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Review: Cartilage tissue engineering treatments for chondral defects and osteoarthritis

Abstract

Osteoarthritis (OA) is one of the most common musculoskeletal disorders, affecting 32.5 million individuals within the United States and more than 590 million globally. Various treatment options exist for cartilage defects and osteoarthritis, including palliative care, surgical intervention, and autologous or allogeneic chondrocyte transplantation, but they contain various limitations that limit their application. Cartilage tissue engineering holds promise as a viable solution for cartilage regeneration. This paper will discuss the anatomy and physiology behind articular cartilage, analyze the pathogenesis of osteoarthritis, explore relevant market information for the cartilage treatments, review existing treatment techniques and products on market, review recent trends in clinical trials, and introduce a potential novel cartilage tissue engineering product.

Keywords: cartilage, tissue engineering, scaffolds, osteoarthritis, chondral defects

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Abbreviations: OA, osteoarthritis; SC, stem cells; MSCs, mesenchymal stem cells; iPSCs, induced-pluripotent stem cells; TGF-β1, transforming growth factor-β1; TGF-β, transforming growth factor-β3; ECM, extracellular matrix; BMPs, bone morphogenetic proteins; IGF-1, Insulin-like Growth Factor-1; IL-1β, Interleukin-1β; IL-6, interleukin-6; TNF-α, Tumor Necrosis Factor-α; MAPK, mitogen-activated protein kinase; NF-κB, nuclear factor kappa B; MMPs, matrix metalloproteinases; ADAMTS, a disintegrin and metalloproteinase with thrombospondin motifs; GBD, global burden of diseases; CAGR, compound annual growth rate; MF, microfracture; ACI, autologous chondrocyte implantation; HA, hyaluronic acid; PLA, polylactic acid; PGA, poly(glycolic acid); PEG, poly(ethylene glycol); FGF-2, fibroblast growth factor 2; 3D, three-dimensional; CD, cartilage defect; CMC, carpometacarpal; PRP, platelet-rich plasma; PVA, poly (vinyl) alcohol; OATS, osteochondral autologous transplantation; SLS, selective laser sintering; SLA, stereolithography; FDM, fused deposition modeling

Introduction

Osteoarthritis is one of the most prevalent joint disorders globally, affecting millions of individuals across various demographics.[1] This disease places a considerable burden on healthcare systems within society, with 32.5 million cases in the United States and over 590 worldwide.[1] As the population ages and obesity rates rise, the prevalence of osteoarthritis is expected to increase, especially in high-income regions such as North America, and the Asia Pacific.[2,3]

Osteoarthritis is characterized by cartilage degeneration, joint inflammation, and new subchondral bone formation.[4] There are various risk factors that increase the likelihood of developing the disease, including traumatic injury, age, genetics, and obesity.[5] Articular cartilage is a tissue that lacks blood vessels and nerves, limiting its intrinsic regenerative ability and contributing to the progressive nature of osteoarthritis.[6]

Various treatment options exist for cartilage defects and osteoarthritis, including palliative care, surgical intervention, and autologous or allogeneic chondrocyte transplantation.[7] Although these treatments may reduce pain or encourage temporary repair, they are insufficient at supporting the long-term regeneration of cartilage tissue.[8]

Cartilage tissue engineering holds promise as a viable solution for cartilage regeneration.[7] Scaffolds of varying materials may be combined with cells, such as mesenchymal stem cells (MSCs), and/or growth factors, such as transforming growth factor-β1 (TGF-β1) to promote tissue repair. In recent decades, there has been an upsurge in research within this field, resulting in the development of new studies and treatments for cartilage defects.[7]

In this paper, the normal anatomy and function of the articular cartilage and the pathogenesis of osteoarthritis will first be introduced. The market trends for cartilage regeneration will then be explored before existing treatment techniques and cartilage tissue engineering solutions are addressed. Next, existing cartilage tissue engineering products and relevant clinical trials for cartilage regeneration will be reviewed. Finally, a novel treatment option will be introduced and future prospects will be explored.

