregionen.

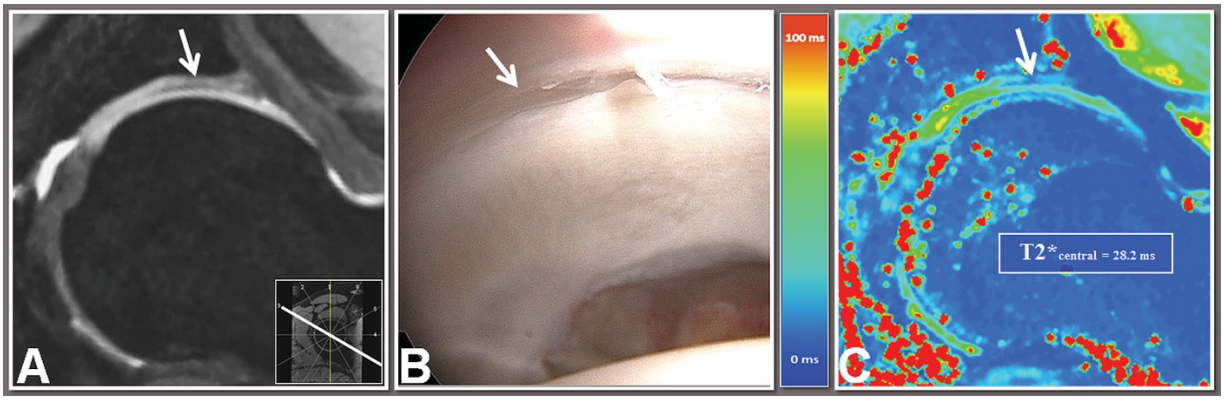

Abb. 4: MRT- und intraoperativer Knorpelbefund bei einem FAI-Patienten superior-anterior. Eine DESS- **(A)** Reformatierung, der intraoperative Befund **(B,** Pfeile) und eine T2*-Karte **(C)** des gleichen 15-jährigen FAI-Patienten, hier in der superior-anterioren Gelenkregion. Es zeigt sich ein Delamination des azetabulären Knorpels (Pfeile) mit Hypointensität in der DESS-Sequenz und niedrigen T2*-Werten. Nachdruck mit freundlicher Genehmigung[44].

Einfluss der Tageszeit und sportlicher Betätigung auf die T2*-Relaxometrie am Hüft- und Kniegelenk

Hesper T, Hosalkar HS, Schleich C, Antoch G, Welsch GH, Krauspe R, Zilkens C, Bittersohl B. T2* Mapping for Hip Joint Cartilage Assessment: Pre-MRI Exercise and Time of Imaging Do Not Bias the T2* Measurement in Asymptomatic Volunteers. *Cartilage.* 2017;8:400-405.

Hesper T, Miese FR, Hosalkar HS, Behringer M, Zilkens C, Antoch G, Krauspe R, Bittersohl B. Quantitative T2(*) assessment of knee joint cartilage after running a marathon. *Eur J Radiol.* 2015;84:284-289.

Bittersohl B, Benedikter C, Franz A, **Hesper T**, Schleich C, Antoch G, Hosalkar HS, Krauspe R, Zilkens C. Elite Rowers Demonstrate Consistent Patterns of Hip Cartilage Damage Compared With Matched Controls: A T2* Mapping Study. *Clin Orthop Relat Res*. Zur Publikation angenommen am 30.10.2018. DOI 10.1097/CORR.0000000000000576.

Eine Kompression von hyalinem Gelenkknorpel, wie sie im Rahmen axialer Gelenkbelastungen auftritt, führt zu einem Zusammendrücken der Proteoglykanketten, einem Wasserausstrom und Abnahme des Knorpel-Matrix-Volumens[46]. Da die T2 / T2*-Relaxometrie vom Knorpel-Wassergehalt und der Integrität des Kollagenfasernetzwerkes abhängt, erscheint es logisch, dass sowohl 1) eine über den Tagesverlauf kumulativ zunehmende axiale Gelenkbelastungen als auch 2) kurzfristige, hohe Belastungsintensitäten zu einer Veränderung des Knorpel-Wassergehalts und der Kollagenfaserstruktur führen und

so Einfluss auf die gemessenen T2*-Werte nehmen können. Daher wurden in einer weiteren Studie tageszeitabhängige Effekte (sog. *Diurnal*-Effekte) sowie der Einfluss einer kurzfristigen Steigerung der Gelenkbelastung unmittelbar vor der MRT-Untersuchung auf die T2*-Relaxometrie am Hüftgelenk untersucht[47]. Hierzu wurden 10 asymptomatische, gesunde Probanden (Durchschnittsalter: 27,4 ± 4,0 Jahre, 5 Männer, 4 Frauen, durchschnittlicher BMI: 22,9 ± 1,6 Kg/m^2) morgens (zwischen 8 und 11 Uhr), am Nachmittag (zwischen 15 und 18 Uhr) sowie unmittelbar im Anschluss an 50 Kniebeugen (MRT im Anschluss an die Nachmittags-Messung) untersucht. Für jeden der 3 Zeitpunkte (vormittags, nachmittags, nach 50 Kniebeugen) wurden T2*-Werte in azetabulärem und femoralem Knorpel nach 0, 15, 30, 45 und 60 Minuten in der Hauptbelastungszone des Hüftgelenkes gemessen. Weder zwischen den verschiedenen Zeitpunkten ($T2^*_{Morgens}$: 22,9 ± 3,0 ms vs. $T2^*_{Nachmittags}$: 23,2 ± 3,2 ms, P = 0,47) noch für die unterschiedlichen Messzeitpunkte (P = 0,67) zeigten sich signifikante Unterschiede in den T2*-Werten. Auch die Messung unmittelbar im Anschluss an die 50 Kniebeugen (21,6 ± 2,6 ms, P = 0,43) zeigte vergleichbare Werte.

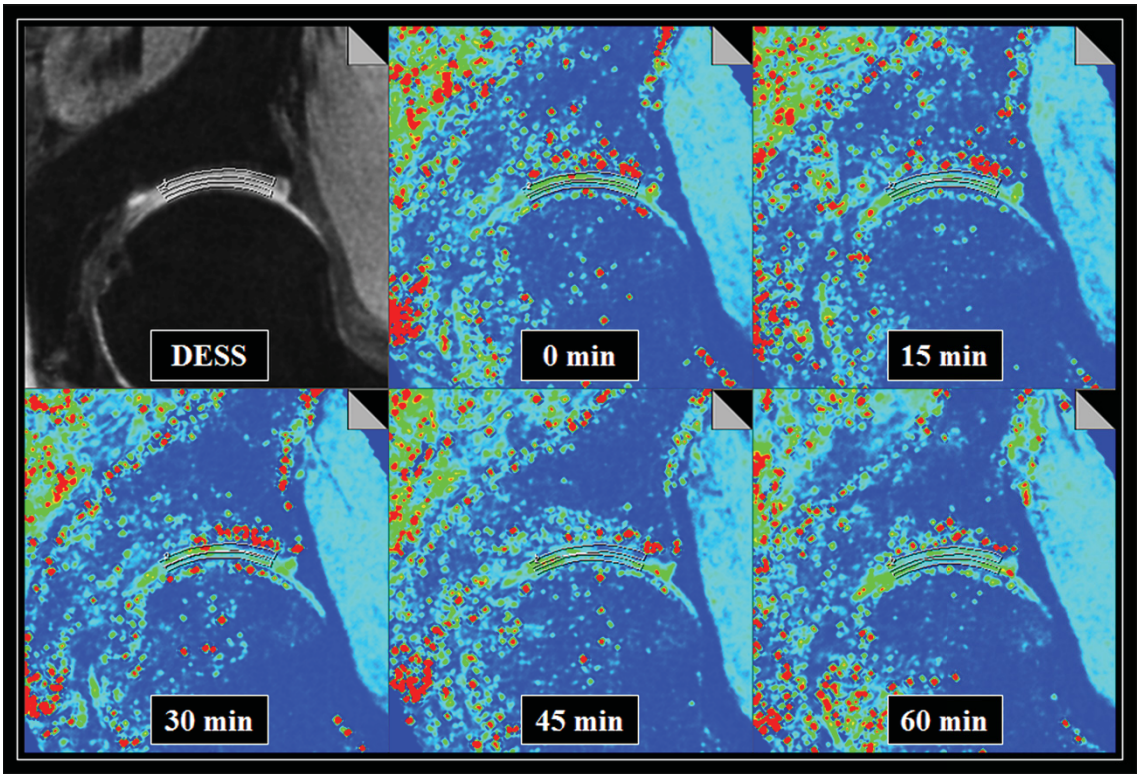

Abb. 5: T2*-Relaxometrie nach unterschiedlichen Zeiten der Entlastung. DESS- und korrespondierende T2*-Reformatierungen der superioren (12 Uhr) Gelenkregion zu verschiedenen Messzeitpunkten. Es zeigten sich keine Unterschiede der gemessenen Werte. Nachdruck mit freundlicher Genehmigung[47].

Neben den tageszeitabhängigen Unterschieden und des Einflusses kurzfristiger, hoher Belastungsintensitäten hinsichtlich des Wassergehalts und der Kollagenfaserstruktur hyalinen Gelenkknorpels und damit verbundenen Einflussfaktoren auf die T2*-Relaxometrie stellt die Frage des Einflusses vermehrter repetitiver Gelenkbelastung auf die T2*-Relaxationszeit – insbesondere bei Patienten mit hohem sportlichen Betätigungsniveau – einen weiteren wesentlichen Aspekt der vorliegenden Arbeit dar. Ziel einer weiteren Studie war es, die intermediären Effekte von repetitiver Gelenkbelastung auf die T2*-Relaxometrie am Kniegelenk zu untersuchen[48]. Hierzu wurden 10 gesunde, asymptomatische Hobby-Marathonläufer (Durchschnittsalter: 28,70 ± 3,97 Jahre, 3 Männer, 7 Frauen, 10 rechte Knie) eingeschlossen. MRT-Untersuchungen wurden bei allen Läufern

innerhalb von 48 Stunden vor dem Marathonlauf (MRT_0), innerhalb von 48 Stunden nach dem Marathonlauf (MRT_1) sowie nach einer Zeit der Rekonvaleszenz von ungefähr 4 Wochen (MRT_2) durchgeführt. T2*-Werte wurden für die folgenden Kniegelenksregionen ermittelt: 1) zentrale laterale Femurkondyle, 2) zentrale mediale Femurkondyle, 3) laterales Tibiaplateau, 4) mediales Tibiaplateau, 5) retropatellar und 6) trochlear. In all diesen Regionen wurden die T2*-Werte sowohl für oberflächlichen (obere 50%) sowie tiefen (unteren 50%) Knorpel ermittelt.

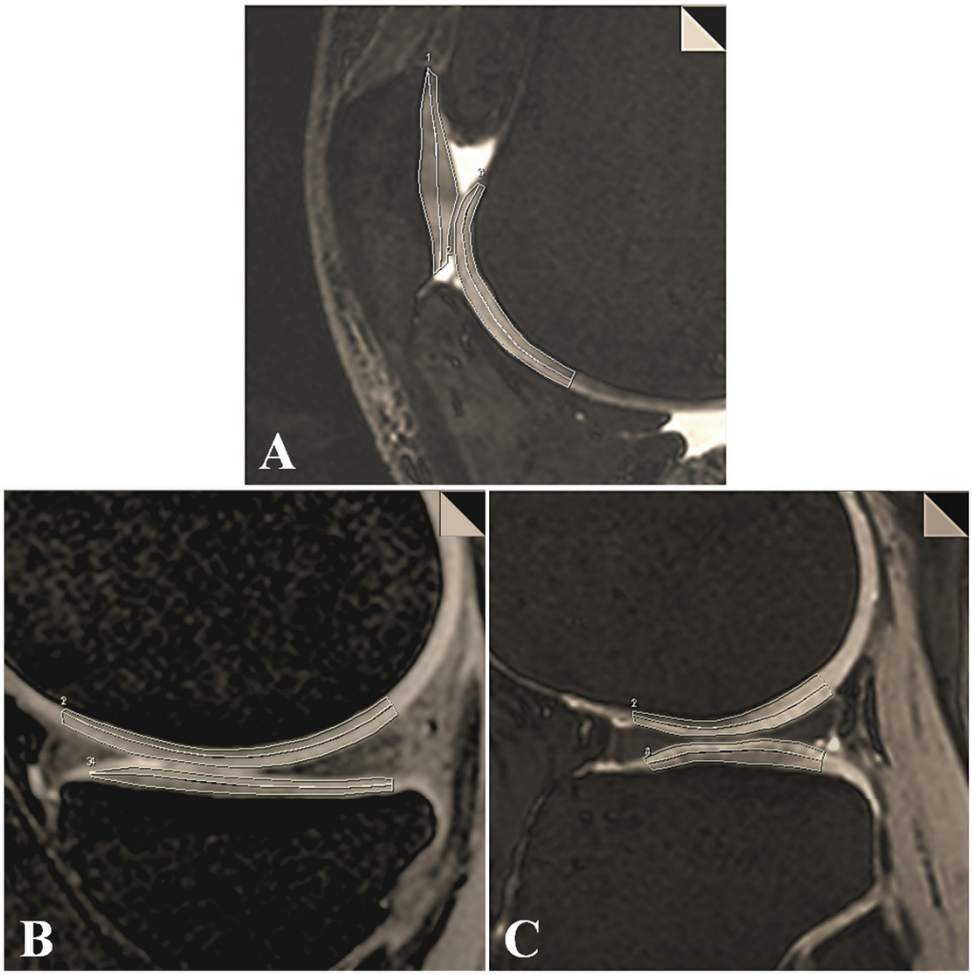

Abb. 6: Knorpelevaluation bei Marathonläufern. Mittels ROI-Analyse wurde oberflächlicher und tiefer Knorpel femoro-patellar **(A)** und im Bereich des medialen **(B)** und lateralen **(C)** femoro-tibialen Gelenkes evaluiert. Nachdruck mit freundlicher Genehmigung[48].

Neben dem zu erwartenden zonalen Verteilungsmuster (höhere T2*-Werte in den oberflächlichen Knorpelregionen aufgrund der vergleichsweise höheren Mobilität der Wassermoleküle) zeigten sich signifikant niedrigere Werte im Bereich des medialen Tibiaplateaus im Vergleich zu allen anderen Gelenkregionen.

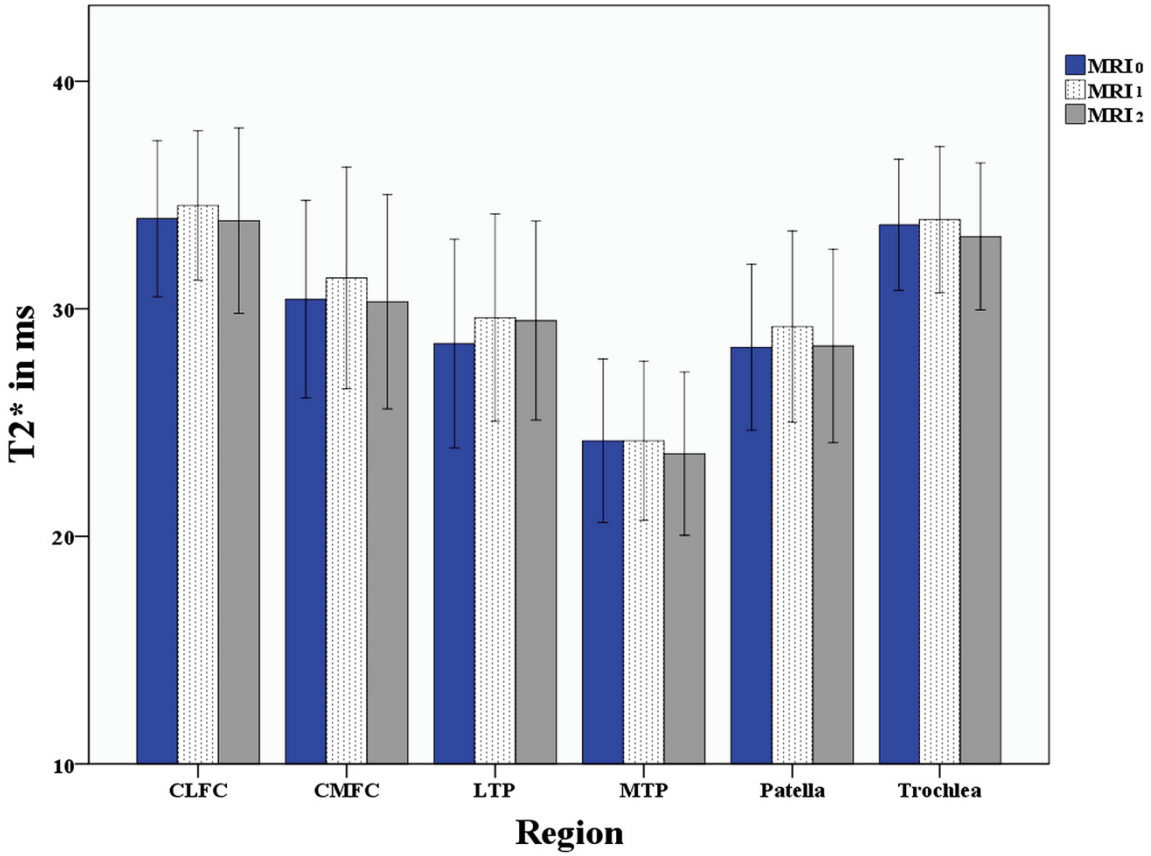

Abb. 7: T2*-Mittelwerte der untersuchten Kniegelenksregionen vor und nach Marathonlauf. Das Balkendiagramm zeigt die T2*-Mittelwerte ± Standardabweichung des Knorpels (oberflächlicher und tiefer Knorpel) in den evaluierten Kniegelenksregionen. Es wurden signifikant niedrigere Werte im medialen Tibiaplateau festgestellt. Nachdruck mit freundlicher Genehmigung[48].

Die wichtigste Erkenntnis dieser Studie war jedoch, dass die T2*-Werte kurz nach dem Marathonlauf nur geringfügig höher lagen als vor dem Lauf (MRT_0= 29,84 ± 4,97 ms vs. MRT_1= 30,47 ± 5,16 ms, P = 0,002), wobei dieser dezente Anstieg der T2*-Werte in

oberflächlichen und tiefen Knorpelschichten nachweisbar war. Nach Rekonvaleszenz der Probanden zeigten sich vergleichbare Werte wie vor dem Marathonlauf (MRT_0= 29,84 ± 4,97 ms vs. MRT_2= 29,81 ± 5,17 ms, P = 0,855). Zwar erreichte der Unterschied der T2*-Werte vor und unmittelbar nach dem Marathonlauf ein signifikantes Niveau, jedoch fiel der Unterschied (<1 ms) deutlich geringer aus als erwartet.

Repetitive Extensions-/Flexionsbewegungen in Kombination mit einer axialen Gelenkbelastung – Bewegungsmuster, wie sie insbesondere beim Rudern vorkommen – können potentielle Schäden am Knorpel des Hüftgelenks und dem Labrum hervorrufen. Ziel einer weiteren Studie war die Analyse des T2*-Relaxationsmusters am Hüftgelenk in einer Population mit hoher repetitiver statischer und dynamischer Mehrbelastung. Wir nahmen an, dass die Population an Spitzensportlern ein typisches T2*-Verteilungsmuster ähnlich wie bei FAI-Patienten (betreffend die anterolaterale Region aufgrund der repetitiven Beugebewegungen und die superiore Region aufgrund der vermehrten axialen Gelenkbelastung) zeigt. Zudem stellten wir die Hypothese auf, dass repetitive tiefe Hüftbeugebewegungen während der Adoleszenz möglicherweise zu einem Stimulus der anterolateralen Wachstumsfuge und so zu einer knöchernen CAM-Deformität nach Wachstumsabschluss in dieser Population führt.

Die Rekrutierung von 20 asymptomatischen Hochleistungs-Ruderern (9 Frauen, 11 Männer, Durchschnittsalter 22,8 ± 2,8 Jahre) erfolgte nach Zustimmung der Trainer und Mannschaftsärzte über den Deutschen Ruderbund. Von 20 U-23 Athleten und 32 Athleten des A-Kaders (≥23 Jahre) waren 30 Athleten bereit an unserer Studie teilzunehmen. Vier Athleten gaben Hüftgelenksbeschwerden an und wurden im Vorfeld ausgeschlossen. Von den verbliebenen 26 Athleten wurden 20 (unter Berücksichtigung einer ausgeglichenen Geschlechterverteilung) eingeschlossen. Aus der Gruppe der Frauen waren sieben Athletinnen aus dem U-23 Kader, zwei aus dem A-Kader. Von den Männern waren fünf

Athleten aus dem U-23 Kader und sechs aus dem A-Kader. Das durchschnittliche Alter bei Beginn mit dem Rudersport betrug 15 ± 2 Jahren, die Dauer des betriebenen Leistungssports im Schnitt 8 ± 3 Jahre. Bei jedem Probanden wurde eine (zufällig ausgewählte) Hüfte untersucht. Azetabulärer und femoraler Knorpel (peripher und zentral) sowie das Labrum wurden in sieben radiären Schichten entlang des Schenkelhalses (von anterior bis posterior) analysiert. Ferner wurde in radiären Schichten von anterior bis superior-posterior der α-Winkel[49] bestimmt und anhand einer subjektiven Einschätzung jede Hüfte auf das Vorliegen einer CAM-Deformität untersucht. Der Knorpelstatus wurde anhand einer modifizierten Outerbridge-Klassifikation[45] morphologisch graduiert (Grad 0 = normal, Grad 1 = Signalveränderter Knorpel, Grad 2 = Knorpelabrasion, Grad 3 = Knorpelverlust) und T2*-Relaxationszeiten wurden erfasst. Morphologische Veränderungen am Labrum wurden folgendermaßen bewertet: Grad 0 = normales Signalverhalten, dreieckig geformt, Grad 1 = Partialruptur, Grad 2 = Komplettruptur, Grad 3 = Labrumdegeneration. Bei mehreren Knorpeldefekten innerhalb einer Region wurde der jeweils höchste Defektgrad gewählt. Im Hinblick auf die Knorpelevaluation mittels T2*-Relaxometrie wurden die so erhobenen Daten der Sportler mit denen der zuvor publizierten[41] altersgematchten Kontrollgruppe (asymptomatische Probanden, kein Rudersport) verglichen.

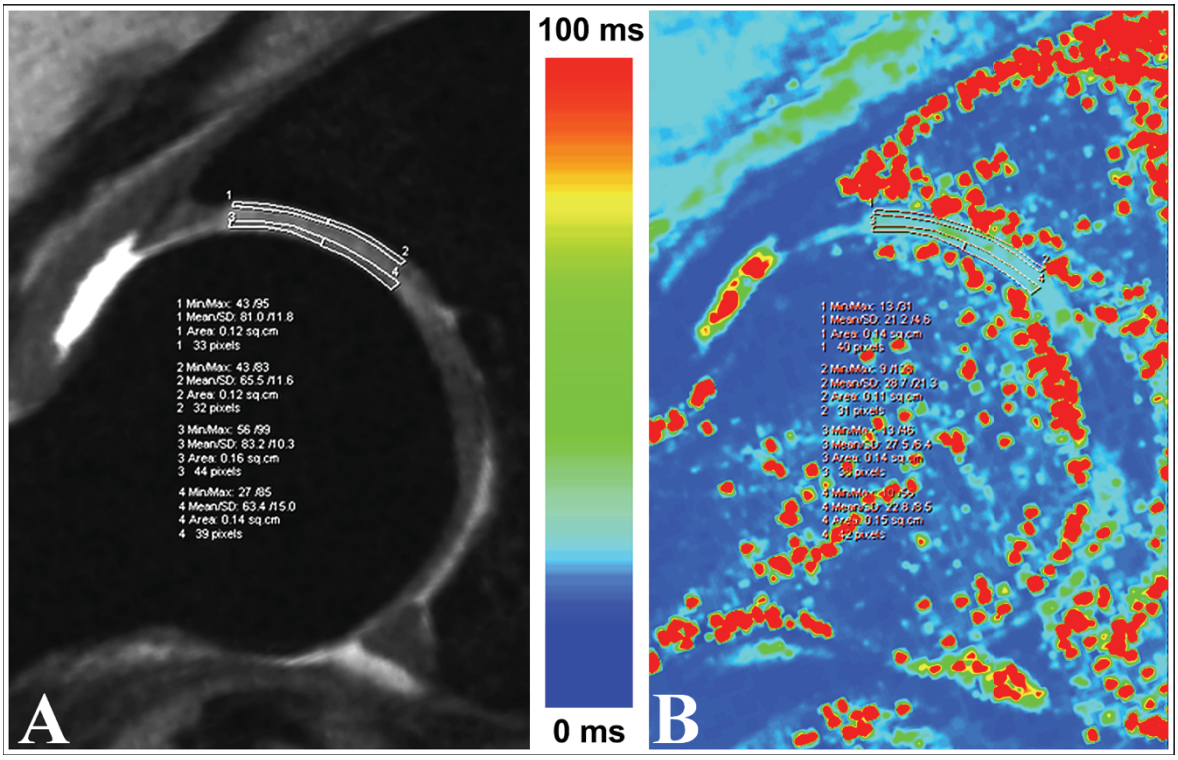

Abb. 8: Knorpel- und Labrumevaluation bei Hochleistungs-Ruderern. In sieben radiären Schichten entlang des Schenkelhalses wurde azetabulärer und femoraler Knorpel sowie das Labrum anhand einer DESS-Sequenz **(A)** morphologisch graduiert. T2*-Werte **(B)** wurden in zentralem und peripherem Knorpel des Azetabulums und des Femurkopfes evaluiert. Nachdruck mit freundlicher Genehmigung[50].

In der Gruppe der Ruderer zeigten drei Hüften (15%) typische Veränderungen einer CAM-Deformität (nicht-publizierte Daten). Verglichen mit der Kontrollgruppe asymptomatischer Probanden zeigte die Gruppe der Ruderer ein hohes Maß an Knorpeldegeneration. In der Gruppe der Ruderer ließen sich in allen untersuchten Hüften Knorpelpathologien feststellen. In azetabulärem Knorpel wurden von 271 untersuchten Regionen 44% (120/271) als „normal“ bewertet, 6% (15/271) zeigten „Signalveränderungen“, 45% (122/271) demonstrierten Knorpelabrasionen und 5% (14/271) einen vollständigen Knorpelverlust. Für femoralen Knorpel zeigten sich deutlich weniger morphologische Knorpelveränderungen.

Verglichen mit der Kontrollgruppe zeigten sich in der Gruppe der Ruderer deutlich niedrigere T2*-Werte (T2* global azetabulär: 20 ± 6 ms vs 25 ± 5 ms; P < 0.001; T2* global femoral: 23 ± 7 ms vs 27 ± 5 ms; P < 0.001). In azetabulärem Knorpel wurden in 10 von 14 evaluierten Regionen erniedrigte T2*-Werte gemessen, in femoralem Knorpel in 11 von 14 Regionen. Insbesondere in peripherem Knorpel der anterior-superioren Region zeigten sich große Unterschiede zwischen beiden Gruppen (16 ± 3 ms vs 26 ± 5 ms; p < 0.001). Wie in der Gruppe der asymptomatischen Probanden (s.o.) zeigte sich ein typisches zonales und regionales Verteilungsmuster der T2*-Werte. Auch in der Gruppe der Ruderer ließen sich in azetabulärem Knorpel niedrigere Werte in peripherem, verglichen mit zentralem Knorpel messen, in femoralem Knorpel zeigte sich dies nur in der posterioren Region. Auch die regionalen Unterschiede der T2*-Werte in der Gruppe der Ruderer – wenn auch mit deutlich niedrigeren Werten im Vergleich zur Kontrollgruppe – zeigten ein ähnliches Verteilungsmuster, wie die Gruppe der asymptomatischen Probanden.

