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Review

Subchondroplasty in the treatment of subchondral bone marrow edema: A bibliometric analysis

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Abstract. *Background and objective:* Osteoarthritis is one of the most prevalent causes of disability worldwide. The presence of subchondral bone marrow edema has a negative prognostic significance in the evolution of osteoarthritis. A novel approach, called subchondroplasty, has been proposed to address the subchondral bone marrow edema, stimulate the subchondral metabolism, and prevent osteoarthritis evolution. This study aimed to investigate the research status concerning subchondroplasty by a bibliometric methodology. *Methods:* Publications about the use of subchondroplasty from 2012 to 2022 were searched from the Scopus database. A bibliometric analysis of the dataset was conducted by using a statistical-descriptive spreadsheet tool and the Bibliometrix® software. *Results:* In total, 121 articles, published from 2012 to 2022 met the criteria and were included in this study. The number of publications concerning subchondroplasty progressively increased since 2014 with an annual growth rate of 35.11%. The country with the highest rate of publications was the United States (about 60% of the overall production). The most productive journal is "Arthroscopy Techniques" while the most cited source is "Osteoarthritis and Cartilage". The most productive scholars were Elizaveta Kon, Steven Brad Cohen, and Peter Sharkey. *Conclusion:* This study analyses the scientific production over time concerning the use of subchondroplasty for the management of subchondral bone marrow edema. It is still a niche topic, with a modest scientific production but this is only a starting point. The promising results of subchondroplasty should be confirmed by higher-quality studies to better understand which patients might concretely benefit from this procedure. (www.actabiomedica.it)

Key words: subchondroplasty, osteoarthritis, subchondral bone marrow edema, bibliometrics, Scopus

Introduction

Osteoarthritis (OA) is one of the most prevalent causes of disability worldwide, especially in the elderly, with an ever-increasing prevalence due to the progressive rise in life expectancy (1). It is a degenerative process affecting not only the articular cartilage and the articular environment in a strict sense but affecting also the subchondral unit, which plays a leading role in the progression of symptoms and functional limitations. The presence of subchondral bone marrow edema (SBME) has a negative prognostic significance in the evolution of OA, with a 7-fold greater probability of OA acceleration (2). SBME can be identified as a decreased bone marrow signal on T1-weighted sequences and a high signal on T2-weighted sequences on magnetic resonance images. In a way, the term SBME could minimize the histopathologic process, since the edema is only a detail of what actually happens, with a bone remodeling process characterized

by vascular abnormalities, microcracks, bone marrow fibrosis, and necrosis (3–5). Based on these premises, a novel approach, known as Subchondroplasty® (SCP) - Zimmer Knee Creations, United States - has been developed and first described in 2007 to address the SBME, stimulate the subchondral metabolism and prevent OA evolution. It consists of a subchondral calcium phosphate (CaP) injection, performed under fluoroscopy when a previous conservative approach has failed. Different commercially available bone substitutes for SCP procedures have been developed in the last 15 years (AccuFill – Zimmer Inc., Graftys HBS - Graftys, Wright Pro Dense -Wright, Beta BSM – Zimmer Inc., StrucSure - Smith & Nephew). As confirmed by Colon et al. most commercially available bone substitutes for SCP differ in their chemical composition, viscosity, and rheologic properties (6).

This study aims to analyze the application of SCP in the management of SBME from 2012 to 2022 through bibliometric analysis. Bibliometrics is a quantitative tool, largely employed in the last years, to analyze the interrelated information inside a dataset, and to examine in detail the bibliographic state of the art in a specific scientific production (7,8).