Cartilage tissue anatomy & physiology

Healthy cartilage tissue

Articular hyaline cartilage is a connective tissue that lines bone surfaces in joints.[9] This tissue is responsible for providing the joint with the ability to withstand compressive loads.[10] In addition to this, articular cartilage greatly reduces friction during joint motion, allowing movements to be sustained with ease.[11] Articular cartilage does not contain nerves, blood vessels, or lymphatics, limiting the regenerative ability of the tissue.[6] Most nutrients are obtained, instead, from the synovial fluid and the subchondral bone marrow.[6]

Articular cartilage consists of a network of extracellular matrix (ECM) and specialized cells called chondrocytes.[12] Collagen, proteoglycans, and water are the primary components of ECM, though non-collagenous proteins, such as fibronectin, may also be found within the network.[9] Although chondrocytes are the main cell type within articular cartilage, they only account for 2% of the total cartilage volume.[10]

Water comprises up to 80% of the articular cartilage weight, with the remaining weight contributors being collagen (12-14%) and proteoglycans (7-9%).[9] Collagen type II is the most abundant protein found within articular cartilage.[12] This protein forms fibrils that provide the cartilage with tensile strength and structural integrity.[13]

Collagen types I, IV, V, VI, IX, X, and XI also contribute to network formation, but are less prevalent and involved than Collagen type II.[9] Proteoglycans are the second most prominent protein, with aggrecans being the most abundant of the group.[12] Aggrecans have hydrophilic properties, contributing to the rise in osmotic pressure which enhances the compressive strength of the tissue.[12] Additional proteoglycans and non-collagenous proteins found in the ECM include link protein, cartilage oligomeric matrix protein, fibronectin, decorin, biglycan, and fibromodulin.[9]

The structure of articular cartilage is zonal, comprising the superficial, middle, deep, and calcified zones, each with their own composition and functions (Figure 1).[6] The uppermost, or superficial, zone represents 10-20% of the total cartilage thickness.[14] This zone, mainly composed of collagen fibers, contains a high density of chondrocytes, which are small and flat in this region.[15] The superficial layer functions as a protective zone for deeper layers, providing initial resistance to shear stresses and contributing to the articular cartilage's tensile abilities.[6,12]

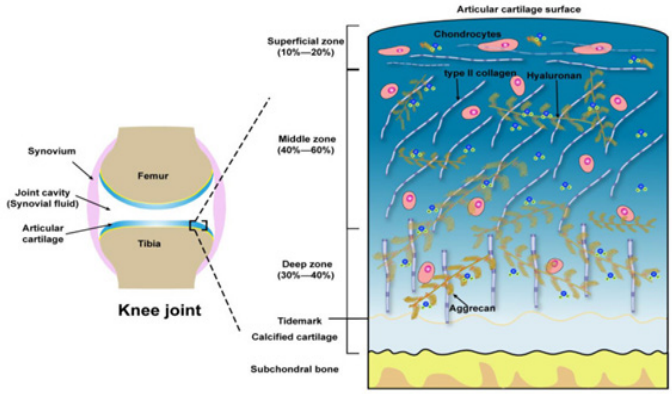

Figure 1 Articular cartilage structure.[11]

The image shows the structure of the articular cartilage of a knee joint, including the different structural zones and their respective cell morphologies and protein compositions.

The middle zone (40-60% of the total volume) consists of proteoglycans and collagen fibrils, as well as a sparse amount of chondrocytes with a round phenotype.[6,12] This layer serves as a transitional zone. 30% of the cartilage's volume is accounted for by the deep zone, which features the largest amount of proteoglycans.[12] In addition, the deep zone is composed of thick collagen fibrils that are perpendicular to the joint surface, providing this layer with the highest resistive ability to compressive forces. The calcified zone, which is the deepest layer, is responsible for forming the attachment between the articular cartilage and the subchondral bone.[9] This zone contains a low density of hypertrophic chondrocytes.[10]