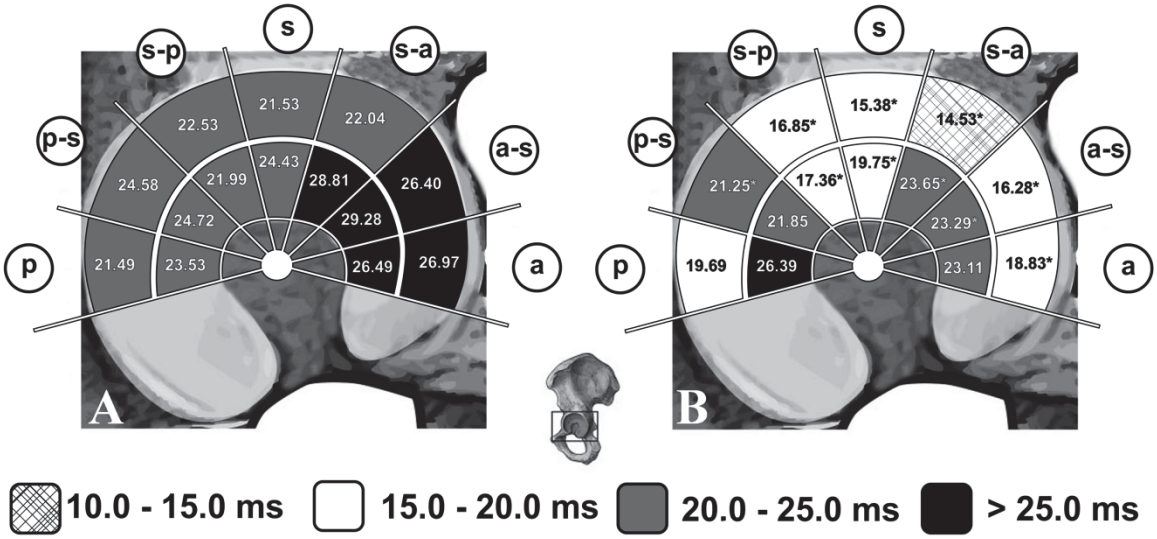

Abb. 9: Regionale und zonale Verteilung der T2*-Mittelwerte in azetabulärem Knorpel der altersgematchten Kontrollgruppe (links) und der Studienpopulation (Ruderer). In der Studienpopulation zeigten sich in nahezu allen Gelenkregionen niedrigere T2*-Werte. a = anterior; a-s = anterior-superior; s-a = superior-anterior; s = superior; s-p = superior-posterior; p-s = posterior-superior; p = posterior. Nachdruck mit freundlicher Genehmigung[50].

Das Labrum wurde in 138 Regionen evaluiert, in 62% (86/138) als „normal“, in 17% (23/138) mit einer „Partialruptur“, in 2% (3/138) mit einer „Komplettruptur“ und in 19% (26/138) mit einer „Labrumdegeneration“ bewertet. Hieraus ergibt sich eine Labrumpathologie in 38% (52/138) aller untersuchten Regionen in der Gruppe der Ruderer.

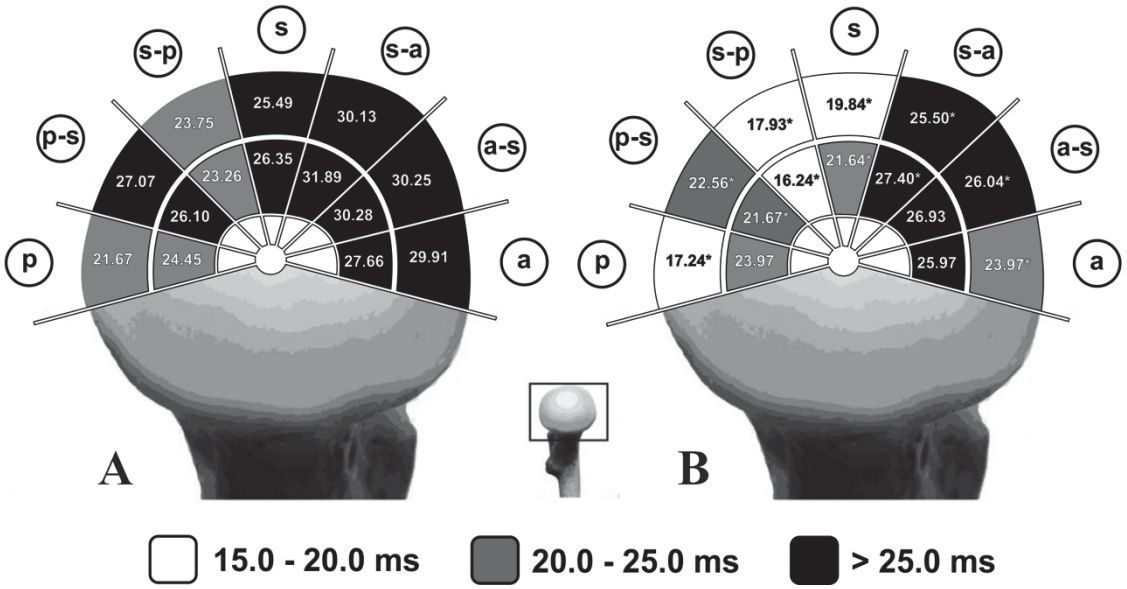

Abb. 10: Regionale und zonale Verteilung der T2*-Mittelwerte in femoralem Knorpel der altersgematchten Kontrollgruppe (links) und der Studienpopulation (Ruderer). In der Studienpopulation zeigten sich in allen Gelenkregionen niedrigere T2*-Werte. a = anterior; a-s = anterior-superior; s-a = superior-anterior; s = superior; s-p = superior-posterior; p-s = posterior-superior; p = posterior. Nachdruck mit freundlicher Genehmigung[50].

Diskussion

In der klinischen Anwendung der T2*-Relaxometrie sind fundierte Kenntnisse über das physiologisch zu erwartende T2*-Verteilungsmuster im gesunden Knorpel notwendig, um zwischen „gesund“ und „krank“ zu unterscheiden, insbesondere bei Vorliegen von Krankheitsbildern, bei denen typische Knorpelschädigungsmuster (wie z.B. beim FAI) auftreten. Erst unter Kenntnis solcher „Normwerte“ lassen sich hieraus möglicherweise Indikationsstellungen (z.B. gelenkerhaltende Therapie vs. Gelenkersatz) ableiten oder ein Therapieerfolg (z.B. nach *salvage procedure* / gelenkerhaltender OP) monitoren.

Verglichen mit anderen in-vivo Studien zur biochemisch-sensitiven Knorpelevaluation am Hüftgelenk[51-53] zeigen die hier vorgestellten Ergebnisse hohe Werte für Sensitivität, Spezifität, PPW und NPW und unterstreichen die Wertigkeit der T2*-Relaxometrie in der Evaluation azetabulärer Knorpelveränderungen am Hüftgelenk. Bei guter Korrelation der T2*-Werte und des intraoperativen Befundes in der anterioren und anterior-superioren Gelenkregion (was möglicherweise die Effektivität der T2*-Relaxometrie bei FAI-Patienten impliziert) ergibt sich eine gewisse Diskrepanz in der diagnostischen Übereinstimmung für die posteriore Gelenkregion. Die Gründe hierfür lassen sich nicht vollständig eruieren. Ein gewisser *selection bias*, mit der Tendenz, Knorpelschäden vermehrt in der anterioren bis superioren Gelenkregion bei FAI-Patienten zu suchen, sowie geringe Unterschiede bei der Anlage der Arthroskopieportale (obwohl von beiden Operateuren jeweils die gleichen, standardisierten Zugangswege gewählt wurden) sind mögliche Ursachen. Bei der Bewertung der hier vorgestellten Ergebnisse müssen die beiden völlig unterschiedlichen Untersuchungsmodalitäten berücksichtigt werden. Mittels T2*-Mapping lassen sich frühzeitige Zeichen der Knorpeldegeneration früher detektieren als es im Rahmen einer morphologischen Knorpelgraduierung möglich ist. Wahrscheinlich spielen auch hier technische Limitierungen des T2*-Mappings sowie der Magic Angle Effekt eine Rolle.

Neben den allgemeinen Limitierungen einer retrospektiven Studie bleibt zu kritisieren, dass die Hüftarthroskopien zwar in gleicher Technik, jedoch von zwei unterschiedlichen Operateuren durchgeführt wurden. Progressive Knorpelveränderungen in der Zeit zwischen MRT und Operation, was unsere Ergebnisse beeinflusst haben könnte, sind denkbar. Da bislang jedoch unklar ist, wann und in welcher Art fortschreitend Knorpeldegenerationen im Rahmen eines FAI auftreten, glauben wir, dass ein Intervall von bis zu 6 Monaten zwischen MRT und Operation als Einschlusskriterium gerechtfertigt ist.

Die Arbeitsgruppe um Ellermann et al. korrelierte in einer Vorstudie T2*-Werte in 28 Hüften von FAI-Patienten (Durchschnittsalter 28,2 Jahre) mit dem intraoperativen Arthroskopiebefund[54]. Hierbei zeigten sich niedrige T2*-Werte in Gelenkregionen mit intraoperativ nachgewiesener Knorpeldegeneration (entsprechend eines modifizierten Beck-Score; T2* = 20,7 ± 6,0 ms versus 35,3 ± 7,0 ms, $P < 0,01$). Obwohl diese Arbeitsgruppe ausschließlich Patienten ohne höhergradigen röntgenologischen Arthrosenachweis (Tönnis Grad 0 und I) einschloss, zeigten sich in 68% der intraoperativ dokumentierten Gelenkregionen Knorpelschäden. Dies unterstreicht die Limitationen röntgenologischer Aufnahmen zur Identifizierung von Knorpeldegenerationen in frühen Stadien. Die Autoren dieser Arbeit postulierten einen T2*-*Cut-Off*-Wert, um zwischen gesundem und geschädigtem Gelenkknorpel zu unterscheiden. Die Autoren geben diesen mit 28 ms an (91% richtig Positive- und 13% falsch Negative-Rate), um zwischen normalem und morphologisch geschädigtem Knorpel zu unterscheiden. Insbesondere vor dem Hintergrund der im Rahmen dieser Arbeit vorgestellten Ergebnisse einschließlich der Heterogenität der T2*-Werte in unterschiedlichen Regionen des Hüftgelenkes erscheint ein solcher *Cut-Off*-Wert jedoch wenig anwendbar, da im Rahmen präarthrotischer Deformitäten erhebliche Unterschiede im T2*-Verteilungsmuster berücksichtigt werden müssen.

Die in der Gruppe asymptomatischer Probanden gemessenen T2*-Mittelwerte am Hüftgelenk zeigen vergleichbare Werte zu bereits publizierten T2*-Mittelwerten in femoralem und azetabulärem Knorpel asymptomatischer Kontrollgruppen (Mittelwerte zwischen 22,9 ± 3,0 ms und 26,0 ± 5,0 ms)[24, 55]. Hervorzuheben ist hierbei das sehr heterogene Verteilungsmuster der T2*-Mittelwerte mit regionalen und zonalen Unterschieden. Im zonalen Vergleich zeigten sich höhere T2*-Werte im zentralen verglichen mit peripherem Knorpel (bei asymptomatischen Probanden nur im azetabulären Knorpel). Unter Berücksichtigung der verschiedenen Regionen von anterior nach posterior zeigten sich höhere T2*-Werte in der anterioren bis superior-anterioren Gelenkregion sowie in der posterior-superioren Region (vergleichbares Verteilungsmuster in der Gruppe der asymptomatischen Probanden und der Ruderer).

In der Literatur finden sich wenige Daten über regionale Unterschiede der T2*-Werte am Hüftgelenksknorpel. Ähnlich der hier vorgestellten Ergebnisse beschrieben Apprich et al.[55] höhere Werte anterior im Vergleich zur superioren Gelenkregion. Die Gründe hierfür sehen die Autoren in Unterschieden in der Kollagendichte, Faserorientierung und des Wassergehaltes in lasttragenden und nicht-lasttragenden Knorpelregionen sowie dem Magic Angle Effekt[29]. Der Magic Angle Effekt spielt insbesondere in sphärisch gewölbten Knorpelregionen (wie am Hüftgelenk) eine Rolle, da es zu einem artifiziellen Anstieg der T2- und T2*-Relaxationszeiten kommt, wenn Kollagenfasern in einem Winkel von 54,7° zum Hauptmagnetfeld ausgerichtet sind. Betrachtet man die Verteilung hoher T2*-Werte in den hier vorstellten Ergebnissen, so scheint der Magic Angle Effekt tatsächlich eine Bedeutung für die Knorpelevaluation am Hüftgelenk zu haben, da gerade die Regionen mit hohen T2*-Werten (insbesondere anterior-superior und posterior-superior) nah am sog. Magic Angle liegen. Während andere Arbeitsgruppen dem Magic Angle Effekt insbesondere im femoralen Knorpel eine große Relevanz zusprachen[56], zeigen unsere Ergebnisse (wenn

auch nicht statistisch signifikant, P = 0,08) einen deutlichen Trend, dass der Magic Angle Effekt auch im azetabulären Knorpel eine nicht zu vernachlässigende Rolle spielt. Neben dem Magic Angle Effekt müssen weitere Einflussfaktoren bei der Interpretation der T2*-Relaxometrie berücksichtigt werden. Hierzu zählen insbesondere am Hüftgelenk MRT-Bildgebungsartefakte wie *chemical shifts*, Suszeptibiltätsartefakte und Volumenmittelungseffekte.

Ein weiterer Aspekt der hier vorgestellten Ergebnisse ist die Beobachtung, dass es in den asymptomatischen Hüften verschiedener Altersgruppen zu keiner Inkonsistenz der gemessenen T2*-Werte kommt. Auch geschlechterabhängige Unterschiede konnten wir nicht nachweisen. Insbesondere die geringe Zahl der untersuchten Probanden muss als Limitierungen des Studiendesigns in diesem Zusammenhang erwähnt werden, wobei es nach unserem Kenntnisstand bislang keine publizierten Daten einer größeren, asymptomatischen Kontrollgruppe gibt. Zur Diskussion steht die heterogene Messzeit sowie das Fehlen eines standardisierten MRT-Protokolls, was die Aktivitäten der Studienteilnehmer vor der MRT-Untersuchung betrifft, dar. Die gewonnenen Ergebnisse legen nahe, dass bei „normalem" Aktivitätsniveau im Vorfeld der MRT-Untersuchung von keinem relevanten Einfluss auf die T2*-Werte auszugehen ist.

Aufgrund seiner molekularen Zielstruktur (Knorpel-Wassergehalt und Wechselwirkungen zwischen freien Wassermolekülen und dem Kollagenfasernetzwerk) müssen verschiedene Aspekte bei der Gelenkknorpelevaluation mittels T2*-Mapping berücksichtigt werden: Repetitive Lastübertragungen führen insbesondere am Hüft-, Knie- und Sprunggelenk zu einer Knorpelkompression, wodurch Proteoglykanketten zusammengedrückt, extrazelluläres Wasser aus dem Knorpel gepresst wird und so eine Reduktion des Knorpel-Matrix-Volumens resultiert[46]. Somit stellen körperliche Belastungen im Vorfeld der MRT-

Untersuchung (hohe Belastungsintensitäten, wie z.B. im Rahmen vermehrter sportlicher Betätigung, aber auch kumulative Knorpelbelastung, wie sie unvermeidbar im Laufe eines Tages, insbesondere an den Gelenken der unteren Extremitäten auftreten) mögliche Fehlerquellen bei der Knorpelevaluation mittels T2*-Mapping dar[57, 58]. Um den Einfluss eben dieser Effekte zu minimieren, beinhalteten bislang verwendete, standardisierte T2*-Protokolle eine ca. halbstündliche Ruhephase vor der MRT-Untersuchung und die T2*-Evaluation erfolgte stets am Ende der Untersuchung (z.B. im Anschluss an morphologische Standard-Sequenzen).

Für die T2*-Relaxometrie im Hüftgelenk konnten wir keine tageszeitabhängigen Effekte nachweisen. Auch die unmittelbar vor der MRT-Untersuchung durchgeführten 50 Kniebeugen hatten keinen signifikanten Einfluss auf die T2*-Werte. Eine längere Entlastung im Vorfeld der MRT-Untersuchung erscheint so unnötig. In diesem Zusammenhang muss berücksichtigt werden, dass bislang keine Daten hinsichtlich biochemisch-sensitiver Knorpelevaluation am Hüftgelenk nach verschiedenen Arten der körperlichen Belastung publiziert wurden. Ein eindeutiger Zusammenhang zwischen dem Durchführen von Kniebeugen und der daraus resultierenden Belastung verschiedener Gelenkregionen am Hüftgelenk kann daher nur angenommen werden. Zudem wurden die hier vorgestellten Ergebnisse in einer Gruppe von gesunden, asymptomatischen Probanden erhoben, welche alle morphologisch gesunden Hüftgelenkknorpel aufwiesen. Eine Übertragung dieser Ergebnisse auf Patienten mit bereits geschädigtem Hüftgelenkknorpel ist daher nur bedingt möglich. Auch tageszeitabhängige Effekte nach der letzten MRT-Messung am Nachmittag können wir nicht ausschließen. Jeder im Rahmen dieser Studie eingeschlossene Proband ließ allerdings 15 MRT-Messungen am Tag über sich ergehen und verbrachte kumulativ ca. 240 Minuten im MR-Scanner. Auf eine ergänzende vierte Messung in den Abendstunden wurde aus diesen Gründen verzichtet.

In der Literatur finden sich nur sehr wenige Studien, die die tageszeitabhängigen Effekte auf biochemisch-sensitive Knorpelevaluation beleuchten. Während in der Studie von Li et al[59] keine tageszeitabhängigen Effekte von T2-Werten am Kniegelenk (Messungen am Morgen zwischen 8 und 10 Uhr, sowie am Nachmittag zwischen 17 und 19 Uhr) festgestellt wurden ($P > 0,05$) beschrieben Apprich et al[55] einen Anstieg der T2*-Werte im Hüftgelenksknorpel von 27 gesunden, asymptomatischen Probanden nach 50 minütiger Entlastung (T2* global 21,75 ± 2,4 ms versus 24,64 ± 3,1 ms, $P < 0,05$). Die Autoren führen dies auf biochemische Kompositionsveränderungen (Rehydratation des Gelenkknorpels nach Entlastung) zurück. Möglicherweise trägt hierzu auch eine Re-Orientierung des Kollagenfasernetzwerkes bei. Da es sich auch in unserer Studie um asymptomatische Probanden mit morphologisch normal erscheinendem Knorpel handelte, wiedersprechen sich unsere Ergebnisse mit denen von Apprich et al[55], was an dieser Stelle nicht erklärt werden kann und Gegenstand weiterer Untersuchungen ist.

Repetitive, axiale Gelenkbelastungen (Marathonlauf) an den Tagen vor der MRT-Untersuchung führten zu einem transienten Anstieg der T2*-Mittelwerte am Kniegelenk. Dieser Einfluss viel jedoch gering aus (Unterschiede < 1 ms) und scheint in der klinischen Anwendung von untergeordneter Bedeutung zu sein.

Unter Berücksichtigung unterschiedlicher Studiendesigns und Techniken der Bildakquisition beleuchten verschiedene Vorarbeiten den Einfluss hoher körperlicher Aktivitätslevel auf die Knorpelevaluation mittels T2-Mapping[57, 60, 61, 62, 16, 63, 64]. Im Gegensatz zu dem von uns beobachteten, geringen T2*-Anstieg in oberflächlichen und tiefen Knorpelschichten, beschreiben verschiedene Autoren T2-Veränderungen lediglich in oberflächlichen Knorpelregionen. Gründe hierfür werden darin gesehen, dass der Netto-Flüssigkeitsfluss durch die vergleichsweise geringe Flüssigkeitspermeabilität der Matrix, die Undurchlässigkeit des subchondralen Knochens und eines nur geringen Druckgradienten in

tiefen Knorpelregionen auf die oberflächliche Knorpelschicht limitiert ist[65]. Andere Autoren führen diese Beobachtung auf die vergleichsweise höhere Komprimierbarkeit der oberflächlichen Knorpelschicht im Vergleich zur tiefen Radiärzone zurück[66, 67]. In diesem Zusammenhang müssen ebenfalls Unterschiede im Sequenzdesign zwischen T2- und T2*-Mapping berücksichtigt werden, wobei die T2-Mapping-Technik vergleichsweise unempfindlich gegenüber T2-Signalen mit kurzer Relaxationszeit (z.B. in tiefen Knorpelschichten) ist und molekulare Veränderungen hier mittels T2*-Mapping sensitiver erfasst werden.

In unserer Kohorte ambitionierter Amateurläufer zeigen sich regionale Unterschiede im T2*-Verteilungsmuster mit deutlich niedrigeren T2*-Werten im Bereich des medialen Tibiaplateaus. Dieses ist möglicherweise durch eine höhere funktionale Beanspruchung dieser Kniegelenksregionen erklärbar. Denkbar sind auch makroskopisch nicht sichtbare, frühe Zeichen der Knorpeldegeneration, die durch repetitive hohe Belastungen in dieser hauptlasttragenden Gelenkregion bedingt sind. Da in einer Vorarbeit unserer Studiengruppe keine Unterschiede hinsichtlich des T2*-Verteilungsmusters zwischen medialem und lateralem Kniegelenkskompartiment bei asymptomatischen Probanden (keine Marathonläufer) festgestellt wurden[58], bleibt der Einfluss hoher repetitiver Gelenkbelastungen, wie sie beim Marathonlaufen auftreten, Gegenstand künftiger Untersuchungen. In diesem Zusammenhang ist auch auf eine Limitierung dieser Studie hinzuweisen: Obwohl sich in unserer Studienpopulation klinisch keine Beinachsenabweichungen zeigten, wäre eine radiologische Evaluation der Beinachse wünschenswert. Aus ethischen Gesichtspunkten war dies jedoch nicht vertretbar.

Im Gegensatz zu dem nur geringen Einfluss axialer Gelenkbelastungen auf die T2*-Relaxometrie am Kniegelenk zeigen unsere Ergebnisse in der Gruppe der professionellen Ruderer am Hüftgelenk häufige Schäden an Labrum und Gelenkknorpel, was mit signifikant

reduzierten T2*-Werten in nahezu allen Gelenkregionen einherging. Besonders niedrige T2*-Werte zeigten sich von anterior (3 Uhr) bis superior (12 Uhr) im peripheren azetabulären Knorpel. Als ursächlich erachten wir hier insbesondere den mechanischen Konflikt am Azetabulumrand während exzessiver Beugebewegungen sowie im Bereich des superioren Knorpels zentral und peripher als Ausdruck repetitiver axialer Belastung, wie sie auftritt, wenn der Ruderer beim Durchzug die Beine kraftvoll durchdrückt. Während manche Autoren hauptsächlich Überlastungssymptome in einer Gruppe von Junioren-Ruderern (mittleres Alter 18 ± 1 Jahr) berichteten[68], zeigte eine MRT-basierte Studie in symptomatischen Ruderern (einschließlich FAI-Hüften, mittleres Alter 18,5 ± 0,6 Jahre) Labrumpatholgien bei allen eingeschlossenen Probanden[69]. Vor dem Hintergrund, dass viele Labrumpathologien mit einer frühzeitigen Knorpeldegeneration assoziiert und häufig durch repetitive Mikrotraumata bedingt sind[70], muss angenommen werden, dass dieses auch auf unsere Studienpopulation zutrifft.

Zu mechanischen Konflikten am Azetabulumrand scheint es auch ohne das Vorliegen einer CAM-Deformität zu kommen. In unserer Studie zeigten drei Hüften (15%) typische morphologische Zeichen eines CAM-FAI (nicht-publizierte Daten). Dieses ist vergleichsweise gering, verglichen mit Raten zwischen 14-24% in größeren Kohorten asymptomatischer Männer und Raten von bis zu 41% in asymptomatischen Adoleszenten, die in Vollkontaktsportarten wie Fußball oder Basketball partizipieren[71-74]. Obwohl die genaue Ätiologie der FAI-Deformität nicht vollständig verstanden ist, postulieren verschiedene Autoren, dass vermehrter Stress im Bereich der Wachstumsfuge - z.B. im Rahmen verschiedener sportlicher Aktivitäten - während der Adoleszenz das Entstehen einer CAM-Deformität begünstigen[71, 75]. Da die Ruderer in unserer Kohorte relativ spät (durchschnittlich mit 14,7 Jahren) im Vergleich zu 6 Jahren[72], 8 Jahren[71] und 10-12 Jahren[76] mit dem Rudersport begannen, haben sportliche Aktivitäten zu diesem Alter möglicherweise

keinen entscheidenden Einfluss mehr auf ein Remodelling im Bereich der Wachstumsfuge und somit auf das Entstehen einer späteren CAM-Deformität.

Limitierungen unserer Studie ergeben sich aus der Tatsache, dass der Rudersport ein vielfältiges Trainingsprogramm beinhaltet, wessen Einflüsse im Rahmen unserer Studie nicht berücksichtigt wurden. Eine weitere Limitierung betrifft die Rudertechnik: Beim einrudrigen Rudern hält der Ruderer das Paddel mit beiden Händen und sitzt auf einer Seite des Bootes. Hieraus resultiert eine asymmetrische Bewegungskette. Viele Ruderer favorisieren eine bestimmte Seite gegenüber der anderen, was bei der Wahl der untersuchten Hüften nicht berücksichtigt wurde.

Vor dem Hintergrund der hohen Anzahl von Knorpel- und Labrumschäden, der sehr niedrigen T2*-Werte verglichen mit asymptomatischen Probanden und FAI-Patienten, dem Wissen über das Krankheitsbild FAI einschließlich dem erforderlichen Bewegungsmuster beim Rudersport, muss angenommen werden, dass Hochleistungsrudern ein Risikofaktor für die Entstehung frühzeitiger Knorpel- und Labrumschäden am Hüftgelenk ist. Weitere Studien mit einer höheren Fallzahl sind erforderlich, um diese Beobachtungen zu verifizieren und zudem die Einflüsse von Hochleistungsrudersport und Freizeitrudern auf das Hüftgelenk zu untersuchen.

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Tab. 1: Übersicht biochemisch-sensitiver MRT-Sequenzen

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Mein besonderer Dank gilt meinem Chef Herrn Univ.-Prof. Dr. med. Rüdiger Krauspe. Ich empfinde es als großes Privileg, meine komplette Facharztausbildung unter seiner Leitung begonnen und durchlaufen zu haben. Neben der breiten klinischen Ausbildung in allen Fachbereichen der Orthopädie hat Prof. Krauspe meine wissenschaftliche Karriere stetig begleitet und gefördert, nicht zuletzt durch die Möglichkeit einen mehrmonatigen Aufenthalt in den USA zu absolvieren.