Methods

Selection criteria and data collection

Data were retrieved from Scopus, one of the most comprehensive databases of peer-reviewed journals on December 31st, 2022. The keyword used for the research was "subchondroplasty" in the string "topic" (that is title, abstract, and keywords). This analysis evaluated articles in all languages performed from 2012 to 2022. A bibliometric analysis of the dataset was conducted by using a statistical-descriptive spreadsheet tool and the Bibliometrix® software on the metadata downloaded from Scopus. Scopus Database is considered to be the most important abstract and citation scientific database of peer-reviewed literature in the world for the depth and transparency of its content. It provides access to a broad scientific production concerning four subject areas: health sciences, physical sciences, life sciences, and social sciences. Scopus database is widely used in bibliometric analyses since it provides tools to track, analyze, and visualize research; for this reason, it was selected to plan and elaborate this study. Bibliometrix® is a software tool developed by Massimo Aria and Corrado Cuccurullo for elaborating and visualizing bibliometric networks through publication maps, country maps, journal maps, and keyword maps. In particular, the following dimensions were analyzed in this study:

- Global scientific production and annual literature growth rate;
- Country scientific production;
- Most relevant sources;
- Most relevant authors and authors cooperation;
- Most cited papers;
- Most cited keywords.

Ethical considerations

Neither ethics committee approval nor informed consent was required since all data had been downloaded from a public bibliographic database. All images were electronically elaborated by the authors themselves (neither copyright nor ethical statement applies to the iconographic support of this study).

Global scientific production

By searching for the topic word "subchondroplasty" in Scopus Database a total of 121 documents were included. We found that the number of publications progressively increased since 2014 with a significant boost in 2018 and an annual growth rate of 35.11% (ranging from 2 documents in 2012 to 28 documents in 2020). In 2020 the number of publications was more than three times that of 2017 (Figure 1a). A slight decrease in scientific production was progressively observed in 2021 and 2022, maybe as a consequence of the COVID-19 pandemic. The trend of publications' number indicated that SCP treatment has received more attention in recent years, though it hasn't generated yet a ubiquitous interest.