Chondrocytes develop from MSCs in a process called chondrogenesis.[10] As shown in Figure 2, MSCs first undergo differentiation and proliferation to develop into chondroprogenitor cells before differentiating into chondrocytes. Following this, chondrocytes may experience terminal differentiation to become hypertrophic chondrocytes.[16] The final potential stage is for endochondral ossification to occur, resulting in bone formation. Throughout this process, various growth factors and transcription factors guide cell differentiation and proliferation.[16] This includes the growth factors bone morphogenetic proteins (BMPs), insulin-like growth factor-1 (IGF-1), and transforming growth factor-β1 and β3 (TGF-β1, -β3), as well as transcription factors SOX-5, 6 and 9.[10]

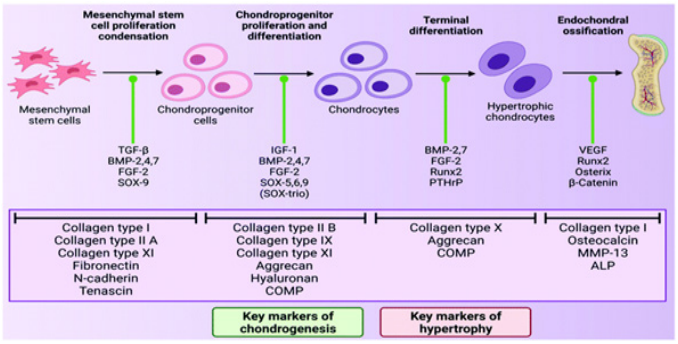

Figure 2 Process of chondrogenesis.[10]

The image shows an overview of chondrogenesis, including the differentiation of a mesenchymal stem cell into chondroprogenitor cells, chondrocytes, hypertrophic chondrocytes, and bone tissue.

Diseased cartilage tissue

Articular cartilage damage, represented by the formation of lesions or microtears within the tissue's surface, may result from sudden acute joint injuries or chronic wear and tear.[6,8,17] Because the articular cartilage lacks considerable regenerative abilities, repeated or prolonged cartilage damage may progress to osteoarthritis, a degenerative joint disease characterized by cartilage degeneration, joint inflammation, and bone formation.[4] Osteoarthritis may impact various joints throughout the body, including the knees, hips, ankles, and toes. Patients with cartilage defects or osteoarthritis may experience joint pain, instability, and mobility issues (Figure 3).[15]

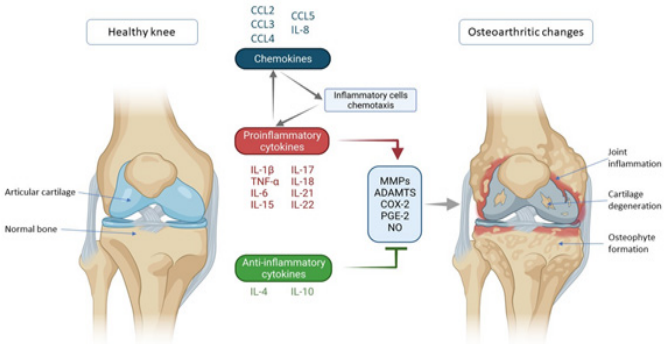

Figure 3 Osteoarthritic Changes.[3]

The image shows the damages that result from osteoarthritis through a comparison of a healthy and osteoarthritic knee joint, showcasing cytokines that contribute to such changes.

The leading physiological factor influencing the development of osteoarthritis is changes to the metabolic activity of articular cartilage, resulting in an imbalance of the synthesis and degradation of the natural ECM.[12] Damage to the articular cartilage matrix triggers an increase in metabolic activity in an attempt to promote matrix repair, represented by a rise in the production of inflammatory cytokines.[6] Pro-inflammatory cytokines, including interleukin-1β (IL-1β), interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α), activate MAPK and NF-kB signaling pathways which further encourage inflammation. During this process, the ECM-degrading enzymes matrix metalloproteinases (MMPs) and ADAMTS are also stimulated.[15] As the disease progresses, the combination of these changes lead to cartilage degradation, chondrocyte apoptosis, and subchondral bone thickening.[15]

Market size & trends

Osteoarthritis (OA) is one of the most common musculoskeletal disorders, affecting 32.5 million individuals within the United States and more than 590 million globally.[1] According to the Global Burden of Diseases (GBD) study conducted in 2019, high income nations of North America, Eastern Europe, and the Asia Pacific have the highest incidences of OA (Figure 4).[1,18]

