Aus der
Klinik und Poliklinik für Orthopädie und Unfallchirurgie
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Die Klassifikation und Therapie von Knochendefekten in der Hüftrevisionsendoprothetik

Habilitationsschrift

zur Erlangung der venia legendi

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Die folgenden aufgelisteten vier Originalarbeiten liegen der kumulativen Habilitationsschrift zu Grunde, welche die wesentlichen Ergebnisse der Publikationen zusammenfasst und diskutiert.

1. **Jaenisch M***, Kohlhof H*, Kasapovic A, Gathen M, Randau TM, Kabir K, Roessler PP, Pagenstert G, Wirtz DC (2021) Femoral defects in revision hip arthroplasty: a therapy-oriented classification. Arch Orthop Trauma Surg. 143(3):1163-1174. https://doi.org/10.1007/s00402-021-04201-7 **(IF: 2,928)**

2. **Jaenisch M**, Wirtz DC, Kohlhof H, Gathen M, Kabir K, Koob S, Jansen TR (2021) APP-guided assessment of acetabular defects in hip revision arthroplasty: a structured approach to a complex situation. Arch Orthop Trauma Surg. 32(3):248-261. https://doi.org/10.1007/s00402-021-04270-8 **(IF: 2,928)**

3. **Jaenisch M***, Kohlhof H*, Wirtz DC, Schildberg FA, Beckmann NA, Kretzer JP, Schonhoff M, Jäger S (2021) Primary Stability in Hip Revision Arthroplasty: Comparison of the Stability of Cementless Fixed Augments on a Modular Acetabular Cage System with and without Cranial Straps. J Clin Med. 10(17):4002. https://doi.org/10.3390/jcm10174002 **(IF: 4,964)**

4. **Jaenisch M**, Guder C, Ossendorff R, Randau TM, Gravius S, Wirtz DC, Strauss AC, Schildberg FA (2023) In-vitro Biocompatibility of a Novel Ceramic Composite for Defect Augmentation in Hip Revision Arthroplasty. J Funct Biomater. 14(10):517. https://doi.org/10.3390/jfb14100517 **(IF: 4.8)**

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1. Inhaltsverzeichnis

Meiner Familie

2. Einleitung

Die Osteoarthrose von Hüft- und Kniegelenk ist die häufigste Gelenkerkrankung weltweit und betrifft etwa 240 Millionen Menschen. Unbehandelt führt sie zu Schmerzen, Gelenkfunktionsstörungen, Immobilität und schließlich dem Verlust der Teilnahme am täglichen Leben. [1,2] Durch die Entwicklung der Hüftendoprothetik, also dem künstlichen Gelenkersatz, kam es zu einer deutlichen Verbesserung der Prognose der Osteoarthrose, sodass die Implantation einer Hüftgelenksendoprothese aktuell eine der erfolgreichsten Operationen ist. [3] Hierdurch kann eine Schmerzlinderung, eine Mobilitätsverbesserung und eine Rückkehr zur physiologischen Gelenkfunktion erreicht werden. Aktuell werden weltweit über 1 Million Primärimplantationen am Hüftgelenk durchgeführt. [4] Auf Grund der guten Ergebnisse und der langen Standzeiten von Hüftgelenksendoprothesen kam es sukzessive zu einer Ausweitung der Indikationsstellung, sodass zunehmend auch junge Patienten mit einem deutlich höheren Aktivitätslevel versorgt werden. [5] Je länger eine Endoprothese einliegt, desto höher ist die Chance für die Notwendigkeit einer Revisionsoperation – einem Prothesenwechseleingriff. Auf Grund der steigenden Implantationszahlen und des jüngeren und aktiveren Patientenkollektivs ist ein deutlicher Anstieg der Anzahl an Revisionsoperationen am Hüftgelenk prognostiziert. Bis zum Jahre 2030 ist von einem Anstieg zwischen 43-70% auszugehen. [6]

Die aseptische Lockerung ist mit einem Anteil von 24%, gefolgt von der periprothetischen Infektion mit 16,7%, die häufigste Ursache für einen Prothesenwechseleingriff am Hüftgelenk. [7] Durch beide Pathologien entstehen Defekte der tragenden Knochensubstanz, welche die erneute primärstabile Verankerung eines Implantates deutlich erschweren.

Die Revisionsendoprothetik des Hüftgelenks stellt einen komplexen Behandlungsschwerpunkt dar und das Ausmaß des zu behandelnden Knochenverlustes bestimmt maßgeblich den Schweregrad und das Ergebnis der Operation.

Die Behandlung von Knochendefekten in einer endoprothetischen Revisionsoperation am Hüftgelenk beruht auf den folgenden Prinzipien [8]:

1. Die Rekonstruktion der physiologischen Gelenkgeometrie. Hierzu zählt besonders die Wiederherstellung des anatomischen Hüftdrehzentrums sowie des femoralen und azetabulären Offsets. Das femorale Offset ist definiert als der Abstand der Schaftachse des proximalen Femurs zum Hüftdrehzentrum. Das azetabuläre Offset ist definiert als der Abstand des Hüftdrehzentrums zur Linea terminalis. [9]
2. Die primärstabile Verankerung des Implantatsystems mit regelhafter Krafteinleitung in die verbleibende azetabuläre und femorale Knochensubstanz.
3. Die biologische Defektverkleinerung, auch „Defekt-Downsizing“ genannt, um bei der Notwendigkeit einer erneuten Revision im weiteren Lebensverlauf noch über operative Versorgungsmöglichkeiten zu verfügen. [10]

Um dies zu ermöglichen bedarf es einer verlässlichen Defekterkennung und Klassifikation von azetabulären und femoralen Defekten. Erst nach klarer Identifikation des Knochendefektes kann im anschließenden Planungsvorgang eine adäquate Therapieoption abgeleitet werden.

Zu diesem Zweck wurden bereits multiple Klassifikationssysteme entwickelt, welche sich in der zugrundeliegenden Struktur und der Schwerpunktsetzung zum Teil deutlich unterscheiden. In der Regel beziehen sich die bestehenden Klassifikationssysteme jedoch auf die, zur entsprechenden Zeit verfügbaren therapeutischen Möglichkeiten. Sie haben entweder ausführlichen, deskriptiven Charakter, oder vereinfachen und untergliedern die Defektstruktur. Das sowohl im klinischen Alltag, als auch in der Literatur am häufigsten verwendete System zur Klassifikation von azetabulären und femoralen Defekten wurde von der Gruppe um Paprosky et al. 1994 bzw. 2003 vorgestellt (siehe Abb. 1). [10,11]

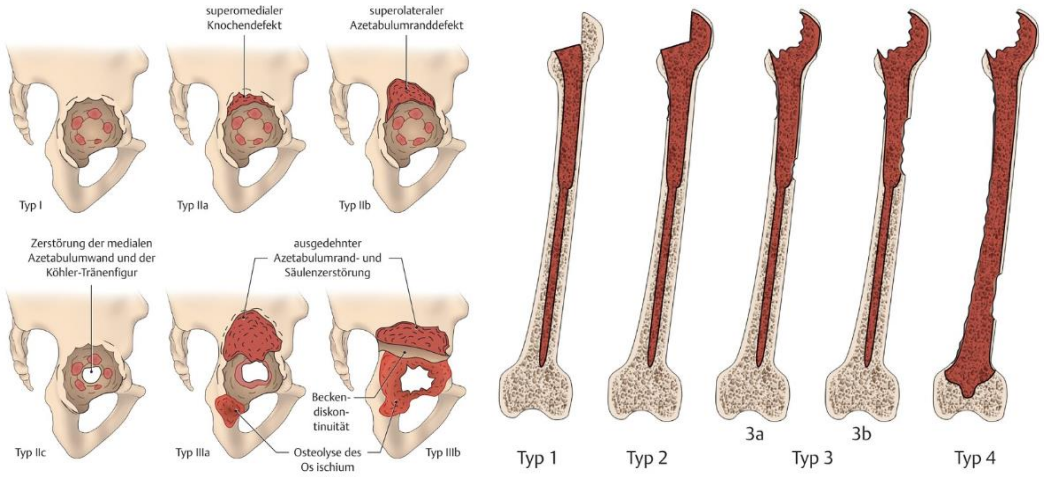

Abbildung 1: Schematische Darstellung der Defektklassifikation nach Paprosky des Azetabulums (links) und des Femurs (rechts) [10,11]. (Aus Wirtz DC, Stöckle U, Expertise Hüfte, Hrsg. 1. Auflage. Stuttgart: Thieme; 2018. DOI:10.1055/b-004-132249)

Das Klassifikationssystem der AAOS (American Academy of Orthopaedic Surgeons) findet ebenfalls eine weite Verbreitung und wurde sowohl für azetabuläre (1989), als auch femorale Defekte (1993) publiziert. [12,13] Beide Klassifikationssysteme unterscheiden sich grundlegend in Ihrem Aufbau. Das AAOS-System folgt einem schematischen Prinzip und teilt das Ausmaß bzw. die Schwere des Defektes ein, ohne eine detaillierte morphologische Beschreibung vorzugeben. Dadurch eignet es sich sehr gut zur wissenschaftlichen Vergleichbarkeit, ermöglicht jedoch kaum Vorteile bei der Operationsplanung oder als intraoperativer Leitfaden. Die Klassifikationen von Paprosky et al. ermöglichen eine Defektbeschreibung bezogen auf typische Versagensmechanismen und bieten zusätzlich einen therapeutischen Leitfaden bezogen auf den Defekt. Auf Grund der großen Zeitspanne von bereits 30 Jahren seit der Erstpublikation bezieht sich dieser therapeutische Algorithmus jedoch auf operative Möglichkeiten, welche zum Teil veraltet sind und nur noch selten Anwendung finden. [8] In der klinischen Praxis stellen sich daher häufig Fragen, welche durch die verfügbaren Klassifikationssysteme nur unzureichend beantwortet werden können.
Auch die alltägliche Anwendbarkeit der etablierten Klassifikationssysteme hat deutliche Defizite. So zeigt sich in der Literatur eine unbefriedigende Verlässlichkeit durch eine unzureichende Übereinstimmung zwischen präoperativer Klassifikation und tatsächlichem intraoperativen Befund. Zusätzlich ergibt sich eine eingeschränkte

Reproduzierbarkeit. [14-17] Mit der steigenden Integration von mobilen Endgeräten (z.B. Smartphones und Tablets) in den medizinischen Alltag könnten moderne digitale Lösungsansätze Abhilfe schaffen. [18] So könnte durch die Etablierung einer Web-basierten Applikation die Anwendung von komplexen Revisionssystemen einfacher und benutzerfreundlicher werden.

Nach Erkennung und Klassifikation der Lokalisation sowie des Ausmaßes der knöchernen Schädigung muss eine adäquate Versorgung - Augmentierung - geplant werden. Die Augmentierung von Knochendefekten in lasttragenden Bereichen unterscheidet sich hierbei grundlegend von der Augmentierung in weniger stark belasteten Bereichen des Azetabulums und des Femurs.

In knöchernen Lokalisationen außerhalb des Hauptkraftvektors bestehen sehr gute Erfahrung mit dem Impaktieren von spongiösem Knochen, dem sogenannten Impaction Bone Grafting (Impaktionstransplantat). Hierbei wird je nach benötigter Menge ein Gemisch aus steril gewonnenem Patientenblut und körpereigener – oder Spenderspongiosa und Knochenmehl angefertigt. Dieses Gemisch wird in den zu augmentierenden Bereich eingebracht und mit unterschiedlichen Stößeln verdichtet (siehe Abb. 2). Langfristig erfolgt ein Umbau der eingebrachten Knochensubstanz in soliden, körpereigenen Knochen. Der Pfannenboden, der superomediale Pfannenerker und die Metaphyse des Femurs eignen sich besonders gut für diese Technik. Im mittleren und langen Nachuntersuchungsintervall konnte eine zunehmende Bildung von vitaler Knochensubstanz nachgewiesen werden. [19, 20] Dies gilt jedoch nur, wenn keine direkte Lasteinleitung ohne ein schützendes Implantat erfolgt.

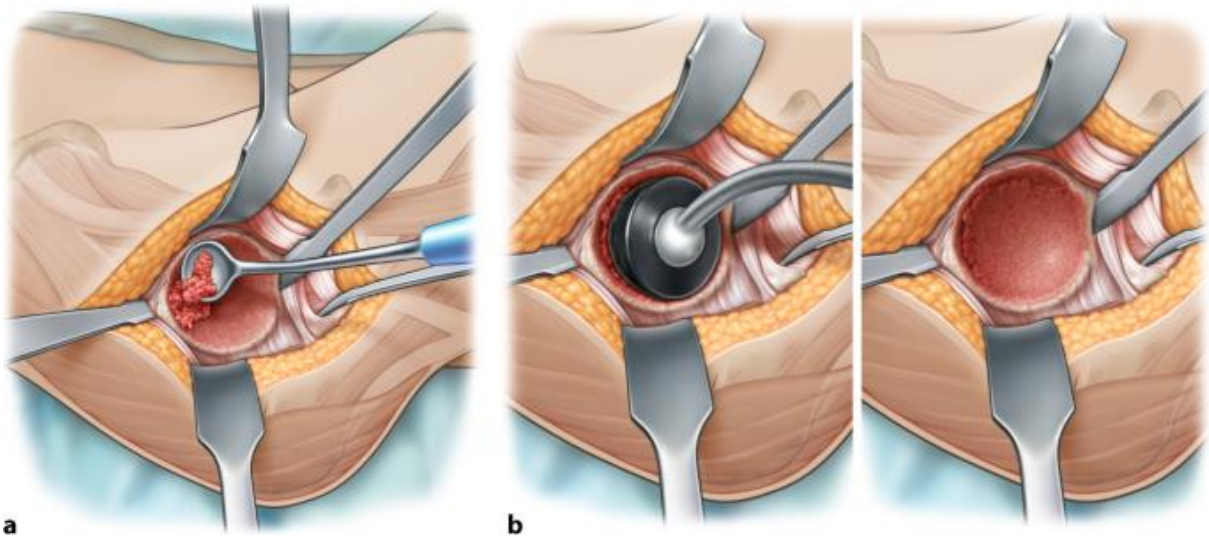

Abbildung 2: Schematische Darstellung des Impaction Bone Grafting. **A** Das Eigenblut-Spongiosa-Gemisch wird schichtweise in den Knochendefekt eingebracht. **B** Anschließend wird es in mehreren Schichten aufsteigend mit hemisphärischen Stößeln verdichtet. (Aus Wirtz DC, Wacker M, **Jaenisch M**, Gravius S, Roessler PP (2019) Hüftpfannenwechsel mit einem neuartigen zementfreien „Augment-and-modular-cage"-Revisionssystem (MRS-C). (Oper Orthop Traumatol 32(3):248-261 DOI:10.1007/s00064-019-00637-8)

Für die lasttragenden Bereiche, speziell der Hüftgelenkspfanne gelten jedoch andere Voraussetzungen. Hierbei sind besonders der kraniolaterale Azetabulumerker und der dorsale Pfannenrand entscheidend, da an ihnen ein Hauptteil der Lasteinleitung erfolgt. Getrieben vom Anspruch einer möglichst biologischen Defektaugmentation erfolgte die Augmentierung der lasttragenden Bereiche des Azetabulums häufig mit strukturellen, sogenannten „Bulk-Allografts". Hierbei wurde Spenderknochen – in der Regel ein oder mehrere Hüftköpfe – mittels Schrauben am Becken fixiert. Trotz erfreulicher Ergebnisse im kurzen Intervall zeigte sich in der langfristigen Nachkontrolle sowohl klinisch, als auch histopathologisch und radiologisch eine eingeschränkte Osteointegration mit bindegewebigem Einwachsen, konsekutiver Resorption und langfristigem Versagen der endoprothetischen Fixierung. [21-24] Der aktuelle Goldstandard zur Versorgung von knöchernen, azetabulären Defekten im lasttragenden Bereich ist daher die Verwendung von makroporösen, metallischen

Augmenten. Die makroporöse, spongiosaähnliche Struktur des Augments bietet mehrere Vorteile. Zum einen ermöglicht sie, durch den hohen Reibungskoeffizienten einen sehr guten primären Pack am Patientenknochen und zum anderen kann in sie neuer Knochen einwachsen und so für eine sehr gute Sekundärstabilität sorgen (siehe Abb. 3). Zusätzlich bietet das metallische Grundmaterial (in der Regel Tantalum oder Titan) eine hohe Primärstabilität. [25]

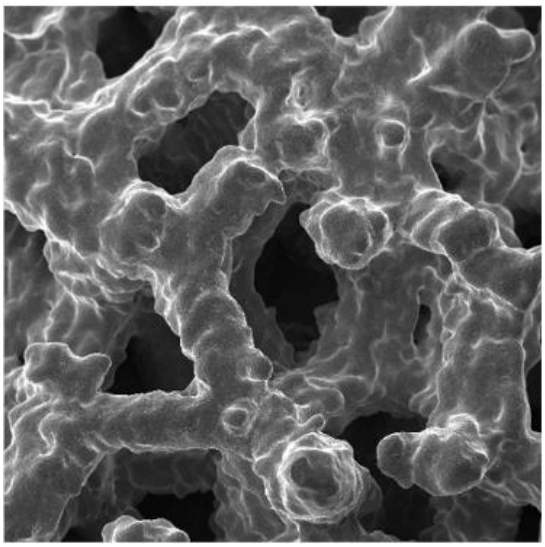

Abbildung 3: Rasterelektronmikroskopische Aufnahme der Oberflächenstruktur eines makroporösen Titanaugments, Vergrößerung 50-fach (Im Internet: https://peter-brehm.de/produkte/huefte/mrs-titan-standard-und-maximum, aufgerufen am 20.07.2023, mit freundlicher Genehmigung von Peter Brehm GmbH)

Während in der Forschung zum aktuellen Zeitpunkt die Nutzung von metallischen Augmenten etabliert ist, sind die möglichen Kombinationen mit unterschiedlichen Implantatsystemen und die Fixierungstechniken vom Augment an Implantat und Knochen zahlreich. Ein modernes Beispiel ist die Nutzung von einer modularen Abstützschale mit einer zementfreien Augmentfixierung über eine Schraubenverbindung, welche in unterschiedlichen Konfigurationen erhältlich ist und so auf die jeweilige intraoperative Situation angepasst werden kann (siehe Abb. 4). Erste Studien zeigen erfreuliche klinische und radiologische Ergebnisse mit einer guten Rekonstruktion des anatomischen Hüftrotationszentrums. [26] Eine Fixierung des Augments mittels Knochenzement (PMMA) an der Prothese ist als sogenanntes Augment-and-Cup ebenfalls möglich. Biomechanische Studien zeigen auch hier eine

stabile Verbindung mit niedrigen Relativbewegungen. [24] Eine mögliche Gefahr für die Langzeitstabilität des Konstruktes ist jedoch das niedrige E-Modul von PMMA. So sitzt es als schwächstes Glied zwischen zwei metallischen Komponenten und könnte im Verlauf zerrütten und einen Metall-Metall-Abrieb ermöglichen. [28] Zusätzliche Implantatmodifikation sind z.B. Verschraubungen in den ilialen Pfannendom, das Schambein und das Sitzbein, kaudale Haken sowie metallische Laschen, welche das Anbringen von weiteren Verschraubungen rechtwinklig zur Krafteinleitung erlauben. Eine optimale Kombination der modularen Implantatmodifikationen zum Erreichen einer möglichst hohen Primärstabilität ist aktuell nicht definiert und weiterhin Gegenstand der aktuellen Forschung.

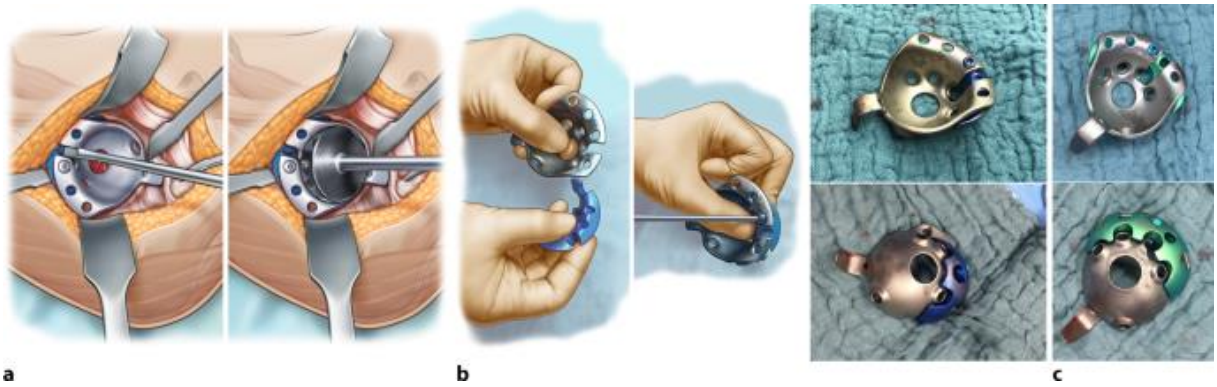

Abbildung 4: Metallische Augmentierung in Kombination mit einer modularen Revisionsabstützschale („Augment-and-modular-Cage“) **A** Das Einpassen des Probeimplantates mit einem Probeaugment im Situs **B** Zementfreie Fixierung des Augmentes an der modularen Abstützschale mit einer Schraubenverbindung **C** Verschiedengroße Probeaugmente adaptiert auf die Defektausdehnung und Lokalisation (angepasst aus Wirtz DC, Wacker M, **Jaenisch M**, Gravius S, Roessler PP (2019) Hüftpfannenwechsel mit einem neuartigen zementfreien „Augment-and-modular-cage“-Revisionssystem (MRS-C). Oper Orthop Traumatol 32(3):248-261 DOI:10.1007/s00064-019-00637-8)

Das grundlegende Streben nach vollständiger, biologischer Defektverkleinerung ist zum aktuellen Zeitpunkt noch nicht erreicht. Die metallische Augmentation ermöglicht eine primärstabile Versorgung, hinterlässt jedoch bei einer weiteren Revision erneut einen großen knöchernen Defekt. Die Nutzung von humaner Knochensubstanz in nicht-lasttragenden Defekten ist limitiert durch die begrenzte Verfügbarkeit und einer

möglichen Entnahmemorbidität. Zusätzlich besteht bei der Nutzung von Spenderknochen die Gefahr von Krankheitsübertragungen und immunologischen Reaktionen sowie eine hohe Kostenbelastung.
Eine mögliche Lösung hierfür sind keramische Knochenersatzmaterialien. Das perfekte Knochenersatzmaterial ist günstig, biokompatibel, fördert das knöcherne Einwachsen und ist erhältlich in unterschiedlichen Konfigurationen (kleinstückig – für Impaction grafting, makroporös Gerüst/Augment – für lasttragende Defekte).
Kalzium-Silikat-Keramiken stellen einen vielversprechenden Ansatz dar und zeigen in experimentellen Studien mechanische Eigenschaften, welche vergleichbar mit spongiösem Knochen sind und den Einsatz in lasttragenden Bereichen möglich erscheinen lassen. [29] Zusätzlich können keramische Knochenersatzmaterialien durch additive Verfahren (3D-Druck) in eine Vielzahl räumlicher Strukturen gebracht werden. [30] Dies ist ähnlich der additiven Herstellung von metallischen Augmenten und könnte eine gute Übertragbarkeit von bereits etablierten endoprothetischen Herstellungsprozessen ermöglichen.

Aufbauend auf den dargelegten Ausführungen ergeben sich verschiedene Fragestellungen:

1. Welche diagnostischen und therapeutischen Verbesserungen können durch die Etablierung eines modernen Klassifikationssystems für knöcherne Defekte in der Revisionsendoprothetik erreicht werden?
2. Kann durch die Kombination mit Web-basierten Applikationen die Nutzung eines komplexen Klassifikationssystems vereinfacht werden?
3. Welche Anpassung an ein Implantatsystem ermöglicht eine Erhöhung der primären Stabilität bei augmentationspflichtigen knöchernen Defekten?
4. Ist eine zementfreie Augmentfixierung am Implantatsystem primär stabil?
5. Stellen Knochenersatzmaterialen zukünftig eine valide Alternative zur metallischen Defektaugmentation dar?

3. Ergebnisteil

3.1 Jaenisch M*, Kohlhof H*, Kasapovic A, Gathen M, Randau TM, Kabir K, Roessler PP, Pagenstert G, Wirtz DC (2021) Femoral defects in revision hip arthroplasty: a therapy-oriented classification. Arch Orthop Trauma Surg. 143(3):1163-1174. https://doi.org/10.1007/s00402-021-04201

Zielsetzung der Arbeit:

Das komplexe Arbeitsfeld der femoralen Knochendefekte in der Hüftrevisionsendoprothetik zeigt einen Mangel an standardisierten und intuitiven präoperativen sowie intraoperativen Analysemöglichkeiten. Um diesen Missstand zu verbessern, stellen wir die Femorale Defekt Klassifikation (Femoral Defect Classification, FDC) vor. Das Ziel dieser Publikation ist die Etablierung eines verlässlichen, reproduzierbaren und intuitiven Klassifikationssystems mit einem klaren, therapeutischen Vorgehen.

Material und Methoden:

Die FDC basiert auf der Integrität der femoralen Hauptsegmente, welche die Funktion und die strukturelle Stabilität des Hüftgelenks ermöglichen. Miteinbezogen sind der Schenkelhals, die Metaphyse (bestehend aus dem Trochanterkomplex) und die femorale Diaphyse. Die vier Hauptkategorien (1-4) beschreiben die Lage des Defektes und die 3 Subkategorien (a-c) klassifizieren den Schweregrad der Knochenschädigung. Insgesamt wurden 218 präoperative Röntgenaufnahmen retrospektiv mit der FDC klassifiziert und mit den beschriebenen intraoperativen Defektkonfigurationen verglichen. Zur Einschätzung der Inter-Rater- und Intra-Rater-Übereinstimmung wurden 80 Fälle durch 5 verschieden Untersucher zu 2 verschiedenen Zeitpunkten analysiert.

Ergebnisse:

In der Bestimmung der Übereinstimmung zwischen präoperativer Analyse und intraoperativem Befund zeigt sich ein Cohens Kappa von 0.832 $\pm$ 0.028. Dies beschreibt eine exzellente Übereinstimmung. In der Bewertung der Übereinstimmung zwischen verschiedenen Untersuchern zeigte sich ein Fleiss Kappa von 0.688, welches im Bereich einer guten Übereinstimmung liegt. Für die durchschnittliche

Übereinstimmung von gleichen Untersuchern zu verschiedenen Zeitpunkten zeigte sich ebenfalls eine exzellente Übereinstimmung mit einem Cohens Kappa von 0.856.

Schlussfolgerung:

Die FDC ist ein verlässliches und reproduzierbares Klassifikationssystem. Es kombiniert eine intuitive Benutzerfreundlichkeit und ein strukturiertes Design und ermöglicht dadurch eine einheitliche präoperative Planung und eine intraoperative Orientierungshilfe. Ein therapeutischer Algorithmus wurde basierend auf Expertenmeinungen und einer Analyse der aktuellen Literatur erstellt. In Kombination mit der bereits veröffentlichten azetabulären Defektklassifikation (Acetabular Defect Classification; ADC) ermöglicht sie eine strukturierte Analyse sämtlicher periprothetischer Defekte in der Hüftrevisionsendoprothetik.