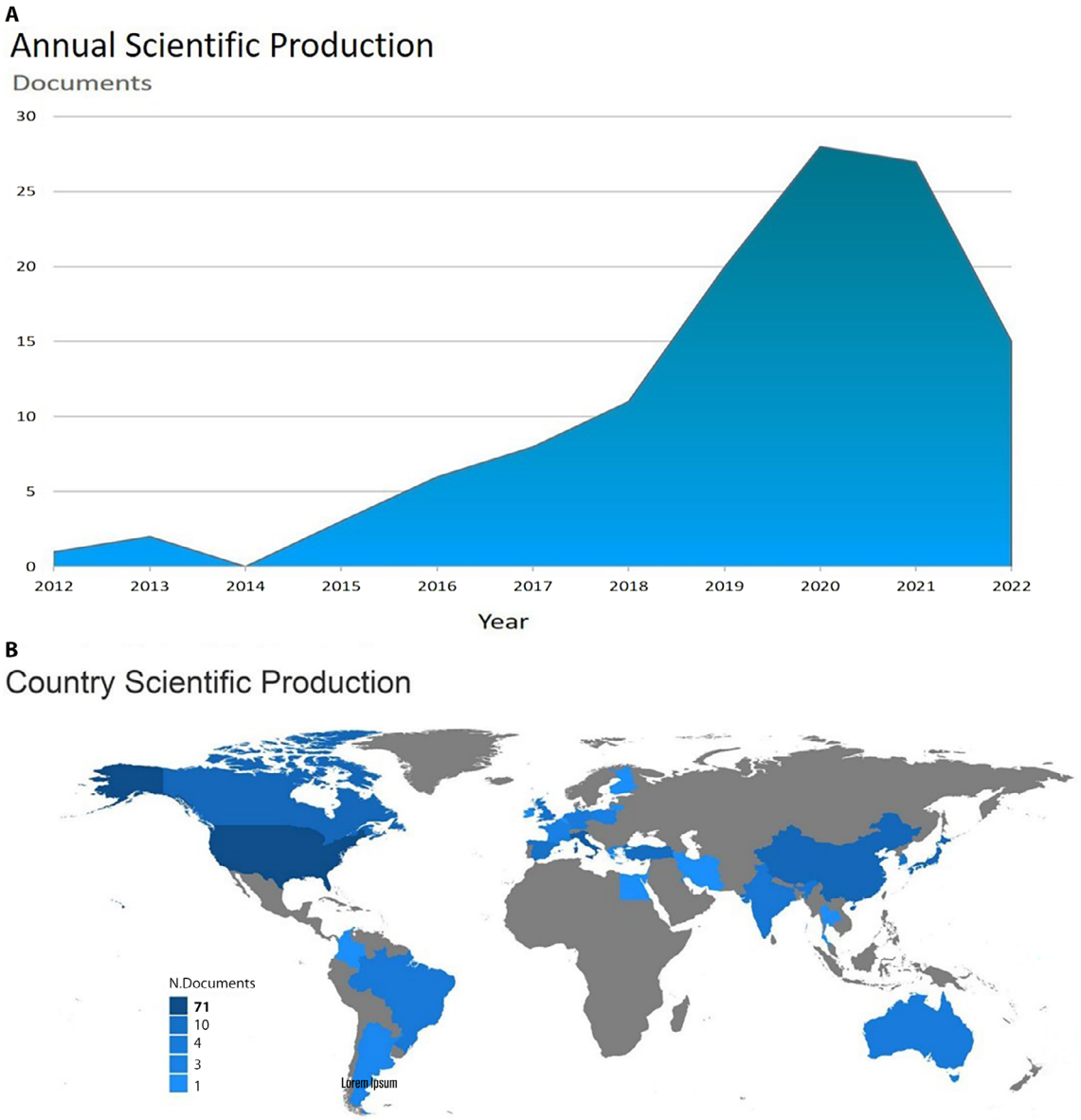

Figure 1. a: trend of the annual number of publications concerning subchondroplasty from 2012 to 2022 - according to Scopus data; b: Country scientific production – number of documents concerning subchondroplasty published by country from 2012 to 2022 according to Scopus data. (All the figures of this paper were originally made by the authors and do not request permission for reproduction).

Country scientific production

The map of countries' distribution is illustrated in Figure 1b. A total amount of 71 papers was published in the United States (by far the most productive country, accounting for about 60% of the overall production). Italy was ranked in the second position with 12 documents, thus being the most productive country in Europe, while Canada completed the podium thanks to 11 publications. China was the most productive country in Asia (7 publications).

Most relevant sources

The top 20 journals with the largest number of publications concerning SCP are listed in Table 1.

The most representative journal is "Arthroscopy Techniques" accounting for 12 documents. The "Journal of Foot and Ankle Surgery" and the "Journal of Knee Surgery" are equally representative with 5 documents respectively, followed by the "Journal of Orthopaedic Research" accounting for 4 papers. Most of the journals belonged to Q2 (second quartile list of the highest impact factor journals according to the Journal Citation Report classification); the median for the H-index was 73.8 (range: 35-162) and for the Impact Score was 2.44 (range: 1.35-3.85). The median of SJR (SCImago journal rank) was 0.6612 (range: 0.462-0.844). The most cited journal (referring to SCP) is "Osteoarthritis and Cartilage" thanks to 216 citations, followed by "The American Journal of Sports Medicine" (207 citations), "Knee Surgery, Sports Traumatology, Arthroscopy - KSSTA" (174 citations), "Foot and Ankle International" (154 citations) and the "Journal of Bone and Joint Surgery – American volume" (130 citations). A complete list of the most cited journals is represented in Table 1.

