Review

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Bibliometric Review of Osteochondral Interface Regeneration

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Keywords: osteochondral; regeneration; tissue engineering; bibliometric; VOSviewer

Review

Bibliometric Review of Osteochondral Interface Regeneration

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Abstract: The topic of OC interface (OCI) has shown an increasing interest in recent years, with a considerable increase in the number of publications. Here, the aim was to reveal trend in OCI research studies and analyze the publications with high citations. An online search was performed on the Web of Science Core Collection (WSCC) for publications on OCI. The journals, publication year, countries, institutions, and citations received were obtained, and the results were analyzed using VOSviewer. Only the most frequently cited top 100 publications on OCI were further considered. Totally, 225 publications were found related to OCI. The number of publications on OCI has increased with time. The US has published the most articles on OCI (n=61). The University of Minho (Portugal) was the most productive institution, with 8 publications and 753 citations. The number of publications on OC interface has recently increased. This study is the first bibliometric study evaluating publications on the OC interface and serves as a valuable source for researchers and practitioners actively working in the field.

Keywords: osteochondral; regeneration; tissue engineering; bibliometric; VOSviewer

Introduction

The osteochondral interface (OCI) refers to the graded region between the cartilage layer and the underlying bone in the joints. It is seen in articulating joints, including articular cartilage, growth plates, and intervertebral discs [1]. The OCI plays an important role in providing mechanical stability to the joint as well as preventing the vascularization and mineralization of uncalcified cartilage [2,3]. Osteochondral interface lesions are more prevalent in countries with a high prevalence of high-impact sports, including football, basketball, and soccer [4]. Additionally, if not treated, osteoarthritis can lead to the initiation and progression of osteochondral interface lesions. Due to its avascular and hypocellular nature, injuries related to articular cartilage do not heal themselves and require surgical treatments, including microfracture, mosaicplasty, and subchondral drilling [2]. Despite reported encouraging results, these currently available treatment options seem far from optimal outcomes, and therefore, alternative strategies are being investigated [5]. Despite the growing research on the osteochondral interface, its pathogenesis and natural history are not fully understood, especially the contribution of the selective membrane called tidemark. Engineering the osteochondral interface using regenerative approaches has the potential to overcome these limits; however, our recent review on the topic demonstrated a need to draw the community's attention to examine the composition and structure of the OCI effectively. Therefore, further research must be performed to recapitulate the native OCI's structure, composition, and function. In this regard, the trends in research and the most impactful studies in the field need to be systematically identified to make plausible recommendations for better outcomes. Bibliometric analysis is used to statistically and visually evaluate quantitative and qualitative trends in research. This study aims to analyze the scientific publications on the osteochondral interface using bibliometric methods to reveal highly cited publications and analyze the trends in OCI related area.

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Material and Methods

Searching WSCC

The data was generated by collecting articles from the WSCC on August 25, 2023. The keywords are obtained using Medical SubjectHeading terms from Pub Med. The search was designed as follows: ((osteochondral interface) [Title]) OR ((osteochondral tissue engineering) [Title]) OR ((osteochondral regenerative engineering) [Title]) OR ((osteochondral tissue regeneration) [Title]) OR (tidemark [Title]) AND Document type (article) AND Period 2000 to 2023.

Analysis Tools

VOSviewer as well as Microsoft Excel 2016 were combined for data analysis. VOS viewer is a tool used to visualize and analyze bibliometric data. Networks of authors, institutions, countries, co-occurrence of the keywords, and co-citation of references were all determined using VOSviewer. Excel 2016 was used to prepare tables and construct figures.

Data Extraction

Two authors independently conducted data extraction, and any differences in findings were resolved through discussions. Data were downloaded from the WSCC database, and Microsoft Excel 2016 and VOSviewer were employed for the analyses. Authors, journals, institutions, countries, total citations, and research trends were the parameters considered.

Results

Publication Trend

A total of 225 publications were identified on OCI research included to the database between 2000 and 2023. The total publications related to OCI increased from 27 between 2000 and 2010 to 79 between 2015 and 2020. In the years after 2020, 41 articles related to OCI were published. (Figure 1A).