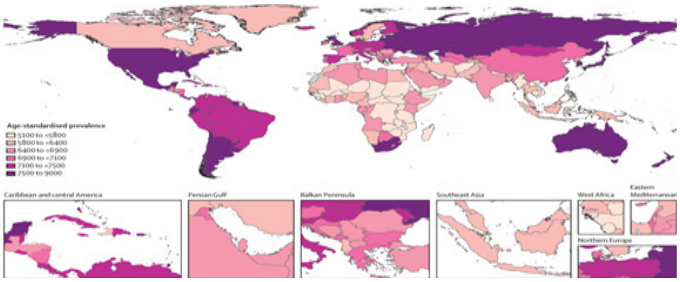

Figure 4 Global prevalence of osteoarthritis.[1]

The image shows the global age-standardized prevalence of osteoarthritis per 100,000 people, represented by a color gradient that associates higher prevalence with darker shades.

This disease places a considerable economic burden on nations, costing the United States roughly $136.7 billion annually.[19] The joint that is the most impacted by OA is the knee, accounting for more than 80% of all cases.[20] Hand OA has the second highest prevalence, with hip OA and all other forms of the degenerative disease following.[1,21] Figure 5 shows that, for all joint types, OA is more prominent in women and increases with age.[5] Women account for approximately 60% of all OA cases, with their higher prevalence possibly resulting from anatomical differences, hormonal influences, and genetics.[2,22]

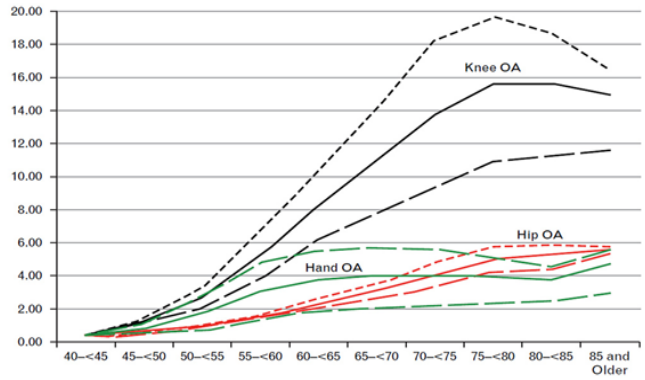

Figure 5 Prevalence of osteoarthritis by age, sex, and joint type.[21]

The image shows the differences in the prevalence of knee, hip, and hand osteoarthritis based on age and sex, with females, males, and the entire population being represented by short-dashed, long-dashed, and solid lines respectively.

Age is a significant factor in the prevalence of OA, showcased by the fact that approximately 73% of the OA patient population exceed the age of 55.[2] Despite this, osteoarthritis is not an inevitable or unavoidable disorder.[2] Rather, it is the culmination of a number of risk factors, including age, sex, genetics, obesity, high activity levels and sports injuries.[19]

It is expected that, as the population ages, the prevalence of osteoarthritis will increase considerably.[2] In addition to this, obesity rates are expected to double in high-income populations by 2035, potentially worsening the future OA rate.[3]

Cartilage regeneration market

In 2023, $1.13 billion was spent globally on cartilage repair treatments, including palliative methods, surgeries, cell-based therapies, and regenerative scaffolds.[19] As a result of aging populations, increasing obesity rates, and high occurrences of cartilage injuries, the cartilage repair market size is projected to grow to $4.62 billion by 2032 with an expected CAGR of 12.13% (Figure 6).[19] Due to expected increased incidences of knee OA, knee cartilage repair is projected to dominate the industry.[23] Ultimately, North America has the largest share of the market (51%) followed by Europe (22%) and then Asia Pacific (20%).[19] Prominent companies within the cartilage repair industry include Zimmer Biomet, Smith + Nephew, Anika Therapeutics, Arthrex, B. Braun Melsungen AG, Stryker, and Vericel.[1]