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Erfahrung, Herzlichkeit und nicht zuletzt Freundschaft, den Weg in die Orthopädie und später auch ans UKD aufgezeigt hat.

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Eidesstattliche Erklärung

Hiermit erkläre ich, Dr. Tobias Hesper, geboren am 21.10.1983 in Bad Pyrmont, an Eides statt, dass:

- Die von mir vorgelegte schriftliche Habilitationsleistung eigenständig und nur unter Verwendung der angegebenen Hilfsmittel und Quellen angefertigt wurde;
- Bei den wissenschaftlichen Untersuchungen, die Gegenstand der von mir vorgelegten schriftlichen Habilitationsleistung sind, ethische Grundsätze und die Grundsätze und Empfehlungen zur Sicherung guter wissenschaftlicher Praxis berücksichtigt wurden;
- An keiner anderen Hochschule ein Habilitationsverfahren von mir eingeleitet oder erfolglos beendet wurde.

Düsseldorf, 20.11.2018

Dr. Tobias Hesper

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Quantitative T2* assessment of knee joint cartilage after running a marathon

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ABSTRACT

Objective: To study the effect of repetitive joint loading on the T2* assessment of knee joint cartilage.
Materials and methods: T2* mapping was performed in 10 non-professional marathon runners (mean age: 28.7 ± 3.97 years) with no morphologically evident cartilage damage within 48 h prior to and following the marathon and after a period of approximately four weeks. Bulk and zonal T2* values at the medial and lateral tibiofemoral compartment and the patellofemoral compartment were assessed by means of region of interest analysis. Pre- and post-marathon values were compared.
Results: There was a small increase in the T2* after running the marathon (30.47 ± 5.16 ms versus 29.84 ± 4.97 ms, $P < 0.05$) while the T2* values before the marathon and those after the period of convalescence were similar (29.84 ± 4.97 ms versus 29.81 ± 5.17 ms, $P = 0.855$). Regional analyses revealed lower T2* values in the medial tibial plateau ($P < 0.001$).
Conclusions: It appears that repetitive joint loading has a transient influence on the T2* values. However, this effect is small and probably not clinically relevant. The low T2* values in the medial tibial plateau may be related to functional demand or early cartilage degeneration.
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1. Introduction

Osteoarthritis (OA) is characterized by progressive changes in the micro- and macrostructure of articular cartilage, including the loss of proteoglycans, changes in extracellular water content, disorganization of the collagen fiber network and eventual cartilage loss [1]. Biochemically-sensitive magnetic resonance imaging (MRI) techniques such as delayed gadolinium-enhanced magnetic resonance imaging (dGEMRIC) [2], T2/T2* mapping [3,4], T1rho mapping [5] and others [6,7], which aid in assessing these changes in the various stages of the disease, have become increasingly relevant and will hopefully evolve towards directing decision and medical management based on the status of the articular cartilage.

T2* mapping features exceptional properties such as a high image resolution and the ability to perform isotropic three-dimensional (3D) cartilage evaluation. In addition, there is no need for special hardware components or contrast media administration, which enables a simple and quickly exercisable examination of cartilage tissue. Similar to the T2 mapping technique, T2* mapping is sensitive to the extracellular water content and interactions occurring between the water molecules and collagen fibers, wherein high T2* values reflect a high water content and superior water molecule mobility. Few studies have noted a correlation between T2 and T2* mapping [8–11]. However, substantial differences between these two imaging modalities need to be considered [12]. T2* mapping is performed with a gradient-echo (GRE) pulse sequence that does not comprise of a 180° refocusing pulse. Therefore, T2* mapping is influenced by both the transverse relaxation (T2) and local susceptibility fields, which may occur as the result of microscopic gradients or variations in the magnetic field strength. At the same time, T2* mapping is less sensitive to errors resulting from stimulated echoes and magnetization transfer [8,13]. Furthermore, with echo readings at ~10 ms–100 ms, standard T2 mapping targets to a large extent bulk water and is rather insensitive to T2 signals that decay

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Table 1
MRI settings for the 3D double-echo steady state (DESS) sequence and 3D multi-echo data image combination (MEDIC).

	3D DESS Water excitation	**3D MEDIC**T2* mapping
TR (repetition time, ms)	14.20	43
TE (echo time, ms)	5.00	5.37, 11.35, 15.35, 21.22, 27.09, 32.96
FA (flip angle)	25	25
NEX (number of excitation)	1	1
FOV (field of view, mm^2)	150	193
Slice thickness (mm)	0.6	0.6
In-plane resolution (mm)	0.6 × 0.6	0.6 × 0.6
Slice gap (mm)	0.2	0.2
Bandwidth (Hz/Pixel)	250	260
TA (acquisition time, min)	7.33	15.15

more rapidly [14,15]. T2* mapping, in contrast, captures shorter echo-times within the net decay that may increase the sensitivity to cartilage degeneration in particular close to the cartilage bone interface [16,17].

With joint loading and cartilage compression, proteoglycan chains are squeezed together, releasing extracellular water and decreasing cartilage matrix volume [18]. For that reason, diurnal effects as well as the level of physical activity prior to the MRI examination need to be considered when performing T2 or T2* examinations for cartilage evaluation [19,20]. To minimize the effects of cartilage loading, standard T2 and T2* protocols include 20–30 min of rest prior to the MR exam. In contrast to these short-term effects of cartilage loading, however, there is no available study providing evidence for or against the influence of physical activity that is performed on the days prior to the T2* articular cartilage assessment, which we believe could be an additional source of error when attempting to achieve a reliable evaluation of the cartilage status.

The aim of this study was to measure the intermediate effects of repetitive joint loading on the T2* mapping values of knee joint cartilage. We therefore initiated a volunteer recruitment enrolling healthy amateur marathon runners who underwent MRI and T2* mapping both prior to and after running a marathon. We hypothesized that running a marathon before the T2* cartilage assessment may contribute to increased T2* values in articular cartilage due to mechanically-mediated reactive cartilage adaptation and osmotic swelling.

2. Materials and methods

This study was approved by the local ethic committee and all subjects provided written informed consent before participation.

2.1. Study population

Ten healthy asymptomatic non-professional marathon runners (mean age: 28.7 ± 3.97 years, range 22–34 years; three males, seven females; 10 right knees) were recruited. All participants had no history of knee pain, no prior orthopedic surgery on the lower extremities, no clinical findings of knee joint pathology or deviation of the mechanical axis of the leg, and no contraindications for undergoing MRI. Demographic data and clinical findings were obtained by an orthopedic consultant with eight years of experience in orthopedic knee joint surgery.

2.2. Magnetic resonance imaging

Magnetic resonance imaging was performed within 48 h before the marathon (MRI_0), within 48 h after the marathon (MRI_1), and after a period of convalescence of approximately four weeks (MRI_2) using a 3-T MR scanner (Magnetom Trio, Siemens Medical Solutions, Erlangen, Germany) and an eight-channel transmit/receive knee array coil (In vivo, Gainesville, FL, USA). All volunteers were examined in the supine position with the extended knee joint in neutral position within the coil. Here, increased efforts were made to stabilize the knee joint within in the coil by using sandbags and sponges to keep motion artifacts to a minimum. The MRI protocol included a 3D double-echo steady state (DESS) sequence with water excitation for the morphological cartilage assessment and, after a period of 30 min of rest to minimize short-term diurnal effects of preliminary joint loading, a GRE-based 3D multi-echo data image combination (MEDIC) sequence with six consecutive echoes to obtain T2* maps (Table 1).

2.3. Data analysis

The 3D MRI data sets were transferred to a "Leonardo" workstation (Siemens Medical Solutions, Erlangen, Germany) and sagittal reformats parallel to the femur and perpendicular to a line connecting the posterior aspects of the medial and lateral femoral condyle were created. Six regions of the knee joint were taken under investigation: (1) central lateral femoral condyle (CLFC); (2) central medial femoral condyle (CMFC); (3) lateral tibial plateau (LTP); (4) medial tibial plateau (MTP); (5) patella; and (6) trochlea in which the anterior and posterior margins of the meniscus were used to define these regions of interest (ROI). Zonal (superficial zone = upper half, deep zone = lower half) and full-thickness (bulk) T2* values (mean value derived from the zonal measures) in each region were obtained by ROI analysis. This was performed manually in which a thorough placement of marker points delineating each ROI allowed for a precise T2* measurement within articular cartilage bounds even in curved cartilage regions (Fig. 1). Morphological cartilage evaluation (to rule out morphologically evident cartilage damage) was performed by an experienced musculoskeletal radiologist (X.X) while the T2* evaluation was conducted by an orthopedic surgeon (X.X) with eight years of experience in biochemically-sensitive MRI. The T2* measurement was repeated in 10 randomly selected data sets to estimate the consistency of the cartilage T2* analysis in this study.

2.4. Statistical analysis

For all statistical analyses, SPSS software (Version 21.0; IBM Corp., Armonk, NY, USA) was used. The T2* values in this study are presented as mean ± standard deviation (SD). A paired student's *t* test was utilized to compare bulk and zonal T2* values before and after running the marathon. Regional differences (bulk T2* values) were assessed pair-wise using a one-way analysis of variance (ANOVA) with Bonferroni correction for multiple comparisons. Intra-observer reliability was quantified with the intra-class correlation coefficient (ICC) using the pair-wise correlation model with absolute agreement. *P* values below 0.05 were considered to be statistically significant.

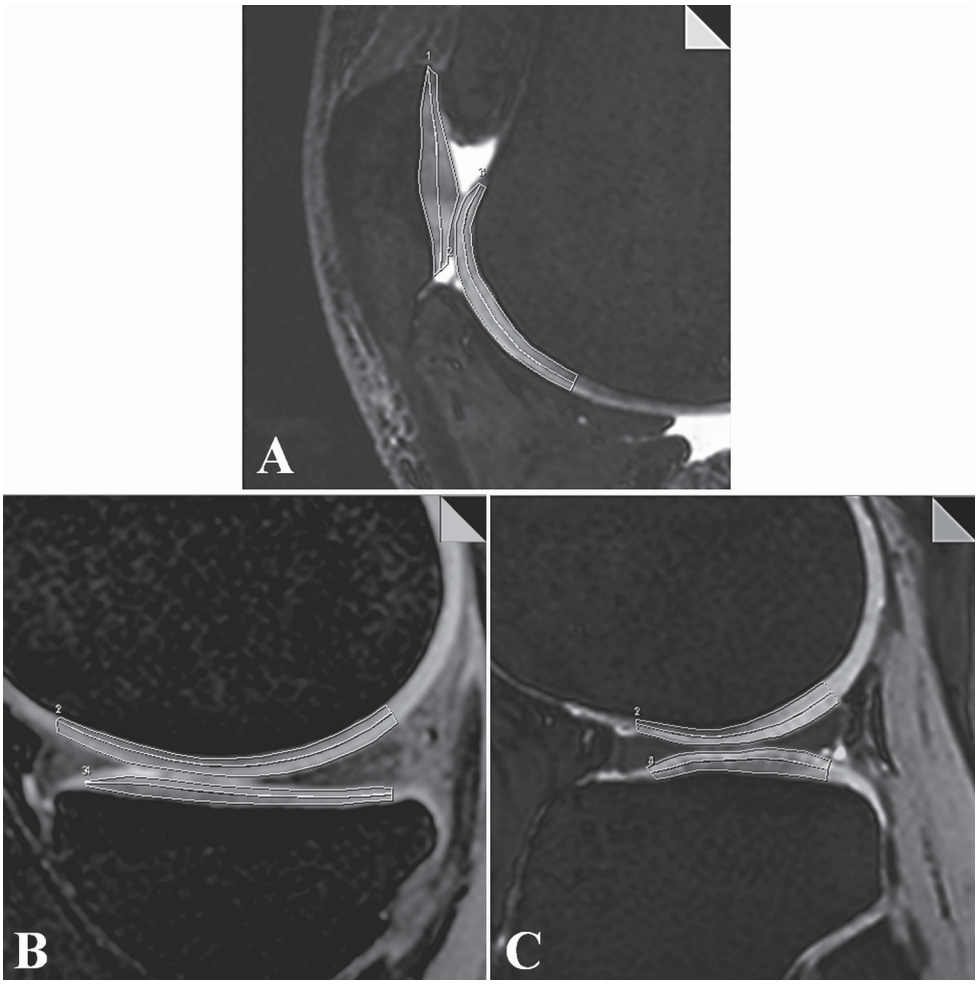

Fig. 1. Cartilage regions of interest defined by multiple marker points at the patellofemoral joint (A), the medial tibiofemoral joint (B) and the lateral tibiofemoral joint (C). Each region was further subdivided into a superficial and deep zone.

3. Results

No volunteer revealed morphologically apparent cartilage damage. Hence, a total of 540 ROIs were analyzed (10 volunteers, measurements at three different time points, six ROIs per knee, three zones [superficial, deep, bulk]). The mean size of these ROIs was $0.37 \pm 0.09\,cm^2$ (101 pixels $\pm$ 25 pixels) ranging from $0.16\,cm^2$ (43 pixels) to $0.70\,cm^2$ (192 pixels). This corresponds to $0.37 \pm 0.09\,cm^2$ (101 ± 25 pixels) ranging from $0.18\,cm^2$ (50 pixels) to $0.70\,cm^2$ (192 pixels) in the superior zone and $0.37 \pm 0.1\,cm^2$ (102 ± 28 pixels) ranging from $0.16\,cm^2$ (43 pixels) to $0.62\,cm^2$ (170 pixels) in the deep zone. ICC analysis proved high intra-reader reliability (ICC value = 0.971, P value < 0.001) for the $T2^*$ analysis in this study.

The comparison of bulk cartilage $T2^*$ values at different time points of measurement before and after the marathon revealed a small increase after the marathon run ($MRI_0 = 29.84 \pm 4.97$ ms [range: 19.3 ms–39.0 ms] versus MRI_1: 30.47 ± 5.16 ms [range: 20.5 ms–38.8 ms]; $P = 0.002$) while the $T2^*$ values following a period of convalescence after the marathon were similar to those prior to the marathon (MRI_0: 29.84 ± 4.97 ms [range: 19.3 ms–39.0 ms] versus MRI_2: 29.81 ± 5.17 ms [range: 19.5 ms–39.3 ms]; $P = 0.855$). Furthermore, zonal variations with the characteristic pattern of higher $T2^*$ values in superficial cartilage layers were noted ($P < 0.001$) in which the response of the $T2^*$ values after the marathon in deep and superficial zones was similar (Table 2). We also observed regional dissimilarities of the $T2^*$ values demonstrating lower $T2^*$ values in the MTP (Table 3, Fig. 2).

4. Discussion

We investigated the intermediate impact of superior levels of physical activity on the $T2^*$ relaxation measures of knee joint cartilage. Therefore, we recruited ten healthy and asymptomatic marathon runners who underwent MRI within 48 h before and after a marathon as well as following a period of convalescence of approximately four weeks. To the best of our knowledge, this is the first descriptive report on intermediate effects of superior levels of physical activity prior to MRI on $T2^*$ relaxation assessment of articular cartilage.

In this study, we noted a small increase in the $T2^*$ values after the marathon in the superficial and deep cartilage zone, while the $T2^*$ values before the marathon and those after a period of convalescence were similar. Contrary to our expectations, the increase in the $T2^*$ values was small (<1 ms) and within the anticipated margin of error in such measurements; therefore, we believe that physical activity, which is performed within 48 h before the $T2^*$ mapping, does not bias the cartilage evaluation (Fig. 3). Notably, in this cohort of ambitious amateur athletes, regional analyses demonstrated considerably lower cartilage $T2^*$ values in the medial tibial plateau that may be related to functional demand and/or macroscopically invisible early signs of cartilage degeneration due

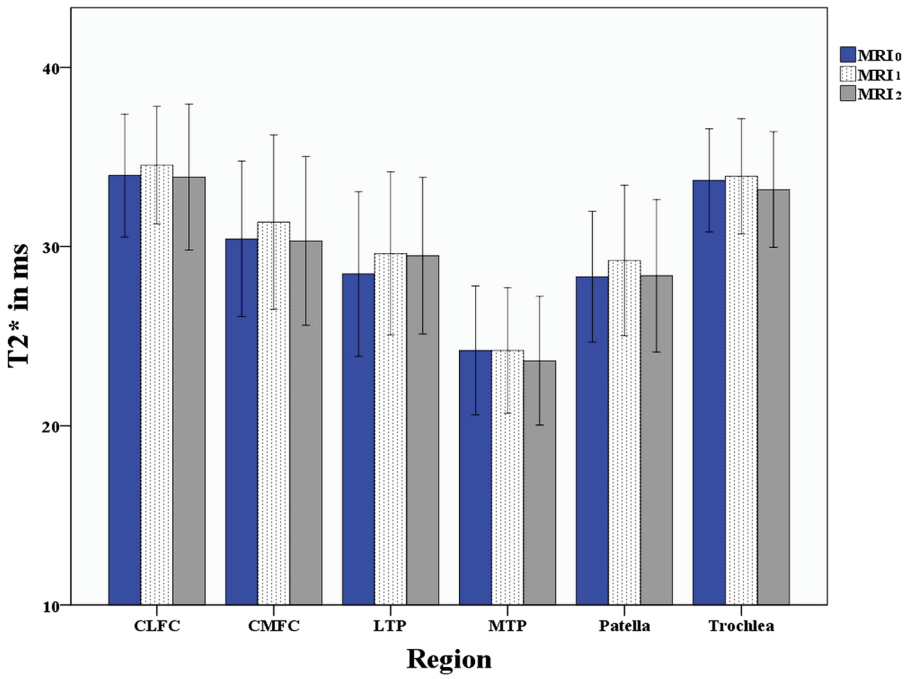

Fig. 2. Bar diagram representing full-thickness (bulk) cartilage $T2^*$ values ± standard deviation (in ms) in various regions of the knee. Considerably lower $T2^*$ values were noted in the medial tibial plateau (MTP).

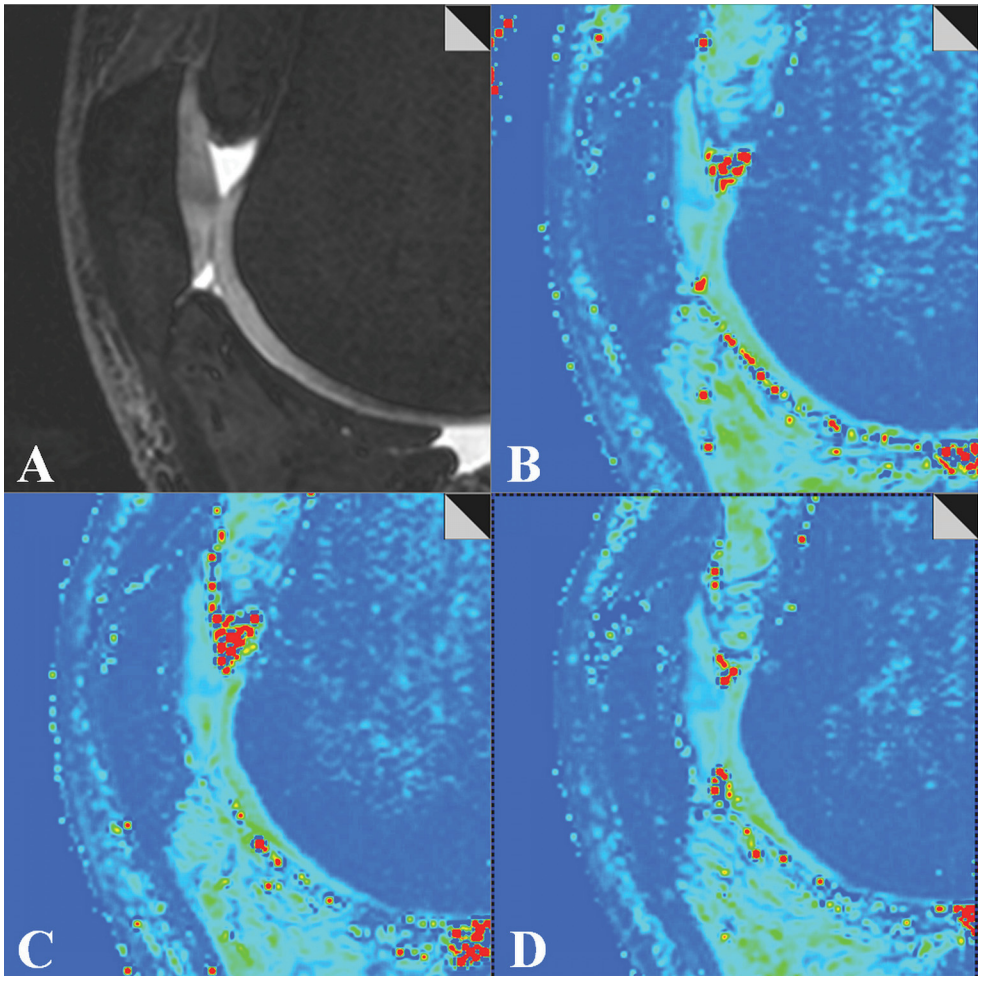

Fig. 3. DESS (A) and corresponding $T2^*$ reformats of one illustrative patellofemoral joint before (B), one day (C) and four weeks after the marathon (D). Note the $T2^*$ maps before and after the marathon were similar.

Table 2
Zonal (superficial, deep) and bulk (full-thickness) cartilage T2* values including T2* mean ± standard deviation (SD), T2* range and 95% confidence interval (CI) within 48 h prior to (MRI_0) and following the marathon (MRI_1) as well as after a period of approximately four weeks (MRI_2).

MRI	Zone	Mean T2* ± SD [ms]	T2* range [ms]	95% CI
MRI_0	SuperficialDeepBulk	32.52 ± 5.4127.12 ± 5.0629.84 ± 4.97	21.0–43.516.1–37.219.3–39.0	31.12–33.9225.81–28.4228.56–31.13
MRI_1	SuperficialDeepBulk	33.10 ± 5.6427.80 ± 5.2030.47 ± 5.16	20.3–43.517.4–38.220.5–38.8	31.64–34.5526.45–29.1429.14–31.81
MRI_2	SuperficialDeepBulk	32.24 ± 5.7527.32 ± 5.1629.81 ± 5.17	19.5–43.218.0–37.119.5–39.3	30.75–33.7225.99–28.6628.47–31.14

Table 3
Full-thickness (bulk) cartilage mean T2* values ± standard deviation (SD) and 95% confidence intervals (CI) at different regions of the knee joint prior to the marathon with pair-wise comparisons revealing regional differences in the T2* measurements. CLFC = central lateral femoral condyle; CMFC = central medial femoral condyle; LTP = lateral tibial plateau; MTP = medial tibial plateau.

Region 1	T2* ± SD in ms[95% CI]	Region 2	T2* ± SD in ms	*P* value
CLFC	34.0 ± 3.4 [31.5–36.4]	CMFC	30.4 ± 4.3	0.619
		LTP	28.5 ± 4.6	**0.031**
		MTP	24.2 ± 3.6	**<0.001**
		Patella	28.3 ± 3.7	**0.023**
		Trochlea	33.7 ± 2.9	1.000
CMFC	30.4 ± 4.3 [27.3–33.5]	LTP	28.5 ± 4.6	1.000
		MTP	24.2 ± 3.6	**0.008**
		Patella	28.3 ± 3.7	1.000
		Trochlea	33.7 ± 2.9	0.881
LTP	28.5 ± 4.6 [25.2–31.8]	MTP	24.2 ± 3.6	0.220
		Patella	28.3 ± 3.7	1.000
		Trochlea	33.7 ± 2.9	**0.048**
MTP	24.2 ± 3.6 21.6–26.8	Patella	28.3 ± 3.7	0.279
		Trochlea	33.7 ± 2.9	**<0.001**
Patella	28.3 ± 3.7 [25.7–30.9]	Trochlea	33.7 ± 2.9	**0.037**
Trochlea	33.7 ± 2.9 [31.6–35.8]			

to repetitive high-impact joint loading in this main weight-bearing area. Although one previously published study on T2* cartilage assessment in healthy volunteers who were not involved in any kinds of high-level sports revealed no differences between the medial and lateral femorotibial joint [19], this observation must be investigated further by ongoing studies and the inclusion of sufficient study cohorts. Of note, although we did not observe gross deviations of the leg axis, no standing anterior-posterior radiographs of the leg were taken to correlate these findings.

Acknowledging differences in study design and imaging techniques, several studies on quantitative cartilage T2 assessment prior and after various loading conditions have been published [8,20–25]. Liess et al. [26] reported their results on T2 measurements in healthy volunteers after an exercise protocol of 60 knee bends that was followed by 45 min of rest. An increase in the T2 value of 2.6 ± 1% in the assessment after 45 min led to the assumption that load-dependent changes in articular cartilage water content were detectable with T2 mapping. Similar observations were made by Mamisch et al. [23], who noted an increase in the T2 values in both native cartilage and cartilage repair tissue after matrix-associated autologous chondrocyte transplantation (MACT) in knee joint cartilage ($n = 30$) following a 45 min period of rest. In their study, T2 assessment was performed without a specific activity protocol immediately after routine daily life activities as well as after a period of 45 min of rest. In contrast to the T2* increase throughout the cartilage depth in our analysis, several studies noted T2 alterations in articular cartilage after compressive loading only in the superficial cartilage layers [20,27,28]. Wong and Carter [29] postulated that the net fluid flux is limited to the superficial zone of articular cartilage due to the relatively low fluid permeability of the matrix, the impermeability of the subchondral bone and the fact that the adjacent cartilage fluid is also under pressure, thereby generating only a small pressure gradient to extrude water from the deep zones under the loading region. Others relate this observation to the greater compressibility of the superficial layers that is in contrast to the low compressive strains noted in the deep radial zone [27,28]. Mosher et al. [20] revealed a decrease in the T2 values in the superficial zones of femoral cartilage after a 30 min running exercise in seven young healthy volunteers that could be associated with the extrusion of extracellular water and the decreasing cartilage matrix volume due to cartilage compression. Of interest, although cartilage thinning was noted to be even higher for tibial cartilage, a decrease of T2 was only apparent in femoral cartilage, pointing towards a pressure-induced increase in superficial collagen fiber anisotropy rather than a net efflux of extracellular water. Because the MRI was conducted immediately before and after exercising, time-dependent changes in the T2 relaxometry after the cessation of exercise were not targeted in this study. Luke et al. demonstrated T1rho and T2 changes in articular cartilage in 10 asymptomatic marathon runners who had knee MRI scans two weeks before, within 48 h after, and 10–12 weeks after running a marathon [30]. In this study, elevated T2 and T1rho values were noted in all articular cartilage areas of the knee ($P < 0.01$) except the lateral compartment after the marathon. While the T2 values recovered to baseline except in the medial femoral condyle after 10–12 weeks of reduced activity, the average T1rho values remained increased. This supports that T1rho reflects changes other than fluid shifts in the articular cartilage. Furthermore, the patellofemoral joint and the medial compartment demonstrated the highest changes suggesting a somewhat increased vulnerability to cartilage degeneration due to high-impact repetitive loading.