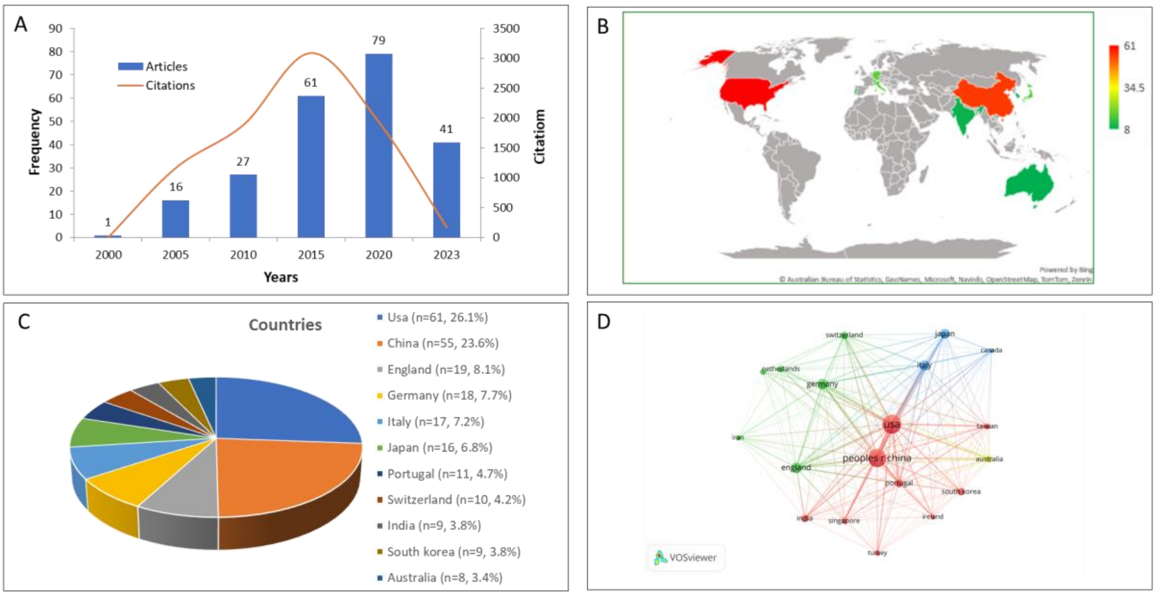

Figure 1. Overview of articles related to osteochondral interface (OCI). (A) Number of articles and citations from 2000 to 2023. B) Geographic map showing regional sources of articles. (C) Top 10 countries where articles were published. (D) Network visualization map showing international collaborations investigating OCI.

Country Distribution

The research published in articles was performed in 31 different countries. The USA published the most articles (n=61), followed by China (n=55), England (n=19), and Germany (n=18) (Figure 1B and C). A total of 22 countries were the home for 2 articles. The network analysis revealed that the USA served as the hub of Osteochondral interface research, while China, England, and Germany were seen as additional centers (Figure 1D).

Institution Distribution

A total of 473 universities or research centers were involved in the extracted publications, with the highest contribution coming from the Chinese institutions (Figure 2). The highest ranking 10 institutions were the University of Minho (Portugal; n=8), Columbia University (USA; n=7), Rice University (USA; n=7), Shanghai Jiao Tong University (China; n=7), Nanjing Medical University (China; n=6), Sichuan University (China; n=6), University of Kansas (USA; n=6), Fourth Military Medical University (China; n=5), University of Connecticut (USA; n=5), and The University of Hong Kong (China; n=5) (Figure 2A). Publications from the University of Minho were the most cited, with a total of 753 times, followed by Columbia University with 614 citations and the University of Kansas with 471 citations (Figure 2B). Regarding co-authorship relationships between institutions, the University of Minho has the strongest network (n=37), followed by Columbia University (n=33), University of Kansas (n=24), and ICVS/3B's—PT Government Associate Laboratory (n=17) (Figure 2C). The number of authorship share between institutions is depicted by the thickness of the line connecting the institutions.

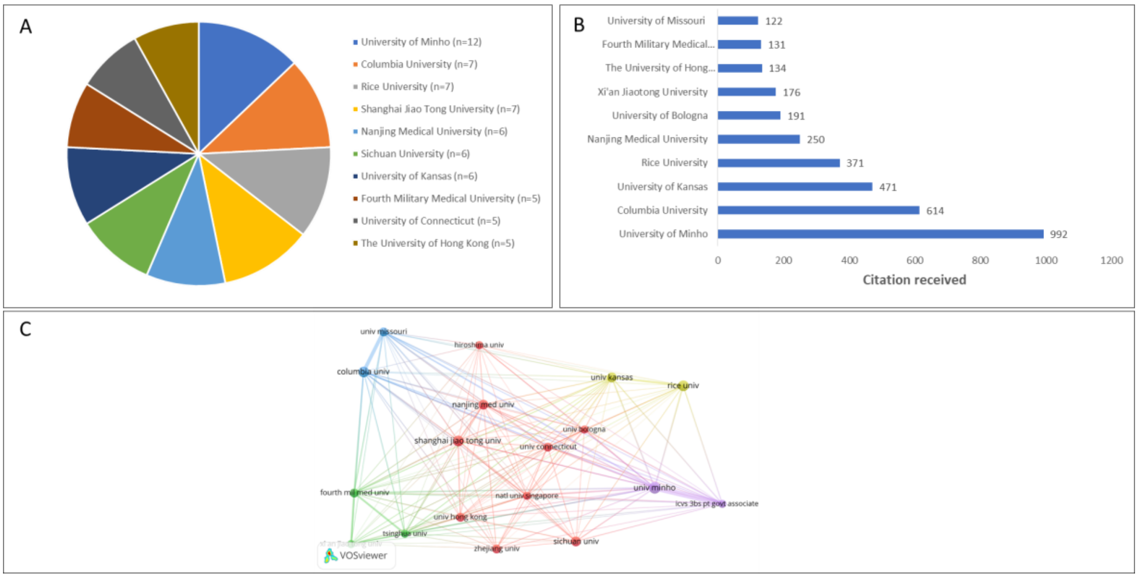

Figure 2. Highest-impact institutions are publishing on the osteochondral interface. (A) The 10 institutions with the most articles. (B) The 10 institutions with the most citations. (C) Network visualization map showing institutional collaborations related to the osteochondral interface.