Most relevant authors and most cited papers

The most productive authors are Elizaveta Kon (IRCCS Humanitas Research Center, Rozzano, Milan, Italy), Steven Brad Cohen, and Peter F. Sharkey (both affiliated with the Department of Orthopedic Surgery, Rothman Institute, Thomas Jefferson University, Philadelphia, Pennsylvania, USA), who published 5 documents concerning SCP respectively. The top 20 most productive authors are reported in Table 1. In addition, Kon E and Cohen SB published the most cited documents: "Bone marrow lesions and subchondral bone pathology of the knee" (published by Kon et al. on "Knee Surg Sports Traumatol Arthrosc" in 2016 - 63 citations) (9) and "Subchondroplasty for treating bone marrow lesions" (published by Cohen et al. on "J Knee Surg" in 2016 - 55 citations) (10). The lowest step on the most-cited papers podium is occupied by "Regenerative Engineering for Knee Osteoarthritis Treatment: Biomaterials and Cell-Based Technologies" (published by Escobar Ivirico JL et al. on "Engineering" in 2017 – 34 citations) (11). The top-five list of the most cited papers is completed by "Expanding applications of the subchondroplasty procedure for the treatment of bone marrow lesions observed on magnetic resonance imaging" (published by Farr et al. on "Oper Tech Sports Med" in 2013 – 33 citations) (12) and "Subchondral Calcium Phosphate is Ineffective for Bone Marrow Edema Lesions in Adults With Advanced Osteoarthritis" (published by Chatterjee et al. on "Clin OrthopRelat Res" In 2015 – 32 citations) (13). The top 20 of the most cited documents concerning SCP are listed in Table 1.

We point out, for completeness of information, that the number of citations depends in part on the year of publication, so the older documents are likely to be more cited. This is an implicit bias of the overall scientific production.

Figure 2a is representative of the authors' cooperation: unlike other orthopedic arguments (and probably due to the sectoral nature of this topic) there is no practical cooperation among different institutions.

Most cited keywords

Figure 2b is representative of the most frequent keywords related to SCP publications: "osteoarthritis" and "bone marrow lesions" are the main players. This keyword analysis graphically confirmed that the most involved joint in this specific research is the knee, which was already the main object of the research regarding the management of cartilage and subchondral unit disorders. Keywords co-occurrence is illustrated in Figure 2c, where the "playmaker" is "nuclear magnetic resonance imaging", given the central role of this radiological modality in the diagnostic definition (and subsequent therapeutic path).

Discussion

SCP is an emerging technique for the management of subchondral bone marrow edema. The progressive understanding of the mechanisms underlying osteoarthritis degeneration (including the role of the subchondral layer in its prognostic evolutions) was

Table 1. a: the top 20 most productive journals; b: the top 20 most cited sources; c: the top 20 most productive authors; d: the top 20 most cited documents concerning subchondroplasty from 2012 to 2022.

a	**TOP 20 MOST PRODUCTIVE JOURNALS**	
	JOURNAL	**NUMBER OF DOCUMENTS**
	ARTHROSCOPY TECHNIQUES	12
	JOURNAL OF FOOT AND ANKLE SURGERY	5
	JOURNAL OF KNEE SURGERY	5
	JOURNAL OF ORTHOPAEDIC RESEARCH	4
	CARTILAGE	3
	CHINESE JOURNAL OF TISSUE ENGINEERING RESEARCH	3
	CLINICS IN PODIATRIC MEDICINE AND SURGERY	3
	FOOT AND ANKLE INTERNATIONAL	3
	FOOT AND ANKLE ORTHOPAEDICS	3
	KNEE SURGERY SPORTS TRAUMATOLOGY ARTHROSCOPY	3
	OPERATIVE TECHNIQUES IN SPORTS MEDICINE	3
	AMERICAN JOURNAL OF ROENTGENOLOGY	2
	ARTHROSCOPY SPORTS MEDICINE AND REHABILITATION	2
	BULLETIN OF THE HOSPITAL FOR JOINT DISEASES	2
	CLINICAL IMAGING	2
	FOOT AND ANKLE SPECIALIST	2
	INTERNATIONAL ORTHOPAEDICS	2
	JBJS CASE CONNECTOR	2
	JOURNAL OF ARTHROPLASTY	2
	JOURNAL OF ORTHOPAEDICS	2
b	**TOP 20 MOST CITED JOURNALS**	
	JOURNAL	**NUMBER OF CITATIONS**
	OSTEOARTHRITIS AND CARTILAGE	216
	AMERICAN JOURNAL OF SPORTS MEDICINE	207
	KNEE SURGERY SPORTS TRAUMATOLOGY ARTHROSCOPY	174
	FOOT ANKLE INTERNATIONAL	154
	J BONE JOINT SURGERY AM	130
	CLINICAL ORTHOPAEDICS AND RELATED RESEARCH	117
	ARTHRITIS & RHEUMATOLOGY	107
	JOURNAL OF KNEE SURGERY	103
	ANNALS OF THE RHEUMATIC DISEASES	92
	ARTHROSCOPY	85
	INTERNATIONAL ORTHOPAEDICS	83
	ARTHRITIS AND RHEUMATISM	72
	SKELETAL RADIOLOGY	66
	JOURNAL OF ORTHOPAEDIC RESEARCH	62
	ARTHRITIS RESEARCH & THERAPY	61