We acknowledge the limitations in this study. Although only young and asymptomatic volunteers were included, there remains some inadvertent possibility of undiagnosed cartilage degeneration. Further validation of healthy articular cartilage, for example by means of arthroscopy, would be desirable. However, this was not feasible due to ethical reasons. In addition, the rather small study sample may have led to statistical power issues in some parts of this investigation. Our study also lacks a potential standardized activity protocol for the interval prior to and after the MRI measurements. For that reason, a certain degree of inconsistency in the T2* measurements must be taken into account. The image

reformatting and cartilage T2* assessment by means of ROI analysis was performed manually which is operator-dependent. Furthermore, instead of a multi-slice segmentation assessment, cartilage T2* was measured in only one representative mid-sagittal reformat per knee joint compartment that included the area with the thickest cartilage in these regions. This bears the risk of confounding selection bias related to a heterogeneous cartilage T2* distribution within these compartments. The rationale for our methodology was the very high probability of cartilage variations in these main load-bearing regions and the intention to assess knee joint cartilage of various regions in a reasonable amount of time with equitable accuracy. A further limitation of this study is that only intra- and not inter-reader reliability was assessed.

In conclusion, it appears that repetitive joint loading has a transient influence on the T2* values. However, it does not confirm our assumption that superior levels of joint loading performed 1–2 days prior to MRI examination would affect relevantly the T2* articular cartilage assessment, as we noted only small differences in the T2* values after intense repetitive joint loading. Despite the small study group and the presence of morphologically normal appearing cartilage, we noted lower cartilage T2* values in the medial tibial plateau that may be related to functional demand or early signs of cartilage degeneration. This observation must be investigated further using ongoing observations and the inclusion of larger study groups.

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Conflict of interest

Every author of the above mentioned article declares that they have no financial or personal relationship with other people or organizations that could inappropriately influence (bias) their work. Examples of potential conflicts of interest include employment, consultancies, stock ownership, honoraria, paid expert testimony, patent applications/registrations, and grants or other funding.

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T2* Mapping for Hip Joint Cartilage Assessment: Pre-MRI Exercise and Time of Imaging Do Not Bias the T2* Measurement in Asymptomatic Volunteers

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Abstract

Objective. To identify if the time of day and pre-imaging exercise matter while performing T2* mapping of hip joint cartilage at 3 T. *Design*. Nine asymptomatic healthy volunteers (mean age 27.4 ± 4.0 years) with no obvious morphological evidence of cartilage damage were enrolled. The MRI protocol included a double-echo steady state (DESS) sequence for morphological cartilage assessment and a multi-echo data image combination sequence for the T2* measurement. T2* values were obtained between 8 and 11 a.m., between 3 and 6 p.m., and after 50 knee-bends at several time points of each measurement (0, 15, 30, 45, 60 minutes). *Results*. We observed no differences ($P = 0.47$) between the T2* values obtained in the morning (T2* = 22.9 ± 3.0 ms) and those measured in the afternoon (T2* = 23.2 ± 3.2 ms). We also observed no statistically significant differences between the T2* values at different time points ($P = 0.67$) or after 50 knee-bends ($P = 0.43$). *Conclusions*. Timing of the scan and pre-imaging exercise clearly did not matter in this modality. This study consolidates the value of T2* imaging in hip joint cartilage that seems to be independent of diurnal effects and physical activity prior to MRI.

Keywords

magnetic resonance imaging, hip, time, exercise

Introduction

Osteoarthritis is characterized by changes in the extracellular water content, continuous glycosaminoglycan depletion, and a progressive loss of integrity of the collagen fiber network.[1] A valid and reproducible assessment of these changes at earlier stages, which may not be easily detected by plain radiography and/or standard magnetic resonance imaging (MRI), could facilitate decision making and management with respect to joint preservation or joint replacement.

A number of biochemically sensitive MRI techniques that include the delayed gadolinium-enhanced MRI of cartilage (dGEMRIC),[2] T2 mapping,[3] and others[4,5] have been documented as robust instruments regarding this early detection of subtle cartilage alterations. More specifically, the T2* mapping technique,[6] which is sensitive to the water content of articular cartilage and interactions between water molecules and collagen fibers, happens to have inherent advantages that may account for the recent emergence of this technique. These mainly include a rather simple implementation into the clinical routine, no need for special hardware components or contrast media administration, short acquisition times, and the ability of high-resolution isotropic 3-dimensional (3D) cartilage evaluation.

Biochemically, T2* values depend to some extent on the bulk water content and changes in articular cartilage hydration. It is intuitively possible that both "water content" and "articular cartilage hydration" may be affected by continuous cartilage strain over the course of the day or by temporary high levels of exercise. Although one previous study[7] did not reveal a clinically relevant difference between the

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Table 1. Imaging Parameters Utilized in This Study.[a]

	3D DESS Water Excitation	3D MEDIC Inline T2* Mapping
TR (repetition time, ms)	14.75	38
TE (echo time, ms)	5.03	4.62, 9.41, 15.28, 21.15, 27.02, 32.89
FA (flip angle, deg)	25	25
NEX (number of excitation)	1	1
FOV (field of view, mm^2)	192	192
Slice thickness (mm)	0.6	0.6
In-plane resolution (mm)	0.6 × 0.6	0.6 × 0.6
Slice gap (mm)	0.2	0.2
Bandwidth (Hz/pixel)	260	260
TA (acquisition time, min)	13.17	13.29

[a]The MRI protocol included a double-echo steady state (DESS) sequence for morphological cartilage assessment and a multi-echo data image combination sequence for the T2* measurement.

T2* values measured prior to running a marathon and those measured after the marathon (T2* measurements within 48 hours prior to and following the marathon and after a period of approximately 4 weeks), we found no data related to effects of diurnal variation and cartilage strain immediately preceding the measurement.

The purpose of this study was to identify if the time of day (diurnal variation) and preimaging exercise matter while performing T2* mapping of hip joint cartilage. We hypothesized that (1) T2* values for the hip joint will demonstrate diurnal variations and (2) preimaging physical activity comprising a set of 50 squats would affect the T2* values for the hip joint from exercise-related cartilage strain. This study was performed on a 3 T system to allow for higher resolution imaging and better distinct assessment of acetabular and femoral head cartilage.

Methods

This study was approved by the local ethics committee. All procedures performed in this study were in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. All subjects provided a written informed consent before participation.

Study Population

Ten asymptomatic volunteers underwent initial MRI of the left hip; 1 subject was excluded following this initial evaluation due to MRI morphological signs of bone marrow edema and femoroacetabular impingement (FAI). Therefore, 9 healthy asymptomatic participants (mean age, 27.4 ± 4.0 years; range, 23-34 years; 5 males, 4 females; mean body mass index [BMI], 22.9 ± 1.6 kg/m^2) were included. None of the participants had a history of hip pain or surgery on their lower extremities, and every individual was examined prior to MRI by an orthopedic surgeon to rule out any abnormality of the hip. Of note, the pre-MRI activities of each participant were not supervised or controlled, although every subject was thoroughly reminded to keep physical activity prior to the morning MRI to a minimum and to avoid any excessive activities other than daily life activities such as running and jumping between the measurements.

Magnetic Resonance Imaging

MRI conducted on a 3 T MR scanner (Magnetom Trio, Siemens Medical Solutions, Erlangen, Germany) was performed in the morning (MRI between 8 and 11 a.m.; $MRI_{morning}$), in the afternoon (MRI between 3 and 6 p.m.; $MRI_{afternoon}$), and after 50 squats (subsequent to the afternoon evaluation). At these measuring points, T2* was assessed 0, 15, 30, 45, and 60 minutes after unloading in the MRI. Therefore, each participant underwent 15 measurements during the day. The MRI protocol included a gradient-echo (GRE) based 3D multi-echo data image combination (MEDIC) sequence with 6 consecutive echoes for the T2* assessment, and a double-echo steady state (DESS) sequence for morphological cartilage assessment that was performed subsequent to the T2* evaluation in the morning. To keep motion artifacts to a minimum, efforts were made to ensure the best possible patient comfort during the examination using blankets and pillows. Two sandbags were placed medially and laterally to the knee on the investigated side to promote higher stability of the leg and decrease rotation in the hip. Furthermore, a soft pillow was placed beneath the ipsilateral foot for a comfortable position and to avoid motion within the ankle during the scans. **Table 1** supplies additional information on the imaging parameters employed in this study.

Data Analysis

The 3D MRI data sets were transferred to a Leonardo workstation (Siemens Medical Solutions, Erlangen, Germany)

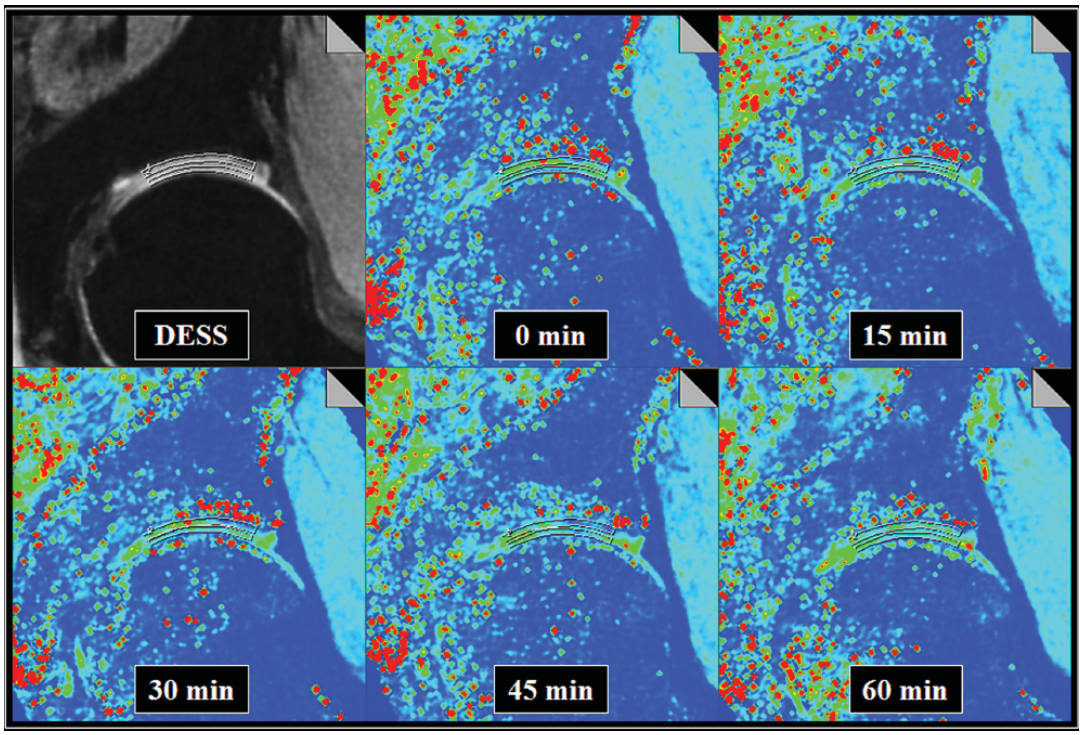

Figure 1. Double-echo steady state (DESS) and corresponding T2* reformats depicting the superior hip joint region at different time points of measurement. Regions of interest were defined by multiple marker points framing the acetabular and femoral cartilage from the acetabular rim to the fovea area. The corresponding morphological DESS images served as anatomical references. T2* values are illustrated in a color scale, whereby the red color represents T2* values increasing towards 100 ms and the blue color represents T2* values decreasing towards 0 ms. The green color reflects T2* values observed in healthy cartilage. Note that the T2* maps at different time points of measurement were similar.

for further assessment. Seven radial reformats with a slice thickness of 2 mm depicting the hip from anterior to superior and posterior were created using multiplanar reconstruction. Region of interest (ROI) analysis was then performed by an orthopedic surgeon (BB; 8 years of experience in MRI of hip joint cartilage including morphological and biochemical cartilage assessment) in the MRI radial reformat depicting the weight-bearing area of the hip including corresponding regions of acetabular and femoral cartilage. ROI placement in acetabular cartilage included the area between the acetabular rim and the fossa acetabuli. In femoral head cartilage, ROIs were placed between the fossa of the femoral head and the acetabular rim. An appropriate placement of marker points that delineated the ROI was conducted using corresponding DESS reformats as a reference to ensure a precise ROI placement within cartilage boundaries (**Fig. 1**). To assess interobserver reliability, a second independent observer (TH) with 5 years of experience in biochemical cartilage imaging repeated the analysis in 5 randomly selected volunteers.

Statistical Analysis

We used SPSS software (Version 21.0; IBM Corp, Armonk, NY, USA) for statistical analysis in this study. All T2* values in this study are referred to as mean values ± standard deviation (SD). In order to compare the T2* values at the different times of day, a paired Student's *t*-test was utilized. A 1-way analysis of variance (ANOVA) with Bonferroni correction for multiple comparisons and a *post hoc* test were used to compare the T2* values at different time points of each measurement. Inter-observer agreement was calculated by intraclass correlation (ICC) analysis utilizing a pairwise correlation model with absolute agreement. *P* values less than 0.05 were considered to reveal a statistically significant difference.

Results

A total of 270 ROIs (9 volunteers, 3 measurements [morning, afternoon, after knee-bends], 2 regions [acetabular and femoral head], and 5 time points of measurement [0, 15, 30, 45, 60

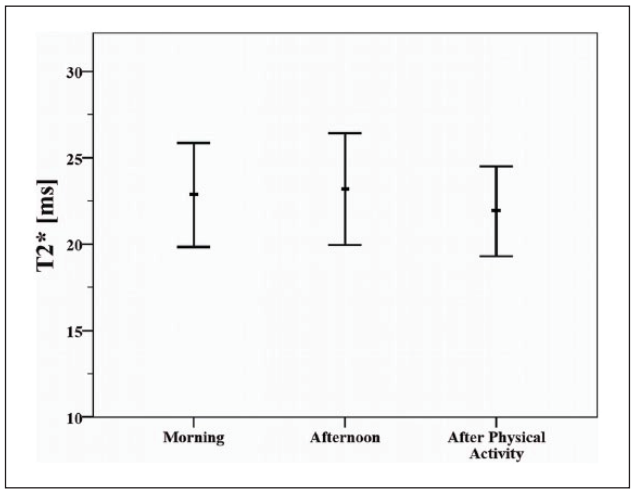

Figure 2. Mean T2* values ± standard deviation in the morning, in the afternoon, and after physical activity.

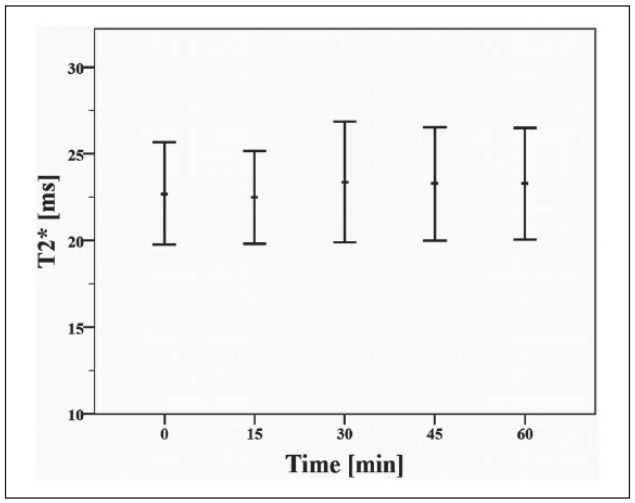

Figure 3. Mean T2* values ± standard deviation at 5 time points of measurement. Note that the T2* values at different time points of measurement were similar.

minutes]) were analyzed. Of these, 4 ROIs were excluded due to MRI artifacts. The mean size of the remaining ROIs was 0.17 ± 0.07 cm^2 (48 pixels), ranging from 0.08 cm^2 (23 pixels) to 0.31 cm^2 (87 pixels). ICC analysis indicated a high interobserver reproducibility of the T2* measurement (ICC = 0.951; 95% confidence interval, 0.907-0.972).

The T2* values measured in the morning ($T2^*_{morning}$, 22.9 ± 3.0 ms, range, 18.0-30.7 ms) were not statistically different ($P = 0.47$) from those measured in the afternoon ($T2^*_{afternoon}$, 23.2 ± 3.2 ms, range, 17.1-31.8 ms; **Fig. 2**). The same applies for the T2* values at different time points of each measurement ($P = 0.67$; **Fig. 3**) and the T2* assessment after 50 squats (T2*, 21.6 ± 2.6 ms, T2* ranging from 15.4 to 28.0 ms; $P = 0.43$; **Fig. 4**).

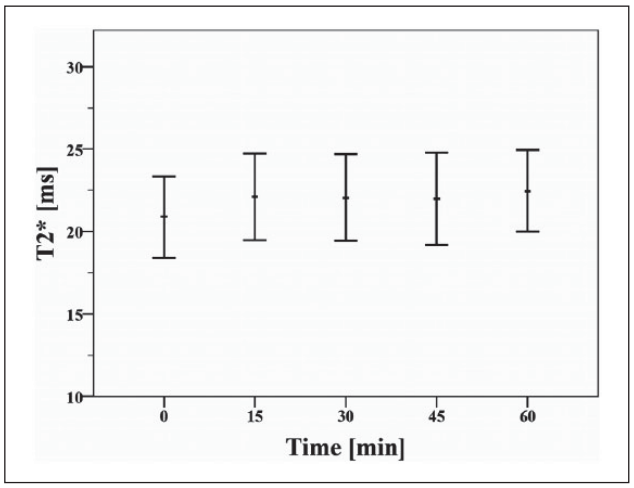

Figure 4. Mean T2* values ± standard deviation at 5 time points of measurement after 50 squats. Note that the marginal trend of higher T2* values after 60 minutes was not statistically significant (difference $T2^*_{0\ minutes}/T2^*_{60\ minutes} = -1.6 \pm 0.9$ ms; $P = 0.43$).

Discussion

We analyzed diurnal effects and the impact of preimaging exercise prior to MRI on the T2* mapping values in hip joint cartilage. Our results did not reveal any statistically significant differences in the T2* values between the different time points of the day (morning and afternoon) and values obtained at different time points of measurement. After 50 squats, a marginal trend of higher T2* values was noted; however, this was not statistically significant (difference $T2^*_{0\ minutes}/T2^*_{60\ minutes} = -1.6 \pm 0.9$ ms; $P = 0.43$).

There are few reports on the effect of various kinds of physical activities on cartilage thickness and dGEMRIC, T2, and T2* values of knee and hip joint cartilage.[8-12] In the study of Widmyer *et al*.,[13] diurnal strains on articular knee cartilage with respect to the BMI were analyzed. Aligned MR images obtained in the morning (8 a.m.) and in the afternoon (4 p.m.) of 10 obese volunteers (BMI = 25-31 kg/m^2) and a control group of 10 normal-weighted (BMI = 18.5-24.9 kg/m^2), age-matched, and sex-matched participants were compared. In the study group, increasing diurnal strains (decrease of cartilage thickness) were observed for the medial and lateral joint compartments. In the control group, such diurnal variations were only noted in the medial compartment. These observations run in concordance with 2 other studies on diurnal variations in knee joint cartilage where only little differences concerning amount and distribution among the joints were reported.[14,15] While these studies included measurements of cartilage volume, thickness, or both, the study of Li *et al*.[16] analyzed diurnal effects on T1ρ and T2 values of knee joint cartilage in six healthy volunteers (age range, 22-35 years) and noted no differences for

both T1ρ and T2 values between the morning (8-10 a.m.) and afternoon (5-7 p.m.) measurements ($P > 0.05$). An analysis of the percentage change in the T1ρ and T2 values in 5 regions of the joint (lateral femoral condyle, medial femoral condyle, lateral tibia, medial tibia, patella) revealed an increasing trend of these values for femoral than for tibial cartilage. Although these studies were obtained in the knee joint and not in the hip like the present study, the results comparable to our study show no clear diurnal effects in cartilage volume or compositional cartilage values.

In their evaluation of articular cartilage in 22 patients with FAI (mean age 28.1 years) and 27 healthy asymptomatic volunteers (mean age, 26.6 years) using T2* mapping at different time points, Apprich *et al*.[17] noted an increase of T2* relaxation times (T2* global, 21.75 ± 2.4 vs. 24.64 ± 3.1 ms, $P < 0.05$) in healthy hip joint cartilage after a period of approximately 50 minutes of unloading. Apprich *et al*.[17] attribute their findings to possible changes in the biochemical composition of healthy cartilage. Because T2* is sensitive to the cartilage water content, a rehydration after unloading could thus lead to superior T2* relaxation as well as to a presumable rearrangement of the collagen fiber network after unloading. Our results are somewhat contrary and as such cannot be fully explained.

Another study on 10 healthy nonprofessional marathon runners with no morphologically evident cartilage damage (mean age, 28.7 ± 3.97 years) revealed that superior levels of physical activity performed on the days prior to MRI scarcely influenced the T2* cartilage evaluation.[7] However, one has to consider that these results were obtained in knee joint cartilage, and the time span between the T2* measurements before and after the marathon was 2 to 3 days in this study, possibly limiting the comparison with the current study.

The present results were obtained in young volunteers, and the lack of diurnal effects or during loading or (afterward) unloading have to be noted with caution. There are nearly no studies on the hip joint available, and to actually assess the value of T2* mapping in the hip, volunteer studies like this are needed and somewhat critical. In the knee joint, however, available studies that mainly used standard spin-echo T2 mapping show an effect of unloading, especially in altered cartilage areas as present after cartilage repair or in osteoarthritis.[18,19] The existing benefits of T2* mapping in comparison with standard T2 mapping are mentioned above. The present study shows that T2* mapping in the hip joint of volunteers is a stable parameter. Nevertheless, the mentioned limitations have to be taken into consideration.

Our study has further limitations. No *in vivo* studies on transchondral stress distribution in the hip joint during motion were found in current literature. Especially no previously reported data on biochemical cartilage assessment after different types of exercise is available. Thus, a safe conclusion between performing squats and joint loading cannot be drawn. In addition to the rather small study group, the daily activities of each volunteer between the MRI in the morning and the measurement in the afternoon were not supervised or documented. Therefore, differences in cartilage strain (e.g., gait pattern, frequency of joint loading) might have altered the T2* measurements. Also, our study group consisted of healthy, asymptomatic volunteers with morphologically apparent normal cartilage and, therefore, our observations may not translate to patients with some form of cartilage degeneration. As MRI scans were performed in the morning and in the afternoon but not in the evening, our results cannot exclude ongoing diurnal effects that occur with further joint loading at a later time of the day. However, the period of time between the 2 T2* measurements was at least 6 hours. It must also be outlined that each participant in this study underwent 15 scans during the day and spent approximately 240 minutes in the MR scanner. Therefore, we believe that an additional scan in the evening would not have been reasonable.

In conclusion, the timing of the scan and preimaging exercise did not matter in this imaging modality. This study consolidates the value of T2* imaging in hip joint cartilage that seems to be independent of diurnal effects and exercise prior to MRI. While aiming for a standardized imaging protocol, diurnal changes in molecular cartilage composition as well as loading conditions immediately prior to MRI do not seem to significantly alter cartilage assessment. However, ongoing studies including a standardized activity protocol and a larger study group, which enrolls patients with cartilage degeneration, may further reaffirm these findings.

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Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical Approval

This study was approved by the local ethics committee.

Informed Consent

Written informed consent was obtained from all subjects before the study.

Trial Registration

Not applicable.

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T2* Mapping of the Hip in Asymptomatic Volunteers with Normal Cartilage Morphology: An Analysis of Regional and Age-Dependent Distribution

Tobias Hesper[1], Christoph Schleich[2], Alexander Buchwald[1], Harish S. Hosalkar[3,4], Gerald Antoch[2], Rüdiger Krauspe[1], Christoph Zilkens[1], and Bernd Bittersohl[1]

Abstract

Objective. To assess age-dependent and regional differences in T2* relaxation measurements in hip joint cartilage of asymptomatic volunteers at 3 T. *Design*. Three age cohorts (cohort 1: age 20-30 years, 15 individuals; cohort 2: age 30-40 years, 17 individuals; cohort 3: age 40-50 years, 15 individuals) were enrolled. T2* values were obtained in the central and peripheral cartilage of the acetabulum and the femoral head in 7 regions (anterior to superior and posterior). *Results*. T2* did not differ among age cohorts in acetabular cartilage (cohort 1: 24.65 ± 6.56 ms, cohort 2: 24.70 ± 4.83 ms, cohort 3: 25.81 ± 5.10 ms, $P = 0.10$) and femoral head cartilage (cohort 1: 27.08 ± 8.24 ms, cohort 2: 25.90 ± 7.82 ms, cohort 3: 26.50 ± 5.61 ms, $P = 0.34$). Analysis of the regional T2* distribution pattern indicates increased T2* values in the anterior, anterior-superior, superior-anterior, and the posterior-superior aspects of acetabular and femoral head cartilage. For acetabular cartilage, higher values were observed in the central region (25.90 ± 4.80 ms vs. 24.21 ± 4.05 ms, $P < 0.0001$) whereas femoral head cartilage did not reveal such differences (26.62 ± 5.74 ms vs. 26.37 ± 5.89 ms, $P = 0.44$). *Conclusions*. The T2* analysis of presumably healthy hip joint cartilage does not seem to be stratified according to age in this population. Regional T2* variation throughout hip joint cartilage is apparent in this modality.

Keywords

T2* mapping, magnetic resonance imaging, hip, cartilage, age groups

Introduction

Due to the awareness of pre-arthritic problems in the hip joint today, which, if left untreated, would lead to early osteoarthritis (OA) over the natural course of time, combined with the continued advances in the field of hip joint preservation surgery and cartilage repair techniques, a precise and reproducible assessment of hip joint cartilage is warranted. Such an assessment would assist as a decision guiding tool for physicians regarding various treatment options, including surgical and nonsurgical approaches, and also provide valuable information regarding disease onset and progression and, therefore, possibly facilitate the process of reviewing surgical outcomes and treatment follow-up objectively and in a reproducible manner.

Magnetic resonance imaging (MRI) is now considered the standard of care in morphological cartilage assessment. Highly precise morphological imaging of hip joint cartilage was initially considered ambitious due to the unique hip anatomy with its location deep in the pelvis, the spherical shaped cartilage, and—in particular regions—limited cartilage thickness. Over the past decade, MR scanners with high (≥3 T [Tesla]) field strengths and evolving cartilage-specific MR sequences have greatly improved the utility of morphological cartilage imaging, albeit the ability to delineate very early changes in the course of OA remains limited.

Supplementary to morphological MR cartilage assessment, biochemical sensitive MRI techniques (i.e., delayed gadolinium-enhanced magnetic resonance imaging of cartilage [dGEMRIC],[1,2] T1rho imaging,[3,4] glycosaminoglycan chemical exchange saturation transfer [gagCEST],[5] sodium imaging,[6] T2 mapping,[7,8] and T2* mapping[9,10]) offer the

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ability to depict subtle cartilage changes before macroscopic alterations are notable; these techniques are well-documented, previously described, and published. Each of these techniques target biochemical changes that occur within cartilage boundaries during the process of cartilage degeneration. However, each method holds different advantages and disadvantages related to its clinical application. While some of these techniques are sensitive to the content of cartilage glycosaminoglycan (dGEMRIC, gagCEST, sodium imaging, T1rho imaging), T2 and T2* mapping is susceptible to the cartilage water content and interactions between water molecules and the collagen fiber network. Notably, while T1rho may not be as specific for proteoglycan as gagCEST, sodium, or dGEMRIC, there are now a moderate number of articles utilizing T1rho demonstrating that T1rho reflects the compositional changes seen in the early stages of OA including cohorts of hip dysplasia, femoroacetabular impingement (FAI), and hip OA.[11,12]

In particular, with recent concerns related to the questionable safety of gadolinium-involving methodologies,[13,14] T2* mapping features substantial safety benefits when compared with other imaging techniques.[15] Without the need for contrast media, 3-dimensional (3D) cartilage assessment can be accomplished with comparatively short acquisition times and a high signal-to-noise ratio and high image resolution. Moreover, T2* mapping is easy to implement on clinical routine MRI systems without the need for specialized hardware components.