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ORTHOPAEDIC SURGERY

Femoral defects in revision hip arthroplasty: a therapy-oriented classification

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Abstract

Introduction The complex field of femoral defects in revision hip arthroplasty displays a lack of standardized, intuitive pre- and intraoperative assessment. To address this issue, the femoral defect classification (FDC) is introduced to offer a reliable, reproducible and an intuitive classification system with a clear therapeutic guideline.

Materials and methods The FDC is based on the integrity of the main femoral segments which determine function and structural support. It focuses on the femoral neck, the metaphysis consisting of the greater and lesser trochanter, and the femoral diaphysis. The four main categories determine the location of the defect while subcategories a, b and c are being used to classify the extent of damage in each location. In total, 218 preoperative radiographs were retrospectively graded according to FDC and compared to intraoperatively encountered bone defects. To account for inter-rater and intra-rater agreement, 5 different observers evaluated 80 randomized cases at different points in time.

Results A Cohens kappa of 0.832 ± 0.028 could be evaluated, accounting for excellent agreement between preoperative radiographs and intraoperative findings. To account for inter-rater reliability, 80 patients have been evaluated by 5 different observers. Testing for inter-rater reliability, a Fleiss Kappa of 0.688 could be evaluated falling into the good agreement range. When testing for intra-rater reliability, Cohens Kappa of each of the 5 raters has been analyzed and the mean was evaluated at 0.856 accounting for excellent agreement.

Conclusion The FDC is a reliable and reproducible classification system. It combines intuitive use and structured design and allows for consistent preoperative planning and intraoperative guidance. A therapeutic algorithm has been created according to current literature and expert opinion. Due to the combination of the FDC with the recently introduced Acetabular Defect Classification (ADC) a structured approach to the entire field of hip revision arthroplasty is now available.

Keywords Femoral · Bone defect · Hip · Arthroplasty · Revision

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Introduction

Modern total hip arthroplasty continues to be on the rise and implantation rates are predicted to keep increasing all over the developed world [1]. In the near future, orthopedic surgeons will be faced with more and more complex cases of bone loss while revision and re-revision surgeries are piling up. Acetabular defects have been sufficiently described and organized with the recent addition of the acetabular defect classification (ADC) published by this group [2]. However, for femoral defects a lack of standardized, intuitive pre and intraoperative assessment is still being experienced.

Successful treatment of femoral bone defects focuses on the reconstruction of the physiological joint geometry [3]. In regard to femoral components, this includes the preservation of leg length and an appropriate femoral offset and rotation. As with any arthroplasty, primary stable fixation, enabling proper force transmission to the remaining femoral bone stock, is essential to achieve long-term stability. Whenever it is possible, circumferential press-fit should be applied caudal to the defect situation [4]. Cancellous, as well as cortical defects should be subjected to augmentation to promote biological downsizing and improve the outcome in following revision procedures [5, 6].

A successful revision arthroplasty, therefore, requires decisive preoperative planning and appropriate choice of implant. Common patterns of defect morphology should be evaluated in a consistent and reproducible demeanor resulting in a clear therapeutic algorithm which then can be applied.

Different classification systems have been published to facilitate the aforementioned goals [7–12]. Most of the established classification systems focus on the description of defect location and extent, but fail to relate to current state-of-the-art treatment options. A consensus has not been reached and different systems are being applied in different areas of the world resulting in difficulties when trying to compare the outcome related to defect morphology.

To the authors' knowledge, no classification system is available that combines intuitive use and structured design while still producing a detailed defect description and offering a therapeutic method according to the current literature and modern state-of-the-art treatment options.

The goal of this publication is to introduce an intuitive guideline for the evaluation and treatment of femoral defects in revision hip arthroplasty. To account for reliability, we compared preoperative grading with intraoperative findings and in the evaluation of reproducibility we evaluated inter- and intra-rater agreement.

We hypothesized that the FDC is a reliable and reproducible classification system. It offers a valid estimation of the defect severity preoperatively and aids with essential planning and preparations. A clear therapeutic algorithm is supplied to help with implant choice and additional interventions according to current literature and expert opinion. The proposed femoral defect classification (FDC) was created to be used alongside the recently introduced acetabular defect classification (ADC). In combination, both defect classification systems offer a structured and holistic approach to hip revision arthroplasty.

Materials and methods

Study design and patients

This single center, cohort study is based on retrospectively collected data of patients that underwent femoral revision surgery between 2011 and 2018. A total of 265 consecutive patients who received THA revision for multiple reasons (aseptic loosening, peri-prosthetic infection, recurrent or chronic luxation, implant failure) with exchange of at least the femoral component were identified. Set criteria for exclusion were irretrievable preoperative radiographs or preoperative radiographs of insufficient quality, as well as incomplete intraoperative recordings that did not allow for a reliable grading. Other recorded patient characteristics including age, sex, date of revision and implant inserted were collected. In total, 13 cases were excluded because no digital copies of preoperative radiographs could be retrieved or because radiographs were of insufficient quality. Furthermore, 34 cases were excluded because intraoperative data did not match the defined requirements (intraoperative evaluation). After exclusion, the preoperative X-rays and intraoperative documentation of 218 patients have been included. As the primary outcome parameter, the agreement between preoperative radiographic grading and intraoperative grading has been evaluated using the data of the whole collective ($n=218$). The evaluation of the rater agreement has been carried out on a randomised sample ($n=80$) of the whole collective.

Intraoperative evaluation

Retrospective collection and conversion into FDC grading of intraoperative data were accomplished by the first author. Surgical documentation was analyzed for information concerning the extent of femoral defect morphology and size and combined with additional information such as implants used and/or use of augmentation to allow for proper grading. Cases were excluded if the exact defect location was not specified and if no measurement of defect size was not recorded.

Radiographic evaluation

To enable blinded assessment, radiographs were striped of any identifying features and anonymized by numerical coding. Therefore, no knowledge of intraoperative findings could distort the grading process. Radiographic grading according to FDC was carried out by the first and last author.

After power analysis according to the formula created by Flack et al., 80 anonymized radiographs were randomly selected and distributed to five raters [13]. The chosen raters are experienced orthopaedic surgeons in the field of hip revision arthroplasty. A teaching session consisting of thorough explanation of the classification system and supervised evaluation of ten random cases was carried out in preparation for the assignment. The 10 sample cases did not include any of the 80 used for later evaluation. A scoring sheet was distributed. None of the raters had any prior knowledge of the FDC or were involved in the creation. To control for distortion due to memory, a wash out period of 2 weeks was established between ratings. Radiographs were re-labelled and randomized prior to the second evaluation.

Preoperative radiographic assessment consisted of standing anteroposterior view and lateral view of the hip joint. Radiographic analysis and grading were carried out using IMPAX EE (Agfa HealthCare GmbH, Bonn, Germany).

Classification system

The FDC is based on the integrity of the main femoral segments which determine function and structural support. It focuses on the femoral neck, the metaphysis consisting of the greater and lesser trochanter, and the femoral diaphysis. The four main categories determine the location of the defect while subcategories a, b and c are being used to classify the extent of damage in each location.

Type 1 defects

Type 1 defects encompass the entire region of the femoral neck while the metaphysis remains uncompromised. Such defects can be encountered during revision surgery of a hip resurfacing prosthesis or in cases of prior osteosynthesis due to femoral neck fractures. An illustration of type 1 is displayed in Fig. 1.

Type 2 defects

Type 2 defects are limited to the area of the metaphysis. The diaphysial bone remains intact. Type 2 A displays total depletion of the metaphyseal cancellous bone, while the compact bone remains supportive on both the greater and lesser trochanter. In type 2B, the lesser trochanter and the thick compact bone called Calcar femoris are rendered non-supportive in addition to the cancellous depletion described above. In type 2C, severe bone loss and disintegration of the greater trochanter is encountered. This presents a structural as well as functional challenge due to the loss of vital muscle attachment. All type 2 defects are displayed in Fig. 1.

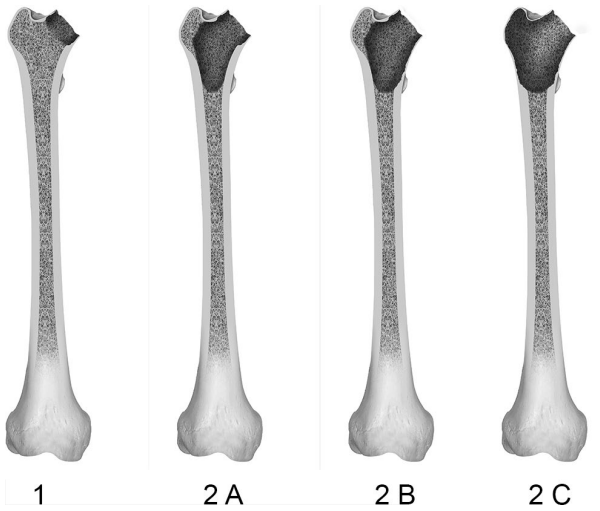

Fig. 1 Shows type 1 and type 2 defects of the femoral defect classification (FDC). Type 1 presents a limited defect of the femoral neck; type 2 defects concern the femoral metaphysis with type 2A presenting a cancellous defect, 2B displaying an insufficient calcar femoris and the region of the lesser trochanter and 2C affects the whole metaphysis with calcar femoris, greater and lesser trochanter

Type 3 defects

In type 3 defects, the extension of bone loss reaches the diaphysis while respecting the isthmus femoris (region of smallest intramedullary diameter of the femoral diaphysis). Type 3A is defined as a hollowed out cortical bone with complete destruction of the cancellous bone structure. The cortical bone remains to provide circumferential support. In type 3B, in addition to the depletion of cancellous bone, the defected encompasses part of the cortical circumference rendering below 50% of it unsupportive. In type 3C, the defect amounts to > 50% of the cortical circumference. Differences between the individual type 3 defects can be seen in Fig. 2.

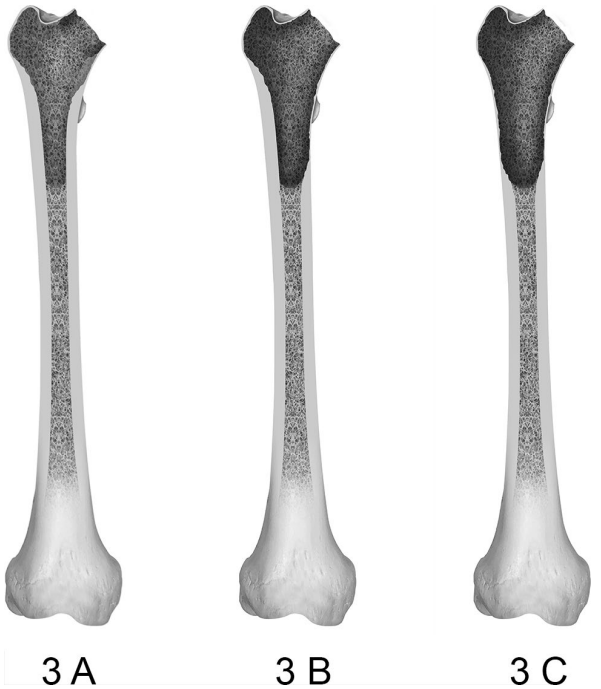

Fig. 2 Displays the subdivisions of type 3 defects of the femoral defect classification (FDC). Type 3 defects affected the proximal diaphyseal bone of the femur while leaving enough viable bone stock in the area of the isthmus femoris. The subdivision narrows down defect severity with 3A presenting a full depletion of cancellous bone, 3B displaying an affection of the cortical bone below 50% of the circumference and 3C rendering above 50% of the cortical bone non-supportive

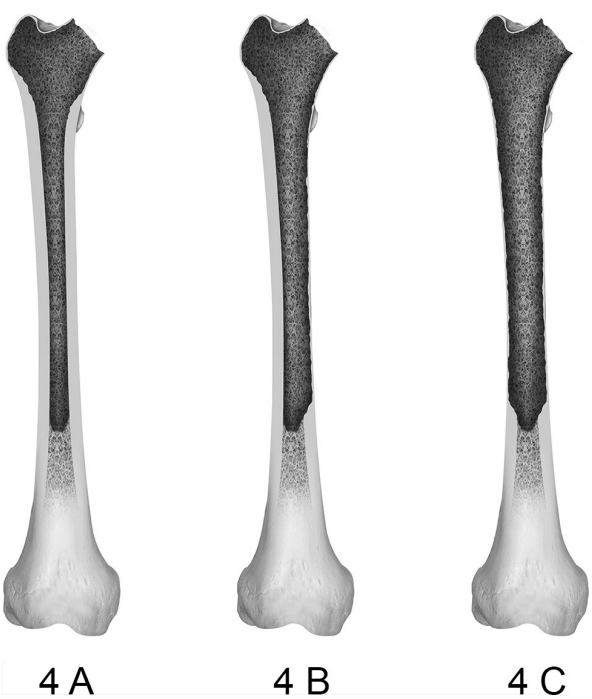

Fig. 3 Displays the subdivisions of type 4 defects of the femoral defect classification (FDC). Type 4 defects affected the bone stock of the isthmus femoris presenting the most severe defects encountered in hip revision arthroplasty. Similar to type 2 defects, 4A describes a depletion of cancellous bone, 3B renders up under 50% of the cortical bone of the isthmus femoris non-supportive and for 4C defects over 50% of the cortical bone of the isthmus femoris is compromised

Type 4 defects

While type 4 defects follow the same structure as type 3 defects, the isthmus femoris is compromised. A graphic representation of type 4 defects is illustrated in Fig. 3.

Statistical analysis

The statistical analysis was carried out using IBM SPSS Statistics 1.0.0.1131 (IBM Inc., Armonk, New York, USA). The level of significance was set at $p < 0.05$. The confidence interval has been set at 95%. As a means to account for inter-rater reliability in the process of comparing ordered categorical data with more than 2 raters, Fleiss Kappa was used. Through the utilization of Cohens Kappa, intra-rater reliability was calculated and compared through the mean kappa of all raters. Kappa values were interpreted utilizing the agreement scale described by Landis and Koch [14]. Kappa values exceeding 0.80 indicate excellent agreement, between 0.61 and 0.8 indicate good agreement, between 0.41 and 0.60 indicate moderate agreement, between 0.21 and 0.4 indicate fair agreement and between 0.20 and below indicates poor agreement.

Results

A total of 218 cases have been included to evaluate the agreement between preoperative radiographic grading and intraoperative grading. Indications for revision were aseptic loosening ($n = 153$), peri-prosthetic infection ($n = 47$), recurrent or chronic luxation (n = 15), implant failure $n = 3$). Preoperative radiographs as well as intraoperative findings have been graded according to FDC. Mean interval between preoperative X-ray and intraoperative assessment was 12.7 ± 13.4 days. According to the intraoperative gradings, the samples proved to be well-balanced and exhibited every defect type. The defect distribution of the whole population and of the randomized sample are displayed in Fig. 4.

A Cohens kappa of 0.832 ± 0.028 could be evaluated, accounting for excellent agreement between preoperative radiographs and intraoperative findings.

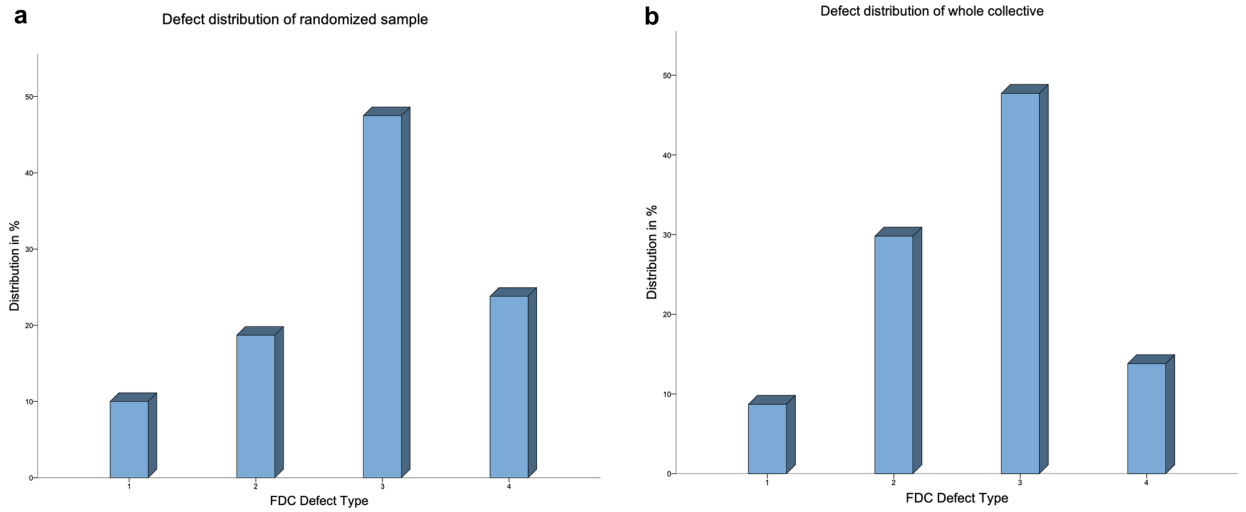

Fig. 4 To allow for proper evaluation of reliability each FDC defect type is in included in the whole collective, as well as in the randomized sample and the distribution is considered to be similar to the occurrence in the clinical practice of femoral revision arthroplasty. The whole collective consisted of 218 cases: 19 Type 1 defects 65, Type 2 defects (2A $n=37$, 2B $n=1$, 2C $n=27$) 103, Type 3 defects (3A $n=72$, 3B $n=15$, 3C $n=16$), 31 Type 4 defects (4A $n=17$, 4B $n=3$, 4C $n=11$), (**a**) Illustration of the distribution of FDC defect types in the whole collective ($n=218$); y-axis: percent out of all cases, x-axis: FDC Defect type 1–4; (**b**) Illustration of the distribution of FDC defect types in the randomized sample ($n=80$); y-axis: percent out of all cases, x-axis: FDC Defect type 1–4

To account for inter-rater reliability, a randomised sample of 80 patients have been evaluated by five different observers. Testing for inter-rater reliability, a Fleiss Kappa of 0.688 (low CI 0.660; high CI 0.716) could be evaluated falling into the good agreement range as defined by Landis and Koch [14]. When testing for intra-rater reliability Cohens Kappa of each of the five raters has been analyzed and the mean was evaluated at 0.856 ± 0.054 accounting for excellent agreement according to Landis and Koch [14]. Individual results for each rater are displayed in Fig. 5.

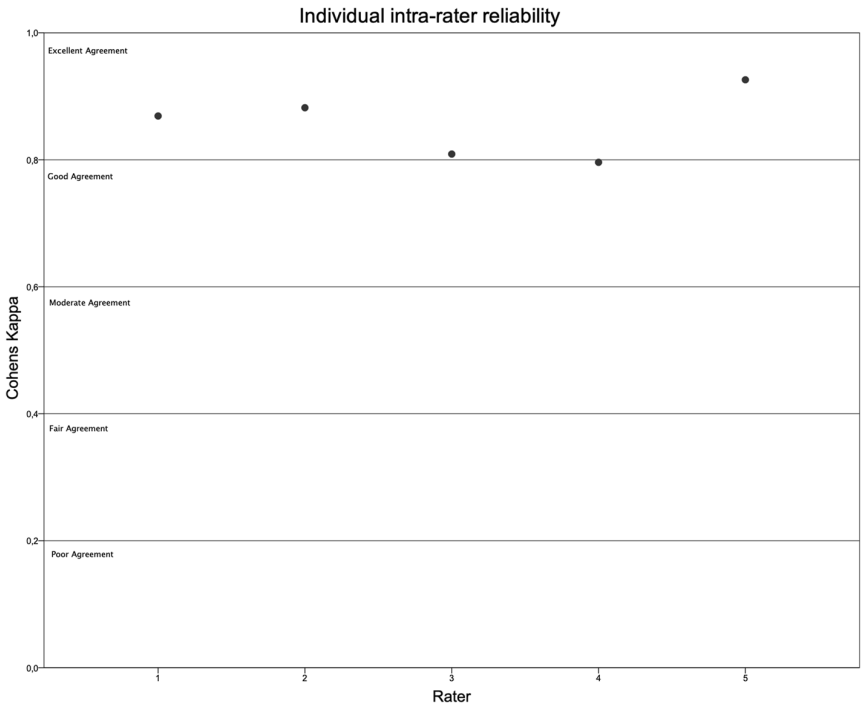

Fig. 5 Illustration of individual intra-rater reliability. All individual raters displayed good to excellent agreement between themselves at different time points. y-axis: Cohens Kappa, x-axis: individual rater

Discussion

The most important feature of a classification system is a clinical usefulness generated through a clear therapeutic algorithm. The loosening of the femoral component of a hip prosthesis is commonly associated with peri-prosthetic bone loss which can hinder primary stable fixation. Reliable defect recognition and classification is essential for successful femoral revision arthroplasty. Depending on defect location and morphology, different treatment options should be applied.

So far numerous classification systems have been introduced to rate femoral bone defects. The AAOS introduced the most extensive one in 1993 describing the full range of femoral abnormalities found in primary and revision hip arthroplasty. This approach resulted in a rather bulky but comprehensive classification system which, however, fails to offer a clear therapeutic guidance [8, 10]. Gross et al. focused primarily on bone allograft augmentation to enable reconstruction and primary stable implantation [10, 11]. Other classification systems mainly cater to a specific therapeutic approach. The Endoklinik's system has been constructed to evaluate the option of cemented revision arthroplasty while Engh and Paprosky aimed for primary stable, diaphyseal implantation of a cementless stem [7, 10, 12]. To improve upon the existing approaches, the FDC takes augmentation, all state-of-the-art implant choices and defect morphology into account, to offer a complete, yet intuitive classification system. The FDC was created to complete the ADC and in union, they offer a holistic approach to hip revision arthroplasty [2]. It is a reliable, reproducible and intuitive classification system which, in addition, offers a clear therapeutic guideline according to state-of-the-art treatment options.

Presenting the same structure as the familiar ADC, it can be applied to native radiographs of the femur. Therefore, it is applicable to a widely available and easily reproducible diagnostic process. In the present analysis the extent of the defect is estimated in preoperative radiographs when compared to intraoperative findings show a k value of 0.83. As defined by Landis and Koch, this indicates excellent agreement [14]. The authors, therefore, conclude that the FDC presents a reliable option to evaluate defect severity preoperatively. As an example, for an esthablished classification the Paprosky system has been evaluated for validity twice. Gozzard et al. reported moderate agreement between preoperative radiographical grading and intraoperative grading ($k = 0.54$) [15]. The group around Käfer confirmed these findings with k values from 0.59 to 0.68 [16]. These results are in contrast to our own excellent agreement, which might be partially contributed to improvements in imaging technique since the conduct of the studies from Gozzard and Käfer and to the structured assessment the FDC provides.

This is especially important for the practitioner to confidently approach a revision case. The good results might be partially contributed to the structured radiographic analysis aided by the provided evaluation spreadsheet and standardized defect definitions according to easily observable radiographic landmarks. In this study, standing anteroposterior view and lateral view X-rays of the affected hip have been evaluated. Due to cost- and practicability-related causes, x-rays of the femur still present the method of choice for most orthopaedic surgeons to monitor bone stock and other stability parameters after primary or revision arthroplasty in the postoperative follow up cycle [17]. A classification system should be applicable to the most common imaging. It is important to mention that radiopaque material can severely impeded defect recognition and assessment of defect severity. In addition, the extent of damage to the bone caused by the revision operation due to implant and/or cement removal is difficult to anticipate and can significantly change the defect type. These points need to be taken into consideration when planning for a revision operation. A wide portfolio of available implants, especially revision stems, is advisable. Advanced diagnostics can be applied for specific questions. Through considerable improvements in diagnostic software and hardware, MARS (metal artefact reduction sequence) MRI has recently been shown to present good sensitivity and specificity to detect component loosening [18]. CT scans offer improved resolution and are useful in the analysis of focal osteolysis, deformities such as rotational abnormalities and improved digital planning capacities [19–21]. X-ray still present the first imaging step when loosening of hip prosthesis is suspected and present with a decent sensitivity and specificity but are not as specific/sensitive as MRI and CT [22].

For a classification system to be widely adopted, it needs to be intuitive and easy to apply. In the creation of the FDC, the authors focused on a structured design and kept it as similar as possible to the ADC to complete the integrated system.

Several studies have evaluated the reliability of established femoral bone loss classifications. The most evaluated system is the Paprosky classification with mixed results in literature. An evaluation carried out by the same group who introduced the initial classification system found substantial agreement between raters and for the same rater at different points in time. Results showed k values of 0.61 for inter-rater reliability and 0.81, 0.78, and 0.75 for intra-rater reliability which is in a similar range to our own findings [23]. These results were confirmed by another study, which also evaluated the classifications system of the AAOS (0.63–0.68) and the Endoklinik (0.83–0.85) [24]. Other groups have reported different results with reliability rating as low as 0.27–0.50 for inter-rater evaluation and 0.09–0.64 for intra-rater evaluation of the Paprosky system [15]. Haddad et al. described

an overall low reliability for the Paprosky, AAOS and Mallory system with inter-rater reliability ranging from 0.12 to 0.29 and intra-rater reliability ranging from 0.43 to 0.63 [25]. A recent systematic review demonstrated good intra-rater reliability for the Paprosky and AAOS systems but only moderate inter-rater-reliability for Paprosky and even poor inter-rater reliability for AAOS [26]. An explanation for the deviating results in different studies might be differences in training [23]. In summary, the FDC appears to be in an equal or even superior range concerning reliability when compared to established classification systems. Due to different results in the evaluation of reliability of established classification systems further independent studies may be helpful to further validated the FDC.

Similar studies have been conducted with acetabular defect classification systems and the results for rater reliability fall into a similar range [27]. A direct comparison is limited.

In the following paragraphs, the therapeutic recommendations according to defect type will be discussed. The therapeutic algorithm was established through expert opinion in combination with a thorough review of the current literature and derived from the therapeutic procedure of the authors' own clinical experiences.

The category of type 1 bone defects presents with a destruction of the femoral neck while leaving the remaining bone stock of the femur, including the metaphysis and diaphysis, utterly intact. These defects can be experienced after a femoral neck fracture or a revision of a hip resurfacing prosthesis. While extensive research shows the higher failure rate of metal-on-metal (MoM) hip resurfacing when compared to a standard total hip replacement, a limited number of studies investigated the revision implant best suited to the consecutive femoral bone defect after implant failure. In most publications, a stable femoral revision after hip resurfacing could be achieved using a short stem or a standard cemented/cementless femoral component [28, 29].

The main defect for FDC type 2 is located at the metaphysis. Type 2A presents a complete depletion of the metaphyseal cancellous bone, while the structure of the compacta remains supportive, leaving especially the muscle attachment at the greater and lesser trochanter intact. This type of defect can occur after extensive loosening of a short stem prosthesis or a cementless or cemented standard stem. As long as the cortical bone stock of the metaphysis is supportive, a metaphyseal anchoring standard stem can be utilized [30–33]. When a cemented fixation is chosen, enough cancellous bone, or at least a roughened up corticalis needs to remain in the diaphyseal aspect to enable proper interdigitation with the cement layer [34]. In case of cementless stem fixation, impaction bone grafting should be applied to allow for biological downsizing of the metaphyseal defect [35–39].

In type 2B, the lesser trochanter and the dense compacta called Calcar femoris are rendered non-supportively in addition to the cancellous depletion of the metaphyseal aspect of the femur. This renders the metaphyseal bone stock non-supportively and dictates to project the fixation of the chosen prosthesis in the diaphyseal portion of the femur. Due to the intact greater trochanter and the muscle attachment of the gluteal group, a cementless or cemented diaphyseal anchoring standard stem can be chosen. Once the stem is inserted, analogous to type 2A defects, impaction bone grafting should be applied to allow for biological downsizing [35–37].