Journal of Publication

The 225 extracted publications appeared in 118 different journals. The top 25 journals published 47.5% of the publications (Table 1). The most publishing 5 journals were Acta Biomaterialia, Biomaterials, Journal of Tissue Engineering and Regenerative Medicine, Journal of BiomedicalMaterials Research-PartA, and TissueEngineering-PartA. The articles published in Biomaterials had the highest total citations (n=1129). In contrast, the Journal of Controlled Release had the highest mean citations (217, not shown in the table of top 25). The impact factor of the journals with greater than 10 publications averaged to 8.44.

Table 1. Journals Publishing Most on OCI.

	Source	Articles	Citations	Mean citation*	Impact factor
1	Acta Biomaterialia	14	789	56.4	10.63 (2021)
2	Biomaterials	12	1129	94.1	15.3 (2021)
3	Journal of tissue engineering and regenerative medicine	12	221	18.4	4.323 (2023)
4	Journal of biomedical materials Research part A	7	353	50.4	4.854 (2021)
5	Tissue engineering part A	7	381	54.4	4.080 (2021)
6	Biofabrication	6	194	32.3	9.954 (2020)
7	Journal of materials chemistry B	6	119	19.8	7.571 (2023)
8	Biomedical materials	5	59	11.8	4.103 (2023)
9	Tissue engineering	5	445	89.0	3.616 (2021)
10	PLOS ONE	4	219	54.8	3.752 (2021)
11	ACS applied materials & Interfaces	3	79	26.3	10.383 (2021)
12	ACS biomaterials science & engineering	3	94	31.3	5.395 (2021)
13	Advanced healthcare materials	3	80	26.7	11.092 (2021)
14	Journal of biomaterials and tissue engineering	3	13	4.3	0.287 (2023)
15	Journal of biomechanics	3	152	50.7	2.789 (2023)
16	Knee surgery sports traumatology arthroscopy	3	122	40.7	4.114 (2021)
17	Materials letters	3	33	11.0	3.574 (2023)
18	Materials science & engineering-biomimetic and supramolecular systems	3	142	47.3	7.328 (2020)
19	Scientific reports	3	131	43.7	4.959 (2023)
20	ACS applied biomaterials	2	15	7.5	3.25 (2023)
21	American journal of sports medicine	2	10	5.0	7.010 (2023)
22	Annals of biomedical engineering	2	178	89.0	4.219 (2021)
23	Applied biochemistry and biotechnology	2	21	10.5	3.094 (2021)
24	Arthroscopy-the journal of arthroscopic and related surgery	2	58	29.0	5.973 (2023)
25	Carbohydrate polymers	2	52	26.0	10.723 (2023)

The Mean citation* is calculated by dividing the total number of citations by the total number of papers

Keywords and Research Clusters

The co-occurrence network analysis tool analyzed keywords from articles related to the osteochondral interface. The number of total occurrences was set at 20, and a total of 15 keywords were used and they were classified into 3 different clusters: "Basic research," "articular cartilage," and "cell culture." In the primary research cluster, the most frequently seen keywords were "bone," "cartilage," "differentiation," "knee," and "regeneration" (Figure 3A). The frequency of "bone" was high during the period selected. In the “articular cartilage” cluster, "articular cartilage repair," "chondrocytes," "defects," "hydroxyapatite," "in-vitro," and "subchondral bone" were the keywords that were most popular. In the cell culture cluster, the most popular keywords were "chondrogenic differentiation," "mesenchymal stem cells," "osteochondral," and "osteogenic differentiation.” To determine variation in research focus over the period examined, we evaluated the trend of the keywords with highest-frequency (Figure 3B). Colors represent the average time in years the keywords appeared in articles. For instance, the purple color shows that the keywords appeared earlier than the keywords in yellow. This analysis demonstrated that “basic science research” attracted more interest early on, which later shifted in favor of “cell culturing”. In recent years, it is seen that the shift was toward keywords "mesenchymal stem cells", "osteogenic differentiation" and "chondrogenic differentiation".

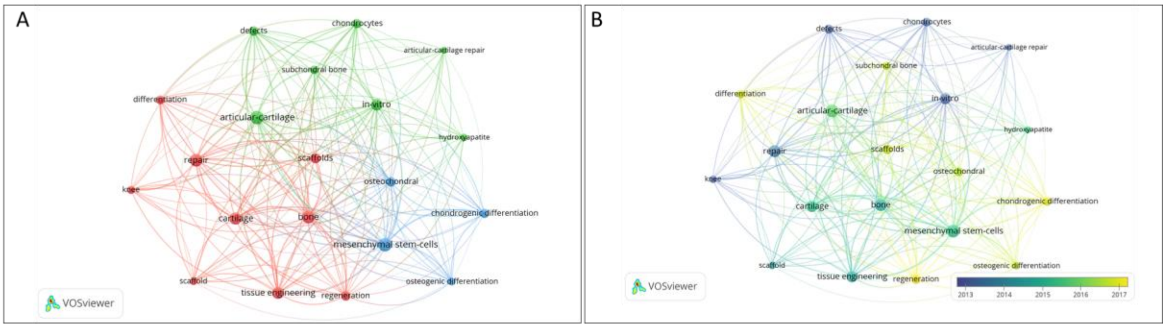

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Figure 3. Keyword analysis. (A) Network visualization map showing cluster analysis of keywords associated with the osteochondral interface. (B) Network visualization map showing the evolution of keyword frequency over time. Colors were assigned according to the average year keywords appeared in articles. Basic science research seems to be a more frequent area of focus early on, with a shift toward clinical focus in recent years.