	CARTILAGE	58
	RADIOLOGY	57
	JOURNAL OF BONE JOINT SURGERY BR	56
	BIOMATERIALS	54
	JOURNAL OF BIOLOGICAL CHEMISTRY	52
c	**TOP 20 PRODUCTIVE AUTHORS**	
	AUTHOR	**NUMBER OF DOCUMENTS**
	KON E.	5
	COHEN SB.	5
	SHARKEY PF.	5
	BOZYNSKI CC.	4
	COOK CR.	4
	COOK JL.	4
	KUROKI K.	4
	STOKER AM.	4
	DALLO I.	3
	DI MATTEO B.	3
	DRAKOS MC.	3
	GIZA E.	3
	GOBBI A.	3
	VULCANO E.	3
	YOUM T.	3
	ANDRIOLO L.	2
	BERNHARD K.	2
	COLE BJ.	2
	DEBERNARDIS D.	2
	FARR K.	2
d	**TOP 20 MOST CITED DOCUMENTS**	
	PAPER (FIRST AUTHOR, YEAR, JOURNAL, DOI)	**TOTAL CITATIONS**
	KON E, 2016, KNEE SURG SPORTS TRAUMATOL ARTHROSCOPY – DOI: 10.1007/s00167-016-4113-2	63
	COHEN SB, 2016. J KNEE SURG – DOI: 10.1055/s-0035-1568988	55
	ESCOBAR IVIRICO JL, 2017, ENGINEERING – DOI: 10.1016/J.ENG.2017.01.003	34
	FARR J, 2013, OPER TECH SPORTS MED – DOI: 10.1053/j.otsm.2013.03.006	33
	CHATTERJEE D, 2015, CLIN ORTHOP RELAT RES – DOI: 10.1007/s11999-015-4311-0	32
	ZHU X, 2021, FRONT CELL DEV BIOLG – DOI: 10.3389/fcell.2020.607764	31
	BONADIO MB, 2017, REV BRAS ORTHOP – DOI: 101016/j.rbo.2016.07.014	30