In type 2C, severe metaphyseal bone loss and disintegration of the greater trochanter is encountered. This presents a structural as well as functional challenge due to the loss of vital muscle attachment. Great care should be taken intraoperatively to re-fixate any remaining bone stock and muscle attachments through wire/suture cerclages. To prevent particle debris and consecutive osteolysis through metallosis, the wire/suture cerclages should not be in contact with any part of the endoprosthesis. To ensure an appropriate intermediate layer, Strut grafts may be applied. Figure 6 demonstrates a type 2C defect caused by severe metallosis for which the deficient bone stock of the greater trochanter is stabilized with wire/suture cerclages.

Caused by the decreased function of the muscular sleeve, instability with the risk of consecutive luxation increases dramatically. While fixation can be handled according to type 2B with a diaphyseal anchoring stem, which can either be cemented or cementless, additional support to provide functional stability needs to be considered. Alternative bearing constructs can include dual mobility articulations, unconstrained tripolar articulations or constrained liners. While constrained liners offer an increased amount of stability, they further the risk of potential catastrophic implant failure requiring additional surgical intervention [40, 41]. Therefore, the addition of a constrained liner should be reserved for severe cases with previous exhaustion of other options. Unconstrained tripolar articulations and dual mobility articulations present less constrained options, while still offering a larger excursion distance, more range of motion prior to impingement and can help in the restoration of appropriate offset and the tensioning of the abductor muscle. First results show promising results for tripolar and dual mobility articulations regarding rate of luxation. The increased number of articulating interfaces may lead to an increased amount of particle debris and consecutive osteolysis, which raises concerns [42–46].

Type 3 defects extend into the diaphyseal aspect of the femur while leaving the isthmus femoris intact. In these cases, a cementless revision stem (modular/monobloc) should be implanted with a sufficient length to anchor in the cortical frame distal to the defect. The required length

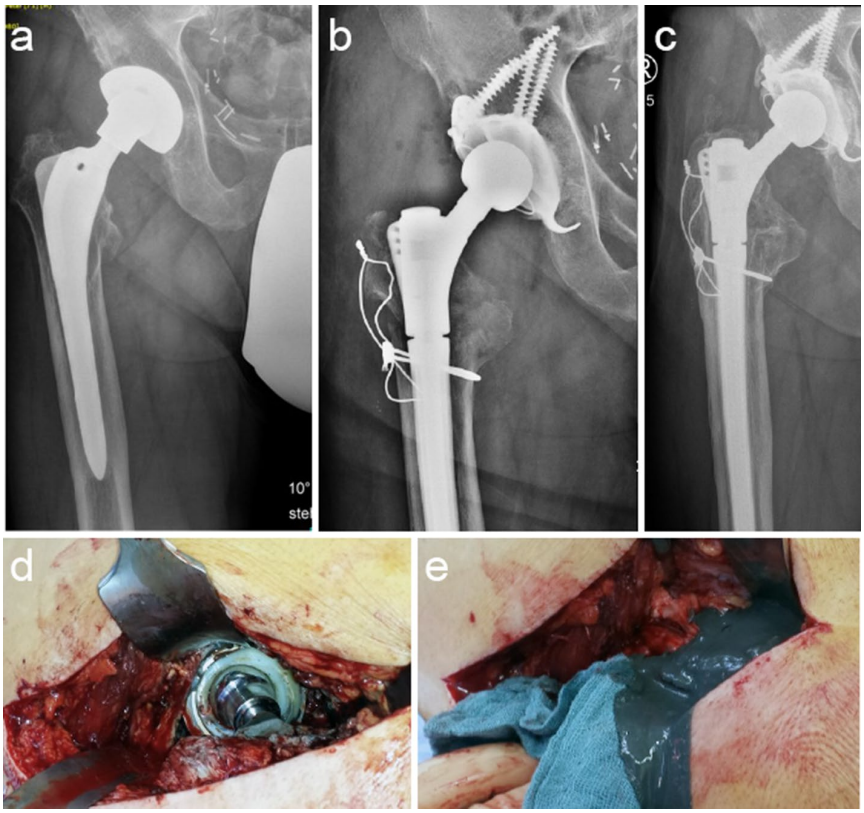

Fig. 6 Clinical case of a 73-year-old, male patient presenting with a type 2C defect caused by severe metallosis due to metal-on-metal particle debris. Primary arthroplasty took place 12 years prior to revision; (**a**) displays the preoperative native radiograph (pelvis ap standing) with osteolytic bone stock at the metaphysis; (**b**) postoperative native radiograph (pelvis ap standing) with a cementless, modular, femoral revision stem and additional wire cerclages to stabilize the remaining bone stock of the greater trochanter combined with impaction bone grafting; (**c**) native radiograph (pelvis ap standing) four years after revision arthroplasty displaying a consolidation of the augmented and stabilized femoral metaphysis; (**d/e**) displays the intraoperative finding of severe metallosis

of circumferential press-fit for cementless revision stems is an ongoing debate. A press-fit distance for tapered stems of less than 2 cm appears to be an independent risk factor for significant stem subsidence [45]. Other authors reported a minimum of 5–7 cm of circumferential press-fit required to prevent subsidence, which appears adequate in our own clinical experience. Drilling of the femoral medullary canal can be utilized to optimize fitting of the stem and to achieve the appropriate contact area [38, 46]. To neutralize applied endo-femoral force generated through the press-fit, wire/suture cerclages can be liberally applied. To allow for biological downsizing, especially in type 3C defects, Strut grafts can be added in the area of the unsupportive bone to provide a framework for wire/suture cerclage stabilized diaphyseal cortical bone. In Fig. 7, Strut grafts are applied to provide additional augmentation in the case of a type 3C defect. If a sufficient press-fit of a minimum of 5 cm cannot be achieved, additional distal locking screws should be added to the construct.

Finally, type 4 defects present the most severe defects of this classification system and in clinical practice. The isthmus becomes increasingly compromised while moving from a to c. Type 4A and B defects may be able to be salvaged through long cementless revision stems and a combination of Strut grafts and wire/suture cerclages to enable at least a limited amount of press-fit. Type 4C defects display the so called "stovepipe configuration" with an insufficient isthmus femoris. In these cases, cemented partial or total femur replacement should be applied as a salvage procedure. A table containing all therapeutic recommendations according to defect type is supplied below (Table 1).

This classification system has several limitations. To keep the structure simple and easy to apply, some defect morphologies are simplified. A standardized classification system will always lack in the all-encompassing description of every possible defect morphology. In clinical practice, different combinations of defects might be encountered and the surgeon must be vigilant to alter the therapeutic algorithm accordingly. While the FDC is applicable to any type of radiographic imaging as well as to an intraoperative setting, it has initially been based on x-rays. As discussed above, x-rays may present with limited reliability in defect recognition. When performing a preoperative evaluation with an implant still in situ, the prospective additional destruction of bone due to implant removal must be taken into consideration and the defect grading must be updated accordingly. The correlation between preoperative grading and intraoperative findings has been evaluated retrospectively. While further prospective studies are ongoing, the current evaluation presents with limited expressiveness. The preoperative

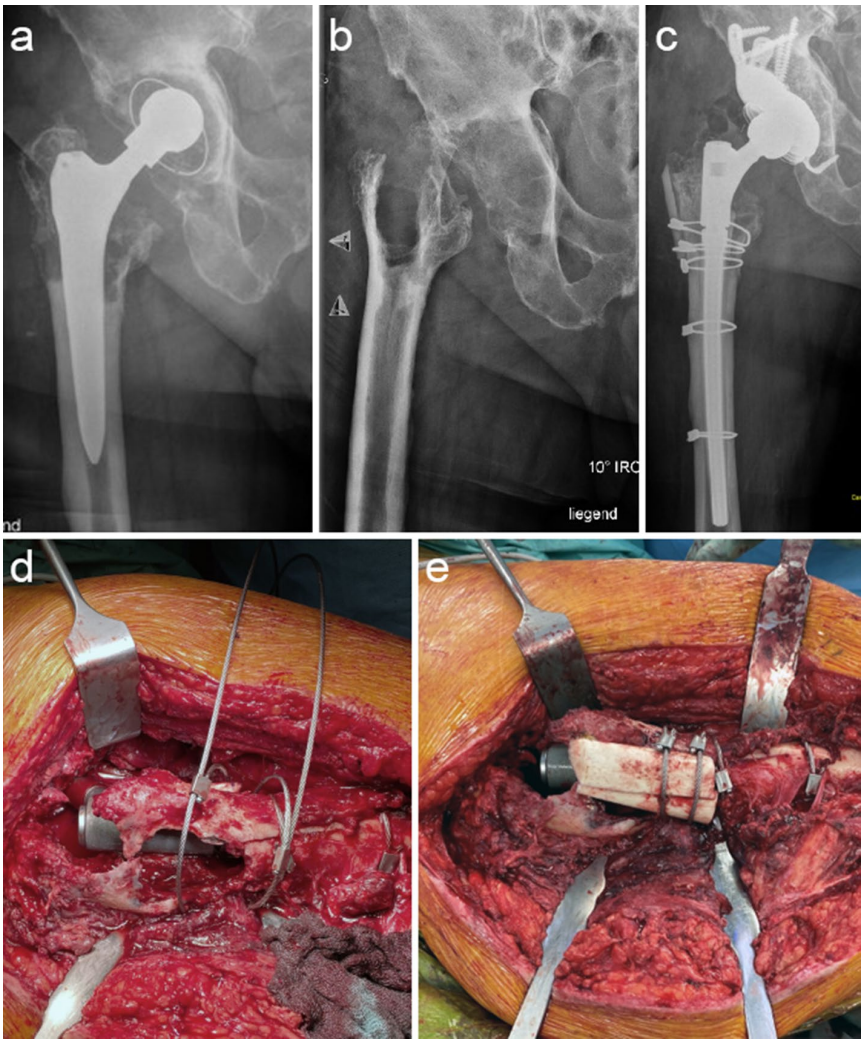

Fig. 7 Clinical case of a 71-year-old, male patient presenting with a type 3C defect and cystic granulomatosis due to particle debris. **a** displays the preoperative native radiograph (pelvis ap standing), which illustrates large cystic osteolysis encompassing the metaphysis and proximal diaphyseal bone; (**b**) postoperative native radiograph (pelvis ap standing) after removing the implant and granuloma visualizing the full extent of the defect situation; (**c**) postoperative native radiograph (pelvis ap standing) after revision arthroplasty utilizing a long, cementless, modular, femoral revision stem and additional allogenous augmentation through impaction bone grafting and Strut grafts fixated with wire cerclages; (**d**) illustrates the extent of the metaphyseal/diaphyseal defect, the stem has been inserted and subsequently wire cerclages are being placed around the femur to receive the Strut grafts; (**e**) finalized femoral revision arthroplasty. Strut grafts act as a shell for the impaction bone grafting

Table 1 Therapeutic recommendation based on defect type according to FDC

Type of defect	Implant choice
1	Cementless or cemented standard stem, short stem if enough of the femoral neck remains
2A	Cementless short stem, cementless or cemented standard stem
2B	Diaphyseal anchoring stem design + impaction bone grafting
2C	Diaphyseal anchoring stem design + impaction bone grafting + alternative bearing construct*
3A	(Modular) Revision stem + impaction bone grafting
3B	(Modular) Revision stem + impaction bone grafting + as an option: diaphyseal wire/suture cerclages
3C	(Modular) Revision stem + impaction bone grafting + strut graft proximal lateral, stabilized with wire/suture cerclages; as an option: diaphyseal wire cerclages
4A	(Modular) Revision stem + impaction bone grafting + strut graft and wire/suture cerclages
4B	(Modular) Revision stem with distal screw fixation + impaction bone grafting + strut graft and wire/suture cerclages
4C	Proximal or total femoral replacement

*Whenever insufficient muscular stability is encountered, alternative bearing constructs (bipolar/tripolar) may be applied

grading and the intraoperative findings have been evaluated by two of the originators of the FDC which can propose a possible bias.

Conclusion

The femoral defect classification (FDC) is a reliable and reproducible classification system and in combination with the recently introduced acetabular defect classification (ADC) offers a structured approach to the entire field of hip revision arthroplasty. The provided therapeutic algorithm has been created according to current literature and expert opinion and should be validated through future prospective clincial research.

Author contributions MJ: Responsible for study design, creation of the classification system, responsible for drafting the manuscript, analyzed the data and interpreted the findings, read and approved the final version of the manuscript before submission. HK: Responsible for study design, responsible for drafting the manuscript, read and approved the final version of the manuscript before submission. AK: Included radiographs and collected the primary data, analyzed the data and interpreted the findings, read and approved the final version of the manuscript before submission. MG: Analyzed the data and interpreted the findings, included radiographs and collected the primary data, read and approved the final version of the manuscript before submission. TMR: Analyzed the data and interpreted the findings, included radiographs and collected the primary data, read and approved the final version of the manuscript before submission. KK: Analyzed the data and interpreted the findings, responsible for drafting the manuscript, read and approved the final version of the manuscript before submission. PPR: Responsible for study design, analyzed the data and interpreted the findings, read and approved the final version of the manuscript before submission. GP: Contributed significantly to the revision process, read and approved the final version of the manuscript before submission. DCW: Responsible for study design, creation of the classification system, creation of therapeutic recommendation, analyzed the data and interpreted the findings, read and approved the final version of the manuscript before submission.

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Declarations

Conflict of interest All authors declare that they have no conflict of interest.

Ethical approval All procedures performed in this study were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent For this type of study, formal consent is not required. All data obtained are part of in-house quality assessment in accordance with National Register procedures. Additional approval for this study was obtained from the institutional review board of our hospital (study no. 369/17).

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3.2 Jaenisch M, Wirtz DC, Kohlhof H, Gathen M, Kabir K, Koob S, Jansen TR (2021) APP-guided assessment of of acetabular defects in hip revision arthroplasty: a structured approach to a complex situation. Arch Orthop Trauma Surg. 32(3):248-261. https://doi.org/10.1007/s00402-021-04270-8

Zielsetzung der Arbeit:

Die Erkennung und Klassifizierung von azetabulären Defekten gestaltet sich für den behandelnden Chirurgen sehr herausfordernd. Die jüngst vorgestellte Azetabuläre Defekt Klassifikation (Acetabular Defect Classification; ADC) ist ein verlässliches, reproduzierbares und intuitives Klassifikationssystem für periprothetische Knochendefekte des Hüftgelenks. Um die Benutzerfreundlichkeit und Effizienz der ADC weiter zu erhöhen wurde eine Browser-basierte Applikation zur Umsetzung des Klassifikationssystems erstellt. Diese Veröffentlichung untersucht, ob die ADC-Applikation das Klassifikationsresultat von Medizinstudierenden verbessert und dadurch ein vergleichbares Ergebnis wie von erfahrenen Operateuren ohne die Hilfe der Applikation erreicht werden kann.

Material und Methoden:

Die ADC basiert auf der Integrität des azetabulären Randes und der stabilitäts-vermittelnden Strukturen. Sie besteht aus vier Hauptkategorien, welche in der Defektschwere ansteigen. Die vier Hauptkategorien sind weiter unterteilt in Subkategorien (a-c), welche die Lokalisation des Defektes beschreiben. Insgesamt 80 randomisierte Röntgenaufnahmen wurden durch 3 Medizinstudierende und 3 erfahrene orthopädische Operateure nach ADC klassifiziert. Medizinstudierende verwendeten hierbei die ADC-Applikation, während die Operateure keine digitale Unterstützung erhielten. Evaluiert wurde der Unterschied zwischen der Untersucherübereinstimmung (Interrater-Übereinstimmung) zwischen den Gruppen. Um die Intrarater-Übereinstimmung zu analysieren erfolgte eine erneute randomisierte Auswertung nach 2 Wochen.

Ergebnisse:

Die Medizinstudierenden zeigten sowohl für die Interrater-Übereinstimmung, als auch für die Intrarater-Übereinstimmung schlechtere Ergebnisse als die Operateure. Allerdings zeigten die Ergebnisse der Medizinstudierenden immer noch eine gute

Übereinstimmung. Die Medizinstudierenden erreichten K-Werte von 0.61 für die Interrater-Übereinstimmung und 0.68 für die Intrarater-Übereinstimmung, während die Operateure 0.72 für die Interrater-Übereinstimmung und 0.83 für die Intrarater-Übereinstimmung erzielten.

Schlussfolgerung:
Die APP-unterstützte Analyse von azetabulären Defekten verspricht einen innovativen Ansatz, um eine komplexe Problemstellung einfacher bearbeiten zu können. Sie erniedrigt die Eingangsbarriere besonders für weniger erfahrene Benutzer und erleichtert die präoperative Defekterkennung.

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ORTHOPAEDIC SURGERY

APP-guided assessment of acetabular defects in hip revision arthroplasty: a structured approach to a complex situation

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Abstract

Introduction Acetabular defect recognition and classification remains a challenging field of practice for orthopedic surgeons. Recently, the Acetabular Defect Classification (ADC) has been introduced to provide a reliable, reproducible and intuitive classification system. In order to improve ease of use and efficiency of the ADC, a browser-based application has been created. We hypothesized that the ADC application can improve rating performance of non-specialists (medical students) to achieve good inter- and intra-rater agreement and will compare favorable to the results of specialists (experienced surgeons) without the help of the application.

Materials and methods The ADC is based on the integrity of the acetabular rim and the supporting structures. It consists of four main types of defects ascending in severity. These defects are further subdivided in A–C, narrowing down defect location. 80 randomized radiographs were graded according to ADC by three non-specialists (medical students) with help of the ADC application and by three specialists (orthopedic surgeons) without help of the application to evaluate the difference in inter-rater agreement between groups. To account for intra-rater agreement, the rating process was repeated after a reasonable wash-out period.

Results Inter-rater and intra-rater agreement within the non-specialist group rated lower when compared to the specialist group while still falling into the good agreement range. The student group presented with k values of 0.61 for inter-rater agreement and 0.68 for intra-rater agreement, while the surgeon group displayed k values of 0.72 for inter-rater agreement and 0.83 for intra-rater agreement.

Conclusion The app-guided assessment of acetabular defects offers a promising innovative approach to simplify complex situations. It makes the challenging field of acetabular revision arthroplasty more approachable especially for less experienced surgeons and offers insight and guidance in the planning stage as well as intra-operative setting.

Keywords Acetabular · Bone defect · ADC · App · Application · Hip · Arthroplasty · Revision

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Introduction

Modern total hip arthroplasty is considered to be the operation of the century, offering pain relief, advanced mobilization and an increased overall quality of life to a vast number of patients [1, 2]. While implantation rates are predicted to increase all over the developed world, due to the limited durability and survival of implants, revision cases tend to accumulate as well. Most cases of hip revision arthroplasty are accompanied by acetabular bone defects of varying degree. Depending on the severity of the damage to the remaining bone stock, primary stable implantation of the revision component and a favorable long-term outcome are demanding to achieve. Detailed and proper defect recognition and meticulous pre-operative planning are essential. To facilitate pre-operative grading of the expected bone loss, numerous acetabular defect classification systems have been established [3–6]. Recently, the Acetabular Defect Classification—short ADC—has been introduced to provide a reliable, reproducible and intuitive classification system, which offers a clear therapeutic guideline [7]. Even though the structured design facilitates intuitive use, acetabular defects present a complex and difficult field of practice and especially for unexperienced surgeons, ways to lower the introductory hurdle are more than welcome.

The omnipresent mobile device commonly known as "smart phone" has altered the way we interact with each other and how we consume information. Many studies have confirmed a significant increase in the number of smart phone users and the time being spent on mobile devices per day [8–10]. The introduction of customizable applications, which can be accessed through app stores or various internet browsers, offer the possibility of individualization and ubiquitous access to web-based information and innovative technologies [11]. Therefore, daily usage for various private and professional applications such as online banking or different modes of communication have become common place [12].

Medical applications are on the rise as well and their number and availability are constantly increasing. While an unified nomenclature is still lacking, most available applications are described as "health", "lifestyle" or "care"-apps and are mostly aimed for individual adoption by private end users. Nevertheless, especially young surgeons in the field of Orthopedics and Trauma Surgery use smartphone apps daily in their clinical practice and the importance in the near future is projected to increase [13].

Due to the corona pandemic a steep increase in web-assisted patient care can be observed in clinical practice. Especially the utilization of telemedical examinations to reduce human contact and prevent a further spreading of the corona virus has increased significantly [14]. In these cases, medical applications such as virtual goniometers may be helpful to increase accuracy of a telemedical examination [15–17].

To further improve the ease of use and efficacy of the ADC, a browser-based application appears to be a natural evolution and has been developed to lead the user along the pre-operative radiographic grading process. To the authors' knowledge, no system is available that applies an established acetabular defect classification system with the practical benefits of a browser-based application. App-guided evaluation of complex defect situations could offer a vast array of potential benefits, such as increased efficacy and a steeper learning curve. The ADC has been proven to offer a reliable pre-operative grading which corresponds closely with the encountered intra-operative findings [7]. Therefore, the following publication will exclusively focus on evaluating the improvement in grading experience generated through an web-based application.

We hypothesized that the ADC application can improve rating performance of non-specialists (medical students) to achieve good inter- and intra-rater agreement according to Landis and Koch, and will compare favorably to the results, which experienced orthopedic surgeons achieved without the help of the application [18].

Materials and methods

Study design

From a sample of 211 patients who underwent acetabular revision for various reasons with exchange of at least the acetabular component, a randomized sample of 80 pre-operative radiographs, after power analysis, was selected. All radiographs were screened for sufficient quality to allow for a reliable grading. To enable blinded assessment any identifying features were removed, and the images were anonymized by numerical coding. Radiographic assessment consisted of pelvis a.p. standing and involved hip axial. Radiographic analysis and grading were carried out using IMPAX EE (Agfa HealthCare GmbH, Bonn, Germany).

Raters were recruited and divided into two different groups. The first group (specialists, S) consisted of experienced orthopedic surgeons in the field of hip revision arthroplasty. The second groups consisted of medical students (non-specialists, nS). None of the raters had any prior knowledge of the ADC or were involved in the creation.

Each rater received a teaching session consisting of an overview of the classification system and the supervised evaluation of ten random cases, which did not include any of the tested 80 cases. A scoring sheet was distributed. Only the nS group received an introduction to the ADC application

and was allowed to use it during the teaching session and further rating.

Radiographic evaluation was carried out at two different stages with a wash-out period of two weeks in between to avoid bias due to memorization. All images were relabeled and randomized prior to the second evaluation.

Browser-based application and classification system

The browser-based application was built using Angular (Version 6, Google LLC, Mountain View, California, USA), a TypeScript-based open-source web application framework. The front-end design was built using Bootstrap (Version 4, Twitter Inc., San Francisco, California, USA). Cordova Apache (Version 4.5.5, Adobe Inc., San José, California, USA) was used to transform the web app to a native iOS application. All data are temporarily stored in the internal storage of the device and are deleted after each run time. No data is stored on the web server. The app itself is designed as a guided walk-through. Each sub-item of the acetabular defect characteristics can be chosen by a simple-selection button. Once a sub-item for each characteristic is chosen, the defect category can be calculated. After calculation, an example image of the chosen acetabular defect and a treatment option are displayed. Figure 1a–d displays the individual steps of the application work flow.

The Acetabular Defect Classification (ADC) is based on the integrity of the acetabular rim and the supporting structures. It consists of four main types of defects ascending in severity, with an additional subdivision into a, b and c. The following defect descriptions are extracted from the original publication introducing the ADC [7].

Type 1 defects

Type 1 defects are characterized as contained defects with the acetabular rim remaining intact and only showing cancellous bone defects in different locations according to subdivision. A 1A defect displays randomly distributed cancellous defects, which respect the superomedial aspect of the acetabulum, as well as the medial wall, leaving these structures intact. A 1B defect exhibits additionally to defects already described for a lysis of the superomedial acetabulum. A 1C defect displays a deficiency of the medial wall, which does not affect the anterior or posterior column.

Type 2 defects

Type 2 defects demonstrate a non-contained defect of the acetabular rim in addition to cancellous bone defects. The defect measures below or equal 10 mm and is considered as non-structural. For 2A the rim defect affects the superolateral portion while in 2B the posterior column is deficient. A type 2C defect is a combination of A and B and displays a defect including the full weight-bearing portion of the rim. Because of its measurement below 10 mm, it is also considered as non-structural.

Type 3 defects

Type 3 defects possess non-contained, structural defects over 10 mm of the acetabular rim. The subdivision follows the same structure as for the type 2 defects with A, including the superior aspect, B, the posterior column and C being a combination of both. An illustration of a type 3 C defect is displayed in Fig. 2.

Type 4 defects

Type 4 defects involve pelvic discontinuity and are the most severe cases of acetabular bone loss. There is a disruption between the bone stock of the ischium and the ilium. The anterior and posterior columns are rendered non-supportive. The subclassification in A, B and C allow for evaluation of the therapeutic options by taking the superior bone support into consideration. For A, the superior bone stock is considered supportive, for B a non-structural superior rim defect under/equal 10 mm is described and for C, a structural superior rim defect over 10 mm accompanies the pelvis discontinuity.

Statistical analysis

For the statistical analysis, IBM SPSS Statistics 1.0.0.1131 (IBM Inc., Armonk, New York, USA) was utilized. The level of significance was set at $p < 0.05$ and the confidence interval at 95%. To account for inter-rater reliability in the process of comparing ordered categorical data with more than two raters, Fleiss kappa was used. Through the utilization of Cohens kappa intra-rater reliability was calculated and compared through the mean kappa of all raters. Interpretation of kappa values was achieved through the agreement scale described by Landis and Koch. Kappa values exceeding 0.80 indicate excellent agreement, between 0.61 and 0.8 indicate good agreement, between 0.41 and 0.60 indicate moderate agreement, between 0.21 and 0.4 indicate fair agreement and between 0.20 and below indicates poor agreement [18].