The Most-Cited 100 Publications

The most highly-cited 100 publications on osteochondral interface appeared between 2000 and 2023 (Table 2). The largest number of articles published on the topic was between 2011 and 2015 (45 articles), followed by 2016 and 2020 (26 articles) (Figure 4A). These 100 articles were produced by twenty countries. The USA contributed 30 articles, followed by China with 14 articles; Germany with 12 articles; the UK with 10 articles; Italy with 9 articles; Japan with 8 articles; and Portugal with 7 articles (Figure 4B). The University of Kansas and Minho contributed 6 articles each to the top 100 most cited articles, followed by Columbia University, with 5 articles, and Rice University and Tsinghua University, with 4 articles each (Figure 4C). The other 23 institutions produced two articles, and the remaining institutions produced only one article in the most-cited 100 groups.

Table 2. The Top 100 Most-Cited Articles on OCI.

Rank	First author	Title	Journals	Years	Citations
1	Oliveira	Novel hydroxyapatite/chitosan bilayered scaffold for osteochondral tissue-engineering applications: Scaffold design and its performance when seeded with goat bone marrow stromal cells	Biomaterials	2006	356
2	Wang	Growth factor gradients via microsphere delivery in biopolymer scaffolds for osteochondral tissue engineering	Journal of Controlled Release	2009	330
3	Shim	Bioprinting of a mechanically enhanced three-dimensional dual cell-laden construct for osteochondral tissue engineering using a multi-head tissue/organ building system	JOURNAL OF MICROMECHANICS AND MICROENGINEERING	2012	274
4	Schaefer	Tissue-Engineered Composites for the Repair of Large Osteochondral Defects	Tissue-Engineered Composites for the Repair of Large Osteochondral Defects	2002	242
5	Gao	Tissue-Engineered Fabrication of an Osteochondral Composite Graft Using Rat Bone Marrow-Derived Mesenchymal Stem Cells	TISSUE ENGINEERING	2001	213
6	Alhadlaq	Tissue-Engineered Osteochondral Constructs in the Shape of an Articular Condyle	THE JOURNAL OF BONE AND JOINT SURGERY	2005	144
7	Shim	Three-dimensional bioprinting of multilayered constructs containing human mesenchymal stromal cells for osteochondral tissue regeneration in the rabbit knee joint	Biofabrication	2016	143
8	Kelly	Mechano-regulation of stem cell differentiation and tissue regeneration in osteochondral defects	Journal of Biomechanics	2005	142
9	Harley	Design of a multiphase osteochondral scaffold III: Fabrication of layered scaffolds with continuous interfaces	Wiley Periodicals	2010	137
10	Mohan	Continuous Gradients of Material Composition and Growth Factors for Effective Regeneration of the Osteochondral Interface	TISSUE ENGINEERING:	2011	121
11	Malafaya	Bilayered chitosan-based scaffolds for osteochondral tissue engineering: Influence of hydroxyapatite on in vitro cytotoxicity and dynamic bioactivity studies in a specific double-chamber bioreactor	Acta Biomaterialia	2009	118
12	Chen	3D printing of a lithium-calcium-silicate crystal bioscaffold with dual bioactivities for osteochondral interface reconstruction	Biomaterials	2019	117
13	Levingstone	Cell-free multi-layered collagen-based scaffolds demonstrate layer specific regeneration of functional osteochondral tissue in caprine joints	Biomaterials	2016	112
14	Gao	Repair of Osteochondral Defect with Tissue-Engineered Two-Phase Composite Material of Injectable Calcium Phosphate and Hyaluronan Sponge	TISSUE ENGINEERING	2002	111
15	Khanarian	A functional agarose-hydroxyapatite scaffold for osteochondral interface regeneration	Biomaterials	2012	110
16	Bittner	Fabrication and mechanical characterization of 3D printed vertical uniform and gradient scaffolds for bone and osteochondral tissue engineering	Acta Biomaterialia	2019	107