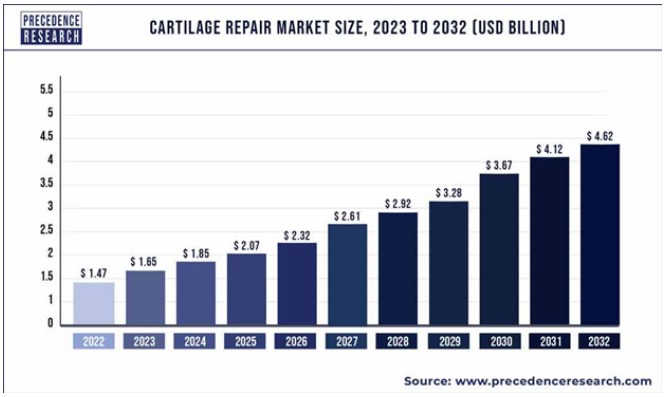

Figure 6 Global Cartilage Repair Market Size.[19]

The image shows the projected growth of the global cartilage repair market from 2023 to 2032, represented in USD billion.

Existing treatment techniques for osteoarthritis

Various strategies exist for the treatment of OA, including palliative care, surgeries, and regenerative scaffolds (Figure 7).[24] Palliative care, which comprises corticosteroids, analgesics, hormones, and hyaluronic acid, may be utilized to treat mild cases of cartilage defects or injuries. Although palliative management options may provide temporary pain relief to patients, these treatments prove to be insufficient at preventing degeneration in the long-term.[25]

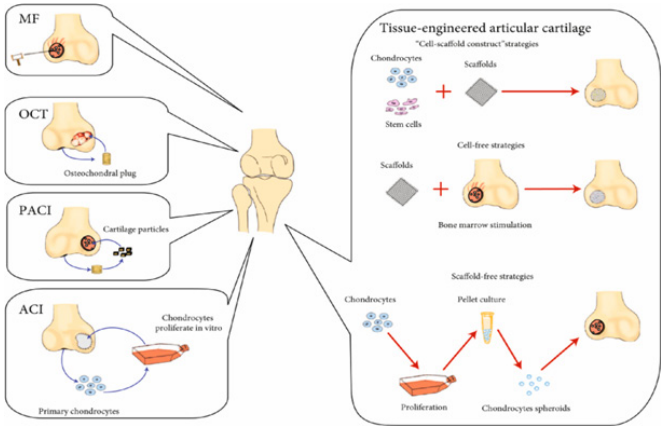

Figure 7 Treatment methods for cartilage degeneration.[24]

The image shows an overview of treatment techniques available for the treatment of osteoarthritis, including surgical methods and tissue engineering solutions.

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For severe OA cases, surgeries like microfracture (MF), osteochondral transplantation, and autologous chondrocyte implantation (ACI) may be employed to promote cartilage regeneration.[26] MF is a technique in which small holes are poked into the bone, leading to the formation of blood clots and the stimulation of bone marrow MSCs.[5] This method is relatively simple and inexpensive, but it is limited by the size of cartilage defects that may be treated.[24]

Osteochondral autologous transplantation is an appealing option for cartilage repair due to the lack of rejection and the facilitated healing process, but because the tissue is coming from the patient, there is a limited source and only small defects may be treated. Allografts, which come from donors, may be utilized for larger defects, but this treatment is also hindered by the supply of donor tissues.[24] ACI is a cell-based autologous approach in which healthy cartilage is taken from the patient and cultured before expanded chondrocytes are redelivered to the defect. Despite being a promising method for cartilage regeneration, the ACI procedure requires more time and is more expensive.[27]

Cartilage tissue engineering treatments

Scaffolds offer a wide range of variability for the treatment of cartilage disorders, as the matrix material, cell type, and growth factors utilized may be altered for different purposes.[28] Natural polymers such as collagen, hyaluronic acid (HA), and chitosan are very biocompatible and promote bioactivity, making them great candidates for scaffolds.[26] Synthetic polymers like polylactic acid (PLA), poly(glycolic acid) (PGA), and poly(ethylene glycol) (PEG) are also suitable materials due to their mechanical stability. A tissue engineering product may be composed of a combination of natural and synthetic materials to ensure favorable properties.[29]