Results

Inter-rater agreement of the nS group was evaluated at a k value of 0.611 ± 0.022, which differed significantly from the inter-rater agreement of the S group ($p < 0.001$), which was evaluated at a k value of 0.721 ± 0.023. Both results

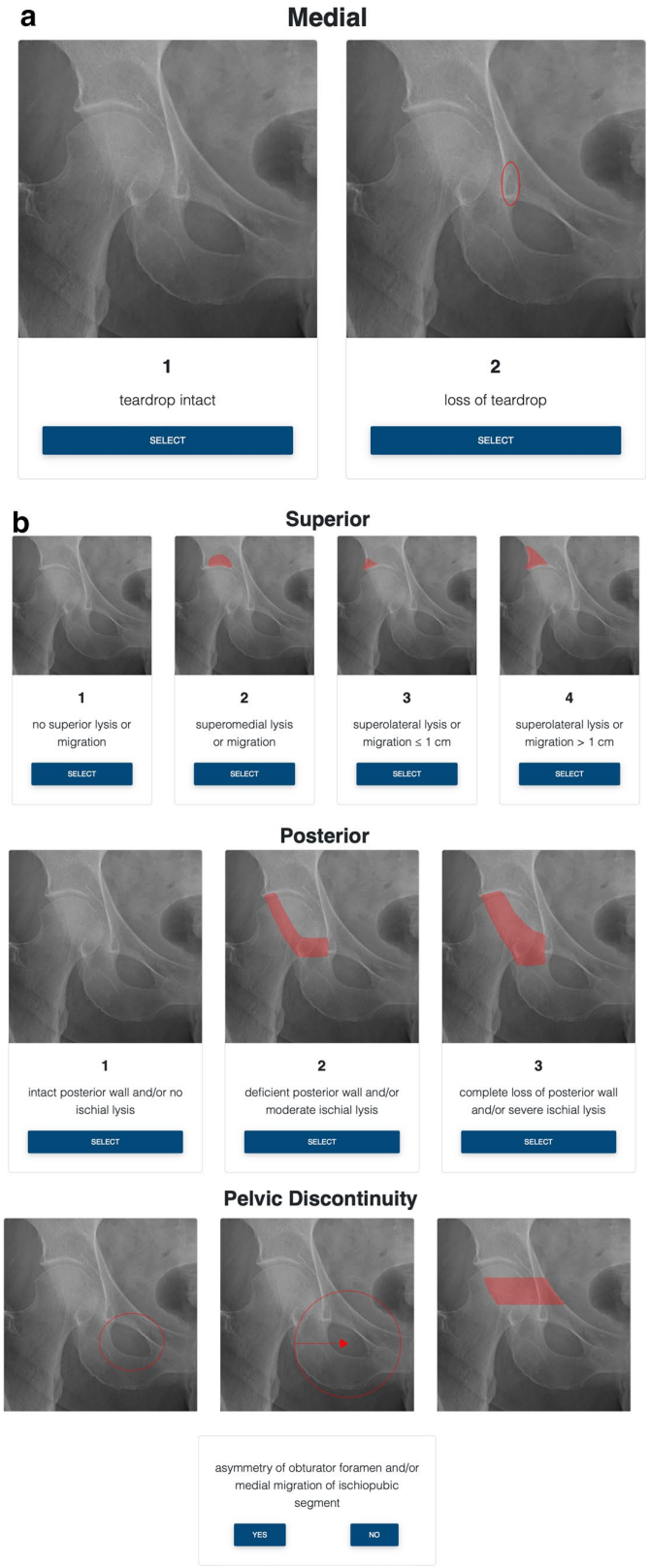


Fig. 1 The ADC application is designed as a walk-through, guiding the end user through a radiographic evaluation of an acetabular defect. Due to the condensation of information by depicting a complex, three-dimensional bone defect on a two-dimensional native radiograph, structured and detailed evaluation is essential to achieve a reliable grading. In all grading steps a native a.p. radiograph of a right-sided, healthy hip joint is provided for comparison. **a** Beginning with the medial portion of the acetabulum, the end user can evaluate the integrity of the "teardrop", a radiographic phenomenon resulting in the overlay of different bone surface encompassing the medial wall. The teardrop is marked with a red oval ellipse. For options, either "teardrop intact" or "loss of teardrop" can be selected. **b** In the next grading step, the superior aspect of the acetabular rim can be evaluated. The region of interest is clearly marked by a red color overlay. Options extend from "no superior lysis or migration", over "superomedial lysis or migration", and "superomedial lysis or migration < 1 cm", to "superolateral lysis or migration > 1 cm. **c** On the following page the posterior aspect of the acetabulum is evaluated. The region of interest is clearly marked by a red color overlay. Possible choices are: "intact posterior wall and/or no ischial lysis", "deficient posterior wall and/or moderate ischial lysis" and "complete loss of posterior wall and/or severe ischial lysis". **d** At the last grading step direct or indirect signs of pelvic discontinuity need to be assessed. If any signs of pelvic discontinuity are present, such as "asymmetry of obturator foramen and/or medial migration of ischiopubic segment" (compare to the first and second marked image) or a visible fracture line can be observed (compare to the third marked image), the user can choose "yes" and continue

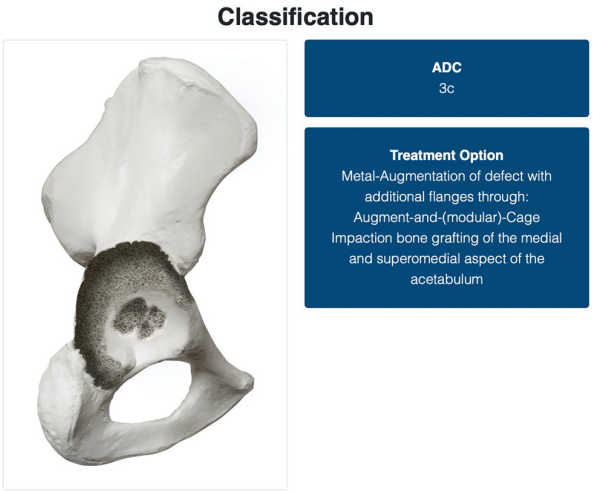


Fig. 2 The depiction of one of the possible results. In this case, in the field "ADC", a 3b defect has been classified. Possible implant choices are provided in the "Treatment Option" field. Each therapeutic recommendation is specifically tailored to the evaluated defect and based on a thorough review of the literature and expert opinion. On the left side of the figure, an anatomical representation of the defect is provided to further convey detailed understanding of the bone morphology

fall into the good agreement range as defined by the scale of Landis and Koch [18]. For the control of the reproducibility of the ADC applications impact on the quality of rating, intra-rater agreement has been examined after a wash-out period of two weeks. The nS group achieved a k value of 0.678 ± 0.040, while the surgeon group achieved a k value of 0.830 ± 0.049. There was once more a significant difference between both k values with the nS group registering lower than the S group ($p < 0.001$). Both values fall above the good agreement range with the nS group even displaying excellent agreement. The individual values for intra-rater reliability are illustrated in Fig. 3a, b.

The feedback provided by the included raters (nS) conveyed a positive attitude and underlined the ease of use and an appreciation for a structured approach to a complex situation. Through the process of this evaluation, no technical issues such as failures to boot, slow servers and loading times or issues in coding were reported. The users displayed a steep learning curve and a quick adaption rate to the operating mode. During the conduct of this study, the web-based application could be utilized thorough out various operating system including Apple iOS, iPadOS and OSX (Apple, Cupertino, California, USA) and Windows 7, 8, 9 and 10 (Microsoft Corporation, Redmond, Washington, USA) and Android Open Handset Alliance (Google Limited Liability Company, Mountain View, California, USA) (Fig. 4).

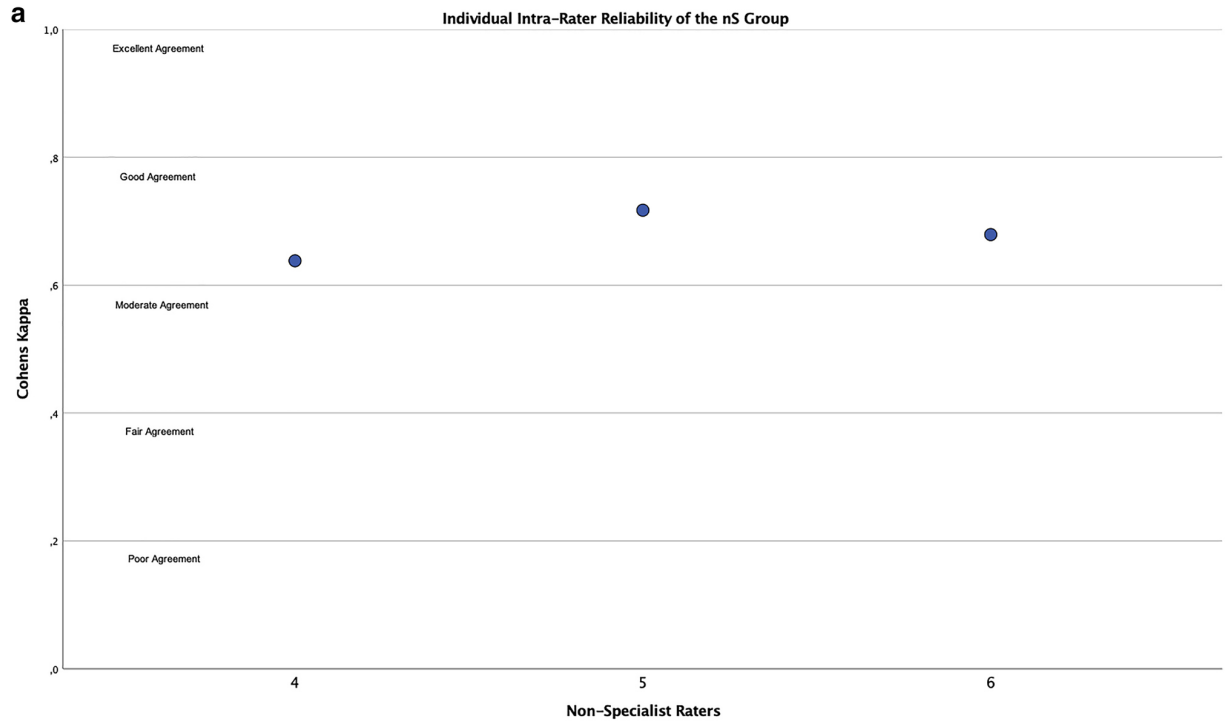
Discussion

The utilization of smartphone and mobile applications is projected to increase in the medical community [19–21]. While mostly younger and less experienced surgeons in the field of orthopedic and trauma surgery use their smartphone on a regular basis in clinical practice, surgeons with > 15 years of experience have shown to employ frequent use of their mobile devices as well [13, 20]. Though the majority of "health" applications are generated for non-medical end users, content provided for medical professionals is projected to increase [22, 23]. Considering the current trend of rapidly increasing smartphone use in the orthopedic community, the creation of mobile applications to aid the professional end users in their clinical practice appears to be a natural evolution [19].

Possible applications for mobile devices are nearly endless and include limited but instrumental tasks like goniometers, or simple but data-secure messaging tools and extend to complex classification systems and surgical reference guides as described below.

Acetabular bone loss in cases of revision hip arthroplasty has been a well-researched scientific field and many classification systems have been introduced as an attempt to manage the complexity [3–6]. In the literature, classification systems such as introduced by Paprosky et al., Gross et al. and the AAOS display varying reliability mostly ranging from moderate to poor [24]. While clinically and methodically well thought through, most classification systems are complex and appear overwhelming, especially when adopted by inexperienced surgeons. To provide a more reliable and easily adoptable classification system, the ADC has been introduced recently [7]. While presenting with good inter- and intra-rater agreement in the initial publication, it contains all clinically relevant defect morphologies while not being overly simplified. To further increase the ease of use, a conversion to a mobile application has been carried out resulting in this publication. Through our results, we were able to show that non-specialist raters (medical students) were able to achieve sufficient results in a complex setting, such as acetabular defects, when compared to experienced orthopedic surgeons. To the knowledge of the authors, no other acetabular defect classification system has been converted to a mobile application and therefore direct comparison is currently not possible.

While the conversion of complex classification systems into mobile applications has not yet been widely adopted in the field of orthopedic and trauma surgery, there is a remarkably similar example in the literature. The group around Riouallon created a smartphone application to aid the utilization of the complex Letournel classification


a
Individual Intra-Rater Reliability of the nS Group
Excellent Agreement
Good Agreement
Moderate Agreement
Fair Agreement
Poor Agreement
Cohens Kappa
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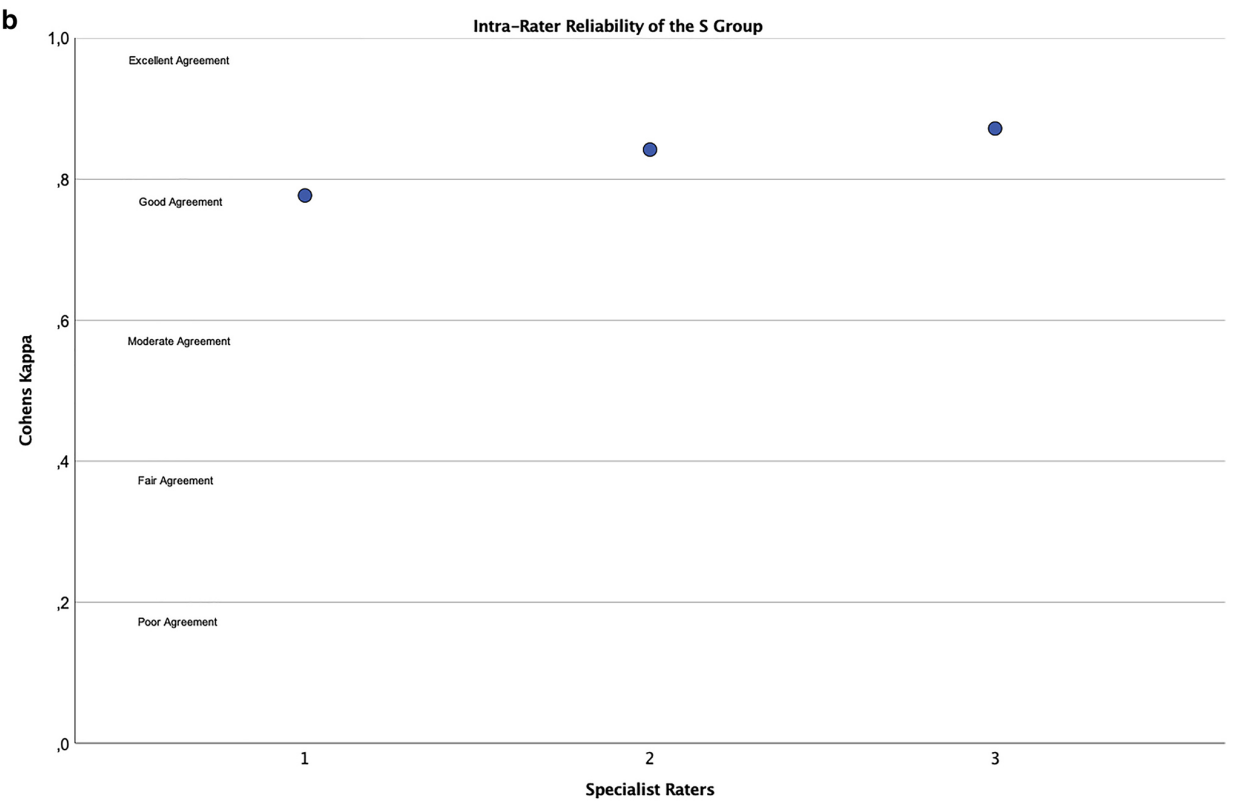
6
Non-Specialist Raters


b
Intra-Rater Reliability of the S Group
Excellent Agreement
Good Agreement
Moderate Agreement
Fair Agreement
Poor Agreement
Cohens Kappa
1,0
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Specialist Raters

◂**Fig. 3** The display of the individual k values for intra-rater reliability of the S group (**a**) and the nS group (**b**). All values fall at least in the good agreement range with two raters in the S group achieving excellent agreement. The different agreement ranges are labeled and divided by horizontal lines to provide an interpretative context to the *k* values. Y-axis features Cohens kappa and X-axis the individual rater ID 1–5 of specialist and non-specialist raters

system for acetabular fractures. Congruent to our own findings, the group discovered a high accuracy even for inexperienced raters through usage of the provided application. In addition, Riouallon observed a significant reduction in average interpretation time when the app was used, which has not been evaluated in this study but would be an interesting question for future research [22].

Another famous and widely adopted example is the browser-based application AOSR (Arbeitsgemeinschaft Osteosynthese Surgery Reference) created by the AO Foundation which helps with the classification of various fractures all over the human and even animal body and offers surgical guidance as well [25]. An assessment of the accuracy of the AO Spine Thoracolumbar Classification as part of the ASOR has been recently conducted by de Araujo Ono and colleagues. They succeeded in showing that residents improved their ability to recognize and classify thoracolumbar spine fractures through app-usage. Therefore, they concluded that their findings reinforce the importance of mobile applications in medical education and clinical practice [26]. The results of both publications support our findings.

The group around Dittrich recently conducted a large survey among orthopedic and trauma surgeons ($n = 836$) in order to investigate the current opinion regarding acceptance, future prospects and risks of the integration and use of smartphones in medical care [13]. Their results coincide strongly with our own aims in the creation of the ADC application. The group discovered that mostly younger and less experienced doctors were prone to regular smartphone use in their clinical practice. The ADC application, while free to use for anyone, is especially aimed at less experienced surgeons entering the field of acetabular reconstruction in order to ingrain a structured and reproducible guideline for diagnostic evaluation from the beginning. To achieve widespread adoption and regular usage, Dittrich found that an intuitive usability is considered favorable, which is produced by the structured algorithm of the ADC application and its walk-through-like design. Applications that are free of charge were also favored, which corresponds with the distribution mode of our application. Two of the major concerns mentioned in the publication by Dittrich were the perceived risk of data misuse and the danger of using untrustworthy apps. As for the first concern, the data storage of the ADC applications is limited to the utilized device and is eradicated once the session has ended. No data is stored on web-based servers. As for the fear of utilizing an untrustworthy application, it is worth noting, that the ADC in itself has been validated by the original publication of this group and therefore can be considered "safe to use" [7].

Our study presents the following limitations: the group of selected raters has not been randomized and was chosen by chance through employment at our institution for the S group and through university-mandated fellowships for the nS group. The number of selected raters is limited and therefore, results achieved by a larger cohort might differ. In this publication only the direct comparison between results of the two different groups has been evaluated. An actual improvement of the medical students (nS) through the app has not been examined, but it is safe to assume that an unaided approach of a non-specialist rater in the task of acetabular defect classification would yield lower k values for both inter- and intra-rater reliability. However, we strongly encourage future research by other groups in order to further evaluate our algorithm and application and gladly provide more detailed methods on request. Lastly, it is important to note that the web-based application merely offers a guided walk-through of the ADC. Visual and lyrical cues aim to increase ease of use of a complex classification system. Known deficiencies of acetabular defect recognition and classification, such as defect obscurrence by radio-opaque material, cannot be addressed by this type of application.

Conclusion

The app-guided assessment of acetabular defects offers a promising innovative approach to simplify complex situations. It makes the challenging field of acetabular revision arthroplasty more approachable, especially for less experienced surgeons and offers insight and guidance in the planning stage as well as during the intra-operative process.

The digitalization of an acetabular defect classification through implementation of a web-based application is a valid approach to align the rating results and rating reproducibility of non-specialists to those of experienced orthopedic surgeons. The introduction of the ADC application will hopefully spawn further advances to make surgical planning more intuitive in the future.

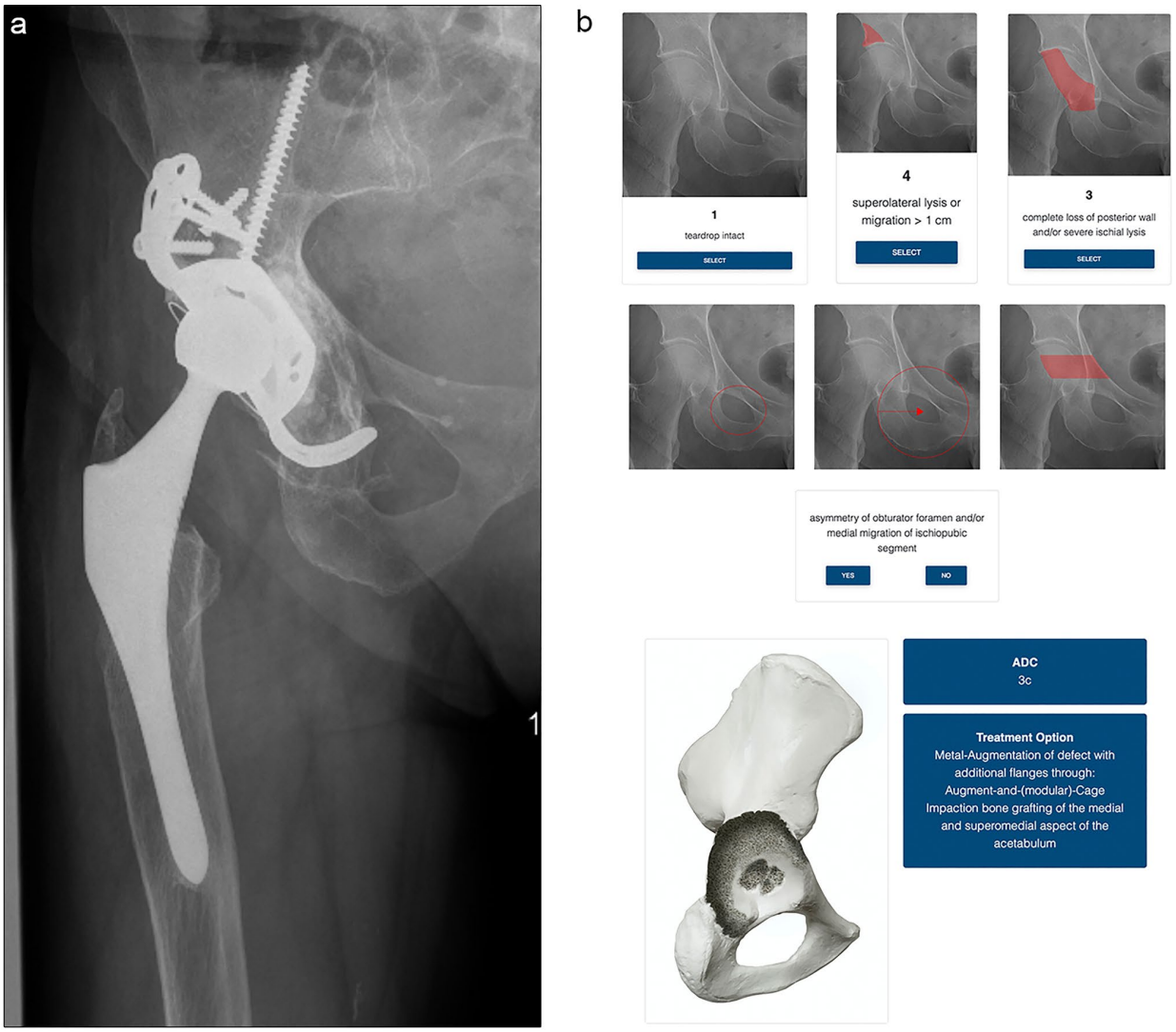

Fig. 4 The presentation of the app-guided classification of a pre-operative X-ray of a 67-year-old, female patient with multiple previous operations of the affected hip. **a** shows the pre-operative AP pelvis view, loosening of the acetabular cage with superolateral migration and consecutive breakage of the screws on the cranial strap; **b** lists the selected subdivisions within the application: medial: the teardrop appears intact due to the superolateral migration; superior: the superolateral migration ensures a superior defect, removal of the fractured screws and bony debridement will further increase defect size, a superior defect of > 1 cm is to be expected; posterior: with the implant still in place radiopaque material limits the visualization of the posterior acetabular wall, cloudy osteolysis of the visible aspects indicate the presents of a bony defect, which should be selected accordingly. To further evaluate the posterior acetabular wall a CT scan can be helpful; pelvic discontinuity: the presented X-ray displays no indicators to suspect pelvic discontinuity. an ADC 3C defect with a treatment option is displayed

Author contributions MJ: responsible for study design. Responsible for drafting the manuscript. Analyzed the data and interpreted the findings. Read and approved the final version of the manuscript before submission. DCW: responsible for study design. Responsible for drafting the manuscript. Read and approved the final version of the manuscript before submission. HK: included radiographs and collected the primary data. Analyzed the data and interpreted the findings. Read and approved the final version of the manuscript before submission. MG: analyzed the data and interpreted the findings. Included radiographs and collected the primary data. Read and approved the final version of the manuscript before submission. KK: analyzed the data and interpreted the findings. Responsible for drafting the manuscript. Read and approved the final version of the manuscript before submission. SK: responsible for study design. Analyzed the data and interpreted the findings. Read and approved the final version of the manuscript before submission. TRJ: responsible for study design. Creation of the Application. Analyzed the data and interpreted the findings. Read and approved the final version of the manuscript before submission.

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Declarations

Conflict of interest All authors declare that they have no conflict of interest.

Ethical approval and informed consent All procedures performed in this study were in accordance with the Ethical Standards of the Institutional and National Research Committee and with the 1964 Helsinki Declaration and its Later Amendments or Comparable Ethical Standards. For this type of study formal consent is not required. All data obtained are part of in-house quality assessment in accordance with National Register procedures. Additional approval for this study was obtained from the Institutional Review Board of our Hospital (Study No. 369/17).

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3.3 Jaenisch M*, Kohlhof H*, Wirtz DC, Schildberg FA, Beckmann NA, Kretzer JP, Schonhoff M, Jäger S (2021) Primary Stability in Hip Revision Arthroplasty: Comparison of the Stability of Cementless Fixed Augments on a Modular Acetabular Cage System with and without Cranial Straps. J Clin Med. 10(17):4002. https://doi.org/10.3390/jcm10174002

Zielsetzung der Arbeit:

Das Hinzufügen von kranialen Laschen an ein Revisionssystem soll zu einer Erhöhung der Primärstabilität führen. Hierzu existieren jedoch aktuell keine fundierten in-vitro Daten. Da das Hinzufügen von kranialen Laschen u.a. das Weichteiltrauma deutlich erhöht, bedarf es zur Indikationsstellung einer ausreichenden wissenschaftlichen Grundlage. Die Zielsetzung dieser Studie ist die Evaluation der primären Stabilität eines zementfrei fixierten Augments an einer modularen Revisionsabstützschale mit und ohne das Hinzufügen von kranialen Laschen unter standardisierten In-Vitro-Bedingungen. Als Surrogatparameter für die Bestimmung der Primärstabilität erfolgte die Messung von Relativbewegungen zwischen den Implantatkomponenten untereinander und zwischen den Implantatkomponenten und dem Knochen.

Material und Methoden:

Die modulare Revisionsabstützschale kombiniert mit einem zementfrei fixierten, trabekulären Metallaugment wurde in ein lebensgroßes, linksseitiges Verbund-Hemipelvis-Modell eingebracht. Die fertigen Konstrukte wurden in 2 Gruppen aufgeteilt: die S-Gruppe mit kranialen Laschen und die nS-Gruppe ohne kraniale Laschen. Insgesamt wurden 1000 Zyklen mit 3 verschiedenen Laststufen durchgeführt. Die Relativbewegungen zwischen den unterschiedlichen Komponenten wurden bestimmt.

Ergebnisse:

Die unterschiedlichen Laststufen zeigten einen signifikanten Effekt bezogen auf die Menge an Relativbewegungen an allen Grenzflächen außer zwischen Schale und Augment. Die Gruppenzuordnung hatte einen Einfluss auf die Relativbewegungen bezogen auf signifikanten Differenzen an allen Grenzflächen. Zwischen Knochen und Schale erhöhten sich die Relativbewegungen bei Erhöhung der Laststufen. Die nS-Gruppe zeigte signifikant höhere Relativbewegungen als die S-Gruppe. Zwischen

Schale und Augment zeigten sich die Relativbewegungen konstant während der Erhöhung der Laststufen. Zwischen Schale und Pfanne zeigte die S-Gruppe höhere Relativbewegungen als die nS-Gruppe, jedoch stiegen die Relativbewegungen in beiden Gruppen mit steigenden Laststufen.

Schlussfolgerung:

Aus den erhobenen Daten konnte geschlussfolgert werden, dass eine signifikante Zunahme der Primärstabilität zwischen Schale und Knochen durch das Hinzufügen von kranialen Laschen erreicht wird. Die Relativbewegungen zwischen Schale und Pfanne erhöhten sich durch das Hinzufügen von kranialen Laschen. Die klinische Konsequenz hieraus ist unklar und bedarf weiterer Untersuchungen. Abschließend zeigte sich die zementfreie Fixierung des Augments gegen den Rand der Schale stabil und erzielte günstige Werte im Vergleich zu Voruntersuchungen mit unterschiedlichen Fixierungstechniken.