Despite the growing interest in the T2* mapping technique for articular cartilage assessment, to the best of our knowledge, no previously reported work has provided data for T2* relaxation among different age groups of healthy volunteers. Furthermore, an analysis of the sectoral/regional T2* distribution within the hip joint has not been performed.

A working knowledge about the "normal" T2* relaxation spectrum among presumably healthy hip joint cartilage is certainly necessary to be able to interpret the results of T2* cartilage assessments in different cartilage disease patterns. Therefore, aiming for T2* baseline values for hip joint cartilage in various age cohorts, this study investigated the age-dependent and regional distribution of T2* relaxation times in the hip joint cartilage of asymptomatic volunteers at 3 T.

Methods

This study met all regulations and was approved by the local ethics committee. All participants provided written informed consent prior to their enrollment.

Study Cohort

In this study, we analyzed the data of 47 healthy, asymptomatic volunteers. Subsequent to their admission, each individual was allocated into 3 age cohorts: cohort 1: age 20 to 30 years, 15 individuals, mean age: 25.9 ± 2.3 years (range: 21.1-29.1 years), 8 females, 7 males, 8 left hips, 7 right hips; cohort 2: age 30 to 40 years, 17 individuals, mean age: 34.1 ± 3.3 years (range: 30.4-39.6 years), 8 females, 9 males, 8 left hips, 9 right hips; cohort 3: age 40 to 50 years, 15 individuals, mean age: 44.7 ± 3.5 years (range: 40.1-49.8 years), 8 females, 7 males, 8 left hips, 7 right hips. As this study was conducted on a clinical MR scanner, data acquisition was limited to weekends and resources regarding measuring time were limited. Therefore, we included data for cohort 1 that had been previously published.[16] In that study, 35 asymptomatic volunteers (mean age 24.9 ± 2.1 years) served as a control for 29 patients with symptomatic FAI who underwent T2* mapping of the hip. For this study, the data of 15 individuals in the control group were randomly selected. Efforts were only made to ensure a balanced ratio of males and females as well as left and right hips. For cohort 2 and cohort 3, we recruited a total of 34 volunteers between 30 and 50 years of age. After reviewing their MRIs, 2 participants had to be excluded due to motion artifacts and an incidental diagnosis of asphericity of the femoral head. Therefore, the data of 47 volunteers underwent statistical analysis.

Although data acquisition for cohort 1 was achieved by a previous study, it has to be noted that there were no differences concerning volunteer recruitment, pre-MRI examination, or MRI protocol issues within all 3 age cohorts in this study. Each participant was asymptomatic regarding musculoskeletal-related pain in either the lower back, groin, or lower extremities, and none reported a history of hip or knee pain, no surgical interventions on the lower extremities, and no contraindications to undergoing MRI. A thorough physical examination was conducted prior to MRI for all individuals by an orthopedic consultant with 8 years of experience in hip joint surgery, revealing no clinical signs of any hip or knee joint pathology or deviation of the mechanical axis of both legs.

Magnetic Resonance Imaging

Magnetic resonance imaging was performed on a 3 T MR scanner (Magnetom Trio, Siemens Medical Solutions, Erlangen, Germany) with a body-matrix phased-array coil in the supine position. Efforts were made to increase the comfort on the examination table by stabilizing the hip with blankets and pillows and, therefore, keep motion artifacts to a minimum. To reduce potential diurnal effects, MRI was performed at the same time of the day, and each participant was reminded to keep physical activities to a minimum, although we did not supervise each study participant before the MRI.

The MRI protocol included a double-echo steady-state (DESS) sequence for morphological cartilage assessment

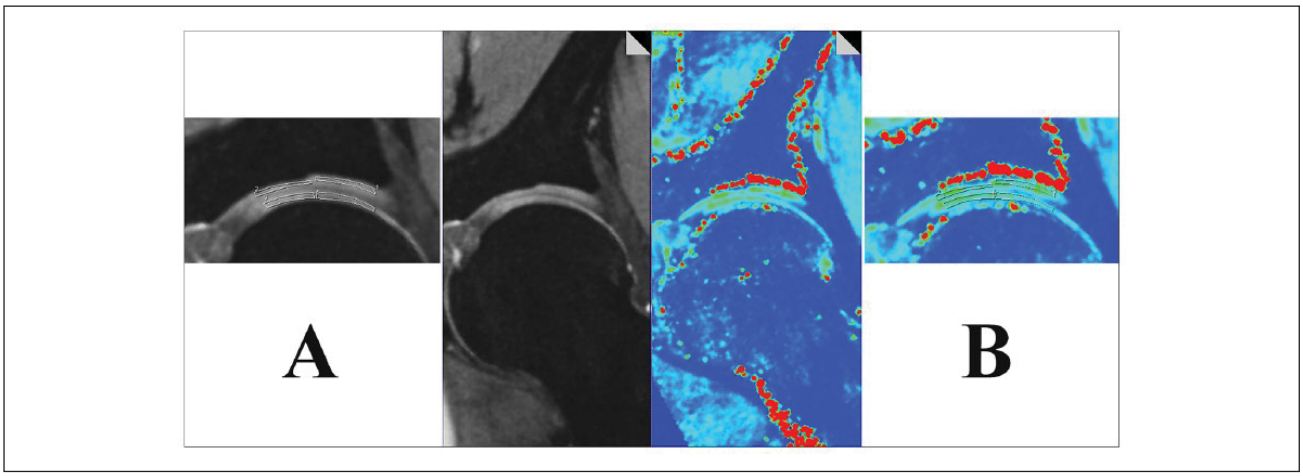

Figure 1. In each of the 7 regions, T2* measurements (**B**) were obtained from central and peripheral cartilage from the acetabulum and the femoral head. Double-echo steady state (DESS, **A**) reformats served as the anatomical reference to ensure precise region of interest placement within cartilage boundaries.

(repetition time: 14.75 ms, echo time: 5.03 ms, flip angle: 25°, number of excitation: 1, field of view: 192 mm^2, slice thickness: 0.6 mm, in-plane resolution: 0.6 × 0.6 mm, slice gap: 0.2 mm, bandwidth: 260 Hz/pixel, acquisition time: 13.17 minutes) followed by a GRE 3D multi-echo data image combination (MEDIC) sequence with 6 consecutive echoes for the T2* measurements (repetition time: 38 ms, echo times: 4.62 ms, 9.41 ms, 15.28 ms, 21.15 ms, 27.02 ms, 32.89 ms, flip angle: 25°, number of excitation: 1, field of view: 192 mm^2, slice thickness: 0.6 mm, in-plane resolution: 0.6 × 0.6 mm, slice gap: 0.2 mm, bandwidth: 260 Hz/pixel, acquisition time: 13.29 minutes).

Data Analysis

Image analysis was carried out by a qualified observer with a special interest in biochemically sensitive cartilage MRI and 8 years of experience in this field. After transferring all 3D MRI data sets to a Leonardo workstation (Siemens Medical Solutions, Erlangen, Germany), 7 radial reformats with a slice thickness of 2 mm were created by multiplanar reconstruction to depict the (1) anterior, (2) anterior-superior, (3) superior-anterior, (4) superior, (5) superior-posterior, (6) posterior-superior, and (7) posterior aspects of the hip joint. Using a region of interest (ROI) analysis, in each of these 7 regions, the articular cartilage of the acetabulum—and the corresponding cartilage of the femoral head—was further divided into central and peripheral cartilage, defined as 2 equally halves between the acetabular fossa and the chondro-labral junction. The corresponding DESS reformats served as guidance to ensure precise ROI placement within cartilage boundaries. **Figure 1** illustrates the ROI placement within acetabular and femoral cartilage in DESS and corresponding T2* reformats.

Statistical Analysis

For the evaluation of age-related and regional dependencies on T2* measurements, a generalized estimated equation (GEE analysis) with Sidak correction for multiple comparisons was utilized and the Wald chi-squared values, mean T2* values ± standard deviation (SD), the 95% Wald confidence interval (CI), as well as *P* values were obtained. For the comparison between the 2 gender cohorts, we utilized Student's *t* test for independent variables. *P* values <0.05 were considered to be statistically significant.

In 10 randomly selected volunteers, T2* values were obtained by a second observer for interobserver agreement (intraclass correlation testing, pairwise correlation model with absolute agreement). Notably, these measurements were obtained from the same reformats as the initial measurements to ensure analysis of the exact same cartilage regions.

Results

In this study, we analyzed a total of 1,316 ROIs (central and peripheral cartilage of the acetabulum and femoral head, 7 radial reformats, 47 participants); 239 ROIs (18.16%) were excluded from further analysis due to imaging artifacts, lacking a clear differentiation between femoral and acetabular cartilage, or apparent cartilage damage. Cartilage damage was obvious in 96 ROIs (44 ROIs in cohort 2, 52 ROIs in cohort 3; no apparent cartilage damage was noted in cohort 1). Therefore, a total of 1,021 ROIs underwent statistical analysis. The mean size of the ROI was 0.10 ± 0.04 cm^2 (27.82 ± 10.55 pixels).

Regarding age-related T2* relaxation, neither for acetabular cartilage (cohort 1: 24.65 ± 6.56 ms, cohort 2: 24.70 ± 4.83 ms, cohort 3: 25.81 ± 5.10 ms, $\chi^2 = 4.70$, $P = 0.10$) nor

Table 1. T2* Values in Acetabular and Femoral Head Cartilage in Different Age Groups.

Age Cohort (Years)	Acetabular Cartilage		Femoral Head Cartilage	
	Mean T2* ± SD (ms)	95% CI (ms)	Mean T2* ± SD (ms)	95% CI (ms)
20-30	24.65 ± 6.56	23.76-25.54	27.08 ± 8.24	25.96-28.19
30-40	24.70 ± 4.83	23.96-25.43	25.90 ± 7.82	24.79-27.01
40-50	25.81 ± 5.10	24.96-26.67	26.50 ± 5.61	25.64-27.35

CI = confidence interval.

Table 2. Pairwise Comparison between T2* Relaxation Measures of Acetabular and Femoral Cartilage in Different Age Groups.

Age Cohort (Years)		Acetabular Cartilage			Femoral Head Cartilage		
		Mean Δ T2* (ms)	95% CI (ms)	Sig.	Mean Δ T2* (ms)	95% CI (ms)	Sig.
20-30	30-40	−0.05	−1.20 to 1.11	1.00	1.17	−0.40 to 2.75	0.96
	40-50	−1.16	−2.39 to 0.07	0.18	0.58	−0.83 to 1.99	1.00
30-40	40-50	−1.11	−2.24 to 0.01	0.15	−0.59	−2.0 to 0.81	1.00

CI = confidence interval.
No significant differences were observed between different age cohorts.

for femoral cartilage (cohort 1: 27.08 ± 8.24 ms, cohort 2: 25.90 ± 7.82 ms, cohort 3: 26.50 ± 5.61 ms, $\chi^2 = 2.13$, $P = 0.34$) were any statistically significant differences noted between the different age cohorts. **Table 1** summarizes the age-dependent distribution of mean T2* relaxation times for acetabular and femoral cartilage, and **Table 2** provides a pairwise comparison testing.

Notably, we did observe regional differences in the T2* relaxation measures. Higher T2* values were detected in central acetabular cartilage when compared to peripheral acetabular cartilage (25.90 ± 4.80 ms vs. 24.21 ± 4.05 ms, $P < 0.0001$), whereas for femoral head cartilage, no significant differences (26.62 ± 5.74 ms vs. 26.37 ± 5.89 ms, $P = 0.44$) were noted between central and peripheral cartilage.

An analysis of the regional distribution of T2* relaxation times within the cartilage of the acetabulum and the femoral head among the 7 radial reformats revealed higher values for the anterior, the anterior-superior, and the superior-anterior aspects of the hip joint. Furthermore, the posterior-superior region of acetabular and femoral cartilage revealed superior values when compared to the adjacent regions (except for posterior-superior compared to superior-posterior in acetabular cartilage, where a P value of 0.08 was noted). Mean T2* values for acetabular cartilage were noted between 23.03 ± 3.31 ms (superior-posterior) and 27.18 ± 5.14 ms (anterior-superior). T2* values for femoral head cartilage amounted between 23.60 ± 4.35 ms (posterior) and 29.64 ± 4.76 ms (superior-anterior). The regional distribution of T2* relaxation times for acetabular and femoral head cartilage is shown in **Figure 2** and **Table 3**. The pairwise comparison is presented in **Table 4**.

An evaluation between the 2 gender cohorts revealed no differences between acetabular (female: 25.12 ± 4.29 ms vs. male: 25.28 ± 4.32 ms, $P = 0.68$) or femoral (female: 26.95 ± 4.85 ms vs. male: 26.37 ± 4.59 ms, $P = 0.15$) cartilage.

Intraclass correlation coefficient (ICC) analysis indicated a high interreader reproducibility of the T2* measurement in this study (ICC 0.74, $P = <0.0001$ for acetabular cartilage; ICC 0.85, $P = <0.0001$ for femoral head cartilage).

Discussion

In this study, we investigated age-dependent differences and the regional/sectoral distribution pattern of T2* relaxation times in the hip joint cartilage of asymptomatic volunteers at 3 T with morphologically normal cartilage. Regarding age, no significant differences in the T2* values for both acetabular and femoral cartilage were observed among the 3 cohorts. In addition, regional disparities in T2* relaxation were apparent with higher values in central acetabular cartilage compared to peripheral acetabular cartilage, as well as superior levels in the anterior to superior-anterior as well as the posterior-superior region of both acetabular and femoral head cartilage.

When assessing hip joint cartilage using the T2* mapping modality, baseline values of presumably healthy cartilage are mandatory to interpret the obtained T2* values in potentially damaged cartilage regions. Our findings are similar to those in previously reported *in vivo* studies on T2* cartilage assessment of hip joint cartilage in which asymptomatic controls served as a source of baseline T2* values for acetabular and femoral cartilage.[16-19] However, there are little data available on the topography of the T2*

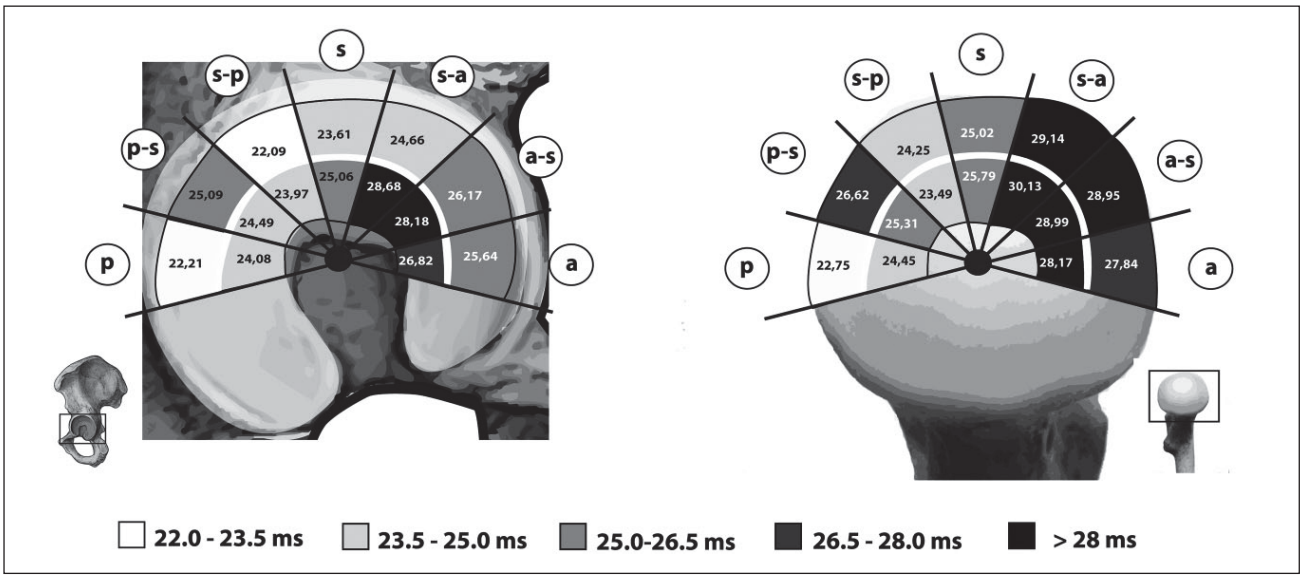

Figure 2. Regional/sectoral distribution of mean T2* values in acetabular (left) and femoral head (right) cartilage. Notably, higher values in the anterior, anterior-superior, and superior-anterior regions were identified. When compared to the adjacent regions, higher values were also observed in the posterior-superior region of both acetabular and femoral head cartilage. a = anterior; a-s = anterior-superior; s-a = superior-anterior; s = superior; s-p = superior-posterior; p-s = posterior-superior; p = posterior.

Table 3. T2* Values in Acetabular and Femoral Head Cartilage in Different Regions of the Hip Joint.

	Acetabular Cartilage		Femoral Head Cartilage	
Region	Mean T2* ± SD (ms)	95% CI (ms)	Mean T2* ± SD (ms)	95% CI (ms)
Anterior	26.23 ± 5.09	25.07-27.39	28.01 ± 5.74	26.72-29.30
Anterior-superior	27.18 ± 5.14	26.04-28.31	28.97 ± 6.40	27.62-30.32
Superior-anterior	26.67 ± 3.29	25.93-27.41	29.64 ± 4.76	28.65-30.63
Superior	24.34 ± 3.41	23.53-25.15	25.40 ± 4.78	24.37-26.44
Superior-posterior	23.03 ± 3.31	22.18-23.88	23.87 ± 3.40	23.07-24.67
Posterior-superior	24.79 ± 3.80	23.99-25.59	25.97 ± 3.32	25.27-26.66
Posterior	23.15 ± 3.53	22.33-23.96	23.60 ± 4.35	22.61-24.59

CI = confidence interval.

relaxation pattern of hip joint cartilage, which becomes increasingly important in pathological conditions such as FAI, where cartilage damage can frequently be observed in distinct cartilage regions (e.g., labral-chondral junction in the cam-type FAI).

The first descriptive report on T2* relaxation in hip joint cartilage was published in 2009.[17] In that study, 10 asymptomatic volunteers (mean age 27.0 ± 1.9 years, range 25-31 years) served as a control for 33 patients with symptomatic FAI. After morphological grading, T2* and dGEMRIC measurements were compared. Regarding the group of asymptomatic volunteers, mean T2* values were reported between 32.7 ± 4.5 ms in cartilage that was graded to have no morphological alterations and values of 29.1 ± 4.0 ms in cartilage with minor surface irregularities and changes in signal intensity. Notably, this study was conducted using a 1.5-T MR scanner, which made a distinct differentiation between acetabular and femoral cartilage impossible. Therefore, acetabular and femoral cartilage was evaluated as one entity during the ROI assessment. As T2* relaxation is sensitive to the water content, joint fluid between the 2 articulating cartilage layers likely biased the T2* evaluation in that study, resulting in slightly higher T2* values compared to our findings. The same limitation was pointed out by Miese *et al*.[18] In their group of 10 healthy participants (mean age 24 years, range 19-29 years) who served as a control for patients with slipped capital femoral epiphysis, T2* values between 23.06 ± 2.68 (central hip cartilage) and 29.83 ± 3.86 (medial hip cartilage) were reported using a 1.5-T MR scanner.

Table 4. Pairwise T2* Comparison of Acetabular and Femoral Head Cartilage in Different Regions of the Hip.

		Acetabular Cartilage		Femoral Head Cartilage	
Region		Mean Δ T2* (ms)	Sig.	Mean Δ T2* (ms)	Sig.
Anterior	Anterior-superior	−0.94	0.80	−0.97	0.89
Anterior	Superior-anterior	−0.44	1.00	−1.63	0.39
Anterior	Superior	1.90	**0.02**	2.60	**0.01**
Anterior	Superior-posterior	3.20	**<0.001**	4.14	**<0.001**
Anterior	Posterior-superior	1.44	0.56	2.04	0.07
Anterior	Posterior	3.08	**0.001**	4.41	**<0.001**
Anterior-superior	Superior-anterior	0.51	1.00	−0.67	1.00
Anterior-superior	Superior	2.84	**<0.001**	3.57	**<0.001**
Anterior-superior	Superior-posterior	4.15	**<0.001**	5.10	**<0.001**
Anterior-superior	Posterior-superior	2.38	**0.02**	3.01	**<0.001**
Anterior-superior	Posterior	4.01	**<0.001**	5.37	**<0.001**
Superior-anterior	Superior	2.33	**<0.001**	4.23	**<0.001**
Superior-anterior	Superior-posterior	3.64	**<0.001**	5.77	**<0.001**
Superior-anterior	Posterior-superior	1.88	**0.01**	3.67	**<0.001**
Superior-anterior	Posterior	3.52	**<0.001**	6.04	**<0.001**
Superior	Superior-posterior	1.31	0.30	1.53	0.27
Superior	Posterior-superior	−0.46	1.00	−0.56	1.00
Superior	Posterior	1.19	0.55	1.81	0.16
Superior-posterior	Posterior-superior	−1.76	0.08	−2.10	**<0.001**
Superior-posterior	Posterior	−0.12	1.00	0.27	1.00
Posterior-superior	Posterior	1.64	**0.03**	2.37	**0.002**

Higher values were observed for the anterior, anterior-superior, and superior-anterior regions when compared with other regions. Also, note the higher values in posterior-superior cartilage compared to its adjacent regions. P values <0.05 are considered to be statistically significant and are highlighted in boldface.

A 3-T MR scanner may remedy this limitation as the higher field strength offers the capability of higher image resolution, which is, in turn, beneficial because it is able to differentiate better between acetabular and femoral head cartilage in most cartilage regions. Acquired in asymptomatic volunteers on a 3-T MR scanner, recently reported T2* baseline values for acetabular and femoral cartilage are very similar to the findings of this study, ranging from 22.9 ± 3.0 ms to 26.0 ± 5.0 ms.[16,19]

There are little available data on hip joint cartilage that provide important clinical information about regional heterogeneities in the T2* relaxation pattern. Similar to our results, Apprich *et al*.[19] noted regional heterogeneity with higher T2* values in the anterior aspect of the hip joint than in the superior region (26.64 ± 4.3 ms vs. 22.67 ± 2.7 ms, $P = 0.012$). The authors contribute these findings primarily to (1) the magic angle effect that promotes an increase in T2/T2* relaxation when collagen fibers are orientated 54.7° to the main magnetic field and (2) possible differences in collagen density, fiber orientation, and water content in weight-bearing and non–weight-bearing cartilage regions.

An increase in T2/T2* relaxation when collagen fibers are orientated at an angle of approximately 55° is referred to as the magic angle effect.[20,21] This phenomenon might have contributed to the heterogeneity of regional T2* distribution in this study, as comparatively higher values were observed in the anterior-superior and posterior-superior region (which are closest to the magic angle). Similar to the findings of Apprich *et al*. and our results, Watanabe *et al*.[22] described increasing T2 mapping measures for femoral head cartilage toward the magic angle. In their study, single-plane radial T2 mapping analysis was conducted in 6 acetabular and 12 femoral head regions (12 healthy volunteers; mean age 29.5 ± 4.9 years), and radial sections were defined stepwise every 10° from a center line that was drawn through the center of the femoral head, perpendicular to the main magnetic field. Femoral T2 values appeared to steadily increase toward the magic angle and were shown to peak between 40° and 50° and (symmetrically with respect to the central line) −40° to −50°. The unexpected findings of lower values at 50° to 60° (respectively −50° to −60°) led to the authors to hypothesize that collagen fiber orientation that is not perpendicular to the subchondral bone might contribute to lowering the expected angle of highest T2 relaxation. Notably, in the study by Watanabe *et al*., these findings were only present in femoral head cartilage, while acetabular cartilage did not show superior values in these particular regions. Although not statistically significant, when comparing the posterior-superior and superior-posterior region ($P = 0.08$), our results strongly point toward an influence of the magic angle in acetabular

cartilage as well. Not only the magic angle effect but also the biomechanics of the hip during motion, loading conditions, and alterations in the biochemical composure of weight-bearing and non–weight-bearing cartilage likely contribute to these regional differences in T2* relaxation of femoral and acetabular cartilage.

We do acknowledge some limitations in this study. Our study group was fairly small and data acquisition for the various age cohorts was obtained at different points in time. Although both MRI protocols were identical and fastidious efforts were made to ensure standardized volunteer recruitment and physical examination before MRI, we cannot rule out the possibility that this might have possibly biased our results. Our study did not comprise a standardized protocol for pre-MRI activities to rule out possible alterations in joint loading among the study cohort. However, while previously published data revealed a load dependency for T2 relaxation in knee cartilage,[8] a recently conducted study [23] provides evidence that joint loading prior to image acquisition and diurnal effects do not seem to bias hip joint cartilage assessment utilizing T2* mapping. Of note, in this study we investigated full-thickness femoral and acetabular cartilage, although—for T2* cartilage assessment—a typically zonal stratification with higher T2* values in superior cartilage regions and lower values toward the radial zone (where water molecule restriction and T2* decay is promoted due to the characteristically perpendicular collagen fiber orientation and high proteoglycan content) is well documented.[15] In a recently published study on zonal and regional T2* relaxation in different morphological grades of knee joint cartilage, Bittersohl *et al*. noted a decrease of T2* values with increasing cartilage degeneration in both superior and deeper cartilage layers, with only a slightly more pronounced decrease in T2* between a modified Mankin grade 1 and grade 2/3 in superficial layers.[24] Given this rather steady decrease of T2* in superficial and deep cartilage layers in normal appearing cartilage and cartilage with higher grades of degeneration, we believe our methodology is appropriate for the purpose of this study. However, future studies, including an analysis of both superficial and deep cartilage layers are needed to shed further light on this topic.

Gradient-echo–based MRI techniques including the DESS and MEDIC (T2* mapping) sequence lack the 180° refocusing pulse making them prone to local susceptibility fields. These susceptibility fields, which are pronounced at the cartilage/bone interface and by foreign body particles like postsurgical debris or artificial implants, can compromise the assessment of cartilage, in particular when MRI is performed in the postoperative setting. Note should be made that minor changes to the highly organized basilar components of cartilage close to the tidemark, which have very short T2* relaxation times (estimated T2* values in deep and calcified cartilage = 1-2 ms[25]), may have been underestimated considering the TE range of our T2* mapping technique (TE min = 4.62 ms). As reported previously, changes in these deep cartilage zones may be better picked up by utilizing ultra-short echo time (TE range: 0.5-40 ms) T2* mapping techniques.[26,27] Nevertheless, limitations in these studies including small study samples have to be taken into account and each method holds different advantages and disadvantages related to its clinical application.