	COHEN SB, 2012, TECH KNEE SURG – DOI: 10.1097/ BTK.0b013e318276e1fe	24
	SASAKI A, 2019. WORLD J STEM CELLS – DOI: 10.4252/wjsc.v11.i5.254	23
	COLLINS JA, 2016, BULL HOSP JT DIS – DOI: NA	23
	KAWAI T, 2020. J TISSUE ENG – DOI: 10.1177/2041731419896446	22
	DELGADO D, 2019, J CLIN ORTHOP TRAUM – DOI: 10.1016/j.jcot .2018.09.017	22
	WANG B, 2017, SCI REP – DOI: 10.1038/s41598-017-17025-6	20
	ABRAMS GD, 2013, ARTHROSCOPY TECH – DOI:10.1016/j. eats.2016.03.001	20
	COLON DA, 2015. KNEE – DOI: 10.1016/j.knee.2015.06.017	17
	ASTUR DC, 2019, CARTILAGE – DOI: 10.1177/1947603518770249	16
	SUNDARAM K, 2019, J KNEE SURG – DOI: 10.1055/s-0039-1677792	16
	SALTZMAN BM, 2018, SPORTS HEALTH – DOI: 10.1177/1941738118782453	15
	ILAS DC, 2017, FUTUR SCI OA – DOI: 10.4155/fsoa-2017-0055	15
	GHASEMI RA, 2019, ORTHOP CLIN NORTH AM – DOI: 10.10106/j.ocl .2018.08.008	14

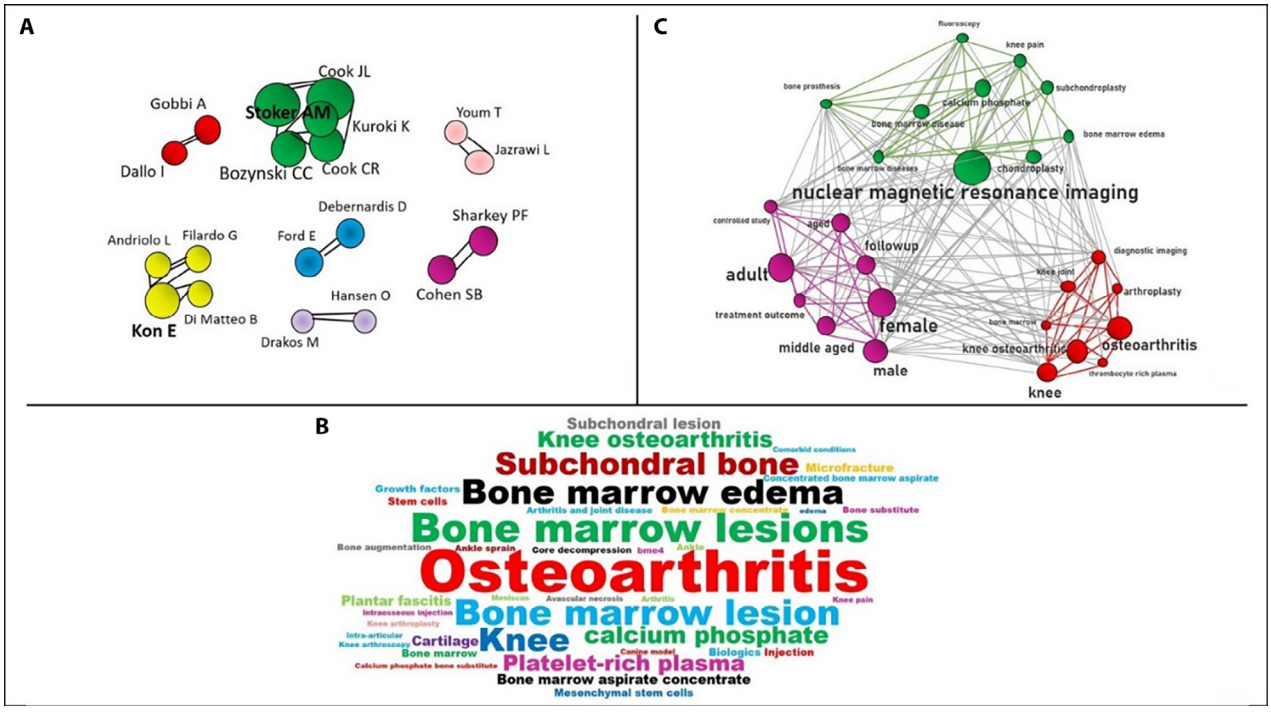

Figure 2. a: the network map of authors' cooperation on the focus "subchondroplasty"; b: iconographic representation of the top keywords with the strongest citation bursts on subchondroplasty; c: the network of keywords distribution (All the figures of this paper were originally made by the authors and do not request permission for reproduction)