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Article

Primary Stability in Hip Revision Arthroplasty: Comparison of the Stability of Cementless Fixed Augments on a Modular Acetabular Cage System with and without Cranial Straps

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Abstract: The goal of this study is to evaluate the primary stability of a cementless augment-and-modular-cage system with and without the addition of cranial straps in a standardized in vitro setting. As the surrogate parameter for the evaluation of primary stability, the measurement of relative motion between the implant components themselves and the bone will be used. Acetabular revision components with a trabecular titanium augment in combination with a large fourth-generation composite left hemipelvis were assembled. These constructs were divided into two groups with (S) and without cranial straps (nS). A total of 1000 cycles was applied at each of three load levels. Relative movements (RM) between the components were measured. Load levels display a significant effect on the amount of RM at all interfaces except between shell/augment. The group assignment appears to have an effect on RM due to significantly differing means at all interfaces. Between bone/shell RM increased as load increased. NS displayed significantly more RM than S. Between shell/augment RM remained constant as load increased. Between shell/cup S showed more RM than nS while both groups' RM increased with load. We conclude a significant increase of primary stability between the shell and the bone through the addition of cranial straps. Relative motion between components (shell/cup) increases through the addition of cranial straps. A clinical impact of this finding is uncertain and requires further investigation. Finally, the cementless fixation of the augment against the rim-portion of the shell appears stable and compares favorably to prior investigation of different fixation techniques.

Keywords: hip; revision; arthroplasty; modular; cementless; augment; cranial strap

1. Introduction

The number of primary hip arthroplasties is rising all over the developed world [1]. Due to bone loss caused by aseptic loosening and periprosthetic infection, surgeons often encounter severe acetabular defects in cases of revision surgery. With an increased number of primary hip arthroplasties, a consecutive rise in revision arthroplasties is to be expected [2]. In order to achieve long-term stability, a primary stable implantation with proper force transmission to the remaining acetabular bone stock is essential. Therefore, non-contained acetabular defects should be transitioned into contained defects [3].

While structural bulk allografts for the weight-bearing area of the acetabular rim present limited integration and consecutive resorption, leading to failure of fixation in the long term, modern macro-porous metal augments present a promising alternative [4–7]. These augments can be combined with different implant components in the means of

an augment-and-cage or augment-and-cup construct. A new alternative is a cementless augment-and-modular-cage construct. In these types of implant systems, the augment, in different shapes and sizes, can be combined with a variety of different shells featuring, e.g., cranial straps, different cup orientations, caudal hooks, and more. While this is a new approach to the treatment, first radiographic and clinical results are promising [8]. In cases of severe acetabular bone loss with the need to augment a non-contained defect, a simple press-fit of the augment and component might not be enough. Additional means of fixation can be added in order to improve primary stability. Cranial straps are supposed to provide a surplus of stability by anchoring the acetabular cage or shell to the remaining stable iliac bone stock. Widespread use in clinical practice and extensive clinical research of implant components combined with cranial straps have been conducted and appear favorable [8–11]. To the best of the authors' knowledge, no publication describes the surplus of stability achieved by the addition of cranial straps alone in objective and isolated terms. This knowledge, however, is highly important due to the increased damage of soft tissue, especially caused by the mobilization of the gluteal muscle group, required to implant cranial straps. Gluteal insufficiency, risk of damage to the gluteal nerves and vessels, as well as other soft tissue-related complications can be experienced [12]. Another important factor is the amount of relative motion between the individual components of a modular construct. Due to the different prosthesis design (with and without cranial straps), there is a possibility that the individual components of the modular system might react differently to each other and thus may lose stability. To provide an optimal therapeutic solution, modular revision systems need to be thoroughly investigated. The amount of relative motion has been discussed to affect osseointegration of implant components and may cause an increased risk of particle debris, which is associated with implant loosening. A detailed analysis of the possible impact of increased relative motion between components and between bone and the revision system will be provided below.

Therefore, the goal of this study is to evaluate the primary stability of two different designs of a cementless augment-and-modular-cage system with and without the addition of cranial straps in a standardized in vitro setting. As the surrogate parameter for the evaluation of primary stability, the measurement of relative motion between the implant components at all interfaces and the bone (composite hemipelvis model) will be used. The Results will be compared to current literature.

2. Materials and Methods

2.1. Study Design

We constructed an experimental setup utilizing an acetabular revision component with a trabecular titanium augment (MRS-Titan® Comfort, Peter Brehm GmbH, Weisendorf, Germany) in combination with a large fourth-generation composite left hemipelvis (#3405 Sawbones; Sawbones Europe AB, Malmö, Sweden). Of these constructs (implant and hemipelvis), 12 were prepared in the manner listed below and consecutively divided into two groups (6 with cranial straps (S) and 6 without cranial straps (nS)). Sample size estimation was carried out using G*Power 3.1 Software (Heinrich-Heine-University, Düsseldorf, Germany), [13] using a Mann–Whitney U test for two groups with an expected effect size of $d = 2.5$ and $\alpha = 0.05$, with power $(1\text{-}\beta) = 0.8$; we based the chosen values on the well-standardized methods of this experiment and laboratory experience, as well as similar literature [14,15].

2.2. Defect Planning and Preparation of Pelvic Models

In order to comply with a frequent clinical setting in cases of acetabular revision arthroplasty, the common morphology of an ADC IIa/Paprosky IIb defect was chosen [3,16]. The segmental bone lesion was located in the superior portion of the acetabular rim with a depth of 1 cm, affecting one-third of the acetabular circumference. To provide a standardized and reproducible defect location, a DICOM format with a layer thickness of 1 mm of the composite hemipelvis was generated through a CT scan using a Philips

Brilliance ICT 6000 (Philips, Amsterdam, Netherlands). The DICOM file was subsequently segmented using Materialize Mimics Medical Version 22.0 (Materialise, Leuven, Belgium). The STL-Format was then adapted to include the above-mentioned ADC IIa/Paprosky IIb defect. In addition, the implant bed and screw holes were planned to allow maximum of reproducibility. A gap in the anterior portion of the acetabulum below the inferior anterior iliac spine outside of the weight baring area was added. The purpose of this addition was to accommodate a rod which later would be outfitted with a marker platform (Figure 1c). For the planning process, Pro Engineer Wildfire 2.0 (PTC Inc., Boston, MA, USA) was utilized, and in order to convert the STL-Format into an applicable format, ESPRIT CAD-CAM Build 19.17.170.1385 (Esprit Inc., Camarillo, CA, USA) was employed (Figure 1a). The composite hemipelvis models were then milled in a CNC milling drill (Hermle C12 U Dynamik TNC 640 340590 06 SP7—6 (Berthold Hermle AG, Gosheim auf dem Heuberg, Germany)) with a milling accuracy of 5µm (Figure 1b). Care was taken during planning to include all processing steps into a single working cycle of the CNC milling drill to avoid any deviations due to repositioning of the hemipelvis models. In Figure 1, different steps of the planning and milling process are displayed.

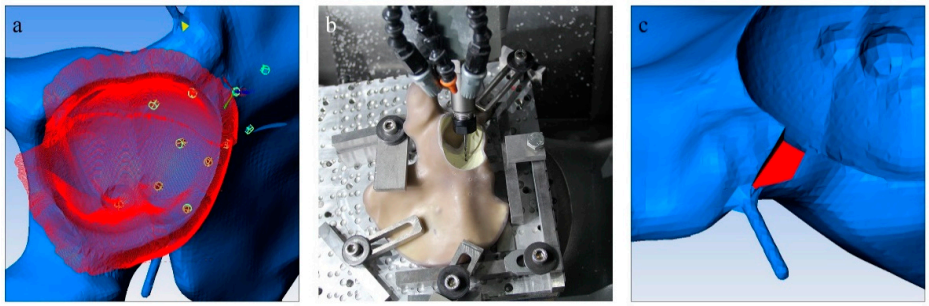

Figure 1. Different steps of the planning and milling process are displayed. (**a**) The segmented bone defect (red) on the digital model of the composite hemipelvis model (blue) and the planned screw holes (green); (**b**) a milling tool in the process of creating the acetabular defect and implant bed as well as the screw holes in the composite hemipelvis model; (**c**) a fabricated gap which enables the addition of a metal rod and a measuring platform to the augment (compare Figure 2).

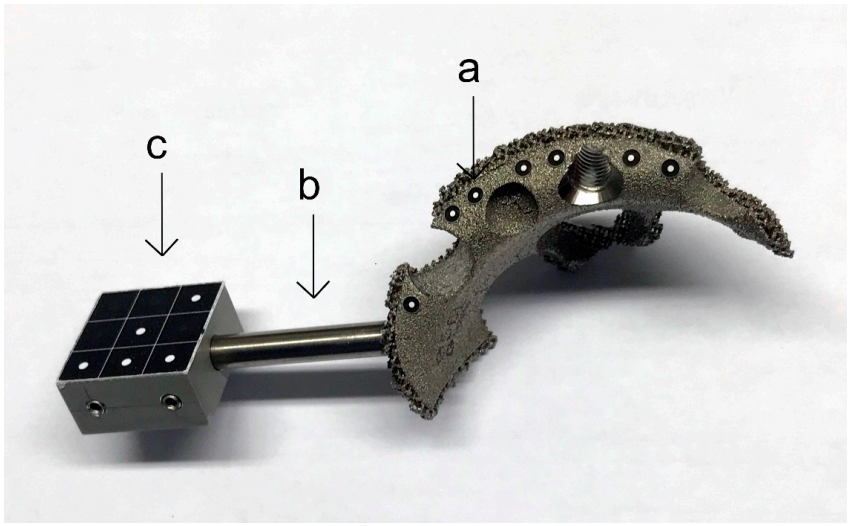

Figure 2. Macro-porous titanium augment with the addition of optical markers (a) and an added metal rod (b) as an extension which holds a metal platform (c) which contains further optical markers. While markers at the implant shell and composite bone were easily attachable (compare Figure 3), the augment was mostly covered by the rim and cranial straps. Therefore, a metal rod was added to the augment as an extension in order to attach a satisfactory number of optical markers.

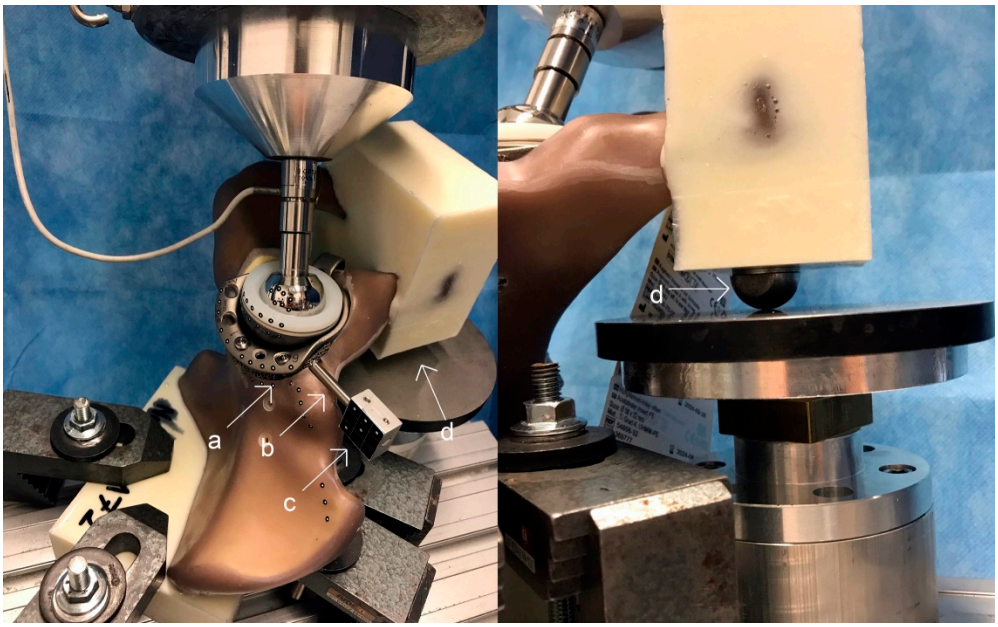

Figure 3. Left: Setup of the implant-hemipelvis-model construct inserted into a material testing machine for the biomechanical stimulation. Visible are multiple optical markers (a) and a metal rod (b) serving as an extension combined with a metal platform (c) in order to attach a satisfying amount of optical markers to the augment. The macro-porous titanium augment is almost entirely covered by the rim portion of the shell. Right: Composite pelvis with the implanted augment-and-modular-cage construct in the polyurethane setting with the addition of the stainless-steel ball on the undersurface (d). Due to this setup the symphysis is only fixed in one degree of freedom and multiplanar movement and rotation is enabled [15].

2.3. Cementless Augment-and-Modular-Cage Construct and Implantation

The cementless augment-and-modular-cage construct with cranial straps (S) and without cranial straps (nS) was implanted in a standardized fashion by an experienced orthopedic surgeon in accordance with the manufacturer's instructions and the preceding digital planning. All shells were size 56 mm left combined with a 14 mm A-Augment and either no cranial straps or two cranial straps (45 mm) with 2 screws holes each extending over the superior aspect of the acetabulum to the iliac bone. The A-Augment was pre-operatively modified by the addition of a metal rod which would later carry marker points during the biomechanical analysis. This step was necessary due to the coverage of the augment by the cage. Therefore, in order to enable a valid measurement of relative motion, the metal rod with marker points was used as an extension of the augment. To compare to a clinical setting, a press-fit implantation prior to the insertion of screws was attempted and achieved in all cases. The press-fit of the implant in combination with an uncontained acetabular defect, however it does not offer the same stability as an undisturbed acetabular rim would.

The porous metal augment was attached to the titanium shell and fixated through a singular screw (6 × 12 mm) with 8 Nm torque prior to implantation. After initial press-fit of the cementless augment-and-modular-cage construct, the following screws were added depending on the assigned group (S/nS): S: cranial strap with 4x flathead spongiosa screw 6 × 25 mm, 6 × 30 mm, 6 × 30 mm, 6 × 40 mm; rim with 1 flathead spongiosa screw 6 × 40 mm; dome with 3 flathead spongiosa screw 6 × 25 mm, 6 × 50 mm, 6 × 60 mm; nS: rim with 1 flathead spongiosa screw 6 × 25 mm; dome with 3 screw 6 × 25 mm, 6 × 50 mm, 6 × 60 mm.

Finally, in preparation for the biomechanical analysis, all hemipelvis models with the implanted acetabular component were secured by submerging the posterior ilium into a containment device filled with a liquid two-component casting resin block. In a separate

step, the symphysis was also secured into a two-component casting resin block with the addition of a stainless-steel ball on the undersurface. In the biomechanical analysis, this ball is in contact with a metal plate only fixating the symphysis in one plane and therefore allowing multiplanar movement and rotation in order to mimic a more physiological fixation [17,18].

Figure 3 shows the composite pelvis with the implanted modular cage-and-augment construct in the polyurethane setting with the addition of the stainless-steel ball on the undersurface.

2.4. Biomechanical Analysis

To enable discrimination and recording of relative movement between the components during loading, the implant-hemipelvis-construct was outfitted with optical markers (uncoded passive white markers with a diameter of 0.8 mm, GOM Item Number: 21874; GOM GmbH, Braunschweig, Germany) along the surface of each component planned to be measured. While markers at the implant shell and composite bone were easily attachable, the augment was mostly covered by the rim and cranial straps. Therefore, the implant manufacturer assembled a specialized augment containing a metal rod as an extension in order to attach a satisfactory number of optical markers (Figure 2).

To record relative movement between the components, an optical measuring system (PONTOS 1; GOM GmbH, Braunschweig, Germany) applying 3D point triangulation detected the optical marker positions in the defined coordinate system. The 3D micro-movements in x-, y-, and z-axes were consecutively measured simultaneously between the different interfaces (bone/augment, bone/shell, shell/cup). The dependent variable was the relative movement between the components (measured in µm). The recorded maximal movements of the component augment, shell, bone and cup were calculated using the formula $\left|\vec{R}\right| = \sqrt{x^2 + y^2 + z^2}$.

The biomechanical simulation was carried out by using a material testing machine (MTS Mini Bionix 359; MTS Systems Corporation, Eden Prairie, Minnesota). The implant-hemipelvis-construct set into the material testing machine is displayed in Figure 3.

The vector of the load application coincided with the direction of the greatest load occurring during normal gait [19,20]. Termination criteria were set as fracture of the hemipelvis model.

According to a publication by Bergmann et al., the maximum load during normal walking relates with 233% to the individual's body weight at 31° of rotation around the x-axis and 5° around the z-axis relative to the described acetabular component system [21].

The experimental body weight was set at 80 kg for each testing (1.8 kN at 100% load). To warrant a proper force closure between the force plate and the implant-hemipelvis-construct, a constant force of 0.2 kN was applied prior to testing. A total of 1000 cycles were applied in a sinusoidal waveform at 1 Hz at each of three load levels: 3% to 30% load (the equivalent of 0.5 kN peak load); then 5% to 50% load (the equivalent of 0.9 kN peak load); and, finally, at 10% to 100% load (1.8 kN peak load). Relative movements between the components were measured at cycles 1 to 50, 51 to 200, 201 to 500, 501 to 800, and 801 to 995 (average and variance).

2.5. Statistical Analysis

The statistical evaluation was performed using SPSS Statistics Version 22 (IBM Corp., Armonk, NY, USA). To test for primary stability, the surrogate parameter of relative movement between the components during different loads (measured in µm) was applied. For each interface a separate analysis was carried out (augment/bone, shell/bone, shell/augment, shell/cup). Initial descriptive statistical analysis was applied utilizing the arithmetic mean, range and standard deviation. Normal distribution was assessed through the Kolmogorov–Smirnov and Shapiro–Wilk Test.

A repeated-measures analysis of variance (ANOVA) was calculated for the transformed relative movement (averaged over cycles, as described above, and weighted by the

inverse variance of these samples). To validate the ANOVA Mauchly's sphericity test was used. In cases where sphericity could not be verified the Greenhouse–Geisser correction was applied. As covariates we defined the application of cranial straps (S, nS), force (30%, 50%, and 100% maximal load), and their interaction. The unpaired *t*-test was applied to test for differences between component design (S/nS) according to load when homogeneity of variance could be established. In cases where homogeneity of variance could not be shown, Welch Test was utilized.

Hemipelvis ID was chosen as a random intercept, and post hoc comparisons between S and nS, and S/nS were performed using differences of 'least-squares' means [22]. The level of significance for two-tailed *p*-value was set at ≤ 0.05.

3. Results

Table 1 displays the detailed results of the descriptive statistical analysis, the analysis of variance and the unpaired *t*-test/Welch Test. Means of maximal relative movement between the different components with and without cranial straps (nS/s) is displayed in Figures 4 and 5.

Table 1. Descriptive statistic evaluation of relative movement between components, ANOVA, and unpaired *t*-test. Means of maximal relative movement (µm) are provided with standard deviation relative to group (nS/S); Load levels (%) relative to interface.

Load, %	Mean Relative Movement (RM), µm ± SD		ANOVA RM—Load		ANOVA Group—RM		Unpaired T-Test/ Welch Test	
	AmC without Cranial Straps (nS)	AmC with Cranial Straps (S)	F	Sig.	F	Sig.	T	Sig.
Shell—Augment			3.52	$p = 0.054$	36.357	$p < 0.001$		
30	8.32 ± 0.68	10.92 ± 1.08					−4.559	$p < 0.003$
50	8.38 ± 0.56	10.77 ± 0.67					−6.110	$p < 0.001$
100	9.52 ± 0.46	10.83 ± 0.70					−3.507	$p < 0.009$
Bone—Augment			89.520	$p < 0.001$	279.101	$p < 0.001$		
30	16.17 ± 1.67	38.72 ± 1.60					−21.798	$p < 0.001$
50	20.72 ± 2.85	40.55 ± 2.92					−10.867	$p < 0.001$
100	35.96 ± 1.46	40.92 ± 1.89					−4.652	$p < 0.003$
Bone—Shell			233.585	$p < 0.001$	219.333	$p < 0.001$		
30	24.186 ± 1.28	12.84 ± 1.00					15.637	$p < 0.001$
50	29.15 ± 4.19	14.61 ± 1.71					7.183	$p < 0.001$
100	53.48 ± 4.36	16.36 ± 0.93					18.607	$p < 0.001$
Shell—Cup			65.582	$p < 0.001$	56.686	$p < 0.001$		
30	15.94 ± 1.20	17.59 ± 1.23					−2.138	$p < 0.065$
50	15.93 ± 1.39	20.17 ± 2.27					−3.557	$p < 0.008$
100	19.15 ± 0.64	26.25 ± 0.66					−17.316	$p < 0.001$

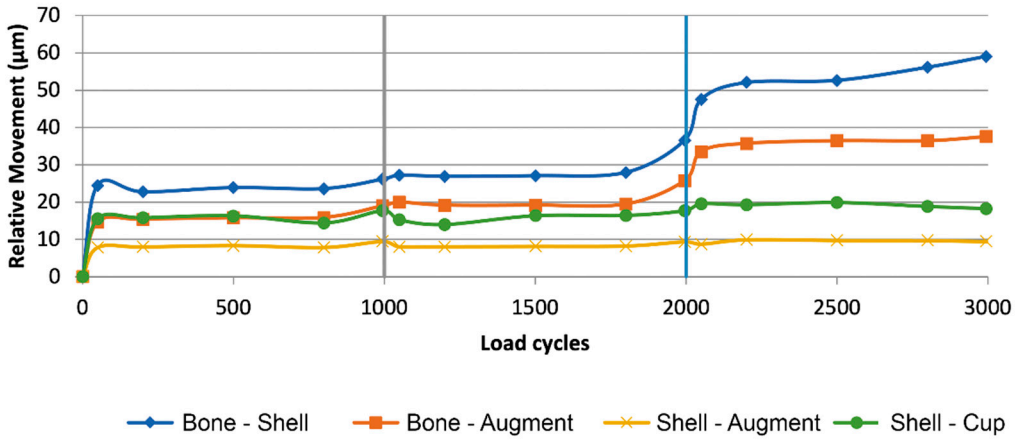

Figure 4. Relative Movement of different interfaces in relation to load (I = 30%, II = 50%, III = 100%) over the accumulation of load cycles in the group without cranial straps (nS), (diamond blue: bone-shell, square orange: bone-augment, cross yellow: shell-augment, circle green: shell-cup). The interface between bone and shell features the largest amount of relative movement with an increase as load levels increase. Followed by the amount of relative motion at the interface of bone and augment which displays an increase with ascending load levels as well. Relative motions at the interfaces of shell and augment and shell and cup remain constant as load levels increase.

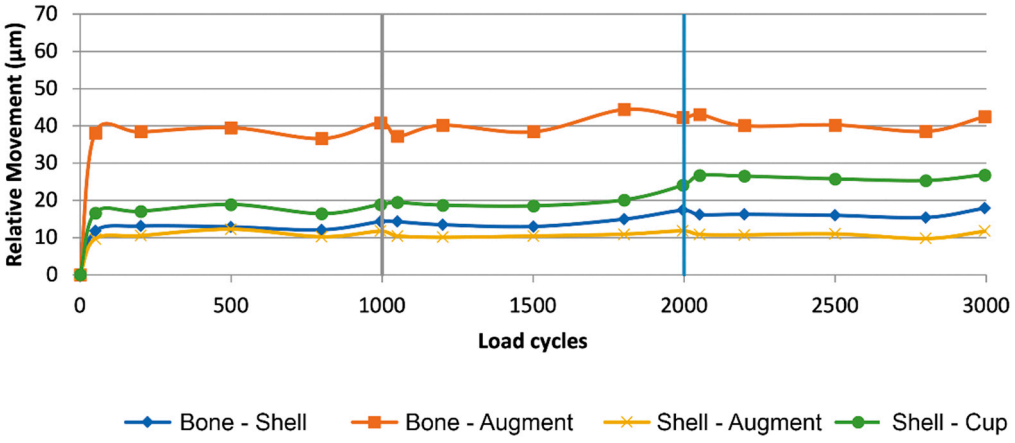

Figure 5. Relative movement of different interfaces in relation to load (I = 30%, II = 50%, III = 100%) over the accumulation of load cycles in the group with cranial straps (S), (diamond blue: bone-shell, square orange: bone-augment, cross yellow: shell-augment, circle green: shell-cup). The interface between bone and augment features the largest amount of relative movement in the construct followed by the interface between shell and cup. Relative motions at the interfaces of shell and augment and shell and bone remain constant as load levels increase.

Load levels display a significant effect on the amount of relative motion between bone and shell ($F(2, 16) = 233{,}585$, $p < 0.001$), bone and augment ($F(1.19, 9.55) = 89.52$, $p < 0.001$), and shell and cup ($F(2, 16) = 65.58$, $p < 0.001$). In the interface between shell and augment, no significant effect of load levels on the amount of relative motion could be assessed ($F(2, 16) = 3.52$, $p = 0.054$).

The group assignment (S/nS) appears to have an effect on relative motion due to significantly differing means in the comparison of bone and shell ($F(1, 8) = 219.333$, $p < 0.001$), bone and augment ($F(1, 8) = 279.101$, $p < 0.001$), shell and cup ($F(1, 8) = 56.686$, $p < 0.001$), and shell and augment ($F(1, 8) = 36.357$, $p < 0.001$).

At the interface between bone and shell, relative movement increased as load level increased for the nS-group while remaining constant throughout for S-group (Figure 6). The nS-group also started with a higher amount of relative movement when compared to the S-group. Relative movement was significantly different between groups for all

load levels (30%: t(8) = 15.64, $p < 0.001$; 50%: t(8) = 7.18, $p < 0.001$; 100%: t(4, 36) = 18.61, $p < 0.001$).

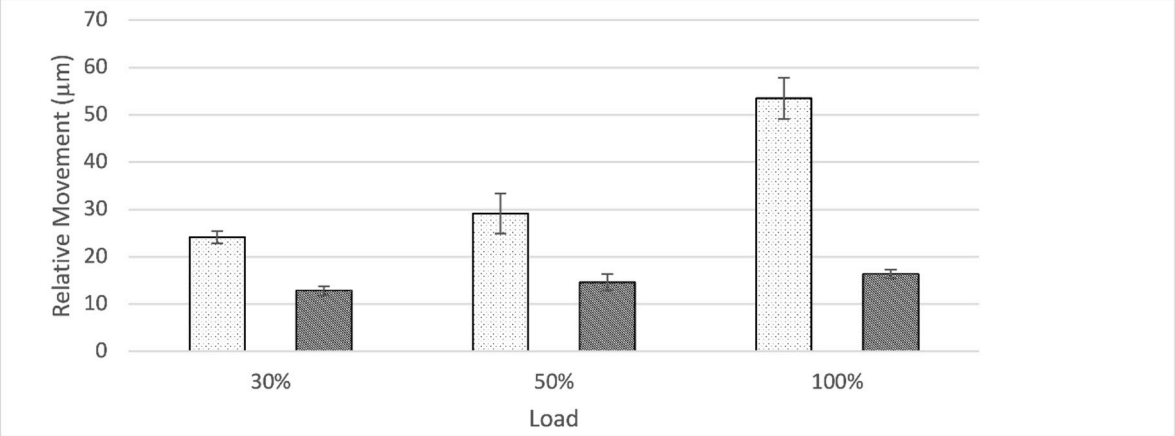

Figure 6. Graph showing relative movement between bone and shell in relation to load divided by group (nS = dotted, S = striped). The S-group displays a constant amount of relative motion as load levels ascend. The amount of relative motion in the nS-group increases as load levels increase.