Adding cells and/or growth factors to a scaffold could greatly enhance the regenerative ability of the treatment.[30] Naturally, chondrocytes are a beneficial selection for cartilage tissue engineering because these cells are responsible for producing ECM components, including glycoproteins.[31] Stem cells (SCs), such as mesenchymal and induced pluripotent SCs, also serve as suitable candidates because they may be differentiated into chondrocytes. Cartilage tissue regeneration may be further encouraged by the addition of growth factors like insulin-like growth factor 1 (IGF-1), fibroblast growth factor 2 (FGF-2), and transforming growth factor beta 1 (TGF-β1).[5]

Cartilage repair treatments on the market

There is currently a diverse range of treatments on the market that address cartilage regeneration, with products varying in treatment type, scaffold composition, and usage conditions (Figure 8 & Table 1).[26] 10 Among the list of treatments, showcased in Table 1, there were cell-based therapies, off-the-shelf allografts, and 3D matrices composed of natural and synthetic polymers.[5] Many of the products were intended to be used in combination with a standard surgical cartilage treatment as well.[26]

Figure 8 Commercially available cartilage tissue engineering products.

The image shows an overview of cartilage tissue engineering products that are on the market. Products are listed as follows: A) HYALOFAST (Anika Therapeutics, Inc.). B) BioCartilage (Arthrex, Inc.). C) NOVOCART 3D (B. Braun). D) Agili-C (Cartiheal, Inc.). E) CartiMax (CONMED). F) CARTISEM (MEDIPOST). G) Cartiform (Arthrex, Inc.). H) BST-Cargel (Smith+Nephew). I) ProChondrix CR (Stryker). J) MACI (Vericel). K) Epicel (Vericel) L) DeNovo NT (Zimmer Biomet).

Table 1 Commercially available cartilage tissue engineering products[5,14,24,26]

Company	Product	Composition	Characteristics	Reference
Anika Therapeutics SRL	HYALOFAST	Hyaluronic Acid	3D Scaffold; Used with microfracture	1A
Arthrex, Inc.	BioCartilage	Natural ECM	Allogeneic cartilage matrix; Used with microfracture	1B
	Cartiform	Chondrocytes, growth factors, ECM proteins	3D scaffold with chondrocytes, growth factors	1C
B.Braun Melsungen AG	NOVOCART Basic	Collagen type I, Chondroitin sulfate	Biphasic collagen scaffold; Used with microfracture	1D
CartiHeal, Inc.	Agili-C	Aragonite-based	Off-the-shelf biphasic scaffold	1E
CONMED Corp., MTF Biologics	CartiMax	Natural ECM	Off-the-shelf allograft with viable chondrocytes	1F
MEDIPOST	CARTISTEM (Korea)	Hyaluronic Acid	Hydrogel with MSCs derived from human umbilical cord blood	1G
Smith+Nephew	BST-Cargel	Chitosan	Chitosan and autologous blood combination; Used with bone marrow stimulation procedure	1H
Stryker, Allosource	ProChondrix CR	Natural ECM	Allograft with viable chondrocytes and growth factors	1I
Vericel Corporation	MACI	Porcine collagen	Collagen scaffold with autologous chondrocytes	1J
	Epicel	Natural ECM	Scaffold with autologous chondrocytes	1K
Zimmer Biomet	DeNovo NT	Juvenile hyaline cartilage	Off-the-shelf allograft	1L

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Clinical trials for cartilage regeneration treatments

There is a wide range of research being conducted to develop innovative cartilage tissue engineering solutions.[39] An overview of clinical trials for cartilage tissue engineering products for the treatment of chondral defects and osteoarthritis is provided in Table 2. These studies were obtained from ClinicalTrials.gov based on varying combinations of the disease search terms "osteoarthritis," "cartilage damage," "cartilage defects," and "chondral defects" with the treatment terms "tissue engineering," "scaffold," or "graft." The term "cartilage" was also searched. Cumulatively, 395 trials resulted from these searches. Trials that were terminated or withdrawn were not considered, and only trials involving scaffold-based products were selected, reducing the number to 40 trials, as presented in Table 2. Many companies that have products currently on the market, including DeNovo NT, CartiStem, and MACI, are included in the list in addition to companies with emerging technologies that have not yet been approved. The majority of the trials focused on treating knee chondral defects. However, ankle, toe, and carpometacarpal defects were also addressed.