the starting point for the expansion of the research on this topic. There is an incomplete comprehension of the molecular, mechanical, and vascular mechanisms promoting the genesis of subchondral bone marrow edema, anyway. Intraosseous injections are a minimally invasive procedure to provide beneficial effects on subchondral bone damage in osteoarthritic patients (while not ruling out the limits of the current short-term evaluation) (9). In this scenario, SCP represents another card left to play to reduce pain, improve articular function, and procrastinate a joint replacement. Most patients report a high degree of satisfaction following SCP (though an incomplete benefit), as confirmed by the improvements in functional PROMs (VAS, IKDC, KOOS, WOMAC, and SF-12) (14). The low conversion rate to knee arthroplasty following SCP is another point in favor as demonstrated by different authors (10,12,15–17), though further research with longer follow-up is fundamental to fully understand these implications.

In this study, we performed a bibliometric analysis to get an instant view of the spatial and temporal distribution of scientific research concerning SCP. It is not a systematic review of the current literature on this topic, but a statistical quantitative computer-assisted evaluation of the scientific production on this topic. This bibliometric analysis aimed to understand research trends on SCP and evaluate the relationships of authors, institutions, countries, and the influence of publications and citations, through some bibliometric indicators, such as the number of publications, trends according to year, journals with the most articles and most cited articles, authors and authors' cooperation. We chose Scopus for the extraction of the publications inheriting this topic since it is a reliable biomedical database providing a complete, wide, and precise research action.

In the last decade, we observed a progressive increase in the clinical application (and scientific analysis) of SCP with an annual growth rate of 35.11% for scientific publications and a peak in 2020 (28 publications). This is remarkable, even knowing that it is still a niche topic, with modest scientific production. The increase in scientific production is the mirror of the growing interest in this technique, maybe given the inadequate therapeutic alternative solutions, the promising results, and fewer post-operative complications (18). The most active institutions were IRCCS Humanitas Research Center (Rozzano, Milan, Italy) and Thomas Jefferson University (Philadelphia, Pennsylvania, USA): these university research teams are especially prolific in basic research and regenerative medicine for musculoskeletal diseases, as confirmed by their collateral publications. Elizaveta Kon, Steven Brad Cohen, and Peter F. Sharkey are the most productive and most cited authors on this topic, thus confirming the quality of their scientific production. When widening our vision to overall country production we observe, as in other fields, the clear prevalence of the United States in the scientific production concerning SCP (accounting for about 60% of the global production). The knee is the most frequently studied joint (as is generally the case with other regenerative medicine approaches); the hip joint and the foot are the other two investigated anatomical districts where SCP was applied. The cross-interest from different reputable sources, the consistent number of author appearances (694), and overall citations are suggestive of a research topic in a slow but gradual phase of expansion. One current limit, in our opinion, is determined by the lack of cooperation among different institutions, maybe as a consequence of the sectoral nature of this topic and the "embryonic" phase of this specific research area. The analysis of the characteristics of the most cited journals (international high-impact peer-reviewed journals) suggests what an important subject it is. However, it is interesting that the more cited journals differ from the most productive journals, which may indicate a different approach to getting research impact. The top five most cited journals are "Osteoarthritis and Cartilage" (216 citations), "The American Journal of Sports Medicine" (207 citations), "Knee Surgery, Sports Traumatology, Arthroscopy - KSSTA" (174 citations), "Foot and Ankle International" (154 citations), and the "Journal of Bone and Joint Surgery – American volume" (130 citations). The most productive journals are "Arthroscopy Techniques" (12 documents), the "Journal of Foot and Ankle Surgery" (5 documents), the "Journal of Knee Surgery" (5 documents), and the "Journal of Orthopaedic Research" (4 papers). The most cited document, "Bone marrow lesions and subchondral bone pathology of the knee" (published by Kon et al. in "Knee Surg Sports Traumatol Arthrosc" in 2016) (9), is an interesting review,