In conclusion, our results emphasize a regional distribution pattern for T2* relaxation among hip joint cartilage in asymptomatic volunteers, with superior values in the anterior to the superior-anterior aspects of the joint. Furthermore, the posterior-superior region appears to have higher T2* relaxation values when compared to its adjacent regions. Asymptomatic hips do not show evidence of any inconsistency in T2* values among different age cohorts. These results may further help establish T2* baseline values for hip joint cartilage that can serve as a reference, especially in cartilage disease studies, where cartilage degeneration might occur with topographic variation.

Authors' Note

This study was conducted at the Heinrich-Heine University Hospital, Düsseldorf, Germany

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Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical Approval

Ethical approval for this study was obtained from the Ethics Committee of the Heinrich-Heine University Düsseldorf (Study number 5218R, Register-ID 2015094276)

Informed Consent

Written informed consent was obtained from all subjects before the study.

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Original Article

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T2*-Mapping of Acetabular Cartilage in Patients With Femoroacetabular Impingement at 3 Tesla: Comparative Analysis with Arthroscopic Findings

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Abstract

Objective. To evaluate the diagnostic accuracy of T2*-mapping for detecting acetabular cartilage damage in patients with symptomatic femoroacetabular impingement (FAI). *Design*. A total of 29 patients (17 females, 12 males, mean age 35.6 ± 12.8 years, mean body mass index 25.1 ± 4.1 kg/m^2, 16 right hips) with symptomatic FAI underwent T2* MRI and subsequent hip arthroscopy. T2* values were obtained by region of interest analysis in seven radially reformatted planes around the femoral neck (anterior, anterior-superior, superior-anterior, superior, superior-posterior, posterior-superior, posterior). Intraoperatively, a modified Outerbridge classification was used for assessment of the cartilage status in each region. T2* values and intraoperative data were compared, and sensitivity, specificity, negative predictive values (NPV) and positive predictive values (PPV) as well as the correlation between T2*-mapping and intraoperative findings, were determined. The mean time interval between MRI and arthroscopy was 65.7 ± 48.0 days. *Results*. Significantly higher T2* values were noted in arthroscopically normal evaluated cartilage than in regions with cartilage degeneration (mean T2* 25.6 ± 4.7 ms vs. 19.9 ± 4.5 ms; $P < 0.001$). With the intraoperative findings as a reference, sensitivity, specificity, NPV and PPV were 83.5%, 67.7%, 78.4% and 74.4%, respectively. The correlation between T2*-mapping and intraoperative cartilage status was moderate ($\rho = -0.557$; $P < 0.001$). *Conclusions*. T2*-mapping enabled analysis of acetabular cartilage with appropriate correlation with intraoperative findings and promising results for sensitivity, specificity, PPV, and NPV in this cohort. Our results emphasize the value of T2*-mapping for the diagnosis of hip joint cartilage pathologies in symptomatic FAI.

Keywords
hip, MRI, FAI, T2*-mapping, arthroscopy

Introduction

In symptomatic femoroacetabular impingement (FAI), the ongoing pathological abutment between the acetabular rim and the femoral head-neck junction leads to early cartilage degeneration, damage to the acetabular labrum and synovitis. Although it remains unclear which specific FAI-related morphology and corresponding damage to the hip really causes symptoms, if left untreated in symptomatic cases, early osteoarthritis (OA) is known to occur.[1,2] As early intervention including different joint preserving approaches can potentially alter the course of disease progression in a prearthritic condition, a reliable and reproducible cartilage assessment at various stages of damage is critical.[3,4]

Magnetic resonance imaging (MRI) remains the modality of choice for morphological hip joint cartilage assessment. However, the ability to detect cartilage lesions using standard MRI is limited particularly in early stages of cartilage degeneration. For an evaluation of subtle changes that occur early in the course of degeneration, different biochemically sensitive MRI techniques have been proven as robust biomarkers that can pick up changes in cartilage composition

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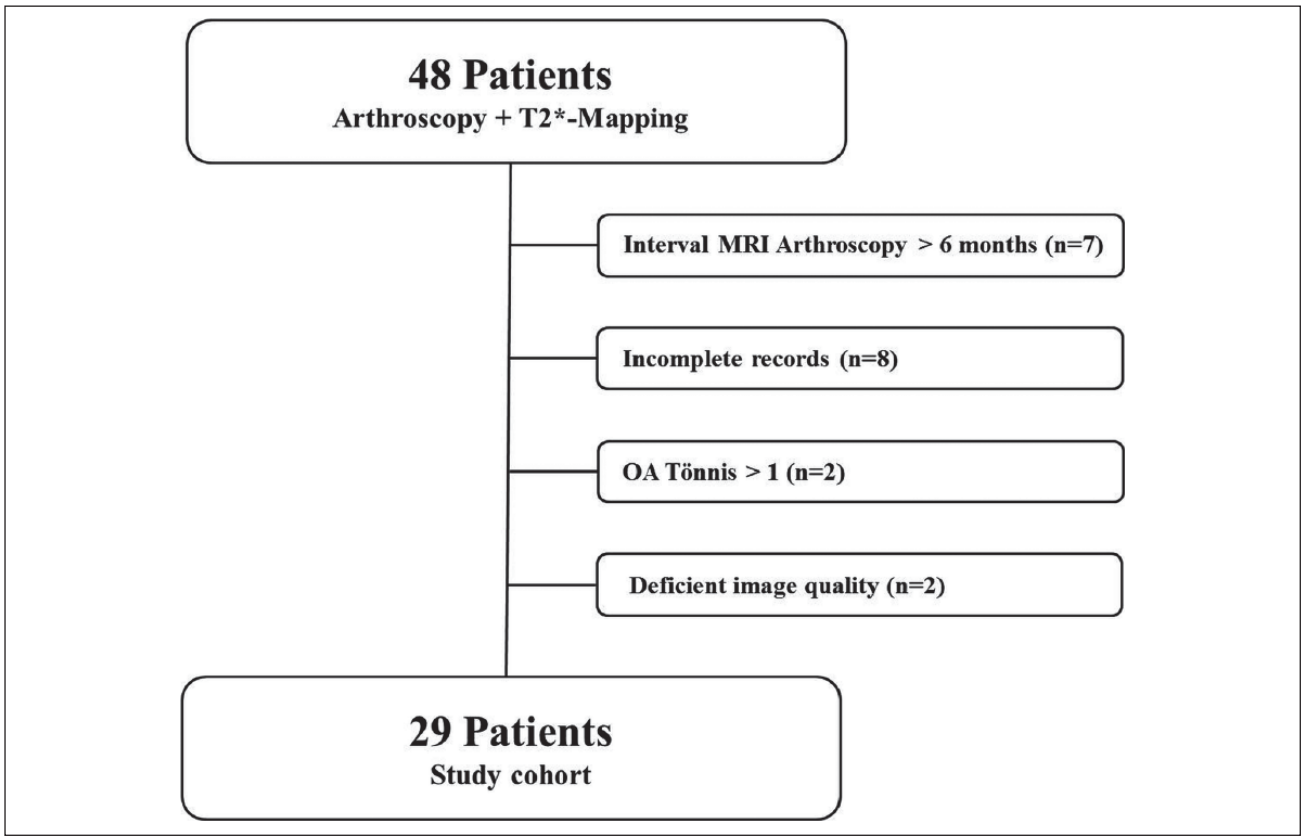

Figure 1. Flowchart for study inclusion and exclusion.

before macroscopic alterations are notable. While some of these techniques are susceptible to cartilage glycosaminoglycan (GAG) content (delayed gadolinium-enhanced magnetic resonance imaging of cartilage, dGEMRIC[5]; T1rho[6]), others are sensitive to the cartilage water content and interactions between water molecules and the collagen fiber network (T2/T2*-mapping[7,8]). T2*-mapping is advantageous in many ways. For example, it does not require the application of contrast media, and it allows for a 3-dimensional (3D), high-resolution, isotropic cartilage evaluation with short acquisition time.[9]

In this study, we sought to determine the accuracy of isotropic 3D T2*-mapping for hip joint cartilage analysis in patients with FAI at 3 T. Using intraoperative data as a reference, we calculated the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) in different regions of the hip joint and determined the correlation between MRI and intraoperative findings.

Method

Study Population

The procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 2000.

We included 29 patients (17 females, 12 males, mean age 35.6 ± 12.8 years, mean body mass index 25.1 ± 4.1 kg/m^2, 16 right hips) who underwent MRI, including T2*-mapping, prior to hip arthroscopy in the clinical setting of symptomatic FAI at our institution between 2010 and 2016. To minimize the risk of bias from possible progressive cartilage degeneration that could occur between MRI and surgery, we included only those patients in whom surgery was performed within 6 months of the MRI (mean time interval between MRI and arthroscopy 65.7 ± 48.0 days, range 5-182 days). All patients were clinically examined by 1 of 2 orthopedic surgeons (B.B., C.Z.). Both are fellowship-trained in Hip Preservation specialty, are currently practicing at a national referral center for hip conditions, and have more than 10 years of experience in clinical management of FAI patients. Regarding surgical experience in hip arthroscopy, both surgeons have, respectively, 9 and 8 years of experience, while coauthors of this study (R.K., H.H.) are national and international hip specialists with more than 2 decades of experience in treating hip conditions individually. The flow chart of inclusion and exclusion criteria is provided in **Figure 1**. Before participation, each patient signed written informed

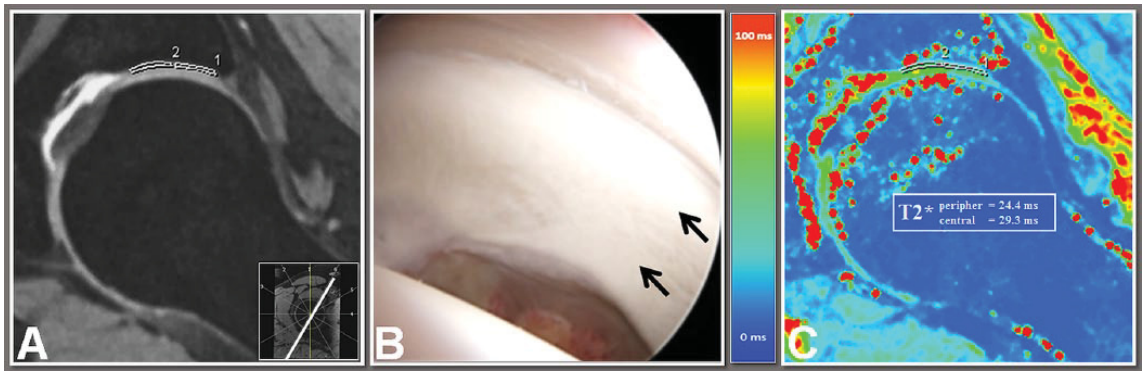

Figure 2. A 10 o'clock double-echo steady-state (DESS) reformat (A), an intraoperative view (B) of the corresponding region (arrows), and a 10 o'clock T2* map reformat (C) of a 15-year-old male patient with anterosuperior femoroacetabular impingement (FAI). T2* values were obtained using a region of interest (ROI) analysis in central and peripheral acetabular cartilage. The corresponding DESS reformat served as a guide to ensure ROI placement within cartilage boundaries. Note no cartilage degeneration was observed in this region, either with DESS MRI, intraoperative correlation or T2* relaxometry.

consent and ethical approval was obtained from the local ethics committee.

Magnetic Resonance Imaging

MRI was conducted on a 3-T scanner (Magnetom Trio, Siemens Medical Solutions, Erlangen, Germany) in the supine position with a 4-channel phased-array, flex surface coil around the hip being investigated. To increase comfort on the examination table and to reduce motion artifacts, the leg was stabilized with blankets and pillows.

Along with localizer images and standard pulse sequences, the MRI protocol included (1) a high-resolution 3D double-echo steady-state (DESS) sequence for morphological cartilage assessment (TR 14.75 ms, TE 5.03 ms, flip angle 25°, NEX 1, FOV 192 mm^2, slice thickness 0.6 mm, in-plane resolution 0.6 × 0.6 mm, slice gap 0.2 mm, bandwidth 260 Hz/pixel, acquisition time 13.17 minutes) and (2) A gradient-echo high-resolution 3D multi-echo data image combination (MEDIC) sequence with 6 consecutive echoes for the T2* measurements (TR 38 ms, TE 4.62 ms, 9.41 ms, 15.28 ms, 21.15 ms, 27.02 ms, 32.89 ms, flip angle 25°, NEX 1, FOV 192 mm^2, slice thickness 0.6 mm, in-plane resolution 0.6 × 0.6 mm, slice gap 0.2 mm, bandwidth 260 Hz/pixel, acquisition time 13.29 minutes).

Image Postprocessing and T2 Relaxometry*

Postprocessing and analyses of images were conducted by one reader (C.S.) with several years of experience in biochemical cartilage imaging who was blinded to patients' clinical information. Following image acquisition, all MR data sets of the DESS and MEDIC, which included the inline T2* maps, were transferred to a Leonardo workstation (Siemens Medical Solutions, Erlangen, Germany). Before analysis, multiplanar reconstruction software was used to create 7 radial reformats with a slice thickness of 2 mm around the femoral neck and with the femoral head as the center of rotation (anterior, anterior-superior, superior-anterior, superior, superior-posterior, posterior-superior, posterior). In each reformat, acetabular cartilage was divided into a peripheral and central zone, separated by a line that bisects the acetabular cartilage between the acetabular fossa and the cartilage-labral junction. T2* relaxometry was conducted by region of interest (ROI) analysis in central and peripheral acetabular cartilage in each reformat. Corresponding DESS reformats served as a guide to ensure ROI placement within cartilage boundaries (**Fig. 2**).

Analysis of Arthroscopic Data

In all 29 patients, hip arthroscopy was carried out using a similar technique by 1 of 2 experienced orthopedic arthroscopy surgeons (B.B., C.Z.). All patients were placed in supine position on the extension table, an anterior and anterolateral portal were established and, in cases that needed labral refixation, a distal anterolateral portal was established. Additional portals were established, if needed, on a case to case basis. Retrospectively, all intraoperative data (intraoperative images, videos and operative notes) were reviewed by 1 reader (B.B.) for cartilage assessment. For localization purposes, a clock-face scheme was implemented, which is consistent with MR interpretation, with 3 o'clock being anterior, 12 o'clock superior, and 9 o'clock posterior (**Fig. 3**). For each region central and peripheral acetabular cartilage was graded according to a modified Outerbridge classification system as follows: grade 0 = normal cartilage; grade 1 = cartilage softening; grade 2 =

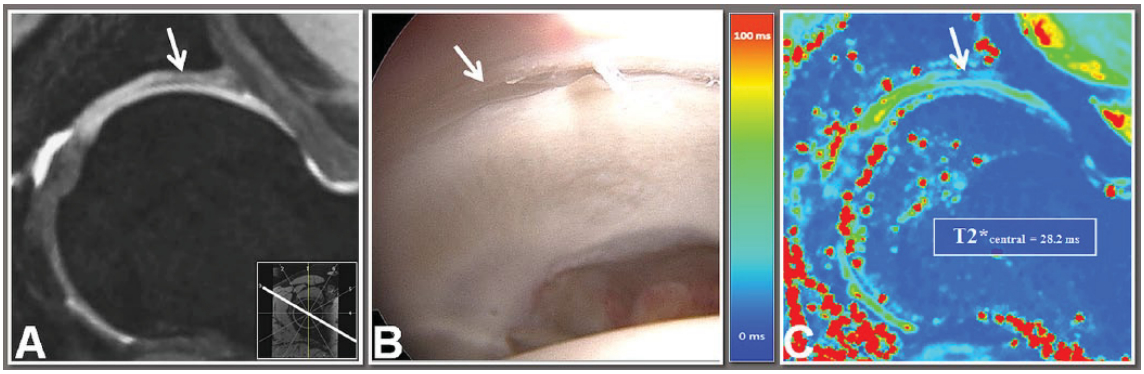

Figure 3. Double-echo steady-state (DESS) reformat (A), arthroscopic view (B) and T2* map reformat (C) of the same 15-year-old male patient with femoroacetabular impingement (FAI) revealing acetabular rim cartilage delamination (arrow; hypointense zone in the DESS image; low T2* values) in the 1 o'clock region. The peripheral region was excluded from this analysis because T2* assessment cannot be performed in areas with severe cartilage loss.

cartilage abrasion; grade 3 = cartilage loss; grade 4 = no evaluation of cartilage possible.[10] In cases of multiple cartilage defects within one region the highest grade of defect was chosen.

Statistical Analysis

Statistical analysis in this study was conducted with the support of a biostatistician who used SPSS software, version 22 (IBM Corp, Armonk, NY, USA). All *P* values <0.05 were considered statistically significant. Exploring the intra- and interreader reliability regarding the retrospective cartilage grading, which was based on intraoperative images, videos, and operative notes, all cases were reviewed again by the first (time interval between both measurements >12 weeks) and a second observer (C.Z.). Then, an intraclass correlation coefficient (ICC) analysis was performed with pairwise comparison and absolute agreement definition. For analysis of correlation between T2*-mapping and intraoperative data Spearman's correlation coefficient (ρ) along with the 95% confidence interval (CI) was calculated. In each investigated region of the hip, cartilage was classified as disease positive or disease negative according to intraoperative data. For MRI evaluation, in each investigated ROI T2* values were classified as either "normal" or "decreased." The ROIs were classified as "decreased" if T2* values were noted below the 95% CI of mean T2* values that were previously published in a population of asymptomatic controls at 3 T.[11] In each case, the mean values of the corresponding hip region were used as baseline values to compensate for regional differences in the T2* relaxation times possibly due to the magic angle effect,[12] which promotes an increase in T2/T2* relaxation when collagen fibers are orientated 54.7° to the main magnetic field, and potential regional differences in collagen density, fiber orientation, and water content. Sensitivity, specificity, PPV, and NPV were obtained via cross-table calculations. For evaluation of variances across the hip joint, correlation, sensitivity, specificity, PPV, and NPV were also evaluated in different subregions (1, anterior, anterosuperior; 2, superoanterior to superoposterior; 3, posterosuperior, posterior).

Results

We investigated 406 ROI (29 patients, 7 regions, central and peripheral acetabular cartilage). A total of 238 ROIs that had complete intraoperative grading and no apparent cartilage loss on MRI underwent statistical analysis. The intra- and interreader variabilities regarding retrospective cartilage grading were low (ICC = 0.89; $P < 0.001$ for intrareader and ICC = 0.92; $P < 0.001$ for interreader agreement).

With superior cartilage degeneration, according to the modified Outerbridge classification, we observed lower T2* values (90 ROIs graded "normal cartilage": mean T2* 25.6 ± 4.7 ms; 11 ROIs graded "cartilage softening": mean T2* 24.2 ± 3.3 ms; 132 ROIs graded "cartilage abrasion": mean T2* 19.9 ± 4.5 ms). The correlation between intraoperative cartilage status and T2* values was moderate ($\rho = -0.557$; $P < 0.001$). However, subregion analysis revealed good correlation in subregion 1 (anterior, anterosuperior; $\rho = -0.750$; $P < 0.001$) compared with subregion 2 (superoanterior to superoposterior; $\rho = -0.486$; $P < 0.001$) and subregion 3 (posterosuperior, posterior; $\rho = -0.331$; $P = 0.004$; **Table 1**). The correlation between T2*-mapping and intraoperative grading in central ($\rho = -0.573$; $P < 0.001$) and peripheral ($\rho = -0.513$; $P < 0.001$) acetabular cartilage was similar.

Sensitivity, specificity, PPV, and NPV were 83.5%, 67.7%, 78.4%, and 74.4%, respectively, in total. Subregion

Table 1. Spearman's ρ Correlation Analysis Assessing Agreement Between Cartilage Grading with Either T2* Relaxometry or Intraoperative Assessment in Various Regions of the Hip Joint.

Region	Correlation	95% Confidence Interval	*P*
Anterior Anterosuperior	−0.750	−0.841 to −0.616	<0.001
Superoanterior Superior Superoposterior	−0.486	−0.622 to −0.322	<0.001
Posterosuperior Posterior	−0.331	−0.522 to −0.110	0.004
Total	−0.557	−0.639 to −0.463	<0.001

analysis revealed values of 85.3%, 89.7%, 90.6%, and 83.9% for subregion 1 (anterior, anterosuperior), 85.5%, 57.6%, 80.8%, and 65.5% for subregion 2 (superoanterior to superoposterior), and 77.8%, 59.5%, 65,1%, and 73.3% for subregion 3 (posterosuperior, posterior; **Table 2**), respectively. For central acetabular cartilage the respective equivalent values were 85.1%, 68.3%, 80.8%, and 74.5%. In peripheral acetabular cartilage, the respective values were 80.0%, 66.7%, 73.5%, and 74.3%.

Discussion

We have continued to expand our understanding of the changing mechanics of the hip joint and nonphysiological abutment motion that occurs in FAI and causes progressive damage of cartilage and early OA in untreated cases of symptomatic FAI. Surgical management via both open and arthroscopic approaches has advanced rapidly to address the pathomorphology, repair the labral tear and damage, treat cartilage defects, and try and restore morphology for an attempted restoration of physiology and function of the hip, thereby altering the course of rapid degeneration to early OA. However, clinical outcomes following these procedures may be unpredictable and sometimes unsatisfactory if higher grades of joint degeneration are already present at the time of surgery.[13-15] Biochemical cartilage evaluation to accurately and reliably assess the cartilage status before cartilage alterations occur will likely provide critical information for decision making related to joint preservation or joint replacement and also for treatment monitoring and postintervention follow-up studies.

In this retrospective study, we sought to determine the accuracy of isotropic high-resolution 3D T2* mapping for hip joint cartilage analysis in patients with symptomatic FAI. Compared with arthroscopic data, T2*-mapping revealed promising results for sensitivity, specificity, PPV, and NPV in this cohort. The ICC measures indicate a high similarity between the surgeon grading of intraoperative cartilage damage in which all intraoperative data, including intraoperative images, videos and operative notes were reviewed. The correlation between MRI and intraoperative cartilage status was moderate. Notably, subregion analysis revealed good correlation in the anterior and anterosuperior aspect of the joint, a region more prone to damage in most FAI patients thereby implying that T2*-mapping is effective in this target group. However, our study raises concerns regarding the relative lack of diagnostic agreement between the T2* mapping values and corresponding intraoperative findings in the posterior aspect of the acetabulum. Although it remains hypothetical, some confirmation and selection bias with the tendency to find more cartilage damage in the anterior aspect while potentially overlooking existent (mild) cartilage degeneration in the posterior portion of the hip may have played a role. Also, T2*-mapping and arthroscopic cartilage evaluation are differently targeted diagnostic modalities where some cartilage degeneration or cartilage alteration picked up with T2*-mapping may not have been seen during hip arthroscopy. The clinical relevance of this finding discrepancy is still unclear, and T2*-imaging artifacts such as magic angle and susceptibility effects[9] may have a further influence. A further critical aspect is the appropriate use of portals for cartilage status assessment in which the anterior or a mid-anterior portal may be advantageous to observe the posterior part of the acetabulum, whereas it might be difficult to observe the superoposterior acetabulum from the anterolateral portal. In the retrospective review of articular surface, it is sometimes difficult to evaluate whole parts of a hip joint and in the retrospective, although viewing portals did not differ between surgeons, it is not absolutely clear which portal was used for the assessment of a specific cartilage region.

Only a few studies on the correlation between biochemical cartilage imaging and intraoperative data in FAI cohorts have been published previously (**Table 3**). In 16 FAI patients (mean age 31.0 ± 11.3 years) who underwent MR arthrography, including dGEMRIC analysis within three months prior to safe surgical hip dislocation, Bittersohl *et al*.[16] noted a moderate correlation between standard MRI and intraoperative data ($r = 0.535$; $P < 0.001$) but a weak correlation between dGEMRIC analysis and such data ($r = 0.114$; $P < 0.126$). However, regions with intraoperative cartilage damage had significantly lower $T1_{Gd}$ values compared with normal cartilage (453.1 ± 113.6 ms vs. 510.1 ± 141.2 ms; $P = 0.003$). In contrast to our study, using a 1.5-T scanner, acetabular and (in FAI patients) presumably healthy femoral head cartilage were analyzed as one ROI, which may have biased the dGEMRIC analysis and correlation with the intraoperative acetabular cartilage status in that study.

Bulat *et al*.[19] noted a correlation of between 0.14 and -0.63 for dGEMRIC analysis and intraoperative cartilage condition. Their retrospective study on 45 FAI patients (47 hips, mean age 29 ± 11 years) included dGEMRIC analysis

Table 2. Sensitivity, Specificity, Positive Predictive Value, and Negative Predictive Value for Cartilage Status Assessment by Means of T2*-Mapping Using Intraoperative Data as a Reference.

				Arthroscopy	
Region				Healthy	Damaged
Anterior Anterosuperior	T2*	Healthy	*n*	26	3
			Negative predictive value	83.9%	
			Specificity	89.7%	
		Damaged	*n*	5	29
			Positive predictive value		90.6%
			Sensitivity		85.3%
Superoanterior Superior Superoposterior	T2*	Healthy	*n*	19	14
			Negative predictive value	65.5%	
			Specificity	57.6%	
		Damaged	*n*	10	59
			Positive predictive value		80.8%
			Sensitivity		85.5%
Posterosuperior Posterior	T2*	Healthy	*n*	22	15
			Negative predictive value	73.3%	
			Specificity	59.9%	
		Damaged	*n*	8	28
			Positive predictive value		65.1%
			Sensitivity		77.8%
Total	T2*	Healthy	*n*	67	32
			Negative predictive value	74.4%	
			Specificity	67.7%	
		Damaged	n	23	116
			Positive predictive value		78.4%
			Sensitivity		83.5%

in six different regions in central and peripheral acetabular cartilage from anterior to posterior that were obtained in radial reformats and in planar $T1_{Gd}$ maps. Although planar $T1_{Gd}$ maps revealed slightly faster cartilage analysis (average of 55 seconds = 27% faster cartilage evaluation compared with radial image analysis), no map-dependent effect on correlation strengths was noted in that study. With a moderate correlation in superior cartilage regions ($r = -0.31$ to $r = -0.63$), cartilage analysis in the anterior aspect of the hip joint was poor to moderate ($r = -0.03$ to $r = -0.35$). This is in contrast to our study, in which we observed a good correlation to the surgical findings in the anterior region, and, on the other hand, a not so good correlation in the superior and the posterior region. Regional differences in the GAG distribution among central weightbearing and peripheral cartilage regions with an increased GAG content toward the superior and central regions (correlates with higher $T1_{Gd}$ values) might account for some of the region-dependent variation in this context. However, detailed information on the surgical procedure (open vs. arthroscopically), sensitivity and specificity were not provided in this study.