At the interface between bone and augment, relative movement increased as load level increased for the nS-group while remaining constant throughout for S-group (Figure 7). The S- group started with a higher amount of relative movement when compared to the S-group. At 100% load the amount of relative movement between the nS- and S-group aligned. Relative movement was significantly different between groups for all load levels (30%: t(8) = −21.89, $p < 0.001$; 50%: t(8) = −10.87, $p < 0.001$; 100%: t(8) = −4.65, $p < 0.003$).

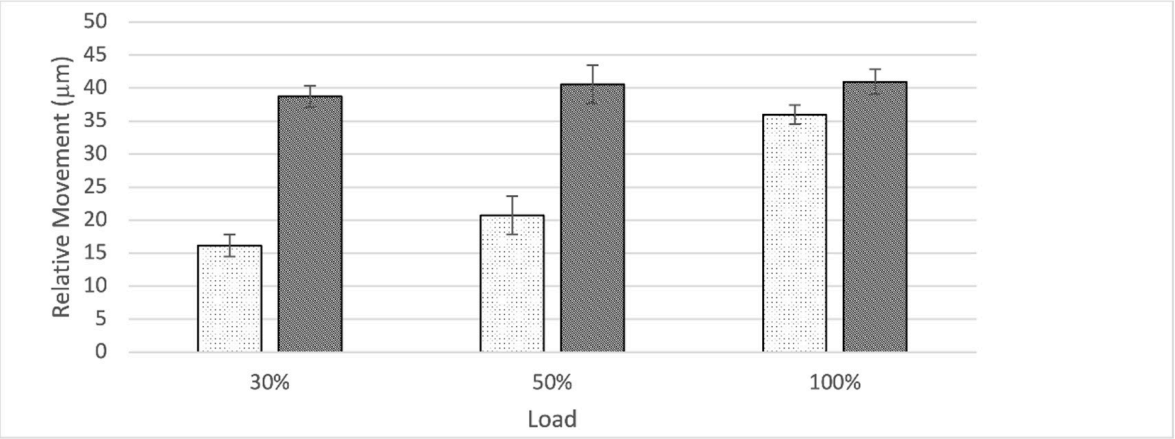

Figure 7. Graph showing relative movement at the interface between bone and augment in relation to load level divided by group (nS = dotted, S = striped). While the S-group started out with a larger amount of relative movement compared to the nS-group, it stayed constant throughout different load levels. The nS-group displayed an increase in relative motion as load levels ascended.

At the interface between shell and cup, relative movement increased as load level increased for both groups. The S-group started with a higher amount of relative movement when compared to the nS-group. Relative movement was significantly different between groups for the 50% and 100% load level, while the difference at the 30% load level was not significant (30%: t(8) = −2.14, $p = 0.065$; 50%: t(8) = −3.56, $p < 0.008$; 100%: t(8) = −17.32, $p < 0.001$).

At the interface between shell and augment, relative movement remained constant as load level increased for both groups (Figure 8). The S-group displayed a slightly higher amount of relative movement when compared to the nS-group. Relative movement was significantly different between groups for all load levels (30%: $t(8) = -4.56$, $p = 0.003$; 50%: $t(8) = -6.11$, $p < 0.001$; 100%: $t(8) = -3.51$, $p < 0.009$).

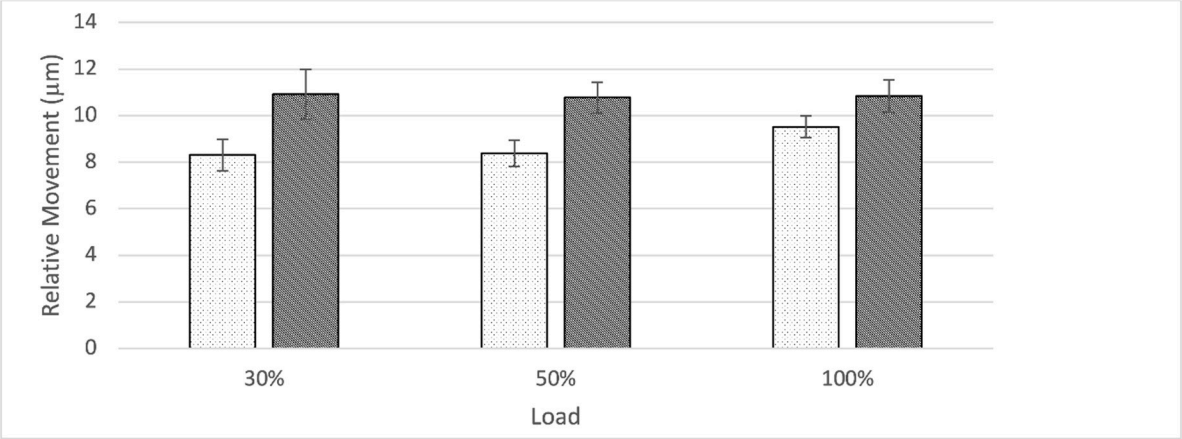

Figure 8. Graph showing relative movement at the interface between shell and augment in relation to load divided by group (nS = dotted, S = striped). Both groups displayed an almost constant amount of relative motion as load level increased. The S-group displays a significantly larger amount of relative motion when compared to the nS-group.

4. Discussion

The aim of this publication is to assess the impact of the addition of cranial straps to a cementless augment-and-modular-cage construct on the amount of relative motion between the different components within the system and between implant and bone. Relative movement is an important in vitro measurement in order to assess primary stability and consecutively determine the potential of osseointegration. The conducted in vitro testing brought many significant results to light. In order to properly interpret these findings, the measurement of relative movement needs to be related to a clinical setting. Prior in-vivo animal and human autopsy studies established cut-off values indicating that successful osseointegration occurs at ~40 µm, while relative movement of 150 µm appears to result only in fibrous attachment [23,24]. Although these values cannot be taken as a gold standard, due to various limitations, they underline the need to keep relative movement between implant and bone bed low in order to optimize in-growth conditions.

Besides, proper osseointegration relative movement also affects the implant system as a whole. One of the most relevant reasons for failure of an implant is particle debris with consecutive osteolysis and loosening. Increased relative movement has been associated with increased wear of the implant surfaces resulting in particle debris [25,26]. Due to the modularity of modern revision systems, the number of interfaces increases, and therefore it is reasonable to assume that the chance for particle debris is amplified. Adverse reactions to metal debris (ARMD) and corrosion increase as the number of interfaces increases and have been described for modular revision implants in numerous previous studies [27–30]. Interestingly, while the amount of relative movement between the shell and the cup increased for both groups, the S-group started with a significantly higher amount of relative movement and remained higher throughout all load levels when compared to the nS-group. This might be due to the increased stiffness of the construct caused by the addition of cranial straps. Therefore, less movement and deformation of the shell is possible and the applied force escapes through an increase of relative motion at the interface between shell and cup. With a maximum amount of relative movement at the highest load level of 26.25 ± 0.66 µm in the S-group, this appears to be a significant effect,

however, to access if this actually poses a clinically relevant alteration, further investigation and different methods are required.

While the usefulness of porous metal augments in cases of severe acetabular bone defects has been established, there remains controversy around the best fixation method between augment and shell or cup. In our findings the form-fitting fixation of the augment against the rim-portion of the shell through a single screw proved stable with a constant amount of relative movement across all load levels for both groups. Even though there was a significant difference between relative movements at all load levels to the disadvantage of the S-group, the small difference is not estimated to present a relevant clinical consequence (nS: 9.52 ± 0.46 µm vs S: 10.83 ± 0.70 µm at 100% load) (Figure 7). The group of Beckmann et al. compared three different fixation techniques between a porous metal acetabular component and augments with similar methods. In this study screw fixation, cement fixation and a combination of both were compared in an in vitro setting also utilizing relative motion as the main outcome parameter. Even though a direct comparison due to slight differences in methods might be biased, it is interesting to compare these results. The cementless fixation method of the augment-and-modular cage system appears to be superior presenting a smaller amount of relative motion especially at the 100% load level (nS: 9.52 ± 0.46 µm vs S: 10.83 ± 0.70 µm at 100% load; Beckmann et al.: cement: 11.3 ± 1.9 µm, screw plus cement: 12.6 ± 4.0 µm, screw 31.4 ± 16.6 µm at 100% load) [15]. Further studies are needed to investigate these findings in a controlled manner.

The initial design of straps or flanges surfaced in reconstruction rings/cages which would bridge an acetabular bone defect in order for the added bone graft below to be protected until it would eventually consolidate. Due to vast improvements in implant design, modern revision systems offer a variety of different modes of fixation such as cranial or dorsal straps/flanges, iliac pegs, caudal hooks, and iliac lag screws. While there are plenty publications assessing the clinical use of implant systems (e.g., cranial socket system, augment-and-cage, augment-and-modular-cage, and individualized partial pelvic implants) which utilize cranial straps, to the knowledge of the authors, no studies exist which objectively quantify the potential gain in stability achieved in a clinical or an in vitro setting. The main objective of this publication is to evaluate if cranial straps provide additional primary stability. To answer this question, the contact surfaces of the implant to the bone are of major concern. In the interface between shell and bone, the addition of cranial straps provided a lower amount of relative movement which remained constant across all load levels. In comparison, in the absence of cranial straps, relative movement started out higher and even increased as load levels increased. Therefore, in addition to the initial design intend, cranial straps seem to provide additional stability to the shell. Especially at the 100% load level, relative movement between the groups were significantly different (nS: 53.48 ± 4.36 µm; S: 16.36 ± 0.93 µm) (Figure 6). In the light of these results, it is reasonable to conclude that cranial straps add additional stability to the implant shell. However, to evaluate the clinical impact of this added stability, further clinical studies are needed.

Finally, the analysis of the interface between augment and bone provided another interesting insight. Even though relative movement between components within the S-group remained constant over all load levels, it started out significantly higher when compared to the nS-group. The nS-group, starting out significantly lower, displayed an increase across ascending load levels and finally almost aligned with the S-group at the 100% load level (Figure 8). Due to the significant but slight difference between groups at 100% load and the constant course of relative movement in the S-group, we interpret these findings as not being evidence of a decrease of stability due to the addition of cranial straps (100% Load; nS: 35.96 ± 1.46 µm; S: 40.92 ± 1.89 µm). Furthermore, these values are within the established threshold for successful osseointegration [23,24].

Our methods present several limitations. We chose to utilize composite pelvic models instead of cadaveric bone in this in vitro setup in order to decrease inter-specimen variability and improve availability and ease of use. In addition, the application of a consistent

acetabular defect in cadaveric bone with varying anatomical setup and bone density is considered challenging. Even though our choice enabled a reproducible in vitro experiment, correlation with the clinical situation might be limited due to different biomechanical properties such as strain distribution and overall stiffness in a fourth-generation composite model [31].

The impact of the addition of cranial straps was only assessed for a specific augment-and-modular-cage revision system. Therefore, a generally valid statement for the many available systems utilizing cranial straps cannot be obtained as of now. We strongly encourage the application of the presented methods to other implant systems and even different set ups of the same augment-and-modular-cage revision systems by other groups. The applied defect morphology (ADC IIa/Paprosky IIb) was chosen due to a wide incidence in the daily reality of hip revision arthroplasty [3,16]. Different defect morphologies and consecutively different choice of augmentation may lead to alternative results and need further investigation as well. Furthermore, the chosen mode of load application, as described in methods, did not replicate the entire cyclical pattern or normal walking with loading on different areas of the acetabulum in differing degrees.

We hope our study inspires future research into the subject. Especially in vivo studies of different fixation techniques between the components within a modular system and the impact of different configuration of that system should be evaluated.

5. Conclusions

Our study evaluated the gain in primary stability through the addition of cranial straps to an augment-and-modular-cage revision system. We utilized a reproducible in vitro setup with composite hemi-pelvis models and measured relative movement between individual components in addition to relative movement between components and the bone as a surrogate parameter for primary stability.

We conclude a significant increase of primary stability between the shell and the bone through the addition of cranial straps. Relative motion between components (shell/cup) increases through the addition of cranial straps. A clinical impact of this finding is uncertain and requires further investigation. Finally, the cementless fixation of the augment against the rim-portion of the shell appears stable and compares favorably to prior investigation of different fixation techniques.

Author Contributions: M.J.: responsible for study design, provided clinical insights, planning and oversight of hemipelvis processing, implantation of revision constructs, analysis and interpretation of data, responsible for drafting the manuscript; H.K.: responsible for study design, provided clinical insights, planning and oversight of hemipelvis processing, implantation of revision constructs, read and approved the final manuscript before submission; D.C.W.: responsible for study design, provided clinical insights, analyzed the data and interpreted the findings, read and approved the final manuscript before submission; F.A.S.: responsible for study design, analyzed the data and interpreted the findings, read and approved the final manuscript before submission; N.A.B.: responsible for study design, provided clinical insights, read and approved the final manuscript before submission; J.P.K.: responsible for study design, provided biomechanical insights, read and approved the final manuscript before submission; M.S.: preparation of hemipelvis-implant constructs for biomechanical analysis, provided the biomechanical measurements, read and approved the final manuscript before submission; S.J.: responsible for study design, analyzed the data and interpreted the findings, preparation of hemipelvis-implant constructs for biomechanical analysis, provided the biomechanical measurements, read and approved the final version of the manuscript before submission. All authors have read and agreed to the published version of the manuscript.

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3.4 Jaenisch M, Guder C, Ossendorf R, Randau TM, Gravius S, Wirtz DC, Strauss AC, Schildberg FA (2023) In-vitro Biocompatibility of a Novel Ceramic Composite for Defect Augmentation in Hip Revision Arthroplasty. J Funct Biomater. 14(10):517. https://doi.org/10.3390/jfb14100517.

Zielsetzung der Arbeit:

Die biologische Augmentation von Knochendefekten in der Hüftrevisionsendoprothetik in der lasttragenden Zone von Azetabulum und Femur ist herausfordernd. Auf Grund der bekannten Limitationen von autologem und allogenem Knochenersatz sind vermehrte Forschungsbemühungen für Knochenersatzmaterialen notwendig. Diese können Alternativen zur Behandlung von Knochendefekten sowohl in der lasttragenden Zone als auch in unbelasteten Arealen bieten. Die Zielsetzung dieser Arbeit ist die Untersuchung der Biokompatibilität eines keramischen Knochenersatzmaterials unter Verwendung von humanen THP-1 Makrophagen und humanen Osteosarkomzellen (MG63). Untersucht wurde die Lebensfähigkeit, Zellteilungsfähigkeit und die Ausschüttung von inflammatorischen Mediatoren.

Material und Methoden:

THP-1 Makrophagen und MG63 wurden in wässriger Lösung einem Calcium-Silikat-basierten Keramiktestkörper für 7 Tage ausgesetzt. Die Lebensfähigkeit wurde durch einen MTT-Test und eine pH-Analyse evaluiert. Die Proliferationsrate beider Zelllinien wurde durch CFSE-Markierung und Durchflusszytometrie gemessen. Die Sekretion von IL-1ß, IL-6 und TFNα wurde durch einen ELISA geprüft.

Ergebnisse:

In der Untersuchung zur Bestimmung der Lebensfähigkeit zeigte sich kein relevanter Unterschied zwischen den Gruppen für beide Zelllinien. Es zeigte sich ein nicht-signifikanter Unterschied in der optischen Dichte des MTT-Tests für MG63-Zellen. Der Vergleich der pH-Wertentwicklung und die Proportion der lebenden Zellen zeigten in beiden Gruppen keinen signifikanten Unterschied in der Testung von THP-1 und MG63-Zellen. Baghdadite hatte keinen relevanten Einfluss auf die Proliferationsrate der untersuchten Zelllinien. Die mittlere Fluoreszenzintensität wurde zwischen den Gruppen ohne einen signifikanten Unterschied berechnet. Die Exposition mit Baghdadite verursacht eine Hochregulation der Produktion von IL-1ß, IL-6 und TNFα

in Markophagen. Ein ähnlicher Effekt auf MG63 wurde nicht beobachtet. Durch die Zugabe von LPS zeigte sich eine weitere Erhöhung der inflammatorischen Potenz in Makrophagen. Es ergab sich eine Synergie zwischen LPS und Baghdadite bezogen auf die IL-1ß-Produktion, während die Sekretion von TNFα und IL-6 unverändert blieb.

Schlussfolgerung:

Es zeigte sich keine relevante Zytotoxizität durch Exposition der Zelllinien zu Baghdadite-Keramik. Baghdadite-Exposition führte zu einem proinflammatorischem Effekt mit einer signifikant erhöhten Sekretion von IL-1ß, IL-6 und TNFα in THP-1 Makrophagen. Ob dieses proinflammatorische Potential in einer klinisch-relevanten Inhibierung der Osseointegration mündet, ist unklar und bedarf weiterer Untersuchungen. Baghdadite-Keramiken sind eine interessante Alternativen zu herkömmlichen Knochenersatzmaterialen. Weitere biomechanische und in-vivo Studien sind zukünftig geplant.

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In Vitro Biocompatibility of the Novel Ceramic Composite Baghdadite for Defect Augmentation in Revision Total Hip Arthroplasty

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Abstract: Biological augmentation of bony defects in weight-bearing areas of both the acetabulum and the femur remains challenging. The calcium-silicate-based ceramic Baghdadite is a very interesting material to be used in the field of revision total hip arthroplasty for the treatment of bony defects in weight-bearing and non-weight-bearing areas alike. The aim of this study was to investigate the biocompatibility of Baghdadite utilizing an osteoblast-like, human osteosarcoma cell line (MG-63) and the human monocytic leukemia-derived cell line (THP-1). THP-1-derived macrophages and MG-63 were indirectly exposed to Baghdadite for 7 days using a transwell system. Viability was assessed with MTT assay and pH analysis. To investigate proliferation rate, both cell lines were labelled using CFSE and flow cytometrically analyzed. ELISA was used to measure the secretion of IL-1ß, IL-6 and TNFα. The investigation of viability, while showing a slight difference in optical density for the MTT assays in MG-63 cells, did not present a meaningful difference between groups for both cell lines. The comparison of pH and the proportion of living cells between groups did not present with a significant difference for both THP-1 and MG-63. Baghdadite did not have a relevant impact on the proliferation rate of the investigated cell lines. Mean fluorescence intensity was calculated between groups with no significant difference. Baghdadite exerted a proinflammatory effect, which could be seen in an upregulated production of TNFα in macrophages. Production of IL-1ß and IL-6 was not statistically significant, but the IL-6 ELISA showed a trend to an upregulated production as well. A similar effect on MG-63 was not observed. No relevant cytotoxicity of Baghdadite ceramics was encountered. Baghdadite ceramics exhibit a proinflammatory potential by significantly increasing the secretion of TNFα in THP-1-derived macrophages. Whether this proinflammatory potential results in a clinically relevant effect on osteointegration is unclear and requires further investigation. Baghdadite ceramics provide an interesting alternative to conventional bone substitutes and should be further investigated in a biomechanical and in vivo setting.

Keywords: ceramic bone substitute; Baghdadite; cytotoxicity; MG-63; THP-1; inflammation; revision total hip arthroplasty

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1. Introduction

Revision total hip arthroplasty (RTHA) is a challenging field of practice with a projected increase in frequency especially for young patients [1]. Aseptic loosening is the most common cause of failure often resulting in large osseous defects of the surrounding host bone stock [2]. In revision arthroplasty of the hip joint, augmentation of the insufficient bone stock is required to achieve a long-term stable implant fixation [3,4]. While metallic, macro-porous augmentation is gaining popularity, the ultimate goal of RTHA should be

biological defect downsizing. To achieve biological defect downsizing, various techniques of autologous and allogenic bone grafts—in bulk or morcalized configurations—have been published [5].

The limitations of autologous and allogenic bone grafts are availability, high cost and osseointegration. For allogenic bone grafts, donor disease transmission, immunological reactions and donor site morbidity are also concerning possibilities for complications. Impaction bone grafting is a well-established technique for the treatment of bone defects in non-weight-bearing areas of the acetabulum and femur. Autologous or allogenic cancellous bone croutons and chips are combined with the blood of the patient and are impacted into the defect. A metallic implant (e.g., reconstruction cage) is implanted on top to protect the bone graft until it is integrated [6]. Depending on defect size and especially in cases of re-revision, large quantities of bone graft are required. Biological augmentation of bony defects in weight-bearing areas of both the acetabulum and the femur remains challenging. While impaction bone grafting cannot be applied in weight-bearing areas, bulk allografts (autologous or allogenic) have been used throughout the years. However, in contrast to promising short term results, multiple analysis of long-term outcome showed a high rate of failure with limited integration, fibrous encapsulation and consecutive resorption and failure [7–10].

Due to the limitations of autologous and allogenic bone grafts, as mentioned above, the research into bone substitute materials is on-going. The perfect bone substitute for revision arthroplasty would be low-cost, biocompatible, promote osseointegration and be available in multiple configurations (morcalized, scaffold). Porous ceramic scaffolds are considered one of the most critical implants for tissue engineering applications in the field of RTHA [11]. The porous structure facilitates the exchange of oxygen and nutrients, the disposal of waste products as well as osteogenesis and vascular invasion into the pores [12]. In addition, the porous surface could facilitate mechanical interlock between the scaffold and the surrounding host bone similar to trabecular metal augments [13]. To be used as a scaffold in weight-bearing areas, the bone substitute would also need to be biomechanically stable, biodegradable, and form-adaptable to individual defect configurations in a porous structure (scaffold).

To meet these requirements, bioceramics have been extensively researched in the recent past. The material group of bioceramics is defined by their ceramic composition and biocompatibility. From this large group of compounds, calcium phosphates (CaP) and silicate-based ceramics have been extensively studied for their potential to be bioactive. In this context, bioactivity refers to the ability to form hydroxycarbonated apatite when exposed to body fluid, which makes up the majority of human bone tissue. Furthermore, they have been introduced in a wide range of clinical applications, including bone reconstruction, toothpastes, dermal fillers and formulations for soft tissue regeneration [14]. However, these conventional bioceramics have limited applications for the reconstruction of critical-sized bone defects in weight-bearing areas due to their limited mechanical strength and fracture toughness [15]. Recently, the reinforcement of CaP and silicate-based ceramics with different ions or metal oxides has been introduced to improve their mechanical and biological properties. This novel class is called “doped” bioactive ceramics and offers a unique set of properties.

The addition of magnesium to CaP can result in improved Young’s modulus, maximum temperature, and ultimate strength [16]. The reinforcement of CaP by Strontium nitrate can increase grain and particle size [17]. Other doped bioceramics such as Akermanite, Sr-Hardystonite and Sr-HT-Gahnite have shown satisfactory structural, mechanical and biological properties for bone regeneration [18]. Other possible effects through the addition of bioactive ions may be enhanced cell proliferation and expression of genes related to osteogenesis and angiogenesis [19].

Another promising contender is Baghdadite, a calcium-silicate-based ceramic, which incorporates Zirconium (Zr), firstly introduced in 2008 by the group around Hala Zreiqat in Sydney, Australia [20]. Baghdadite has been reported to offer improved physical and

mechanical properties when compared to conventional calcium-silicates due to the addition of Zr, which is a quadrivalent ion and can be linked to Ca ions [21]. To enable load transmission to the remaining stable host bone and minimize stress shielding, the elastic modulus of a bone substitute scaffold in weight-bearing areas should be analogous to that of the bone tissue to reduce resorption and degradation [22]. Baghdadite has been reported to meet the lower end of the range for trabecular and cortical bone [12]. Additionally, the ability to manufacture Baghdadite scaffolds through 3D printing has been described and is similar to the production of trabecular metal augments and individualized implants being used for RTHA [23]. Therefore, already existing planning and production pathways could be utilized. Due to these properties, Baghdadite is a very interesting material to be used in the field of RTHA for the treatment of bony defects in weight-bearing and non-weight-bearing areas alike.

The aim of this study is to investigate the biocompatibility of Baghdadite utilizing a human monocytic leukemia-derived cell line (THP-1) and osteoblast-like, human osteosarcoma cells (MG-63). We tested for viability, ability to proliferate and inflammation mediators.

2. Materials and Methods

2.1. Cell Culture

The human monocytic leukemia-derived cell line THP-1 (American Type Culture Collection, Manassas, VA, USA) and the osteoblast-like, human osteosarcoma cell line MG-63 (American Type Culture Collection, Manassas, VA, USA), were cultivated in RPMI 1640 medium supplemented with 10% fetal bovine serum and 1% penicillin/streptomycin at 37 °C in a humidified atmosphere with 5% CO_2. To trigger macrophage differentiation, the THP-1 cells were stimulated with 50 ng/mL phorbol 12-myristate 13-acetate (PMA) (Sigma-Aldrich, Taufkirchen, Germany) overnight. Dense Baghdadite microplates with a diameter of 2 mm were added to the corresponding wells using a transwell system, thus allowing the cellular response to be studied in indirect contact without causing any mechanical stress on the cells.

2.2. Preparation of Baghdadite

Baghdadite ($Ca_3ZrSi_2O_9$), a calcium-silicate-based ceramic, was synthesized by sol-gel method using zirconia oxide nitrate ($ZrO(NO_3)_2$), calcium nitrate tetrahydrate ($Ca(NO_3)_2{\cdot}4H_2O$) and tetraethyl orthosilicate (TEOS, $(C_2H_5O)4Si$) as raw materials. TEOS, ethanol and HNO_3 were mixed at a mol ratio of 1:8:0.16 and hydrolyzed under stirring for 30 min. $ZrO(NO_3)_2$ and $Ca(NO_3)_2{\cdot}4H_2O$ were added at a mol ratio of 1:3:2 ($ZrO(NO_3)_2$/$Ca(NO_3)_2{\cdot}4H_2O$/TEOS). The reactants were stirred for 5 h at room temperature. The solution was maintained for 1 day (60 °C) and dried to obtain dry gel for another 2 days at 100 °C. Calcination was carried out at 1150 °C for 3 h. The Baghdadite was manufactured as cell culture microplates with a diameter of 2 mm. To achieve this, the calcinated Baghdadite powders were sieved to 230 meshes and mixed with 6% (*w*/*v*) polyvinyl alcohol water solution binders using a 1:9 weight ratio of PVA solution and Baghdadite powders. To finalize the process, the mixture was pressed uniaxially at 200 MPa into the form of microplates and sintered at 1400 °C for 3 h with a heating rate of 2 °C/min.

2.3. MTT Viability Assay

An MTT assay was used to indirectly measure the growth properties of the THP-1 and MG-63 cell lines. The corresponding cells were cultured at a density of 25,000 cells/well for THP-1 cells and 2000 cells/well for MG-63 cells in a 96-well plate as a monolayer culture under standard conditions. The culture medium was changed twice per week. The measurements were carried out at the indicated time points according to the manufacturer's protocol of the MTT assay kit (Boster Biological Technology Co., Ltd., Pleasanton, CA, USA).

2.4. CFSE Proliferation Assay

To assess proliferation rate, THP-1 and MG-63 cells were labeled using carboxyfluorescein succinimidyl ester (CFSE) (Molecular Probes, Leiden, Netherlands) to track CFSE dilution over time and thereby examine cell division. The cells were cultured at a density of 200,000 cells/well for THP-1 cells and 15,000 cells/well for MG-63 cells in a 96-well plate as a monolayer culture under standard conditions in the presence or absence of Baghdadite. Cell proliferation was flow cytometrically assessed by analyzing the CFSE dilution. A BD FACS Canto II cell analyzer and FlowJo software (BD Biosciences, Heidelberg, Germany) were used.