developed to provide the most updated evidence for the differential diagnosis and the most effective treatment for bone marrow lesions around the knee. As reported by the authors it is still a controversial argument, conditioned by the presence of a heterogeneous range of underlying pathological conditions (transient bone marrow edema syndrome, subchondral insufficiency fractures, traumatic lesions, cyst erosions, hematopoietic disorders, overuse and disuse, osteonecrosis). The authors describe the clinical, radiological, and histopathological aspects of these different conditions, focusing on etiology and evolution. The final section is dedicated to the management options, including both conservative and surgical solutions. The key message of this article is the leading role of the distinction between reversible and irreversible conditions to define an appropriate therapeutic path. The second most cited document is "Subchondroplasty for treating bone marrow lesions" (published by Cohen et al. on "J Knee Surg" in 2016) (10), examining in more detail the topic "SCP". It is a retrospective study examining 66 patients with documented bone marrow lesions and advanced OA who underwent SCP associated with arthroscopy. The authors reported a significant improvement in both function and pain, 2 years after surgery, as measured by the International Knee Documentation Committee (IKDC) Subjective Knee Evaluation Form and the visual analog scale (VAS). Considering the poor results generally associated with advanced OA with bone marrow lesions, the authors point out that the durability in terms of pain resolution and functional improvement of this therapeutic modality is noteworthy. The podium of the most-cited papers is completed by "Regenerative Engineering for Knee Osteoarthritis Treatment: Biomaterials and Cell-Based Technologies" (published by Escobar Ivirico JL et al. on "Engineering" in 2017) (11). It is an extensive review discussing the pathogenesis of cartilage damage and pain in knee OA, exploring novel treatment options including advanced biomaterials and stem cells (in an independent or in a synergic way). A brief paragraph is dedicated to SCP, describing its potential ability to prevent severe OA and the need for total knee arthroplasty, while stressing the usefulness and the limits of this procedure.

This study has some limitations that should be noted. First of all the bibliometric analysis we performed is unavoidably dependent on the selected database (i.e. Scopus): while appreciating the quality and "universality" of the Scopus database, we are aware that the results may not be comprehensive of the overall scientific production. There are other available scientific databases, such as Web of Science, Google Scholar, and Medline, but none of them can be unequivocally considered superior (19). Another limitation is determined by the nature itself of the bibliometric analysis, being dependent on the temporal variability of the search, so that the results may be different when carried out at a different period. Moreover, the bibliometric analysis can be vitiated by the inclusion of documents not completely related to the specific topic and by the citation mechanism. Though the implicit qualitative value of each cited document, older articles may be favored in this mechanism while at the same time, the citation analysis can be altered by incomplete citing or author and journal self-citations. In the end, bibliometrics is a "snapshot", providing a large quantity of information illustrating the status quo, and as such, it should be interpreted.

Conclusions

At present, this scientific production concerning SCP shines a light on a cost-effective and technically easy procedure, bringing a new opportunity in the management of BME. We think that this could be an important field of investigation and we are aware that this is only a starting point. The promising results of SCP (still limited by the low-quality evidence currently available) should be confirmed by higher-quality clinical trials and systematic reviews to better frame which patients might concretely benefit (and what they have to attend) from this procedure, and to obtain strong long-term data (in terms of pain relief, functional improvement and conversion rate to arthroplasty).

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Authors Contribution: conception: MV performance of work: MV, IS, GC; interpretation or analysis of data: IS; preparation of the manuscript: MV, MA; revision for important intellectual content: ER, VC; supervision: VC. All authors read and approved the final manuscript.

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