To overcome limitations in the dGEMRIC interpretation due to technical alterations and inter- and intra-subject variances in GAG distribution and gadolinium uptake, Lattanzi *et al.*[17] proposed a technique in which standard scores (z) were calculated from $T1_{Gd}$ values that were obtained from the mean and the standard deviation of $T1_{Gd}$ of presumably healthy femoral head cartilage. Compared with arthroscopic data, this approach showed better diagnostic ability (sensitivity, specificity, and accuracy were 88%, 51%, and 62%, respectively, when assuming $z = -2$ as the threshold between normal and degenerated cartilage) to identify cartilage damage than applying threshold values (500 ms) or morphological cartilage grading. This study included only 10 patients and (following femoral head cartilage assessment for z-score calculation) acetabular and femoral head cartilage were evaluated as one entity. In our study, sensitivity and specificity were 83.5% and 67.7%, respectively, in total (85.3% and 89.7% for subregion anterior, anterosuperior, 85.5% and 57.6% for subregion superoanterior to superoposterior, and 77.8% and 59.5% for subregion posterosuperior to posterior, respectively). Accuracy was not measured in our study. These results are roughly similar although considerable differences (example radial vs. coronar planes, 1,5 T vs. 3 T MR scanners, analyzing acetabular and femoral head cartilage as one ROI in

Table 3. Synopsis of Studies Performed as a Comparative Analysis of Magnetic Resonance Imaging (MRI) and Intraoperative Data Assessing the Reliability of Biochemically Sensitive MRI in the Evaluation of Hip Joint Cartilage.

Study	Cohort	Methodology	Fiel -Strength (Tesla)	Selected Sequences /Resolution (mm)	Results	Further Key Findings and Limitations
Bittersohl *et al.* (2011)[16] Correlation dGEMRIC, open hip surgery Interval MRA/OP: >3 months	16 FAI patients Mean age: 31 years (range 17-57 years)	ROI: Acetabulofemoral cartilage ant., ant.-sup., sup.-ant., sup., sup.-post., post.-sup., post. peripheral, central $T1_{Gd}$ threshold 500 ms	1.5	Dual FA 3D GRE VIBE (coronal oblique) 0.78 × 0.78 × 0.78	Correlation dGEMRIC/Surgery k = 0.114 (P = 0.126) Correlation MRI / Surgery k = 0.535 (P < 0.001) SE (peripheral/central): 50% / 37% SP (peripheral/central): 60% / 76%	$T1_{Gd}$ evident damage: 453 ms $T1_{Gd}$ no evident damage: 510 ms P = 0.003 Small study group Femoral and acetabular ROI combined
Lattanzi *et al.* (2012)[17] Correlation dGEMRIC, arthroscopy Interval MRI OP: <4 months	10 FAI patients Mean age: 19.9 years (range 14-32 years)	ROI: acetabulum ant.-sup., sup., post.-sup. central femoral head (=control) Cartilage damage: Mod. Outerbridge classification + grade 5 = delaminated cartilage dGEMRIC: absolute $T1_{Gd}$ values & $z=\frac{\left(T1_{Gd}-T1_{Gd\ femoral}\right)}{SD\ T1_{Gd\ femoral}}$ $T1_{Gd}$ threshold 500 ms dGEMRIC: standardized values (z) z threshold < −1, < −2, < −3	1.5	T1 spin echo fat suppression 0.4 × 0.4 × 3 dGEMRIC 0.3 × 0.3 × 4	dGEMRIC z < −2 / dGEMRIC $T1_{Gd}$ < 500 ms / Outerbridge SE (%): 88 / 47 / 47 SP (%): 51 / 58 / 79 ACC (%): 62 / 55 / 70 62 55 PPV (%): 42 / 31 / 47 NPV (%): 92 / 74 / 79	Small study group Retrospective study Femoral and acetabular ROI combined Selected group of patients Central femoral head cartilage may not be healthy in other pathologies
Ellermann *et al.* (2014)[18] Correlation T2*-mapping, arthroscopy Interval MRA / OP: 3 months	26 FAI patients (28 hips) Mean age: 28.2 years (range 12-53 years)	ROI: acetabulum ant.-sup.: 5 ROIs (superficial and deep zone) acetabulum post.-med. (=control): 2 ROIs (superficial and deep zone) Cartilage damage: Mod. Beck scale Cartilage segmentation and generation of T2* surface map	3	T2* GRE fat saturated (sagittal) 0.52 × 0.52 × 3 interpolated: 0.26 × 0.26 × 3	Beck Grade / T2* values: Bulk / Superficial Zone / Deep Zone 1: 35 / 40 / 31 2: 21 / 24 / 17 3 + 4: 20 / 23 / 17 5 + 6: 17 / 18 / 16	Interobserver reliability: 0.88 Differentiation between 1 and higher grades No differentiation between higher grades T2* variation due to orientation to B_0 (magic angle) max. 2% Retrospective study
Bulat *et al.* (2015)[19] Correlation dGEMRIC, hip surgery (surgery n/s) Interval MRA / OP: <6 months	45 FAI patients (47 hips) intraoperative evaluation in 44 hips Mean age: 29 years (range: n/s)	ROI: acetabulum ant.-post., ant.-cor., sup.-post., sup.-cor., post.-post., post.-cor. Cartilage damage (MRI): Mod. Outerbridge classification Cartilage damage (surgery): Mod. Beck scale dGEMRIC: Radial and planar $T1_{Gd}$-maps	1.5	3-dimensional VFA VIBE (dGEMRIC) 0.83 × 0.83 × 2 TrueFISP 0.63 × 0.63 × 0.63 sagittal, oblique = source 18 radial reformats (10° interval)	Planar $T1_{Gd}$ correlation (range) with Beck scale specific to subregions Outerbridge: 0.16-0.52 dGEMRIC: 0.14 to −0.57 No planar map-dependent effect on correlation strength	Faster cartilage evaluation with planar map (av. 55 s = 27%) Intraobserver agreement: Beck: κ = 0.80 Outerbridge: κ = 0.64 dGEMRIC: κ = 0.89 Retrospective study SE, SP not reported

ACC = accuracy; dGEMRIC = delayed gadolinium-enhanced magnetic resonance imaging of cartilage; FA = flip angle; FISP = fast imaging with steady-state precession; GRE = gradient echo; MRA = magnetic resonance arthrography; NPV = negative predictive value; PPV = positive predictive value; ROI = region of interest; SE = sensitivity; SP = specificity; VFA = variable flip angle; VIBE = volumetric interpolated breathhold examination.

the study of Lattanzi *et al*.[17]) in the methodology need to be considered.

With recent concerns and debates related to the safety of gadolinium involving MR methodologies,[20,21] noncontrast MRI for biochemical cartilage assessment has received increasing attention. Including 28 hips in FAI patients (mean age 28.2 years, range 12-53 years), Ellermann *et al*.[18] correlated T2*-mapping with arthroscopic cartilage assessment (according to a modified Beck score). Their group reported significantly lower T2* values in areas with intraoperative cartilage damage compared with areas with normal appearing cartilage (T2* = 20.7 ± 6.0 ms vs. 35.3 ± 7.0 ms; $P < 0.001$). Although this study group included only patients with Tönnis grade 0 or Tönnis grade 1 on plain radiographs, 68% of the intraoperatively documented cartilage areas had apparent cartilage damage. This again highlights the limitations of plain radiography in identifying and picking up cartilage degeneration in early stages. Using receiver operating characteristic curve analysis, the authors proposed a T2* threshold value of 28 ms to differentiate healthy from damaged cartilage (91% true-positive and 13% false-positive rate to differentiate Beck score 1 from all other cartilages). However, given the previously published heterogeneity of T2* values in different cohorts of asymptomatic volunteers owing to differences in cartilage composition, cartilage thickness, and the magic angle effect, we believe it is crucial to thoroughly scrutinize T2* in each case, especially when a distinctive cartilage disease pattern is present. Our T2* values in normal appearing cartilage were lower (mean T2* = 25.6 ± 4.7 ms vs. 35.3 ± 7.0 ms) while the mean T2* values in damaged cartilage were similar (mean T2* = 19.9 ± 4.5 ms vs. 20.7 ± 6.0 ms). A potential explanation for this discrepancy is the different average age of both study cohorts. We included patients with a mean age of 35.6 ± 12.8 years while the average patient age in the study by Ellermann *et al*.[18] was 28.2 years. Therefore, age-dependent differences of T2* relaxation times despite morphologically normal appearing cartilage have to be considered in these patient groups with a prearthritic hip condition.

Our study has a few limitations. This study cohort of 29 patients is small, and the retrospective study design, including possible errors of documentation for pre-, intra-, and postoperative assessment have to be considered. There may also have been some individual variations in reading the intra-operative damage due to human error. Also, the study-period was long in which changes to the background information and the documentation may have some effect on its scientific value. On the other hand, hip arthroscopy was performed by orthopedic surgeons specialized in hip arthroscopy with similar technique, and the MR imaging protocol, including hardware and the T2* assessment was not changed at all within this study period. Therefore, we believe this time-window bias is likely slight and not contradicting our conclusion. Furthermore, the possible progressive cartilage degeneration between the time points of MRI and surgery that might have biased our results should be considered, although it remains entirely unclear how and when the changes in cartilage damage become apparent in a hip joint with symptomatic FAI. For this reason, we believe that keeping this interval within 6 months is reasonable. One limitation was the lack of a diagnostic gold standard in the form of specimens and histological analysis. Therefore, knowing the sensitivity of T2* mapping to changes in water content and collagen fiber network, which may occur without macroscopically visible change, it is not surprising that the correlation between T2*-mapping and arthroscopic findings was only moderate. Finally, the T2* measurement using ROI analysis obtains mean values that represent the entire encircled area. Consequently, minor but remarkable changes may have been underestimated.

In summary, T2*-mapping reliably assisted in the assessment of acetabular cartilage in patients with symptomatic FAI in which the correlation with intraoperative findings revealed promising results for sensitivity, specificity, PPV, and NPV. Our results certainly emphasize the value of T2*-mapping for the diagnosis of hip joint cartilage pathologies, including FAI and other prearthritic hip conditions.

Acknowledgments and Funding

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Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical Approval

This study was approved by the local ethics committee (Study-ID: 5574R).

Informed Consent

Written informed consent was obtained from all subjects before the study.

Trial Registration

Not applicable.

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Elite Rowers Demonstrate Consistent Patterns of Hip Cartilage Damage Compared With Matched Controls: A T2* Mapping Study

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Abstract

Background Rowing exposes the femoral head and acetabulum to high levels of repetitive abutment motion and axial loading that may put elite athletes at an increased risk for developing early hip osteoarthritis.

Questions/purposes Do elite rowers demonstrate characteristic hip cartilage lesions on T2* MRI sequences compared with asymptomatic individuals who do not row?

Methods This study included 20 asymptomatic rowers (mean age, 23 ± 3 years; nine females, 11 males) who had a minimum of 5 years of intensive (≥ 12 hours/week) training. The recruiting of the rowers took place from the central German federal rowing base, which has inherent intense training and selection requirements to declare these athletes as "elite rowers." We investigated one hip per study participant. MRI was performed on a 3-T scanner. The protocol included standard sequences, a double-echo steady-state sequence, and a multiecho data image combination sequence with inline T2* calculation (= the decay of transverse magnetization arising from molecular interactions [T2] and inhomogeneities in the magnetic field resulting from tissue susceptibility-induced field distortions and variations in the magnet itself), which detects changes in water content and the disruption of collagen structure. Although extrinsic and intrinsic influences on the T2* values including diurnal effects, MR technic-derived variations, and anatomic-related regional disparities need to be taken into account, low T2* values well below 20 ms indicate cartilage degeneration. Cartilage was morphologically analyzed in the anterior, anterosuperior, superoanterior, superior, superoposterior, posterosuperior, and posterior regions of the hip and graded as follows: Grade 0 = normal; Grade 1 = signal changes; Grade 2 = cartilage abrasion; Grade 3 = cartilage loss. Labrum was classified as follows: Grade 0 = normal; Grade 1 = partial tear; Grade 2 = full-thickness tear; Grade 3 = labrum degeneration. The T2* measurement was done through a region of interest

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Each author certifies that his or her institution approved the human protocol for this investigation, that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participation in the study was obtained. This study was performed at the University Hospital of Düsseldorf, Düsseldorf, Germany.

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analysis. For reliability assessment, morphologic evaluation and T2* measurement were performed by two observers while one observer repeated his analysis with a time interval > 2 weeks. Intra- and interobserver reliability was determined using κ analysis and intraclass correlation coefficients. Control T2* data were derived from a previous study on 15 hips in 15 asymptomatic volunteers of similar ages (seven males and eight females) who were not competitive rowers with similar MR hardware and imaging sequences.

Results Compared with the control group of asymptomatic volunteers who were not competitive rowers, we noted a high level of labrum and cartilage degeneration in the cohort of elite rowers. In the group of elite rowers, cartilage degeneration was noted in all hips. Regarding the acetabular cartilage, 271 zones could be evaluated. Of those, 44% (120 of 271) were graded normal, 6% (15 of 271) revealed signal alteration, 45% (122 of 271) demonstrated cartilage abrasion, and 5% (14 of 271) were noted to have full-thickness cartilage loss. Morphologic cartilage degeneration in the femoral head was less frequent. T2* values were lower than the control hips in all zones except for the posterior central acetabular zone (global T2* acetabular: 20 ± 6 ms, range, 9–36 ms, 95% confidence interval [CI], 19–21 ms versus 25 ± 5 ms, range, 14–44 ms, 95% CI, 24–25 ms, $p < 0.001$; global T2* femoral: 23 ± 7 ms, range, 9–38 ms, 95% CI, 22–24 ms versus 27 ± 5 ms, range, 17–45 ms, 95% CI, 26–28 ms, $p < 0.001$). The difference in T2* between the two study groups was superior in the peripheral zone of the anterosuperior region (16 ± 3 ms; range, 10–22 ms, 95% CI, 15–18 ms versus 26 ms ± 5 ms, range, 18–38 ms, 95% CI, 24–29 ms, $p < 0.001$).

Conclusions We found signs of hip cartilage degeneration to a much greater degree in elite rowers than in asymptomatic controls. Although causation cannot be inferred, this is concerning, and future investigations including controlled longitudinal studies both on elite and nonelite athletes with sufficient cohort size are warranted to clarify our findings.

Level of Evidence Level III, therapeutic study.

Introduction

Modern young athletes are pushing themselves harder and harder in competitive sports, sometimes at the cost of musculoskeletal injuries or increasing wear and tear. Different sports expose these athletes to different and perhaps unique patterns of joint or musculoskeletal injury. Much is known about hip injuries in sports like basketball, golf, ice hockey, and others [3]. Rowing is a common sport and known to cause its own set of musculoskeletal injuries, although hip involvement has not been specifically studied.

Rowing involves repeated cyclical axial loading with notable flexion, both motions capable of potentially causing hip cartilage or labral damage in the long run and possibly causing a unique characteristic pattern of damage. Radial or three-dimensional (3-D) cartilage-specific MRI sequences with high resolution to accurately assess the spatial morphology and joint structures such as the labrum and articular cartilage have proven to be reliable [7, 9, 12]. Biochemical-sensitive MRI techniques such as delayed gadolinium-enhanced MRI (dGEMRIC) [17], T2 mapping [15], T1rho imaging [11], chemical exchange saturation transfer imaging of glycosaminoglycan [13], and diffusion-weighted sequences [1] may be added to the protocol because they have the potential to detect early changes in the articular cartilage matrix. T2* mapping is a noncontrast MRI technique that is sensitive to water content and collagen anisotropy; it detects changes in water content and the disruption of collagen structure in cartilage damage and also allows for high-resolution isotropic 3-D imaging on standard clinical MRI systems [6].

We therefore sought to determine whether elite rowers demonstrate characteristic hip cartilage lesions on T2* MRI sequences compared with asymptomatic individuals who do not row. We hypothesized that there would be a pattern of cartilage degeneration involving the anterolateral region and axial loading comprising the superior region based on the specific demands on the hip in this sporting activity. We performed an observational, cross-sectional study in elite rowers with a descriptive and analytical assessment to prove our hypotheses.

Patients and Methods

The procedures in this study adhered to the ethical standards of the institutional review committee on human research. Each volunteer signed a written informed consent, and we obtained ethical approval from the local ethics committee.

Study Population

This study was performed on 20 selected elite rowers (nine females, 11 males; 15 sweep-oar rowers, five sculling rowers). Recruitment took place in the central German federal rowing base. After agreement of the trainers and the supervising physicians was obtained, the elite athletes from the under (U-)23 and senior level competing for Germany were asked for interest in the study. Of the 20 U-23 athletes and 32 senior (≥ 23 years old) athletes, 30 elite athletes volunteered. Of these, in turn, only asymptomatic (n = 26) participants were selected. Finally, nine female and 11 male subjects were selected to provide gender balance.

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Seven of the women belong to the U-23 and two to the senior squad. Of the men, five compete for the U-23 team, whereas six male rowers compete for the senior team. The mean age was 23 ± 3 years. Age when high-level rowing began was 15 ± 2 years; the mean years of high-level rowing was 8 ± 3 years. All volunteers underwent a thorough physical examination conducted before MRI by an orthopaedic consultant with more than 5 years of experience in dedicated hip surgery. Briefly summarized, this included an investigation of pain, discomfort, tenderness, ROM, and the anterior femoroacetabular impingement test (groin pain provoked by hip flexion, internal rotation, and adduction). In the 20 rowers, 10 right and 10 left hips (one from each rower) were further investigated. The first five women and five men each had their right hip examined. In the remaining rowers, the left hip was scanned.

Foundation of T2 and T2*

Biochemical-sensitive MRI techniques such as T2 and T2* mapping have the potential to detect early changes in the articular cartilage matrix. Although there are similarities between T2 and T2*, the distinction between T2 and T2* relaxation is essential [6]. T2 is defined as a time constant for the decay of transverse magnetization (signal decrease caused by dephasing of the spins) arising from interactions between the spinning water atoms (spin-spin-relaxation). T2* refers to the loss of transverse magnetization arising both from spin-spin-relaxation and from local field inhomogeneities, which may be related to imperfections in the scanner magnets themselves and local magnetic susceptibility effects inside the patient. The typically lower spectrum of T2* values reflects the additional contribution of these coherent dephasing effects. In spin-echo techniques, 180° radiofrequency pulses are applied to cancel the local field inhomogeneities (not the interactions between the spinning water atoms) by reversing and rephasing the spins. T2* relaxation is noted only with gradient-echo imaging. Both T2 and T2* are sensitive to water content and the interaction between water molecules and collagen fibers in which a high T2 or T2* reflects high water content and superior water molecule mobility. This explains the decrease in T2 and T2* in deep cartilage zones where the vertically aligned collagen fiber orientation and high proteoglycan content are believed to cause water molecule restriction. The advantage of the spin-echo-based T2 mapping technique is the insensitivity to local field inhomogeneities (that may be substantial in the presence of postsurgery debris). Disadvantages include the long acquisition time that increases the risk for motion artifacts and prevents high-resolution isotropic 3-D MRI at tolerable measurement time. The T2* mapping technique has its advantages here because it offers fast imaging with the prospect of high image resolution, isotropic 3-D biochemically sensitive cartilage evaluation. These gains are of particular importance in the hip with thin, narrow, and spherically arranged cartilage surfaces.

The control T2* data for this study were derived from a previous study in which T2* relaxation measurements in the hip cartilage of asymptomatic volunteers were obtained in various age cohorts using similar MR hardware and imaging sequences [8]. To maximize the comparability of the study cohorts, we used the subgroup between the ages of 20 and 30 years. This group included 15 healthy individuals with no history of hip surgery and no hip complaints (eight females, seven males; mean age, 25.9 ± 2.3 years; seven right and eight left hips).

MRI

The MRI was performed on a 3-T machine (Magnetom Trio; Siemens Medical Solutions, Erlangen, Germany) with the volunteer in the supine position and a four-channel phased-array, flex surface coil placed around the hip being examined. The leg was stabilized with cushions and elastic straps to increase the comfort of the examination and to minimize movement artifacts.

The study MRI protocol included localizer images; standard pulse sequences with T1-, T2-, and PD-weighting in various planes; an isotropic high-resolution 3-D double-echo steady-state (DESS) sequence for morphologic cartilage assessment; and a 3-D gradient-echo high-resolution multiecho data image combination sequence with similar image resolution, six consecutive echoes, and inline T2* decay calculation according to a nonlinear least square fitting routine (Table 1).

Postprocessing and Cartilage Assessment

The 3-D volumes of the DESS and the T2* maps were processed on a Leonardo workstation (Siemens Medical Solutions). We used multiplanar reconstruction software to reformat seven 2-mm thick radial images around the femoral neck axis that depicted the anterior, anterosuperior, superoanterior, superior, superoposterior, posterosuperior, and posterior regions of the hip (Fig. 1). This postprocessing was done by an orthopaedic surgeon (BB) with > 11 years of experience in generating radial scans from a 3-D data set to depict the hip structures such as the labrum and articular cartilage in a perpendicular fashion with minimal distortion.

We analyzed acetabular and femoral cartilage as well as the labrum in these regions, whereas the acetabular and opposite femoral cartilage layers between the acetabular fossa and the chondrolabral junction were bisected into a peripheral and central zone.

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Table 1. MRI protocol and imaging parameters utilized in this study

Imaging parameters	T1 TSE transverse	PD TSE FS transverse	STIR paracoronal	3-D DESS water excitation	3-D MEDIC T2* mapping
Repetition time (ms)	650	3400	5500	14.75	38
Echo time (ms)	9.5	11	32	5.03	4.62, 9.41, 15.28, 21.15, 27.02, 32.89
Flip angle (°)	130	150	120	25	25
Number of excitations	3	2	2	1	1
Field of view (mm^2)	200	180	260	192	192
Number of slices	33	40	20	176	144
Slice thickness (mm)	3	3.2	3	0.6	0.6
In-plane resolution (mm)	0.5 x 0.5	0.5 x 0.5	0.8 x 0.8	0.6 x 0.6	0.6 x 0.6
Bandwidth (Hz/pixel)	221	176	200	260	260
Acquisition time (minutes)	3:10	4:47	3:36	13:17	13:29

Partial Fourier acquisition (6/8 phase, 6/8 slice) combined with parallel imaging (GRAPPA, acceleration factor 2) was applied for the MEDIC sequence to achieve shorter imaging times; TSE = turbo spin echo; PD = proton density; FS = fat-saturated; STIR = short tau inversion recovery; 3-D = three-dimensional; DESS = double-echo steady-state; MEDIC = multiecho data image combination.

Cartilage status was graded as follows: Grade 0 = normal; Grade 1 = signal changes; Grade 2 = cartilage abrasion; or Grade 3 = cartilage loss. The labrum was classified as Grade 0 (normal, triangular-shaped); Grade 1 (partial tear); Grade 2 (full-thickness tear); or Grade 3 (degenerated, hypertrophied, and deformed labrum). In every instance, the worst possible grade was chosen if regions/zones revealed multiple features of cartilage or labrum degeneration. Cartilage and labrum assessment was performed by one orthopaedic surgeon (BB; reader 1) who is an expert in hip MRI with approximately 12 years of clinical experience in musculoskeletal radiology and one radiologist (GA; reader 2) who has 15 years of clinical experience in musculoskeletal radiology. Reader 1 repeated the grading with a time interval of at least 2 weeks to minimize recall effects. In every hip, the grading was performed independently. The T2* measurement was done through a region of interest (ROI) analysis where the ROI fields were placed in the four zones (peripheral acetabular cartilage, central acetabular cartilage, peripheral femoral head cartilage, and central femoral head cartilage) of each region using the corresponding DESS reformats as a guide to ensure that the ROI placement is within cartilage boundaries (Fig. 2). For the ROI placement, the DESS and corresponding T2* maps were loaded into a two-screen layout image area. DESS and the corresponding T2* image were displayed large enough with optimal image contrast and brightness to see details. Hip cartilage was then delineated on the DESS image using a freehand drawing tool. By selecting both images, the ROI drawn in the DESS image was automatically transferred to the T2* map, which reflects in some ways a copied and pasted approach. Afterward, the ROI outlines were reevaluated in the T2* map and, if necessary, only minimally shifted to correct for any ROI offset. The T2* measurement was done independently by one radiologist (CS; reader 1) and by one orthopaedic surgeon (CZ; reader 2) who had 6 years (reader 1) and 10 years (reader 2), respectively, of experience evaluating biochemical cartilage MRIs. Reader 1 repeated the T2* measurement with a sufficient time interval (minimum 2 weeks) between its first and its second analysis. Both T2* evaluators were blinded to the cartilage grades given by the other evaluators. Notably, T2* values well below 20 ms indicate cartilage degeneration [7]. A total of 560 cartilage zones (20 hips, seven regions, two zones per region, acetabular and femoral cartilage) and 140 labra (20 hips, seven regions) were assessed. In 19 zones, morphologic cartilage evaluation was abandoned. Either cartilage was absent in this zone (n = 13) or was not evaluable (n = 6) in a reliable fashion as a result of poor image quality. Therefore, 541 cartilage zones (97%) underwent morphologic grading. Two of 140 labra were not evaluable as a result of image quality issues, leaving 138 labra (99%) for further analysis. Kappa analysis was used to evaluate the intra- and interreader agreement on the cartilage and labrum grading scales. Intra- and interobserver agreement for the cartilage grading was high, revealing κ values ranging from 0.906 to 0.937 ($p < 0.001$). Intra- ($\kappa = 0.886$; $p < 0.001$) and interreader ($\kappa = 0.765$; $p < 0.001$) agreement for the labrum assessment was also high. T2* measurements could not be performed in a total of 72 cartilage zones because cartilage was absent (n = 13), inaccurate delineation of cartilage (n = 25) either as a result of poor tissue contrast or partial-volume effect related to insufficient in-plane resolution in this specific zone of the hip, imaging artifacts (n = 14),

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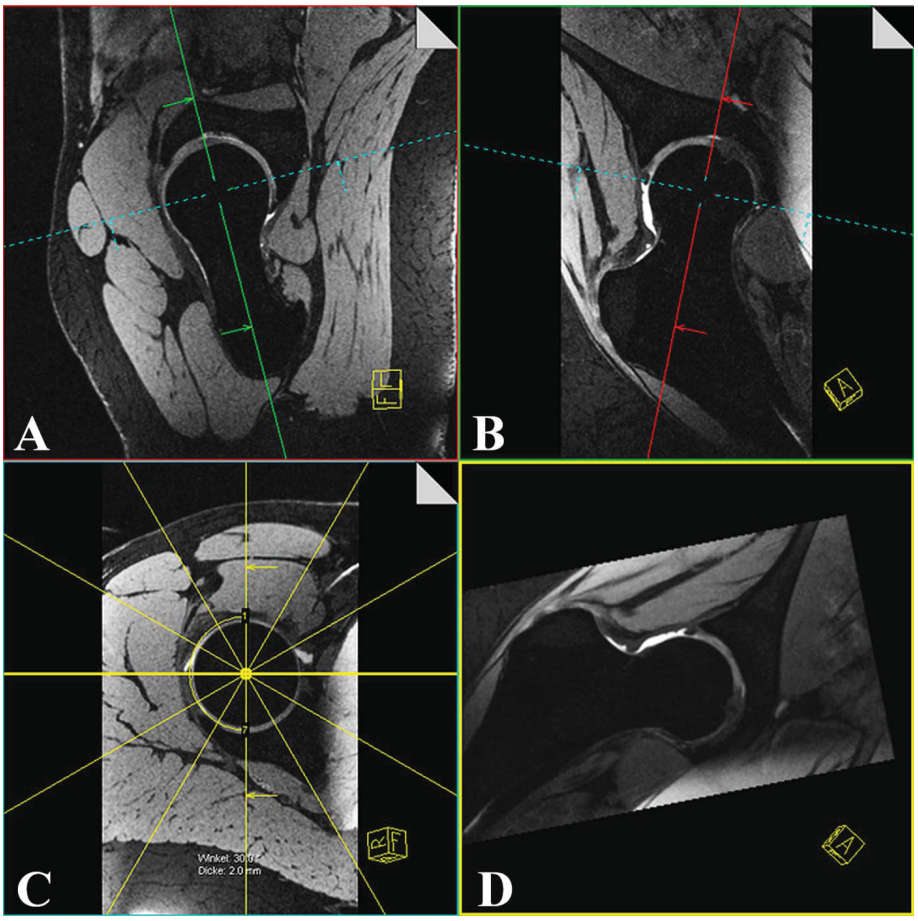

Fig. 1 A-D Multiplanar reconstruction (MPR) allows images to be created in any desired plane. (**A-B**) MPR was performed to generate a plane perpendicular to the femoral neck axis and (**C**) in the center of the femoral head. On this plane, radial reformats with an interval of 30° were generated. (**D**) This image depicts the superior region, which is the highlighted yellow line shown in C.

severe cartilage abrasion (n = 2), or cartilage loss (n = 18). Therefore, 488 T2* values (87%) underwent statistical assessment. Intraclass correlation coefficient (ICC) analysis with pairwise comparison and absolute agreement definition for reliability testing indicated high intra- and interreader agreement regarding the T2* measurement in acetabular (ICC, 0.906 and 0.915; $p < 0.001$) and femoral head (ICC, 0.937 and 0.927; $p < 0.001$) cartilage.