2.5. Enzyme-Linked Immunosorbent Assay

PMA-differentiated THP-1 and MG-63 cells were treated with Baghdadite for 1 day, 2 days, 5 days, and 7 days. Cell-free supernatants were collected and centrifuged (200× *g*, 10 min, 4 °C), and aliquots were stored at −80 °C. The production of the cytokines TNFα, IL-1ß and IL-6 was determined with an ELISA kit according to the manufacturer's protocol (R&D Systems, Wiesbaden, Germany) using a microplate ELISA reader.

2.6. pH Analysis

The corresponding cells were cultured at a density of 25,000 cells/well for THP-1 cells and 2000 cells/well for MG-63 cells in a 96-well plate as a monolayer culture under standard conditions. pH values were measured in the cell culture medium at the indicated time points in the presence or absence of Baghdadite.

2.7. Statistical Analysis

For the statistical analysis GraphPad Prism 7 software (GraphPad, La Jolla, CA, USA) was used. All values are reported as the mean ± SD. The Shapiro–Wilk test was used to test for normal distribution. For data with normal distribution, Student's *t*-test was used for comparison between two groups. One-way ANOVA was used to determine statistical difference between several groups. Mann–Whitney U testing was used for not-normally distributed data. The level of significance was set at * $p < 0.05$, ** $p < 0.01$, and *** $p < 0.001$.

3. Results

In this study, we evaluated the biocompatibility of the calcium–silicate–zirconium compound Baghdadite. We utilized a human monocytic leukemia-derived cell line (THP-1) and an osteoblast-like, human osteosarcoma cell line (MG-63) to mimic both an immediate immune response, and the reaction of a bone-producing cell line.

3.1. Viability

Analyzing cell viability is crucial to rule out relevant cytotoxicity. Macrophages have a multifaceted role in bone healing and can facilitate inflammation as well as regeneration. A complete failure of bone healing was shown if macrophages were depleted [24]. Therefore, the survival of both macrophages and osteoblasts is essential to enable proper osseointegration of implants and scaffolds. THP-1-derived macrophages and MG-63 human osteosarcoma cells were exposed to a Baghdadite test body for up to 7 days. An MTT assay was carried out and did not display any significant difference in optical density (OD) between groups for THP-1 macrophages (Figure 1A). For both groups, the OD decreased slightly over time. MG-63 cells showed an increase in OD for both groups (Baghdadite and control) due to the strong proliferative behavior of the cell line. No significant difference was found between the Baghdadite and control groups. The comparison of pH and the proportion of living cells between groups did not present with a significant difference for both THP-1 and MG-63 (Figure 1B,C). The comparison of viability did not present a meaningful difference between groups for both cell lines.

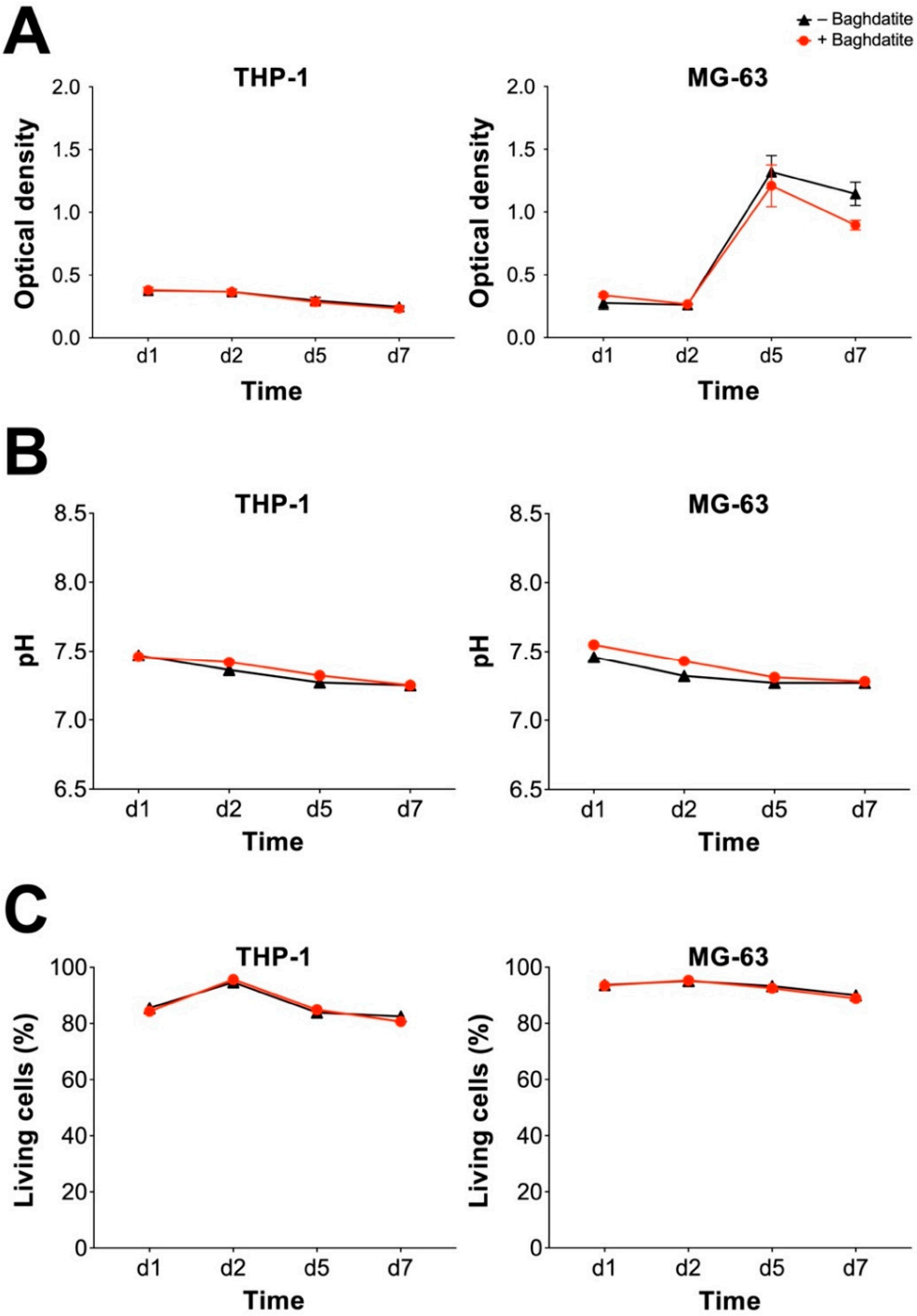

Figure 1. Cytotoxic potential of Baghdadite test bodies on THP-1 and MG-63. OD of MTT assay (**A**), pH of culture medium (**B**) and percentage of live cells (**C**) in the evaluation for THP-1-derived macrophages (**left**) and MG-63 human sarcoma cells (**right**). No significant differences were observed between the presence and absence of Baghdadite.

3.2. Proliferation

To evaluate the rate of cell division in the presence and absence of Baghdadite, THP-1 and MG-63 cells were labeled with CFSE and evaluated at different time points. Loss of CFSE intensity was investigated and cells were analyzed using a flow cytometer. Figure 2 shows the percentage distribution of proliferating and non-proliferating cells sorted by groups (Baghdadite −/+) for THP-1-derived macrophages (Figure 2A) and MG-63 human osteosarcoma cells (Figure 2B). Both THP-1-derived macrophages and MG-63 human

osteosarcoma cells did not display a meaningful difference in proliferation percentage between groups. The presence of a Baghdadite test body did not appear to have a relevant impact on the proliferation rate of the investigated cell lines. To further quantify any potential difference in proliferation rate between groups, the corresponding mean fluorescence intensity was calculated (Figure 2C) with no significant difference.

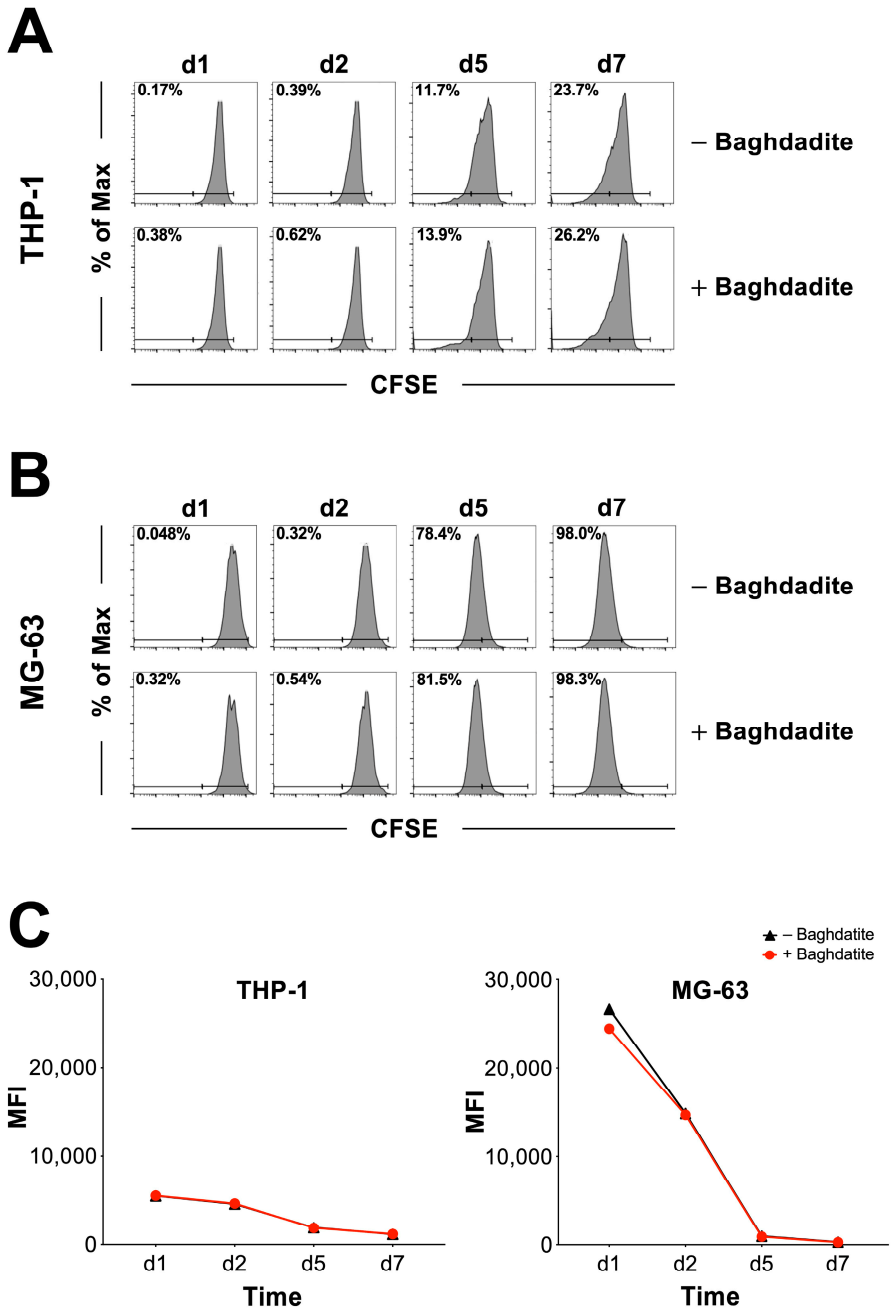

Figure 2. Analysis of cell proliferation rate. Proportion of proliferating and non-proliferating cells based on CFSE proliferation assay for THP-1-derived macrophages (**A**) and MG-63 human sarcoma cells (**B**). Part (**C**) shows the mean fluorescence intensity for THP-1-derived macrophages (**left**) and MG-63 human sarcoma cells (**right**). No significant differences were observed between the presence and absence of Baghdadite.

3.3. Proinflammatory Activity

A common problem in orthopedics and trauma surgery is aseptic loosening. This process can be caused by a chronic inflammation by inducing osteoclastic bone resorption and

suppressing bone formation [25]. This inflammatory reaction can be triggered by various byproducts of joint replacements and is mainly driven by macrophages. Among all proinflammatory mediators, IL-1ß and TNFα are the primary initiators and significant mediators of this inflammatory cascade [26]. IL-6 can be produced by macrophages and osteoblasts alike and has been reported to stimulate osteoclast formation and bone resorption [27]. We, therefore, investigated the proinflammatory effect of Baghdadite by evaluating the induction of IL-1ß, IL-6 and TNFα on the THP-1 and MG-63 cell lines (Figure 3).

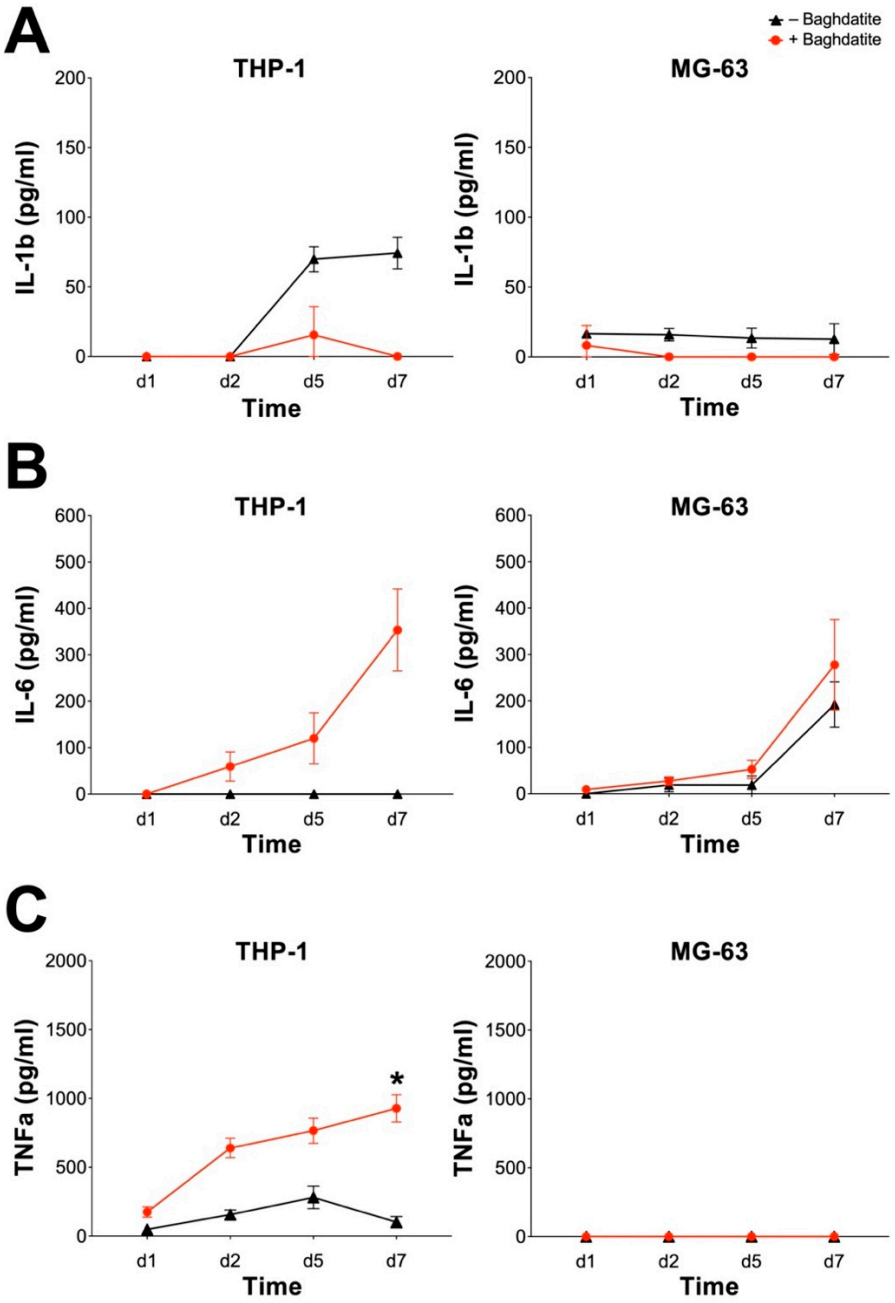

Figure 3. Proinflammatory potential of Baghdadite on THP-1-derived macrophages and MG-63 human sarcoma cells. The THP-1-derived macrophages and MG-63 cells were incubated with Baghdadite test body for up to 7 days. Release of IL-1ß (**A**), IL-6 (**B**) and TNFa (**C**) was measured by ELISA for THP-1-derived macrophages (**left**) and MG-63 human sarcoma cells (**right**). * indicates significant differences between presence and absence of Baghdadite (* p <0.05).

IL-1ß secretion was detected in both cell lines with and without a Baghdadite test body (Figure 3A). THP-1-differentiated macrophages secreted slightly increased amounts of IL-1ß starting at day 2, which might be due to the differentiation process. However, this phenotype was not seen in the presence of Baghdadite, and there was no significant difference between its absence or presence. MG-63 cells in both groups exhibited only minimal secretion of IL-1ß. IL-6 production was enhanced in THP-1 macrophages through the addition of Baghdadite with a solid increase after day 5. These results, however, did not prove statistically significant in comparison to the control group (Figure 3B). Although there was a general trend for MG-63 to produce more IL-6 over time in culture in the absence or presence of Baghdadite, no significant differences were observed between the two groups. TNFα production was significantly increased in the presence of Baghdadite in THP-1 macrophages. The increase was steady in the Baghdadite group, with the highest measurement on day 7, while the TNFα secretion of the control group increased only slightly, resulting in a significantly different TNFα level between the control and Baghdadite groups. The MG-63 cell line did not produce measurable TNFα level with or without Baghdadite (Figure 3C).

In summary, the presence of Baghdadite may result in a proinflammatory effect on macrophages resulting in an upregulated production of IL-6 and TNFα. However, only the difference in TNFα production was statistically significant. A similar effect on MG-63 was not observed.

4. Discussion

Cases of RTHA often present with large uncontained defects of the weight-bearing area of the acetabulum and of the stability-generating aspects of the femur. Biological augmentation and consecutive defect downsizing have been challenging and often result in suboptimal long-term clinical results. Therefore, the idea of a mechanically stable, 3D-printable, and biocompatible ceramic bone substitute is exciting for surgeons and researchers alike.

However, care must be taken to evaluate each aspect separately before progressing to an in vivo model. In this publication, we investigated the biocompatibility of Baghdadite with the focus on a later employment in the field of RTHA. Our group is made up of surgeons and basic science researchers combining scientific experience with clinical expertise. We present a structured and easily reproducible experimental setup.

Our study reported good biocompatibility of a Baghdadite test body without significant differences in cytotoxicity and proliferation rate between groups after 7 days. Other in vitro experimental setups support these results. The group around Arefpour et al. examined the behavior of Baghdadite nanoparticles on mesenchymal bone marrow stem cells and reported no significant cytotoxicity [28]. Ramaswamy et al. investigated the effect of Baghdadite ceramics on the proliferation and attachment of human osteoblast-like cells (HOB), osteoclasts and endothelial cells (HMEC-1) and demonstrated that the ceramic material supports cell attachment and differentiation. A significant difference of proliferation of HOB on day 7 compared to a blank control was not established. Additionally, cell attachment and proliferation/differentiation appeared to be higher in comparison to $CaSiO_3$ ceramics [21]. By exposing human adipose tissue-derived stem cells (ASCs) and primary osteoblasts (HOBs) to Baghdadite and Hydroxyapatite scaffolds, the group of Lu et al. reported an improved promotion of the osteogenic differentiation in the Baghdadite group [29]. While our study provides results of the effects of a Baghdadite ceramic on the viability and proliferation rate of macrophages, the publication of Graney et al. reports an in vitro modulation of macrophage behavior. Baghdadite appears to affect the M1-to-M2 transition to a similar ratio observed in normal healing and thereby may aid in bone repair [30]. In regard to our results and the available literature, Baghdadite appears to have a sufficient biocompatibility in an in vitro setting to warrant further in vivo investigation.

In this study, we also investigated the proinflammatory potential of Baghdadite on THP-1 and MG-63 cells. MG-63 cells did not exhibit any significant increase or upregulation

in the secretion of IL-1ß, IL-6 and TNFα. THP-1-derived macrophages, however, in the presence of Baghdadite, showed an upregulated production of IL-6 and TNFα. Only the upregulation of the production of TNFα proved to be statistically significant. To our best knowledge no other studies investigated the effect of Baghdadite on the secretion of proinflammatory markers such as IL-1ß, IL-6 and TNFα. Therefore, comparability with other results cannot be achieved.

IL-1ß is one of the essential proinflammatory mediators promoting osteolysis in bone–implant interfaces [26]. A dramatic increase in IL-1ß can be achieved through stimulation with LPS, mimicking the situation of an additional low-grade infection and further aggravating inflammation. In an aseptic revision case, a clinical effect may not be as drastic, but needs to be kept in mind. An increase in IL-1ß might also be caused by a simultaneous increase in TNFα, which can act as a priming factor. Such combined increases have been observed in chronic but aseptic low-grade periprosthetic inflammation [31]. TNFα is considered a master cytokine during inflammation and can induce other proinflammatory chemokines and cytokines. According to our results, Baghdadite does possess a proinflammatory capacity due to its induction of TNFα. Whether this is clinically relevant and alters or inhibits bone formation is unclear. The IL-6 cytokine family displays almost contrasting roles and can stimulate the expression of RANKL by osteoblasts to promote the formation of bone-resorbing osteoclasts, but it can also stimulate osteoblast differentiation and promote bone formation [27]. A clinically relevant negative effect on bone formation due to IL-6 induction caused by the presence of Baghdadite needs further investigation.

Baghdadite ceramics present an interesting bone composite material and after evaluating biocompatibility and inflammatory potential in vitro, an in vivo evaluation fitted to the field of RTHA is the logical next step. In vivo, animal models have been published in the literature with promising first results. An interesting publication by the group around Luo evaluated the osteogenic potential of Baghdadite microspheres in a similar setting to impaction bone grafting, as described in the introduction. Ceramic spheres were implanted into the supracondylar region of the femur in Wistar rats. In an immunohistochemical evaluation, Baghdadite presented with enhanced osteogenic potential when compared to silicate-based diopside and ß-tricalcium phosphate [32]. Another investigation was launched by Roohani-Esfahani et al. repairing a critical-sized, segmental bone defect of the radius with a highly porous Baghdadite scaffold in rabbits. Micro-computed tomography and histological analysis after 12 weeks under normal load showed extensive new bone formation with complete bridging of the radial defect [33]. The first large animal model was carried out and published by Li et al. In this study, critical-sized, segmental defects of sheep tibia were treated with Baghdadite scaffolds and analyzed after 26 weeks through electron microscopy, multiphoton microscopy, and histology. The authors report extensive new bone formation that directly abuts the implant surfaces. Furthermore, no evidence of chronic inflammation of fibrous capsule formation, both common with conventional bulk allografts, have been found [34]. A next progression could be the treatment of an uncontained defect and/or a contained defect in a large animal model in combination with a hip revision implant. However, there remains some concern regarding the mechanical strength of Baghdadite as bulk and porous scaffolds. Although the Baghdadite scaffolds have reportedly reached the lower end of the range for cortical and trabecular bone, application for high load-bearing musculoskeletal applications may still be limited [12]. Further biomechanical investigation is required in the future.

5. Conclusions

In summary, our investigation of the biocompatibility of Baghdadite ceramics, which was based on testing the viability and proliferation rate of THP-1-derived macrophages and the human osteosarcoma cells MG-63, presented with no significant differences when compared to a control group. We therefore conclude that, in our in vitro setup, no relevant cytotoxicity of Baghdadite ceramics was encountered. However, Baghdadite ceramics exhibit a proinflammatory potential by significantly increasing the secretion of TNFα in

THP-1-derived macrophages. Whether this proinflammatory potential results in a clinically relevant inhibition of bone ingrowth is unclear and requires further investigation. Baghdadite ceramics provide an interesting alternative to conventional bone substitutes and should be further investigated. Before a large animal model can be carried out, further biomechanical testing is needed to establish sufficient evidence regarding the required stability for an application in the treatment of bone defects in RTHA.

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4. Diskussion

Die Behandlung von ausgeprägten knöchernen Defekten des Hüftgelenks bleibt eine der größten Herausforderungen im Bereich der Revisionsendoprothetik. Um die definierten Grundprinzipien - also eine primärstabile Verankerung, eine Rekonstruktion der anatomischen Gelenkgeometrie und eine Verkleinerung des Defektes - zu erreichen, bedarf es einer dezidierten Defekterkennung, um eine möglichst verlässliche und detaillierte präoperative Planung zu ermöglichen. Die komplexe dreidimensionale Anatomie des Beckens und des Femurs erschwert die Defekterkennung deutlich. Native Röntgenbilder des Hüftgelenks gelten weiterhin als Routinediagnostik vor endoprothetischen Revisionseingriffen. Durch die Eigenschaft des Nativröntgens als Überlagerungsaufnahme ist die detaillierte Defektanalyse herausfordernd. Besonders knöcherne Schädigungen des hinteren Pfeilers zeigen in der radiologischen Auswertung eine stark eingeschränkte Sensitivität von 15%, sind jedoch entscheidend für die Auswahl des Implantatsystems. [31] Ein häufiger Grund hierfür sind einliegende, röntgenundurchlässige Implantate. [32] Zur Erleichterung der Defekterkennung und um einen informierten wissenschaftlichen Dialog zu ermöglichen, wurden bereits zahlreiche Klassifikationssysteme publiziert. Als Inhalt dieser kumulativen Habilitationsarbeit wurde ein integriertes Klassifikationssystem für azetabuläre Defekte (ADC) und für femorale Defekte (FDC) vorgestellt. Dieses kombinierte Klassifikationssystem bietet entscheidende Vorteile gegenüber den etablierten Klassifikationssystemen wie z.B. von Paprosky et al. und der AAOS, welche im Folgenden ausführlich dargelegt werden sollen. [10-13]

Ein entscheidendes Kriterium für die Verwendbarkeit eines Klassifikationssystems ist dessen Verlässlichkeit. So sollte idealer Weise ein präoperativ klassifizierter Defekt in der Operation entsprechend vorgefunden werden. Zusätzlich sollten unterschiedliche Anwender oder gleiche Anwender zu unterschiedlichen Zeitpunkten, stets zu dem gleichen Ergebnis kommen. Ein Blick in die Literatur zeigt jedoch ernüchternde Resultate für die etablierten Klassifikationssysteme. So zeigen sich regelhaft unzureichende Übereinstimmungen zwischen präoperativer Klassifikation und intraoperativem Befund für azetabuläre Klassifikationssysteme. [17, 33, 34] Die femorale Klassifikation zeigen in der präoperativen-intraoperativen Übereinstimmung bessere Werte, aber lassen sich auch nur in die Kategorie der moderaten Übereinstimmung definiert nach Landis und Koch einordnen. [14, 15, 33] In der

vorliegenden Auswertung zeigten im Kontrast dazu sowohl die ADC, als auch die FDC eine sehr gute Übereinstimmung zwischen präoperativer Ästimation und intraoperativer Befunderhebung. [8] Auch die Übereinstimmung zwischen verschiedenen Untersuchern und gleichen Untersuchern zu unterschiedlichen Zeitpunkten konnte jeweils mit "gut" evaluiert werden. [8] Dies steht im deutlichen Kontrast zu den übrigen azetabulären Klassifikationen, die in der Regel mit Übereinstimmungen von schlecht bis moderate evaluiert wurden. [17, 33, 34] Die meisten femoralen Klassifikationen zeigen gemischte Resultate von schlecht, über moderat bis gut, sodass hier eine definitive Einschätzung schwerfällt. [14, 35-38] Für das deutlich bessere Abschneiden der ADC/FDC können verschiedene Gründe diskutiert werden. Beide Klassifikationen folgen einem logischen und intuitiven Aufbau, der sich an der therapeutischen Versorgung und an den lasttragenden Strukturen orientiert. Alle Untersucher erhielten eine ausführliche Unterweisung. Die Etablierung einer Unterweisung zeigte auch bei anderen Klassifikationssystemen eine deutliche Verbesserung der Reproduzierbarkeit. [32]

Um die Benutzerfreundlichkeit, die Reproduzierbarkeit und die Verlässlichkeit der ADC weiter zu verbessern, wurde eine Web-basierte Applikation entwickelt, die den Benutzenden sowohl bei der präoperativen als auch bei der intraoperativen Auswertung unterstützen kann. Die Nutzung von medizinischen Applikationen im Klinikalltag nimmt immer weiter zu und besonders junge orthopädische Kollegen benutzen ihre Smartphones täglich zur klinischen Arbeit. [18] Eine Integration von modernen IT-gestützten Lösungen zur Erleichterung komplexer diagnostischer Vorgänge ist daher der nächste logische Schritt. Durch die ADC-Applikation konnte der diagnostische Erfolg von Studenten ohne vorherige revisionsendoprothetische Erfahrung auf ein gutes Niveau gehoben werden. Die Ergebnisse der "Nicht-Spezialisten" mit Unterstützung der App lagen damit sogar höher als multiple Auswertungen von anderen Klassifikationssystemen in der Literatur. Die erreichten Ergebnisse in der Auswertung der ADC-Applikation sind nicht überraschend. Die Klassifikation von Azetabulumfrakturen nach Letournel ist ebenfalls äußerst komplex. Auch hier konnte mit der Hilfe einer entsprechenden Applikation eine gute Verlässlichkeit und Reproduzierbarkeit der Klassifizierung durch unerfahrene Benutzer erreicht werden. [39] Ein weiteres Beispiel für die erfolgreiche Etablierung einer Applikation ist die so genannte AOSR-Applikation (Arbeitsgemeinschaft Osteosynthese Surgery Reference). In ihr können Frakturen des ganzen Körpers nach

dem etablierten AO-Schema klassifiziert werden. Zusätzlich gibt die Applikation Therapieempfehlungen und Operationsanleitungen. [40] Es konnte im Rahmen dieser Habilitationsschrift dargestellt werden, dass die ADC und FDC reproduzierbare und verlässliche Klassifikationssysteme sind, die durch die Integration in eine Web-basierte Applikation den Einstieg in die komplexe Welt der Revisionsendoprothetik auch für unerfahrene Kollegen deutlich erleichtern.