Rank	First author	Title	Journals	Years	Citation
18	Santo	Controlled Release Strategies for Bone, Cartilage, and Osteochondral Engineering—Part I: Recapitulation of Native Tissue Healing and Variables for the Design of Delivery Systems	TISSUE ENGINEERING	2013	105
19	Kim	Osteochondral tissue regeneration using a bilayered composite hydrogel with modulating dual growth factor release kinetics in a rabbit model	Journal of Controlled Release	2013	104
20	Sutherland	Decellularized Cartilage May Be a Chondroinductive Material for Osteochondral Tissue Engineering	PLOS ONE	2015	102
21	Panseri	Osteochondral tissue engineering approaches for articular cartilage and subchondral bone regeneration	Springer	2012	97
22	Dormer	Osteochondral Interface Tissue Engineering Using Macroscopic Gradients of Bioactive Signals	Ann Biomed	2010	97
23	Yan	Bilayered silk/silk- nano CaP scaffolds for osteochondral tissue engineering: In vitro and in vivo assessment of biological performance	Acta Biomaterialia	2015	96
24	Tuli	Human Mesenchymal Progenitor Cell-Based Tissue Engineering of a Single-Unit Osteochondral Construct	TISSUE ENGINEERING	2004	93
25	Mazaki	A novel, visible light-induced, rapidly cross-linkable gelatin scaffold for osteochondral tissue engineering	SCIENTIFIC REPORTS	2014	90
26	Khanarian	A functional agarose-hydroxyapatite scaffold for osteochondral interface regeneration	Biomaterials	2012	89
27	Li	Demineralized bone matrix gelatin as scaffold for osteochondral tissue engineering	Biomaterials	2006	89
28	Bian	Fabrication of a bio-inspired beta-Tricalcium phosphate/collagen scaffold based on ceramic stereolithography and gel casting for osteochondral tissue engineering	Rapid Prototyping Journa	2012	83
29	Steinmetz	Mechanical loading regulates human MSC differentiation in a multi-layer hydrogel for osteochondral tissue engineering	Acta Biomaterialia	2015	82
30	Castro	Recent Progress in Interfacial Tissue Engineering Approaches for Osteochondral Defects	Annals of Biomedical Engineering	2012	81
31	Cheng	In vitro generation of an osteochondral interface from mesenchymal stem cell–collagen microspheres	Biomaterials	2011	80
32	Chen	Preparation of a biphasic scaffold for osteochondral tissue engineering	Materials Science and Engineering: C	2006	73
33	Dormer	Osteochondral interface regeneration of the rabbit knee with macroscopic gradients of bioactive signals	Biomedical Materials research	2012	71
34	Abarrategi	Chitosan scaffolds for osteochondral tissue regeneration	WILEY PERIODICALS	2010	69
35	Farre-Guasch	Buccal Fat Pad, an Oral Access Source of Human Adipose Stem Cells with Potential for Osteochondral Tissue Engineering: An In Vitro Study	TISSUE ENGINEERING	2010	69
36	Jeon	Perspectives in MultiphasicOsteochondral Tissue Engineering	THE ANATOMICAL RECORD	2014	67
37	Gotterbarm	The minipig model for experimental chondral and osteochondral defect repair in tissue engineering: retrospective analysis of 180 defects	Laboratory Animals	2008	67
38	Christakiran	Mimicking Hierarchical Complexity of the Osteochondral Interface Using Electrospun Silk–Bioactive Glass Composites	applied biomaterials	2017	67
39	Barbeck	Analysis of the in vitro degradation and the in vivo tissue response to bi-layered 3D-printed scaffolds combining PLA and biphasic PLA/ bioglass components e Guidance of the inflammatory response as basis for osteochondral regeneration	Bioactive Materials	2017	67
40	Li	Glycosylated superparamagnetic nanoparticle gradients for osteochondral tissue engineering	Biomaterials	2018	66
41	Galperin	Integrated Bi-Layered Scaffold for Osteochondral Tissue Engineering	Adv. Healthcare Mater	2013	65
42	Graessel	Tissue-engineering strategies to repair chondral and osteochondral tissue in osteoarthritis: use of mesenchymal stem cells	Current rheumatology reports	2014	65
43	Mahmoudifar	Tissue engineering of human cartilage and osteochondral composites using recirculation bioreactors	Biomaterials	2005	64

Rank	First author	Title	Source	Years	Citation
44	Murata	A preliminary study of osteochondral regeneration using a scaffold-free three-dimensional construct of porcine adipose tissue-derived mesenchymal stem cells	Journal of Orthopaedic Surgery and Research	2015	63
45	Liang	Bilayered PLGA/PLGA-HAp Composite Scaffold for Osteochondral Tissue Engineering and Tissue Regeneration	ACS Biomaterials Science & Engineering	2018	61
47	Bernstein	Microporous calcium phosphate ceramics as tissue engineering scaffolds for the repair of osteochondral defects: Histological results	Acta Biomateriaalia	2013	59
48	Yang	Icariin conjugated hyaluronic acid/collagen hydrogel for osteochondral interface restoration	Acta Biomaterialia	2018	58
49	Zoeger	Lead accumulation in tidemark of articular cartilage	Osteoarthritis and Cartilage	2006	57
50	Campbell, Sara	Nanomechanical mapping of the osteochondral interface with contact resonance force microscopy and nanoindentation	Acta Biomaterialia	2012	55
51	T.J. Lyons	The tidemark of the chondro-osseous junction of the normal human knee joint	Journal of molecular histology	2005	53
52	Scotti	Engineering human cell-based, functionally integrated osteochondral grafts by biological bonding of engineered cartilage tissues to bony scaffolds	Biomaterials	2010	51
53	Saha	Osteochondral Tissue Engineering In Vivo: A Comparative Study Using Layered Silk Fibroin Scaffolds from Mulberry and Nonmulberry Silkworm	PloS one	2013	50
54	Battaglia	Arthroscopic autologous chondrocyte implantation in osteochondral lesions of the talus: mid-term T2-mapping MRI evaluation	Knee Surgery, Sports Traumatology, Arthroscopy	2011	50
55	Kang	Functionally graded multilayer scaffolds for in vivo osteochondral tissue engineering	Acta Biomaterialia	2018	49
56	Da	The Impact of Compact Layer in Biphasic Scaffold on Osteochondral Tissue Engineering	PLoS One	2013	49
57	Dormer	Osteochondral Interface Regeneration of Rabbit Mandibular Condyle With Bioactive Signal Gradients	Journal of oral and maxillofacial surgery	2011	49
58	Bal	In Vivo Outcomes of Tissue-Engineered Osteochondral Grafts	Journal of Biomedical Materials Research Part B	2010	48
59	Sartori	A new bi-layered scaffold for osteochondral tissue regeneration: In vitro and in vivo preclinical investigations	Materials Science and Engineering: C	2017	48
60	Petersen	Long term results after implantation of tissue engineered cartilage for the treatment of osteochondral lesions in a minipig model	Journal of Materials Science: Materials in Medicine	2008	48
61	Cui	Repair of articular cartilage defects with tissue-engineered osteochondral composites	Journal of bioscience and bioengineering	2011	47
62	Needham	Osteochondral Tissue Regeneration Through Polymeric Delivery of DNA Encoding for the SOX Trio and RUNX2	Acta biomaterialia	2014	43
63	Yunos	Stratified scaffolds for osteochondral tissue engineering applications: Electrospun PDLLA nanofibre coated Bioglass-derived foams	Journal of biomaterials applications	2013	43
64	Mayr	Microporous calcium phosphate ceramics as tissue engineering scaffolds for the repair of osteochondral defects: Biomechanical results	Acta biomaterialia	2013	43
65	Shimomura	Osteochondral Repair Using a Scaffold-Free Tissue-Engineered Construct Derived from Synovial Mesenchymal Stem Cells and a Hydroxyapatite-Based Artificial Bone	Tissue Engineering Part A	2014	42