Table 2 Clinical trials for cartilage regeneration treatments of CD and OA

	Trial Number	Status	Condition	Product	Treatment
1	NCT01733186	Completed	Knee CD	CARTISTEM	Hydrogel with MSCs
2	NCT02309957	Completed	Knee CD	BioMatrix CRD	Allogeneic cartilage scaffold; Used with arthroscopic microfracture
3	NCT03307668	Unknown	Knee CD	CaReSR-1S	Collagen type I gel with autologous chondrocytes
4	NCT02423629	Completed	CD	Agili-C	Biphasic aragonite-based scaffold
5	NCT01471236	Completed	CD	Agili-C	Biphasic aragonite-based scaffold
6	NCT03299959	Active	Knee CD	Agili-C	Biphasic aragonite-based scaffold
7	NCT03696394	Unknown	CD	BioCartilage	Micronized cartilage matrix; Used with microfracture
8	NCT02203071	Completed	CD	BioCartilage	Micronized cartilage matrix; Used with microfracture
9	NCT01791062	Completed	Knee CD	HYTOP	Scaffold with collagen & hyaluronan
10	NCT01656902	Completed	Knee CD	NOVOCART-3D	Biphasic collagen scaffold; Used with ACI
11	NCT01957722	Active	Knee CD	NOVOCART-3D	Biphasic collagen scaffold; Used with ACI
12	NCT03219307	Recruiting	CD	NOVOCART-3D	Biphasic collagen scaffold; Used with ACI
13	NCT02348697	Completed	CD	NOVOCART-3D	Biphasic collagen scaffold; Used with ACI
14	NCT03808623	Completed	Knee CD	NOVOCART Basic	Biphasic collagen scaffold; Used with microfracture
15	NCT02993510	Completed	Knee CD	Chondro-Gide	Bilayer collagen membrane; Used with ACI
16	NCT05785949	Recruiting	Knee CD	Chondro-Gide	Bilayer collagen membrane; Used with ACI
17	NCT05685316	Recruiting	Knee CD	COPLA	Cartilage scaffold
18	NCT00729716	Unknown	Knee CD	BioCart	Scaffold with autologous chondrocytes
19	NCT05440370	Active	Knee CD	MegaCarti	Allogeneic scaffold
20	NCT06249828	Recruiting	Knee CD	MegaCarti	Allogeneic scaffold
21	NCT06278480	Active	CD	MegaCarti	Allogeneic scaffold
22	NCT01041885	Completed	Knee CD	INSTRUCT	Scaffold with autologous chondrocytes
23	NCT01251588	Completed	Knee CD	MACI	Porcine collagen membrane with autologous chondrocytes
24	NCT03588975	Recruiting	Knee CD	MACI	Porcine collagen membrane with autologous chondrocytes
25	NCT01329445	Unknown	Knee CD	DeNovo NT	Off-the-shelf allograft
26	NCT01347892	Unknown	Ankle CD	DeNovo NT	Off-the-shelf allograft
27	NCT03873545	Active	Knee CD	ProChondrix	Cryopreserved osteochondral allograft
28	NCT00548119	Completed	Knee CD	NeoCart	Cartilage scaffold; Used with ACI
29	NCT05186935	Recruiting	Knee CD	H2Care	Injectable hydrogel
30	NCT06163573	Active	Knee OA	N-TEC	Autologous nasal chondrocyte tissue engineered cartilage
31	NCT03247439	Unknown	CMC OA	Cartiva	PVA hydrogel
32	NCT00969969	Completed	Toe OA	Cartiva	PVA hydrogel
33	NCT02978573	Completed	Toe OA	Cartiva	PVA hydrogel
34	NCT02391506	Completed	CMC OA	Cartiva	PVA hydrogel
35	NCT02659215	Active	Knee CD	HyaloFAST	3D scaffold; Used with microfracture
36	NCT04955548	Unknown	CD	N/A	Autologous adipose gel
37	NCT04955548	Unknown	CD	N/A	Autologous adipose gel
38	NCT00821873	Completed	CD	N/A	Allogeneic scaffold; Used with OATS procedure
39	NCT00850187	Completed	Knee CD, OA	N/A	Collagen I scaffold with MSCs
40	NCT06028763	Active	Ankle CD	N/A	Heparin-conjugated hydrogel