Nach dem die Erkennung und Klassifikationen des Defektes präoperativ sicher und reproduzierbar durchgeführt werden kann, zeigt sich ein weiterer Vorteil des integrierten Klassifikationssystems aus ADC und FDC: die klare therapeutische Konsequenz. Etablierte Klassifikationssysteme basieren häufig, bedingt durch das große Zeitintervall seit der initialen Veröffentlichung, auf veralteten therapeutischen Empfehlungen.

Da der grundlegende Aufbau von ADC und FDC auf der Integrität der lasttragenden Strukturen basiert, erfolgt die Auswahl von Implantatsystemen und Augmentierungsverfahren mit dem Ziel des Erreichens einer biomechanischen Primärstabilität. Damit wird einem Grundprinzip der revisionsendoprothetischen Versorgung gefolgt. Für beide Klassifikationssysteme wurde ein Therapiealgorithmus basierend auf den Erfahrungen aus der klinischen Praxis, Expertenmeinungen und einer ausführlichen Literaturrecherche bereitgestellt. Dieser Algorithmus ist auch nach erfolgter Klassifikation in der Web-Applikation einsehbar. Die Therapieempfehlung der FDC basiert abhängig von der Defektkonfiguration auf dem Erreichen eines zirkumferenten, diaphysären Press-Fits, in der Regel kaudal zur jeweiligen Defektsituationen. Dies kann in der Regel mit einem zementfreien, konischen Revisionsschaft erreicht werden. Das häufig vorhandene modulare Halsteil des Revisionsschaftsystems erlaubt eine intraoperative Einstellung von Rotation, Länge und femoralen Offset zur Rekonstruktion der anatomischen Hüftgeometrie. Bestehende Defekte sollten biologisch augmentiert werden. Hier kommt das oben beschriebne Impaction-Bone-Grafting besonders im Bereich der Metaphyse zum Einsatz. [41-43] Zusätzlich kann durch die metaphysäre Defektaugmentation bei Revisionsschäften mit modularer Halskomponente ein Konusschutz erreicht werden, um Brüche zu verhindern. [44, 45]

Ein zentraler Pfeiler des Klassifikationssystems der ADC ist die metallische, makroporöse Augmentation von lasttragenden Defekten des Azetabulums. Hierdurch kann ein unumschlossener ("uncontained") Defekt wieder in einen umschlossenen

("contained") Defekt umgewandelt werden und so eine Primärstabilität und ggf. sogar eine Verkeilung ("Press-fit") des Implantatsystems erreicht werden. Während in der Frühzeit der Hüftrevisionsendoprothetik häufig strukturelle Allografts (z.B. ganze oder halbierte Hüftköpfe) zur lasttragenden Augmentation genutzt wurden, zeigte die Nachuntersuchung der entsprechenden Fälle ein eingeschränktes Einwachsverhalten, limitierte knöcherne Integration und konsekutive Resorption sowie das Versagen der revisionsendoprothetischen Versorgung. [21, 22, 24, 46] Metallische, makroporöse Augmente aus Titan oder Tantal ermöglichen eine primärstabile Versorgung durch einen hohen Reibungskoeffizienten und ein daraus resultierendes gutes Press-fit. Zusätzlich ermöglicht die makroporöse, Spongiosa-ähnliche Struktur das Einwachsen von vitalem Knochen und damit eine stabile sekundäre Osseointegration. [47] Die Augmentation des lasttragenden Defektes kann zum einen durch Monobloc-Implantate, wie z.B. Oblong-Pfannen und Kranialsockelpfannen, oder durch modulare Augmente an unterschiedlichen Revisionssystemen erreicht werden. Die modulare Anbringung von Augmenten ermöglicht ein hohes Maß an Flexibilität innerhalb der operativen Versorgung. Bezogen auf die Fixierung des Augments am jeweiligen Implantatsystem gibt es aktuell keinen Goldstandard. Während einige Autoren die zementfreie Schraubenfixierung bevorzugen, wird auch häufig eine Fixierung mittels einer dünnen Schicht aus Knochenzement durchgeführt. Eine Kombination aus Knochenzement und Schraubenverbindung ist ebenfalls möglich und etabliert. Bislang konnte keine klare Überlegenheit einer Fixierungsform nachgewiesen werden. In-vitro Untersuchungen zeigen, dass eine singuläre Schraubenfixierung zu bis zu 3-fach erhöhten Relativbewegungen verglichen mit einer Zementfixierung führt. [27] Ob sich hieraus jedoch eine klinische Relevanz ergibt, ist nicht untersucht. Der Nachteil einer Zementfixierung besteht darin, dass der Knochenzement mit seinem deutlich niedrigeren E-Modul zwischen zwei Metallflächen als schwächstes Glied langfristig zerrütten könnte. Hierdurch würde dann Metall-Metall-Abrieb entstehen, welcher als besonders aggressiv und osteolytisch gilt. [48]

Eine attraktive und moderne Möglichkeit zur Versorgung von ausgeprägten knöchernen Defekten des Azetabulums ist die Verwendung einer modulare Abstützschale, abgewandelt nach dem etablierten Burch-Schneider-Prinzip. [49] An ihr können Augmente verschiedener Größe und räumlicher Orientierung zementfrei befestigt werden (siehe Abbildung 4). Die Verwendung von sogenannten Pfannendomschrauben ermöglicht eine Fixierung im Hauptkraftvektor und liefert einen

deutlichen Zugewinn an Stabilität. [50] Zusätzlich ist die modulare Revisionsschale in verschiedenen Konfiguration wahlweise mit anatomischen Iliumlaschen unterschiedlicher Länge erhältlich. Die Verwendung von Iliumlaschen ist ein etabliertes Vorgehen in der Hüftrevisionsendoprothetik und ermöglicht das Einbringen einer weiteren Verschraubung rechtwinklig zum Kraftvektor und den Pfannendomschrauben. Hierdurch wird eine stabile Aufhängung des Implantats am Pfannenerker erreicht. Zur klinischen Evaluation von Implantatsystemen mit kranialen Laschen existieren bereits zahlreiche Studien, die insgesamt positive Ergebnisse aufzeigen. [51-54] Eine isolierte Auswertung des Zugewinns an Primärstabilität durch kraniale Laschen wurde jedoch bis zur der hier vorliegenden Studie nicht durchgeführt. Dies ist besonders wichtig, da die Nutzung von kranialen Laschen zu einer deutlich größeren Weichteilschädigung führt. Zur regelhaften Präparation und Fixierung bedarf es einer Mobilisation der glutealen Muskulatur von der Iliumschaufel. Hierdurch werden eine gluteale Insuffizienz und das Risiko für eine Schädigung von glutealen Gefäßen und Nerven erhöht. [55] Bei großen kranialdorsalen Defekten > 1 cm (ADC 3) und/oder Verlust der kaudomedialen Abstützung mit der Gefahr des "Einkippens" des Revisionsimplantats ist eine zusätzliche Fixierung über Laschen unbedingt notwendig. Doch ob bei kleineren Defekten (ADC 2) der mutmaßliche Zuwachs an Primärstabilität die erhöhte Invasivität rechtfertigt ist unklar.

Ein etablierter Surrogatparameter zur In-vitro Evaluation der Primärstabilität von Implantaten ist das Ausmaß von Relativbewegungen unter physiologischer Belastung zwischen Implantat und Knochen. Initial definiert durch In-vivo Studien an Mensch und Tier konnte ein Sicherheitsbereich in µm definiert werden. So kann bei Relativbewegungen von ~40 µm von der biomechanischen Möglichkeit einer erfolgreichen Osseointegration ausgegangen werden. Werte > 150 µm resultieren dagegen in einer fibrösen Einheilung und langfristigem Scheitern der endoprothetischen Versorgung. [56, 57] Auch, wenn auf Grund von diversen Limitationen der aufgeführten Studien hier keine absoluten Grenzwerte definiert werden können, unterstreichen sie doch die Bemühung möglichst geringe Relativbewegungen unter Belastung im Rahmen der Primärstabilität zu erreichen. Erhöhte Relativbewegungen unter Belastung betreffen jedoch nicht nur die Grenzfläche zwischen Implantat und Knochen, sondern wirken auf das gesamte Revisionssystem. Besonders bei modularen Systemen - im Kontrast zu z.B. einer Monobloc-Versorgung - gibt es viele nicht-artikulierende Grenzflächen, in welchen es

ebenfalls zu Abrieb kommen kann. So beschreiben zahlreiche Studien das Auftreten von Komplikationen durch Abriebpartikel und Korrosion in modularen Revisionssystemen. [58-61]

In der vorliegenden Untersuchung ergab sich ein signifikanter Unterschied mit deutlich weniger Relativbewegungen im Interface zwischen Knochen und Implantat durch die Verwendung von kranialen Laschen. Die Relativbewegungen der Gruppe ohne kraniale Laschen waren bereits bei leichten Belastungen höher und verstärkten sich mit Lastzunahme weiter, während die Relativbewegung bei der Gruppe mit kranialen Laschen über die ansteigenden Laststufen konstant blieb. Es kann daher geschlussfolgert werden, dass die Verwendung von kranialen Laschen tatsächlich einen Zugewinn and Primärstabilität auch bei ADC 2 - Defekten ermöglicht. Ob dieser Zugewinn jedoch die zusätzliche Invasivität rechtfertig, muss individuell entschieden werden. Hierzu können weitere Faktoren, wie z.B. das Ausmaß an Sklerose und die Knochendichte entscheidende Hinweise liefern.

Die zementfreie Fixierung des kraniolateralem, makroporösen Augments and der modularen Revisionsabstützschale mit einer einzelnen Schraube zeigte sich in dieser Auswertung primärstabil mit einem konstanten Ausmaß an Relativbewegungen innerhalb der unterschiedlichen Laststufen. Interessanterweise zeigte sich signifikant höherer Relativbewegungen bei der Verwendung von kranialen Laschen in der Grenzschicht zwischen Implantat und Augment (ohne Laschen: 9.52 ± 0.46 µm vs. mit Laschen: 10.83 ± 0.70 µm bei 100% Belastung). Trotz der statistischen Signifikanz ergibt sich auf Grund des geringen Unterschiedes hieraus am ehesten keine klinische Relevanz. Vergleicht man diese zementfreie Augmentbefestigung mit der Auswertung von zementierten und hybriden (Zement und Schrauben) Augmentbefestigung zeigen sich in unserer Auswertung geringere Relativbewegungen. [27] Zusätzlich schneidet die zementfreie Schraubenbefestigung in unserer Studie deutlich besser ab, als in der Vorstudie (9.52 ± 0.46 µm vs. 31.4 ± 16.6 µm bei 100% Belastung). Hieraus lässt sich ableiten, dass nicht nur das grundlegende Fixierungsprinzip (zementfrei, Schraubenbefestigung) entscheidend ist, sondern auch die Umsetzung im Implantatdesign. So verwenden verschiedene Hersteller das gleiche Prinzip in unterschiedlichen Ausführung. Hierbei divergieren sowohl die Anzahl, Form und Länge der Schrauben, als auch das Drehmoment, Einbringwinkel und die Beschaffenheit der angrenzenden Oberflächen von Augment und Implantatschulter. Dies erschwert eine einheitliche Bewertung deutlich.

Zusammenfassend ermöglichen makroporöse, metallische Augmente eine gute Option zur Überführung eines unumschlossenen in einen umschlossenen Defekt und ermöglichen so eine primärstabile Verankerung von Revisionimplantaten auch bei ausgeprägten Knochendefekten. Sollte es im weiteren Verlauf jedoch zu einer erneuten Revision, z.B. auf Grund von einer periprothetischen Infektion kommmen, hinterlassen diese Augmente bei der Explantation erneut einen großvolumigen Knochendefekt und ermöglichen keine biologische Defektverkleinerung in der lasttragenden Zone.

Die Verwendung von der beschriebenen modularen Abstützschale ermöglicht intraoperativ eine hohe Flexibilität und eine sehr gute Primärstabilität auch bei ausgeprägten Knochendefekten. Sie ermöglicht darüber hinaus eine biologische Augmentation des Pfannenbodens mit Spongiosa über Impaktionstransplantation und schützt durch die flächige Überbrückung des Defektes das Transplantat bis zum finalen Umbau. Gäbe es jetzt noch ein Möglichkeit, die krafttragenden Anteile durch ein Augment aus vitalem Knochen zu ersetzen, wäre eine nahezu vollständige biologische Defektverkleinerung geglückt. Jedoch scheitert, wie oben ausgeführt, in der Regel die Transplantation von soliden Knochenblöcken langfristig. Eine moderne Möglichkeit zur Augmentation von Knochendefekten ist die Verwendung von Knochenersatzmaterial. Während Knochenersatzmaterialen bereits seit vielen Jahren erforscht werden, gewannen in den letzten Jahren Kalziumsilikat-basierte Keramiken immer mehr an Bedeutung. Ähnlich metallischen Augmenten, können Sie durch additive Verfahren (3D-Druck) in die Form von makroporösen Gerüsten gebracht werden. [62] Die poröse Struktur unterstützt den Austausch von Sauerstoff und Nährstoffen, die Abfallproduktentsorgung sowie die Osteoneogenese und Gefäßeinsprossung in die Poren. [29] Zusätzlich könnte bei einem stabilen Konstrukt die poröse Oberfläche, ähnliche wie bei metallischen Augmenten, eine gute Primärstabilität durch den hohen Reibungskoeffizienten und eine gute Verklemmung ermöglichen. [63] Auch für die Augmentierung von nicht lasttragenden Bereichen, wie z.B. dem Pfannenboden und der Femurmetaphyse (bei Verwendung eines diaphysär-verankernden Schaftes), sind durch den Einsatz von keramischen Knochenersatz gute Ergebnissen möglich. [64,65] In dieser Habilitation erfolgte die Untersuchung von Baghdadite, einer Calcium-Silikat-Keramik, welche durch das Hinzufügen von Zirconium (Zr) verbesserte physische und mechanische Eigenschaften besitzt. [66] Dies ist dadurch begründet, dass Zirkonium als quadrivalentes Ion an Kalzium bindet.

[60] Biomechanische Untersuchungen haben ergeben, dass 3D-gedruckte makroraue Baghdadite-Gerüste sich bezogen auf das E-Modul im unteren Bereich der beschriebenen Werte für Spongiosa und Kortikalis befindet. [29] Dies ist essentiell für die Augmentierung in gewichtsbelasteten Bereichen, um die vorzeitige Resorption und den Abbau zu verhindern. [68] In der durchgeführten Studie konnte nun gezeigt werden, dass Baghdadite eine gute Biokompatibilität besitzt. Wir konnten keinen Unterschied bezogen auf die Zytotoxizität und die Zellteilungsrate bei humane Osteoblastomzellen (MG63) und THP-1 Makrophagen nach Exposition zu Baghdadite im Vergleich zu einer Testgruppe evaluieren. Andere Autoren haben Baghdadite ebenfalls auf Zytotoxizität untersucht. In der Regel handelte es sich jedoch dabei um grundlegend andere Versuchsaufbauten. Dennoch konnte in den vorliegenden Studien keine Zytoxizität auf mesenchymale Knochenmarksstammzellen, aber einen ungehemmt Proliferation and Adhäsion von humanen Osteoblasten-ähnlichen Zellen, Osteoklasten und Endothel Zellen (HMEC-1) nachgewiesen werden. [67,69] Die Exposition mit Baghdadite scheint bei humanen Fettgewebs-abgeleiteten Stammzellen (ASCs) und primären humanen Osteoblasten die osteogenetische Differenzierung zu fördern. [70] Zusätzlich könnte das Vorhandensein von Baghdadite zu einer Unterstützung der Knochenheilung führen, da die M1-zu-M2 Transition von Makrophagen in einem ähnlichen Verhältnis beeinflusst wird, wie beim physiologischen Heilungsprozess des Körpers. In Zusammenschau der eigenen Ergebnisse in Kombination mit der bereits vorhandenen Studienlage, scheint Baghdadite eine ausreichende Biokompatibilität ohne Hinweise auf Zelltoxizität zu besitzen, um weitere Versuche zu rechtfertigen.

Jedoch zeigte sich ein mögliches proinflammatorisches Potential durch eine signifikante Erhöhung der Sekretion von IL-1ß, IL-6 und TNFα in THP-1 Makrophagen in der eigenen Untersuchung. Zum Zeitpunkt dieser Habilitation existieren keine weiteren Studien, welche die Sekretion von IL-1ß, IL-6 und TNFα in THP-1 Makrophagen nach Exposition mit Baghdadite untersuchen und so einen Vergleich erlauben würden. Daher sind diese Daten einzigartig und werfen zwar einen interessanten Diskussionspunkt auf, bedürfen jedoch noch weiterer Evidenz um ein abschließendes Urteil zu fällen. Ob dieses proinflammatorische Potential einen relevanten Einfluss auf die Osseointegration des Materials hat, ist aktuell unklar. Baghdadite-Keramiken präsentieren sich als für die Revisionsendoprothetik äußerst interessantes Material. Die Kombination aus mechanischer Stabilität, guter

Bearbeitbarkeit durch additive Verfahren, guter Biokompatibilität und osteogenetischem Potential rechtfertig eine weitere Evaluation in In-vivo Modellen. Hierzu wurde bereits Vorarbeit durch diverse Gruppen geleistet. So konnte bereits ein Impaction-Bone-Grafting-ähnliches Verfahren an Ratten getestet werden und zeigte ein besseres osteogenetisches Potential im Vergleich zu anderen Knochenersatzmaterialen. [71] Auch die Untersuchung von makrorauen Baghdadite-Gerüsten in segmentalen Defekten des Radius bei Hasen zeigte deutliche, vitale Knochenformationen und eine vollständige Überbrückung des knöchernen Defektes unter Vollbelastung nach 12 Wochen. Als erstes Großtiermodell am Schaf zeigten sich bei der Behandlung von segmentalen Defekten an der Tibia ebenfalls eine ausgeprägte Knochenbildung und kein Hinweis auch chronische Entzündung oder fibröses Einwachsen, wie es bei konventionellen Allografts beobachtet wird. [72]

5. Zusammenfassung und Ausblick

Zusammenfassend stellen knöcherne Defekte in der Hüftrevisionsendoprothetik eine sehr herausfordernde Komplikation dar. Da die primäre Hüftendoprothetik so erfolgreich ist, werden die Implantationszahlen meiner Ansicht nach stetig steigen und auch die Indikationsstellung auf jüngere und aktivere Patienten ausgeweitet werden. Im klinischen Alltag an einer Universitätsklinik und an einem Endoprothesenzentrum der maximalen Versorgung ist es mittlerweile üblich Patienten mit der 3. oder 4. Revision zu indizieren. Wie bei allen komplexen Schädigungen, welche einer operativen Therapie zugeführt werden sollen, ist die Erkennung und Analyse des zugrunde liegenden Problems entscheidend. Mit der Vorstellung der integrierten Klassifikation für knöcherne Defekte des Hüftgelenks steht erstmalig ein intuitives und modernes System zur Verfügung, welches sich an der grundlegenden Biomechanik und der therapeutischen Versorgung orientiert. Eine hohe Verlässlichkeit und Reproduzierbarkeit konnten durch die vorliegenden Studien nachgewiesen werden. Um die Benutzerfreundlichkeit weiter zu erhöhen und damit auch die Verbreitung des Klassifikationssystems zu verbessern, wurde eine Web-basierte Applikation vorgestellt, welche den Benutzenden schrittweise durch die komplexe Analyse eines azetabulären Defektes führt. Am Ende der Bearbeitung steht eine 3D-Darstellung des Defektes und eine entsprechende therapeutische Versorgungsoption bezogen auf die knöcherne Schädigung zur Verfügung. Dies ermöglicht auch ein großes Potential für die Lehre und Weiterbildung in der Revisionsendoprothetik, ein Fachgebiet, welches auf Grund der hohen Komplexität in der Regel schwer zugänglich ist. Es konnte gezeigt werden, dass sogar Studierende mit geringen Vorkenntnissen eine validen Einschätzung der Defektsituation vornehmen konnten. Ist der Defekt erkannt, klassifiziert und das operativen Vorgehen geplant kommt es zur eigentlichen Therapie. In den letzten Jahren haben sich modulare Implantatsysteme mit verschiedenen metallischen Augmentationsmöglichkeiten etabliert. Reichhaltige klinische Daten konnten gute Ergebnisse beschreiben, die sich auch in der eigenen Erfahrung widerspiegeln. Jedoch fehlt es weiterhin an isolierten Auswertungen zu den einzelnen modularen Elementen, um definitive Indikation für jegliche Konfiguration definieren und validieren zu können. Es konnte gezeigt werden, dass kraniale Laschen einen deutlichen Zugewinn an Stabilität auch bei geringen lasttragenden Defekten erreichen können. Die zementfreie Augmentfixierung zeigt eine hervorragende Primärstabilität

und geringe Relativbewegungen. Das Fachgebiet der Revisionsendoprothetik ist getrieben von dem stetigen Wunsch nach biologischer Defektverkleinerung. Dies können modulare Implantatsysteme mit metallischen Augmenten in der lasttragenden Zone aktuell nicht erreichen. Nachdem die Resultate von allogener biologischer Rekonstruktion durch Bulk-Allografts unzureichend waren, liegt die Hoffnung auf Knochenersatzmaterialien. Baghdadite, eine Zirkonium-haltige Kalzium-Silikat-Keramik zeigt eine sehr gute Biokompatibilität, eine zureichende mechanische Stabilität und ein gutes osteogenetisches Potential. Die zusätzliche Möglichkeit zur freien Formgebung durch additive Verfahren ermöglicht eine einfache Verarbeitung in bereits etablierten Herstellungsprozessen der Implantathersteller. Zukünftig soll die Verbreitung des integrierten Klassifikationssystem weiter ausgebaut werden. Mit weiteren biomechanischen und klinischen Studien müssen besonders Teilaspekte der modularen Möglichkeiten untersucht und eingeschätzt werden, um klare therapeutische Empfehlungen zu validieren. Die Integration von makrorauen Baghdadite-Augmenten an modularen Revisionsimplantaten im Tierversuch zur Augmentation von Knochendefekten in der lasttragenden Zone ist der nächste logische Schritt um der Vorstellung einer vollständigen biologischen Defektverkleinerung näher zu kommen.

6. Überlappung durch geteilte Autorenschaften

Die vorliegende Habilitationsschrift hat vier publizierte Originalarbeiten zur Grundlage. Von diesen Arbeiten wurden zwei mit einer geteilten Erstautorenschaft publiziert:

Jaenisch M*, Kohlhof H*, Kasapovic A, Gathen M, Randau TM, Kabir K, Roessler PP, Pagenstert G, Wirtz DC (2023) Femoral defects in revision hip arthroplasty: a therapy-oriented classification. Arch Orthop Trauma Surg. 143(3):1163-1174. https://doi.org/10.1007/s00402-021-04201

Die vorliegende Arbeit wurde gemeinsam mit Herrn PD Dr. Kohlhof durchgeführt, welcher zu dieser Zeit der Sektionsleiter der Endoprothetik war. Gemeinsam arbeiteten wir am Studiendesign und der grundlegenden Gliederung der Klassifikation. Die Erstellung von Bild- und Grafikmaterial gemeinsamen mit einem Grafiker erfolgte durch mich. Die Datenerhebung, Datenanalyse, Auswertung und Erstellung des Manuskripts erfolgte durch mich. Eine Durchsicht und Korrektur des Manuskripts vor Veröffentlichung erfolgte durch PD Dr. Kohlhof.

Jaenisch M*, Kohlhof H*, Wirtz DC, Schildberg FA, Beckmann NA, Kretzer JP, Schonhoff M, Jäger S (2021) Primary Stability in Hip Revision Arthroplasty: Comparison of the Stability of Cementless Fixed Augments on a Modular Acetabular Cage System with and without Cranial Straps. J Clin Med. 10(17):4002. https://doi.org/10.3390/jcm10174002

Die vorliegende Arbeit wurde gemeinsam mit Herrn PD Dr. Kohlhof durchgeführt, welcher zu dieser Zeit der Sektionsleiter der Endoprothetik war. Gemeinsam arbeiteten wir am Studiendesign und waren für das Einbringen der klinischen Perspektive bei der vorwiegend biomechanischen Studie verantwortlich. Die Planung, Aufsicht und Durchführung der Hemipelvis-Modell-Präparation erfolgte durch mich, genauso wie die Erstellung von Bild- und Grafikmaterial. Die Implantation der Revisionsabstützschalen supervidierte Herr PD Dr. Kohlhof und ich konnte Sie als damaliger Assistenzarzt unter seiner Anleitung durchführen. Die Datenanalyse, Auswertung und Erstellung des Manuskripts erfolgte durch mich. Eine Durchsicht und Korrektur des Manuskripts vor Veröffentlichung erfolgte durch PD Dr. Kohlhof.

Eine Überlappung mit anderen Habilitationsschriften ist nicht gegeben.

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