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Rank	First author	Title	Journals	Years	Citation
66	Studle	Spatially confined induction of endochondral ossification by functionalized hydrogels for ectopic engineering of osteochondral tissues	Biomaterials	2018	41
67	Ghosh	Bi-layered constructs based on poly(L-lactic acid) and starch for tissue engineering of osteochondral defects	Materials Science and Engineering: C	2008	39
68	Li	A biphasic scaffold based on silk and bioactive ceramic with stratified properties for osteochondral tissue regeneration	Journal of Materials Chemistry B	2015	38
69	Lopiz-morales	IN VIVO COMPARISON OF THE EFFECTS OF RHBMP-2 AND RHBMP-4 IN OSTEOCHONDRAL TISSUE REGENERATION	Eur Cell Mater	2010	38
70	Zhang	The effect of interface microstructure on interfacial shear strength for osteochondral scaffolds based on biomimetic design and 3D printing	Materials Science and Engineering: C	2015	38
71	Stagnaro	Alginate-polymethacrylate hybrid hydrogels for potential osteochondral tissue regeneration	Carbohydrate polymers	2018	37
72	Haasper	Tissue engineering of osteochondral constructs in vitro using bioreactors.	Injury	2008	37
73	Ito	Repair of osteochondral defect with tissue-engineered chondral plug in a rabbit model.	Arthroscopy: The Journal of Arthroscopic & Related Surgery	2005	37
74	Jin	The maturity of tissue-engineered cartilage in vitro affects the repairability for osteochondral defect	Tissue Engineering Part A	2011	37
75	Di	Covalent Binding of Bone Morphogenetic Protein-2 and Transforming Growth Factor-β3 to 3D Plotted Scaffolds for Osteochondral Tissue Regeneration	Biotechnology journal	2017	37
76	Rameshbabu	Investigating the potential of human placenta-derived extracellular matrix sponges coupled with amniotic membrane-derived stem cells for osteochondral tissue engineering	Journal of Materials Chemistry B	2016	37
77	Yao	Bioglass®/chitosan–polycaprolactone bilayered composite scaffolds intended for osteochondral tissue engineering	Journal of Biomedical Materials Research Part A	2014	36
78	Wang	Cryogenic 3D printing of heterogeneous scaffolds with gradient mechanical strengths and spatial delivery of osteogenic peptide/TGF-β1 for osteochondral tissue regeneration	Biofabrication	2020	36
79	Zheng	Evaluation of novel in situ synthesized nano-hydroxyapatite/collagen/alginate hydrogels for osteochondral tissue engineering	Biomedical Materials	2014	35
80	Mendes	Advancing osteochondral tissue engineering: bone morphogenetic protein, transforming growth factor, and fibroblast growth factor signaling drive ordered differentiation of periosteal cells resulting in stable cartilage and bone formation in vivo	Stem cell research & therapy	2018	33
81	Pereira	Injectable gellan-gum/hydroxyapatite-based bilayered hydrogel composites for osteochondral tissue regeneration	Applied Materials Today	2018	32
82	Wang	Human umbilical cord mesenchymal stromal cells in a sandwich approach for osteochondral tissue engineering	Journal of tissue engineering and regenerative medicine	2011	31
83	Zhang	Osteochondral Interface Stiffening in Mandibular Condylar Osteoarthritis	Journal of dental research	2018	31
84	Lee	Enzyme-crosslinked gene-activated matrix for the induction of mesenchymal stem cells in osteochondral tissue regeneration	Acta Biomaterialia	2017	31
85	Nover	Porous titanium bases for osteochondral tissue engineering	Acta Biomaterialia	2015	30
86	Chen	Osteochondral tissue engineering using a PLGA–collagen hybrid mesh.	Materials Science and Engineering	2006	30
87	Lima	The effect of devitalized trabecular bone on the formation of osteochondral tissue-engineered constructs.	Biomaterials	2008	30
88	Amadori	Multi-Layered Scaffolds for Osteochondral Tissue Engineering: In Vitro Response of Co-Cultured Human Mesenchymal Stem Cells.	Macromolecular Bioscience	2015	30
89	Giannoni	Design and characterization of a tissue-engineered bilayer scaffold for osteochondral tissue repair.	Journal of tissue engineering and regenerative medicine	2015	29