CD, cartilage defect; OA, osteoarthritis; CMC, carpometacarpal; PRP, platelet-rich plasma; MSCs, mesenchymal stem cells; ACI, autologous chondrocyte implantation; PVA: poly(vinyl) alcohol; OATS, osteochondral autologous transplantation.

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Emerging developments

In recent years, there has been considerable growth in the development of novel treatments for cartilage tissue engineering, marked by the increase in studies on 3D printed matrices and the production of stimuli-responsive smart scaffolds.[33]

Within the past decade, the use of 3D printing in tissue engineering has skyrocketed, enabling the production of customizable scaffolds with preferable mechanical properties. Various 3D printing techniques exist, including direct ink writing, selective laser sintering (SLS), stereolithography (SLA), and fused deposition modeling (FDM).[34] In regards to cartilage treatments, the utilization of biomaterials with 3D printing enables the production of biomimetic scaffolds with the enhanced ability to integrate with surrounding cartilage tissues.[28]

Stimuli-responsive smart scaffolds are scaffolds that respond to particular signals or triggers, such as changes in temperature, light, pH, and enzyme or ion concentration, to treat cartilage damage. These scaffolds may also be loaded with a drug so that, when their response is triggered, the drug will be released to the cartilage, possibly promoting cell proliferation and differentiation, leading to regeneration.[35]

Conclusion

As the population ages and obesity rates climb, the prevalence of osteoarthritis will increase, creating a demand for innovative solutions in cartilage repair and regeneration.[2] The market for cartilage regeneration treatments of osteoarthritis is expected to grow to $4.62 billion by 2032.[19]

Osteoarthritis, which is characterized by cartilage degeneration, joint inflammation, and new subchondral bone formation, may develop as a result of sudden injury, age, genetic predisposition, or obesity.[5] Changing metabolic activity within the articular cartilage, as well as increased pro-inflammatory cytokines, including IL-1β, IL-6, and TNF-a, has a strong influence on the development of osteoarthritis.[36,37]

Existing treatments include palliative care, surgical procedures, and autologous or allogeneic chondrocyte transplantation, but these treatments are limited. Cartilage tissue engineering has the potential to greatly enhance the regenerative ability of osteoarthritis treatments.[7] Various companies, including Arthrex, Stryker, and Verticel, have released cartilage tissue engineering products to the market, with many of them aiming to treat knee osteoarthritis.[5] There are also many studies to develop innovative solutions and test emerging products for cartilage tissue engineering.[38]

Ultimately, new cartilage tissue engineering solutions are being developed to treat chondral defects and osteochondral.[39] 3D printing and stimuli-responsive hydrogels represent examples of novel treatments with great potential.[34]

Appendix

Products

1A. HYALOFAST: https://anika.com/medical/products/hyalofast/

1B. BioCartilage: https://www.arthrex.com/orthobiologics/biocartilage-extracellular-matrix

1C. Cartiform: https://www.arthrex.com/orthobiologics/cartiform

1D. NOVOCART Basic: https://www.bbraun-vetcare.com/en/products/b11/novocart-basic.html

1E. Agili-C: https://www.cartiheal.com/agili-c/

1F. CartiMax: https://www.conmed.com/en/products/allograft-cartilage-and-tissue/allograft-cartilage/cartimax

1G. CARTISTEM: https://en.medi-post.co.kr/cartistem/

1H. BST-Cargel: https://arthroscorp.com/product/bst-cargel/

1I. ProChondrix CR: https://allosource.org/products/prochondrix-cr/

1J. MACI: https://www.vcel.com/advanced-therapies/

1K. Epicel: https://www.vcel.com/advanced-therapies/

1L. DeNovo NT: https://www.zimmerbiomet.com/en/products-and-solutions/specialties/biologics/denovo-nt-natural-tissue.html

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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