Statistical Analysis

The collected data were entered in an Excel spreadsheet (Version 14, Microsoft Office Professional; Microsoft Corp, Redmond, WA, USA) and later transferred to SPSS software (Version 25; IBM Corp, Armonk, NY, USA) by a biostatistician (SU) who conducted the statistical analysis in this study. The statistical analysis comprised descriptive data including mean values ± SD, range, 95% confidence intervals (CIs), and statistical tests such as κ analysis to evaluate the intra- and interreader agreement on ordinal (cartilage and labrum grading) scales and an ICC analysis with pairwise comparison and absolute agreement definition for reliability testing of quantitative measurements (T2* assessment). For the evaluation of regional differences on the T2* measurements and for group comparison (rower versus control cohort), a univariate analysis of variance with Bonferroni adjustment for multiple comparisons was conducted. Regarding the comparison with the control group, the mean values of the corresponding hip region were used as baseline values to compensate for regional differences in the T2* values possibly resulting from the magic angle effect [16], which promotes an increase in T2/T2* relaxation when collagen fibers are oriented 54.7° to the main magnetic field and possible regional differences in collagen density, fiber orientation, and water content. Probability values < 0.05 were considered to be statistically significant.

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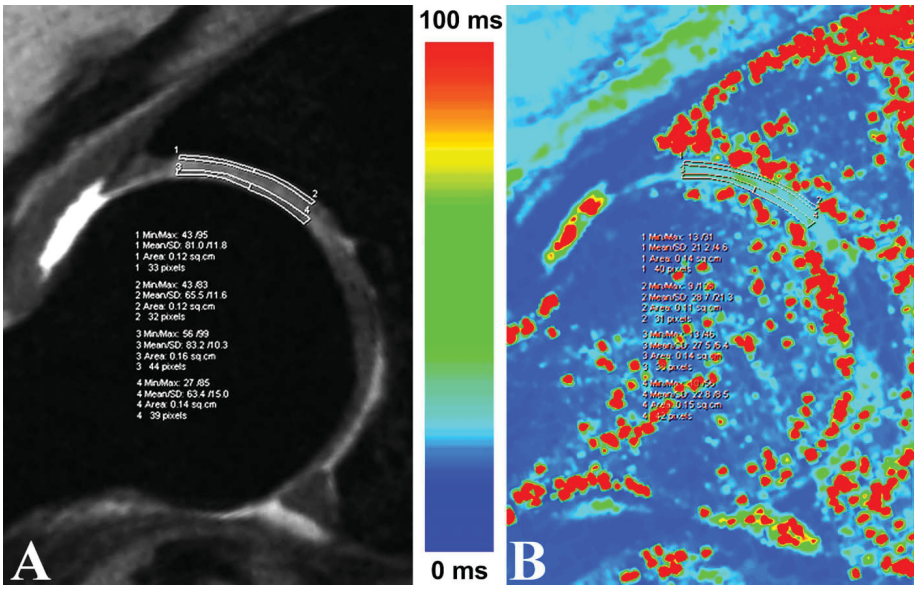

Fig. 2 A-B ROI analysis in central and peripheral acetabular and femoral head cartilage is shown. (**A**) The corresponding DESS image served as a guide to ensure ROI placement within cartilage boundaries. (**B**) T2* values are illustrated in a color scale whereby green reflects T2* values observed in healthy cartilage.

Results

Nineteen of 20 rowers' hips exhibited labral pathology. Of the 138 evaluated labral regions, 86 of 138 (62%) were graded normal, 23 of 138 (17%) were seen with a partial tear, three of 138 (2%) revealed a complete tear, and labrum degeneration was noted in 26 regions (approximately 19%). Therefore, 52 of 138 regions (approximately 38%) revealed some form of labrum damage.

We noted some grade of cartilage degeneration in all of the rowers' hips. Regarding the acetabular cartilage, 120 of 271 zones (44%) were graded normal, 15 zones (6%) revealed signal alteration, 122 zones (45%) demonstrated some degree of abrasion, and 14 zones (5%) were noted to have a full-thickness cartilage loss; this means that 56% of all cartilage zones revealed some degree of cartilage damage. With femoral head cartilage, morphologic cartilage degeneration was less frequent; 193 of 270 zones (72%) had normal-appearing cartilage, nine zones (3%) had signal alteration, 67 zones (25%) demonstrated cartilage abrasion, and only one zone (0.4%) had cartilage loss.

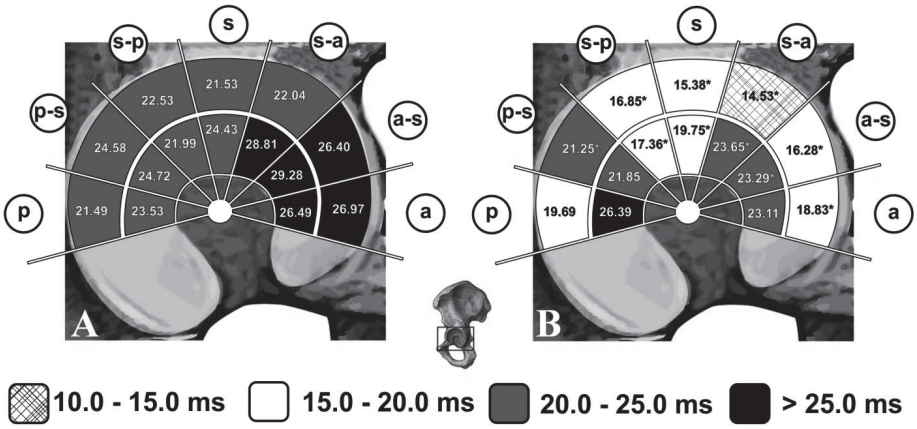

Fig. 3 A-B Regional and zonal distribution of mean T2* values in acetabular cartilage of healthy controls (**A**) and elite rowers (**B**) is shown. In the study cohort, lower T2* values were noted in almost all zones. A = anterior; A-S = anterosuperior; S-A = superoanterior; S = superior; S-P = superoposterior; P-S = posterosuperior; P = posterior. *p < 0.05.

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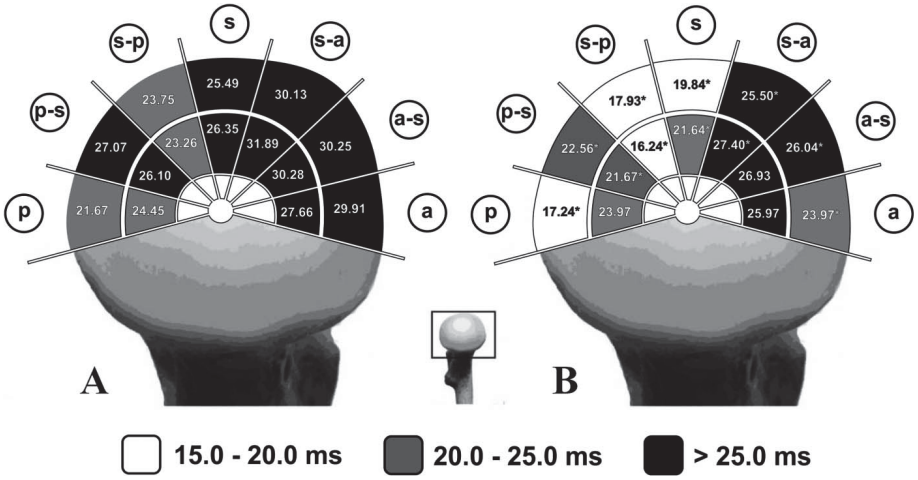

Fig. 4 A-B Regional and zonal distribution of mean T2* values in femoral head cartilage of healthy controls (**A**) and elite rowers (**B**) is shown. In the study cohort, lower T2* values were noted in all zones. A = anterior; A-S = anterosuperior; S-A = superoanterior; S = superior; S-P = superoposterior; P-S = posterosuperior; P = posterior. *p < 0.05.

The T2* values in acetabular (Fig. 3) and femoral head cartilage (Fig. 4) were lower than those in the control cohort. Differences were noted in 10 of 14 zones on the acetabulum (Table 2) and 11 of 14 zones on the femoral head (Table 3). The comparison between the peripheral and central zones revealed lower values in the acetabular peripheral zones in all regions except for the superoposterior and posterosuperior regions (Table 4). This pattern of lower cartilage T2* values in the peripheral zone was not noted in the femoral head except for the posterior region (Table 5). The acetabular T2* values in the posterior (23 ± 7 ms; range, 14–35 ms; 95% CI, 21–26 ms) and posterosuperior (22 ± 6 ms; range, 12–34 ms; 95% CI, 20–24 ms) regions were higher than those in the superior (18 ± 5 ms; range, 9–27 ms; 95% CI, 16–19 ms; p values, 0.002 and 0.030) and the superoposterior (17 ± 6 ms; range, 9–35 ms; 95% CI, 15–19 ms; p values, 0.001 and 0.009) regions. Within femoral head cartilage, we saw higher T2* values in the anterosuperior (27 ± 7 ms; range, 10–38 ms; 95% CI, 24–29 ms) and superoanterior (26 ± 6 ms; range, 12–37 ms; 95% CI, 25–28 ms) regions compared with the superior (21 ± 5 ms; range, 10–29 ms; 95% CI, 19–22 ms; p values < 0.001), superoposterior (17 ± 5 ms; range, 10–29 ms; 95% CI, 16–19 ms; p values < 0.001), posterosuperior (22 ± 6 ms; range, 9–34 ms; 95% CI, 20–24 ms; p values, 0.023 and 0.024), and posterior (21 ± 6 ms; range, 13–38 ms; 95% CI, 19–23 ms; p values < 0.001) regions. However, this pattern, albeit with overall higher T2* values, was also apparent in the control cohort.

Discussion

Damage to hip cartilage and labrum emanating from high levels of repetitive abutment flexion motion and axial loading can lead to a painful hip, restricted motion, and progressive cartilage damage that can occur in childhood and/or adulthood [2, 5]. The present study was performed to investigate whether a young cohort of elite rowers demonstrates a characteristic pattern of hip cartilage degeneration on standard and T2* MRI sequences compared with asymptomatic individuals who do not row. We noted a high level of labrum and cartilage degeneration, which was further underlined by significantly reduced T2* values in almost all joint regions. The T2* decrease was particularly prominent from anterior to superior in the peripheral zones (Fig. 5), probably reflecting the abutment at the acetabular rim during excessive flexion, and at the superior sector centrally and peripherally, consistent with progressive axial loading that likely begins as soon as the rower begins to apply power to the blade by pushing with their legs.

This study has limitations. Our study cohort included only athletes who were elite rowers. Therefore, our observations may not necessarily relate to recreational rowers. Further studies on nonelite athletes are needed to clarify whether this form of degeneration also occurs in recreational/nonelite rowers. The generalizability is further limited even for elite rowers because the numbers are still somewhat limited, leading to statistical power issues. Intraoperative validation was not available in our study and was a limitation. Nevertheless, reliability of cartilage and labrum assessment with the DESS and a T2* mapping technique has been confirmed in other studies [4, 7]. Although the cartilage was evaluated by morphologic grading and quantitative T2* relaxation time mapping, one of the limitations is comparison of the T2* values to a previously performed study on healthy volunteers likely because interfering variables that include changes in the MRI system over time cannot be entirely controlled. However, we

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Table 2. T2* values in milliseconds in various regions and zones of acetabular cartilage in study and control groups*

Region	Zone	Cohort	Number	Mean	SD	95% CI	p value
Anterior	Peripheral	Rower	15	18.83	5.05	16.27-21.38	**< 0.001**
		Normal	15	26.97	7.22	23.31-30.62	
	Central	Rower	13	23.11	6.36	19.65-26.57	0.073
		Normal	14	26.49	4.93	23.91-29.08	
Anterosuperior	Peripheral	Rower	18	16.28	3.21	14.79-17.76	**< 0.001**
		Normal	15	26.40	5.45	23.64-29.16	
	Central	Rower	20	23.29	5.32	20.95-25.62	**< 0.001**
		Normal	15	29.28	5.02	26.74-31.82	
Superoanterior	Peripheral	Rower	16	14.53	3.50	12.81-16.24	**< 0.001**
		Normal	15	22.04	3.52	20.26-23.82	
	Central	Rower	19	23.65	4.87	21.46-25.84	**0.002**
		Normal	15	28.81	4.28	26.65-30.98	
Superior	Peripheral	Rower	18	15.38	4.03	13.52-17.25	**< 0.001**
		Normal	15	21.53	3.13	19.94-23.11	
	Central	Rower	18	19.75	4.62	17.62-21.88	**0.006**
		Normal	15	24.43	4.53	22.13-26.72	
Superoposterior	Peripheral	Rower	18	16.85	3.89	15.05-18.65	**0.001**
		Normal	15	22.53	4.27	20.36-24.69	
	Central	Rower	17	17.36	7.63	13.74-20.99	**0.008**
		Normal	15	21.99	2.84	20.55-23.43	
Posterosuperior	Peripheral	Rower	19	21.25	4.98	19.01-23.49	**0.049**
		Normal	15	24.58	2.65	23.24-25.92	
	Central	Rower	19	21.85	7.39	18.53-25.18	0.090
		Normal	15	24.72	4.69	22.35-27.09	
Posterior	Peripheral	Rower	12	19.69	5.50	16.58-22.80	0.344
		Normal	15	21.49	1.55	20.70-22.27	
	Central	Rower	14	26.39	6.23	23.13-29.66	0.116
		Normal	15	23.53	4.04	21.49-25.58	

*Significant differences were observed in many regions/zones (p values < 0.05 are highlighted in bold); CI = confidence interval.

believe that the data, in particular, the comparison of both cohorts, are reliable, because the MRI examination was performed on exactly the same MRI machine and with the identical sequence protocol. The patient and coil positionings were similar and were conducted by the same person (ER) who has been responsible for MRI measurements for several years. The data analysis was carried out using a model that has been tried and tested for many years by the authors. Of note, in asymptomatic hips, differences in age, the timing of the scan, and preimaging exercise did not show evidence of any inconsistency in the T2* values of hip cartilage. Given these circumstances and information, a high level of reproducibility can indeed be considered. When conducting a ROI analysis, one averaged value (in this case T2* value) per ROI will be obtained assuming that all voxels in this ROI reflect only cartilage tissue. However, the effects of partial (signal) volume averaging by mixing values of different tissues, for example superficial cartilage and synovial fluid or deep cartilage and subchondral bone, have to be taken into account, particularly when considering the thin and curved cartilage layers of the hip and the cubic voxel form. This limits the diagnostic accuracy and may potentially bias measurements, in particular when performing some form of quantitative assessment such as dGEMRIC, T2, and T2* mapping. Extensive research that includes high-resolution MRI and the generation of perpendicular planes has been undertaken to overcome this limitation. Although we appreciate this potential pitfall, our methodology is appropriate and therefore the results are valid. In our study, high isotropic resolution with an image resolution of 0.6 mm^3 was performed, which allowed us to create radial images with a slice thickness of 2 mm with sufficient signal-to-noise ratio and negligible image quality loss. The ROIs were outlined freehand by experienced investigators who did their best to measure cartilage tissue with a considerable amount of

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Table 3. T2* values in milliseconds in various regions and zones of femoral head cartilage in study and control groups*

Region	Zone	Cohort	Number	Mean	SD	95% CI	p value
Anterior	Peripheral	Rower	18	23.97	5.92	21.24-26.71	**0.001**
		Normal	15	29.91	5.53	27.12-32.71	
	Central	Rower	13	25.97	5.69	22.88-29.06	0.406
		Normal	14	27.66	5.91	24.57-30.76	
Anterosuperior	Peripheral	Rower	19	26.04	7.26	22.78-29.31	**0.022**
		Normal	15	30.25	6.75	26.83-33.66	
	Central	Rower	19	26.93	7.66	23.48-30.37	0.067
		Normal	15	30.28	7.45	26.51-34.05	
Superoanterior	Peripheral	Rower	20	25.50	5.48	23.10-27.90	**0.011**
		Normal	15	30.13	3.42	28.40-31.86	
	Central	Rower	19	27.40	5.68	24.85-29.95	**0.014**
		Normal	15	31.89	4.79	29.47-34.32	
Superior	Peripheral	Rower	20	19.84	5.18	17.57-22.11	**0.002**
		Normal	15	25.49	4.03	23.46-27.53	
	Central	Rower	20	21.64	4.75	19.56-23.72	**0.010**
		Normal	15	26.35	3.80	24.42-28.27	
Superoposterior	Peripheral	Rower	20	17.93	4.27	16.06-19.80	**0.001**
		Normal	15	23.75	4.53	21.45-26.04	
	Central	Rower	18	16.24	4.99	13.94-18.55	**< 0.001**
		Normal	15	23.26	3.92	21.28-25.24	
Posterosuperior	Peripheral	Rower	20	22.56	5.47	20.16-24.95	**0.013**
		Normal	15	27.07	2.28	25.91-28.22	
	Central	Rower	18	21.67	6.59	18.63-24.72	**0.017**
		Normal	15	26.10	3.92	24.12-28.08	
Posterior	Peripheral	Rower	13	17.24	3.39	15.40-19.08	**0.028**
		Normal	15	21.67	1.78	20.77-22.57	
	Central	Rower	15	23.97	6.62	20.61-27.32	0.801
		Normal	15	24.45	3.54	22.66-26.24	

*Significant differences were observed in many regions/zones (p values < 0.05 are highlighted with bold); CI = confidence interval.

accuracy. Conversely, a few border pixels of potential cartilage tissue, which are also at risk of partial volume averaging, may not have been included within the ROI to ensure further that the data are not biased by partial volume averaging. This approach, however, reveals some risk for selection bias and variability in the outlining of the ROIs. A potential solution for this limitation is automatic cartilage segmentation by implementing some form of automatic surface and volume processing software. Notably, an increase in T2/T2* relaxation, when collagen fibers are oriented at an angle of nearly 55° (which is referred to as magic angle effect), needs to be taken into account [16]. This phenomenon might have contributed to the heterogeneity of the regional T2* distribution in this study (expected T2* increase in the anterosuperior and superoanterior as well as the posterosuperior and superoposterior regions, which are, depending on the pelvis and hip alignment during MRI, closest to the magic angle). However, in our study, this effect can be reproduced (only to some measure) both in the group of elite rowers and the control group. Furthermore, because this was an observational study, where the exposure to rowing started years before, we have no standardized activity protocol, which would include the daily activities of each rower. Also, in addition to the actual rowing, the sport comprises a variety of training techniques leading to different joint loading that we could not study. For that reason, a certain degree of inconsistency in the degeneration pattern must be considered. In sweep oar rowing, each rower has one oar held with both hands. Therefore, the rowers have to be paired so that there is an oar extending on each side of the boat. When the selection of which hip was further assessed, no specific consideration was given to whether the rowers favored the right or the left side. Therefore, side-dependent differences may have influenced the intraarticular findings. Finally, the participants included in our studies began rowing at a mean

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Table 4. T2* values in milliseconds in peripheral and central zones in various regions of acetabular cartilage in elite rowers*

Region	Zone	Number	Mean	SD	95% CI	p value
Anterior	Peripheral	15	18.83	5.05	16.27-21.38	**0.034**
	Central	13	23.11	6.36	19.65-26.57	
Anterosuperior	Peripheral	18	16.28	3.21	14.79-17.76	**< 0.001**
	Central	20	23.29	5.32	20.95-25.62	
Superoanterior	Peripheral	16	14.53	3.50	12.81-16.24	**< 0.001**
	Central	19	23.65	4.87	21.46-25.84	
Superior	Peripheral	18	15.38	4.03	13.52-17.25	**0.014**
	Central	18	19.75	4.62	17.62-21.88	
Superoposterior	Peripheral	18	16.85	3.89	15.05-18.65	0.775
	Central	17	17.36	7.63	13.74-20.99	
Posterosuperior	Peripheral	19	21.25	4.98	19.01-23.49	0.726
	Central	19	21.85	7.39	18.53-25.18	
Posterior	Peripheral	12	19.69	5.50	16.58-22.80	**0.002**
	Central	14	26.39	6.23	23.13-29.66	

Lower T2 values were observed in the acetabular peripheral zones in all regions; all were statistically significant except for the superoposterior and the posterosuperior region (p values < 0.05 are highlighted with bold); CI = confidence interval.

age of 14.7 ± 2.4 years, which may already be too old for the development of a decided cam deformity through growth plate remodeling processes. Further prospective, randomized, blinded, controlled studies involving a study group that started rowing earlier may provide answers to this question.

In summary, we found characteristic hyaline cartilage lesions in the hips of our group of young elite rowers compared with nonrowers. These lesions were present on both the acetabular side and femoral head and were accompanied by characteristic labral defects as well. Our observations are similar to those of previous studies. Although Smoljanovic et al. [14] reported mostly minor hip injuries classically related to overuse in their cohort of junior competitive rowers (mean age 18 ± 1 years), a separate MRI-based examination of rowers with a symptomatic hip including femoroacetabular impingement (mean age 18.5 ± 0.6 years) revealed labral pathology in all participants, ranging from degenerative tearing to complex longitudinal tears [3]. Because many labral tears are associated with an earlier onset of articular cartilage degeneration and often originate with repetitive

Table 5. T2* values in milliseconds in peripheral and central zones in various regions of femoral head cartilage in elite rowers*

Region	Zone	Number	Mean	SD	95% CI	p value
Anterior	Peripheral	18	23.97	5.92	21.24-26.71	0.342
	Central	13	25.97	5.69	22.88-29.06	
Anterosuperior	Peripheral	19	26.04	7.26	22.78-29.31	0.637
	Central	19	26.93	7.66	23.48-30.37	
Superoanterior	Peripheral	20	25.50	5.48	23.10-27.90	0.305
	Central	19	27.40	5.68	24.85-29.95	
Superior	Peripheral	20	19.84	5.18	17.57-22.11	0.324
	Central	20	21.64	4.75	19.56-23.72	
Superoposterior	Peripheral	20	17.93	4.27	16.06-19.80	0.369
	Central	18	16.24	4.99	13.94-18.55	
Posterosuperior	Peripheral	20	22.56	5.47	20.16-24.95	0.638
	Central	18	21.67	6.59	18.63-24.72	
Posterior	Peripheral	13	17.24	3.39	15.40-19.08	**0.002**
	Central	15	23.97	6.62	20.61-27.32	

A pattern of lower cartilage T2 values in the peripheral zone was not noted in the femoral head except for the posterior region (p values < 0.05 are highlighted with bold); CI = confidence interval.

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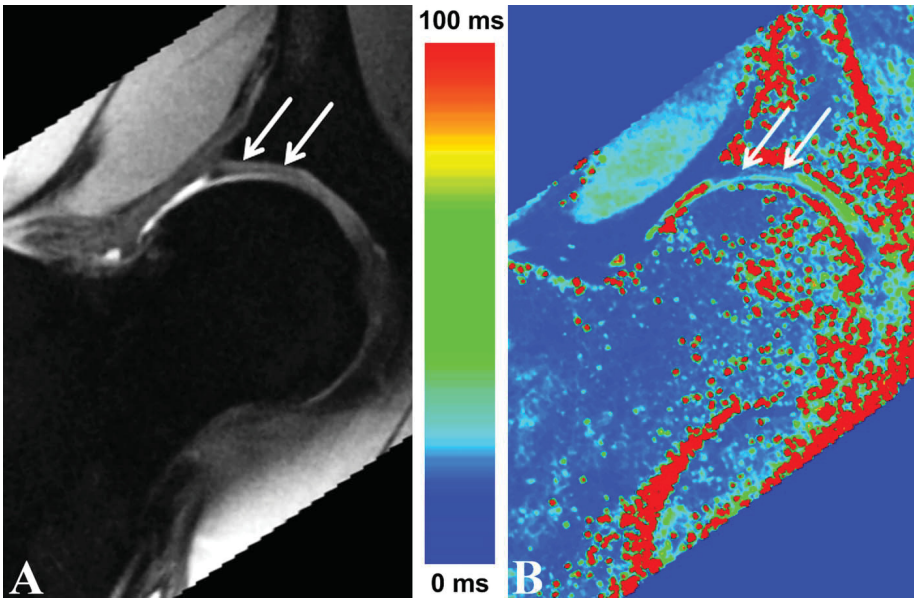

Fig. 5 A-B (**A**) DESS reformat, T2* color scale bar and (**B**) T2* map reformat of an asymptomatic rower are shown revealing mild cartilage thinning and a T2* decrease (white arrows in DESS image and T2* map) at the acetabular roof.

microtrauma [10], it may be assumed that our results are in agreement.

To understand abnormalities of hip morphology, and particularly, to correctly interpret the imaging findings, it must be understood that all quantifiable aspects are subject to a continuum, and there is a wide range of so-called normal sphericity of the femoral head or a normal extent of femoral head coverage or a reasonable ROM or a certain amount of joint loading within a given population. This also applies to the T2* mapping values. Thus, setting a certain threshold to define the normal or abnormal will always include outliers. In other words, these are numbers, not clinical symptoms. In fact, like with other diseases, we would not and should not base any diagnosis and any management therapy on a single number. Importantly, this study cohort included (still) asymptomatic individuals wherein morphologic and even MRI findings do not dictate or necessitate treatment. It is still unknown whether, and if so, in which time window the focal chondral defects necessarily progress to generalized joint degeneration and deterioration. Longitudinal, controlled and prospective studies, which should include a control group and various alternative therapies, should hopefully answer these questions.

Regarding the high amount of cartilage and labral damage noted in this study, and the low T2* values in pretty much all regions (which were more pronounced in the hip areas where the loading occurs), it is reasonable to conclude that extensive rowing in elite rowers may be a risk factor for early hip degeneration, including cartilage and labral damage, yet, although the morphologic and T2* changes were frequently observed in these hips, the data for a highly probable causation theory related to rowing are currently insufficient.

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