Rank	First author	Title	Source	Years	Citation
90	Deng	Construction of tissue-engineered osteochondral composites and repair of large joint defects in rabbit	Journal of Tissue Engineering and Regenerative Medicine	2014	29
91	Emans	Tissue-engineered constructs: the effect of scaffold architecture in osteochondral repair	Journal of Tissue Engineering and Regenerative Medicine	2013	28
92	Mesallati	TISSUE ENGINEERING SCALED-UP, ANATOMICALLY SHAPED OSTEOCHONDRAL CONSTRUCTS FOR JOINT RESURFACING	European Cells and Materials	2015	28
93	Bonde	The area of the tidemark in osteoarthritis - a three-dimensional stereological study in 21 patients	Apmis	2005	28
94	Abdulghani	Biofabrication for osteochondral tissue regeneration: bioink printability requirements	Journal of Materials Science: Materials in Medicine	2019	27
95	Mahmoudifar	Osteogenic Differentiation and Osteochondral Tissue Engineering Using Human Adipose-Derived Stem Cells	Biotechnology Progress: AIChE	2013	27
96	Singh	Hierarchically structured seamless silk scaffolds for osteochondral interface tissue engineering	Journal of Materials Chemistry B	2018	26
97	Ayan	Aspiration-assisted bioprinting of the osteochondral interface	Scientific reports	2020	26
98	Murata	Osteochondral Regeneration with a Scaffold-Free Three-Dimensional Construct of Adipose Tissue-Derived Mesenchymal Stromal Cells in Pigs	Tissue Engineering and Regenerative Medicine	2018	26
99	Aurich	Treatment of Osteochondral Lesions in the Ankle: A Guideline from the Group "Clinical Tissue Regeneration" of the German Society of Orthopaedics and Traumatology (DGOU)	Zeitschrift fur Orthopadie und Unfallchirurgie	2017	26
100	Roschger	Differential accumulation of lead and zinc in double-tidemarks of articular cartilage	Osteoarthritis and Cartilage	2013	25
101	Li	3D-printed scaffolds with calcified layer for osteochondral tissue engineering	Journal of bioscience and bioengineering	2018	24

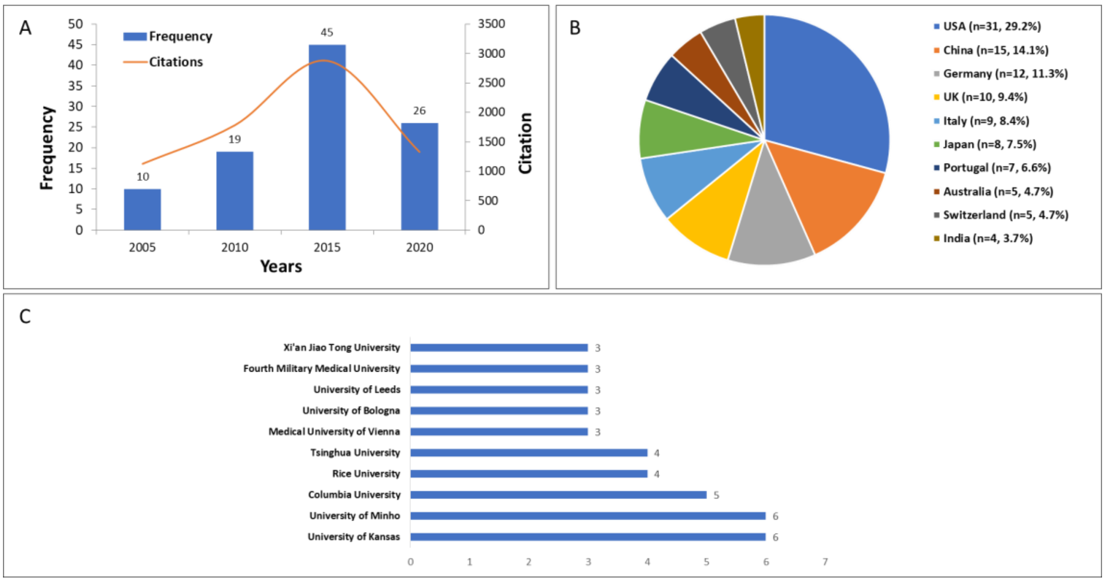

Figure 4. Analysis of the top 100 most-cited articles on osteochondral interface. (A) Year of publication. (B) Distribution of articles by country of origin. (C) Institutions with >2 Articles.

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The most highly-cited studies were published in 52 journals. Biomaterials was at the top of the list, with 12 publications and 1205 citations that was followed by Acta Biomaterialia with the same number of articles (771 citations), and Tissue Engineering, which published 6 articles (652 citations) (Table 3).

Table 3. Top Journals Publishing the 100 Most-Cited Articles on OCI.

Journal	Articles	Citations	Mean Citation	Impact Factor
Biomaterials	12	1205	100.4	15.3 (2021)
Acta Biomaterialia	12	771	64.3	10.63 (2021)
TISSUE ENGINEERING	6	652	108.7	3.616 (2021)
Journal of tissue engineering and regenerative medicine	4	117	29.3	4.323 (2023)
Materials Science and Engineering: C	4	198	49.5	7.328 (2020)
Journal of Materials Chemistry B	3	101	33.7	7.571 (2023)
PLOS ONE	3	201	67.0	3.752 (2021)
Biofabrication	2	179	89.5	11.061 (2023)
Journal of bioscience and bioengineering	2	71	35.5	3.185 (2023)
Journal of Controlled Release	2	434	217.0	11.467 (2023)
Journal of Materials Science: Materials in Medicine	2	75	37.5	4.727 (2021)
Osteoarthritis and Cartilage	2	82	41.0	7.507 (2023)
Tissue Engineering Part A	2	79	39.5	4.080 (2021)
Wiley Periodicals	2	206	103.0	15.153 (2021)

Concerning authorship in most-cited articles, Detamore and Berkland contributed 5 articles, followed by Dormer and Reis. They contributed 4 articles each, followed by Mikos and Martin, who had 3 articles each (Table 4).

Table 4. Top Authors Contributing to the 100 Most-Cited Articles on OCI.

Author	Articles	First author	Last author	Co-authors	Times cited
Rui L. Reis	6	0	4	2	746
Michael S. Detamore	6	0	6	0	471
Cory J. Berkland	5	0	0	5	440
Nathan H. Dormer	4	1	0	3	338
Antonios G. Mikos	3	0	2	1	254
Ivan Martin	3	0	1	2	334
Guoping Chen	2	2	0	0	103
Jizong Gao	2	2	0	0	324
Mahmoudifar	2	2	0	0	91
Murata	2	2	0	0	89
Nora T. Khanarian	2	2	0	0	199

Discussion

Kroner first reported the osteochondral defect of the patella in 1905 and described in detail by HM Coleman in 1948 [6]. The primary function of the cartilage as load-bearing tissue is to resist and absorb the load exerted on the joint. Thus, osteochondral defects resulting from diseases, trauma, and aging may lead to severe consequences that cannot heal themselves due to their avascular nature.[7] We have detected significant interest in osteochondral interface-related research. This study reports the first bibliometric analysis of osteochondral literature to demonstrate OCI-related research data over time and to determine the articles with the highest impact.

Publication Trends in the Osteochondral Interface Research

Recently, the number of osteochondral interface-related articles has increased rapidly. The articles originated from 31 countries, with the highest contribution coming from the USA. This can be due to high prevalence of osteochondral defects in the United States. Concerning institutional contributions, the University of Minho (Portugal) produced the most articles and topped the list of total citations. Analysis of joint work between countries and institutions showed a regional cluster formation. However, despite the geographic separation, the highest frequency of collaborations occurred between China and the United States. England also significantly contributed to the OCI research, ranking number 3 after China. In addition, Actabiomaterilia, Biomaterials, Tissue Engineering, Journal of Controlled Release, and Tissue Engineering Part A published the most articles on the osteochondral interface.

Research Focus

Our analysis determined that articular cartilage, biomaterials, and chondrogenic differentiation were the cluster centers. Essential science keywords were seen more frequently at the beginning, with more focus on in-vitro investigation keywords later. In this regard, keywords used more frequently in earlier included mesenchymal stem cells, scaffolds, differentiations, and design.

The Most Impactful Publications

The study with the most citations was "Novel hydroxyapatite/chitosan bilayered scaffold for osteochondral tissue-engineering applications: Scaffold design and its performance when seeded with goat bone marrow stromal cells," authored by Joaquim M. Oliveira et al. in 2006 [8]. In this article, the authors aimed at evaluating hydroxyapatite / chitosan (HA / CS) bi-layered construct, and goat marrow stromal cells were tested for their differentiation capacity on these scaffolds. It was demonstrated that the scaffold may provide an adequate environment for the regeneration of osteochondral defects.

The earliest publication in 100 most-cited list was authored by Jizong Gao et al. in 2001 and titled "Tissue-Engineered Fabrication of an Osteochondral Composite Graft Using Rat Bone Marrow-Derived Mesenchymal Stem Cells" [9]. These researchers demonstrated the possibility of constructing a tissue-engineered composite osteochondral graft using MSCs, biomaterials and biofactors.

The latest publication in the list of top 100 most-cited was authored by Chong Wang et al. in 2020. It was titled "Cryogenic 3D Printing of Heterogeneous Scaffolds with Gradient Mechanical Strengths and Spatial Delivery of Osteogenic Peptide/TGF-β1 for Osteochondral Tissue Regeneration" [10]. These investigators found that osteochondral scaffolds obtained gradient rBMSC osteogenic/chondrogenic differentiation.

Limitations

In this study, there may be impactful articles in other databases excluded from our study. Second, the most recent date of publication was August 25, 2023. Although the numbers are unlikely to differ dramatically since then, the findings are subject to change slightly.

Conclusions

Findings revealed that research efforts on the OC interface have dramatically increased in the last 23 years, despite limited success in the field. Our search results indicated that only 225 papers have been published in this field, with the specified keywords, between 2000 and 2023. Characterization of the OC interface, designing biomimetic biomaterials, and applying these to regenerate the OC interface appear to be the priorities on this topic. This bibliometric analysis is expected to serve as a helpful guide for clinicians and researchers in portraying the most impactful literature in the field.

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Conflicts of Interest The authors declare no conflict of interest.

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