Bioactive Knee Sleeve for Osteoarthritis: A Small Cohort Study

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Objectives: Osteoarthritis (OA) is one of the most prevalent musculoskeletal ailments worldwide. Numerous conservative therapies exist, but evidence for such treatments remains conflicting. Recently, there has been growing interest surrounding bioactive sleeves for managing knee arthritis; however, the literature on their efficacy for relieving pain and improving function in the setting of knee OA is limited. As such, we sought to investigate the effect of a bioactive sleeve on patient-reported outcome measures in a small cohort of patients with OA.

Methods: Patients with knee OA were given a bioactive sleeve (Reparel, Chico, CA) and asked to refrain from lifestyle modifications and intraarticular corticosteroid injections. Lysholm Knee Score, Oxford Knee Score, Knee Injury and OA Outcome Score (KOOS), Single Assessment Numeric Evaluation, and Visual Analog Scale score were obtained at baseline, 2 weeks, 6 weeks, and 3 months. OA severity was evaluated using the Kellgren and Lawrence (KL) classification system. The Wilcoxon signed rank test was used to compare baseline patient-reported outcomes with 2-week, 6-week, and 3-month time points. Bivariate correlation was used to evaluate the relation between patient-reported outcome measures and KL classification.

Results: The cohort was composed of 14 participants—4 males and 10 females—with a mean age of 62.2 ± 13.2 years and a body mass index of 33.7 ± 5.8. The average KL grade was 2.9 (range 2–4). KOOS pain, symptoms, activities of daily living, and quality of life increased significantly at 2 weeks, 6 weeks, and 3 months. KOOS sport and recreation significantly increased at 3 months. The Oxford Knee Score was significantly greater at 2 weeks, 6 weeks, and 3 months. The Lysholm Knee Score was significantly greater at 6 weeks and 3 months. The Single Assessment Numeric Evaluation attained significant improvement at 3 months, and the Visual Analog Scale improvement was significant at 2 weeks. No statistically significant difference was attained with University of California at Los Angeles activity score. Outcome scores did not correlate with KL classification.

Conclusions: These data suggest that a bioactive sleeve may improve patient-reported pain, symptoms, and function in the setting of knee OA. Further research is needed to better understand the role of bioactive sleeves for patients with knee arthritis.

Key Words: bioactive sleeve, knee, osteoarthritis (OA), patient-reported outcomes

Osteoarthritis (OA) is one of the most common musculoskeletal ailments, affecting approximately 250 million people worldwide.[1] Often described as a disease of wear and tear, OA is marked by the gradual loss of articular cartilage and osteophyte formation, frequently affecting weight-bearing joints.[2] Patients with OA experience joint pain and muscle weakness, which limit function and mobility. In an effort to reduce pain and promote function, knee OA is initially managed conservatively with oral nonsteroidal anti-inflammatory drugs, unloader knee braces, intraarticular corticosteroid injections, physical therapy, and biologics.[1,3,4] There are no clear recommendations for these therapies, however.[5]

Because of numerous factors negatively influencing long-term adherence to physical therapy and oral medication for OA,[6,7] interest has grown for alternative treatments. In recent years, bioactive knee sleeves have emerged as a new treatment method to alleviate knee pain. Early studies suggest that sleeves embedded with nontoxic metalloids, such as germanium, may provide beneficial anti-inflammatory properties.[8] Marino et al recently demonstrated that patients with low grade OA (Kellgren and Lawrence [KL] grades 1 and 2) could benefit from a bioactive sleeve, providing pain relief and promoting increased function and quality of life.[9] One sleeve specifically uses synthetic fibers that incorporate finely processed, nonmetallic, elemental semiconductor nanoparticles. Such composition is thought to improve circulation and decrease pain and swelling.[10] The mechanism of action is thought to be the result of reflecting body

Key Points

- The use of a bioactive knee sleeve provided statistically significant improvements in patient-reported outcomes throughout the study.
- Pain improvement was greatest within the first 2 to 6 weeks of use.
- Significant functional improvements were noted by 3 months of use.
- There was no correlation with outcomes and osteoarthritis severity.

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Reparel, the company that produced the sleeves used in the study, provided the investigated product without charge to the authors' institution.

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Table 1. Patient demographics

	Male	Female	*P*
No. enrollees	4	10	0.057
Age, y	66.0 ± 11.9	60.5 ± 12.8	0.571
BMI	33.7 ± 2.6	34.3 ± 6.6	1.000

BMI, body mass index.

heat as near-infrared light, which promotes vasodilation, and thereby improves nutrient delivery to the synovium, removes inflammatory mediators, and accelerates adenosine triphosphate production. No study has investigated patient-reported outcomes after the use of this bioactive sleeve, however.

In this study, we followed a cohort of nonoperatively managed OA patients after the use of this bioactive sleeve. The purpose of this study was to evaluate patient-reported outcomes with sleeve use in the setting of OA during a 3-month span. We hypothesize that bioactive sleeve use will provide clinically significant pain relief and functional improvement.

Methods

Patient Recruitment and Inclusion

Following institutional review board approval and registration with ClinicalTrials.gov (NCT04743921), the authors prospectively followed a series of patients at an outpatient orthopedic sports medicine clinic between February and July 2021. Patients who opted for nonoperative management of knee OA were informed and consented for the study. Patients were included if they had radiographic evidence of knee OA, no previous surgery on the symptomatic knee, no corticosteroid knee injection within 3 months of the study, and agreed to abstain from a knee injection during the 3-month study period. Patients were excluded if diagnosed as having bilateral symptomatic knee OA, had previously undergone knee surgery, were grossly unstable on physical examination, or had a history of knee malignancy. Patients were instructed to wear the sleeve (Reparel, Chico, CA) as long as tolerated throughout the day and to refrain from modifying usual activities and diet.

Patient Assessment

Participants were asked to complete the following patient-reported outcome measures (PROM): the University of California at Los Angeles Activity Score (UCLA),[11] which measures current activity level; the Lysholm Knee Score (LKS),[12] which measures joint stability and function; the Oxford Knee Score (OKS),[13] which measures knee-related health status; the Knee Injury and OA Outcome Score (KOOS),[14] which assesses difficulties with physical activity; the Single Assessment Numeric Evaluation (SANE),[15] which assesses perceived functional level; and the Visual Analog Scale (VAS),[16] which assesses perceived pain level. These surveys were administered at the initial visit and subsequently over the telephone at 2 weeks, 6 weeks, and 3 months later. Patients also were asked about average daily sleeve usage, product satisfaction, and complaints/issues.

OA Severity Assessment

OA severity was defined by clinical radiographic imaging using the KL classification system at the baseline clinical visit.[17] The radiographs were read and graded by a sports medicine fellowship–trained orthopedic surgeon (A.M.M.).

Statistical Analysis

Post-hoc power analysis was performed to evaluate the minimum number of patients needed to demonstrate a clinically important difference for KOOS subsections. According to Lyman and colleagues,[18] a 12- to 13-point difference is needed to achieve a 90% certainty of minimal detectable change (MDC) for each survey subsection. To demonstrate a 13-point difference, with a power of 0.8 and an α of 0.05, our study required at least 18 patient assessments (9 at baseline and 9 at a follow-up time point).

Statistical analysis was performed using SPSS version 27.0 (IBM SPSS Statistics for Macintosh, Armonk, NY). Given the small sample size, the Mann-Whitney test was used to compare baseline demographics between male and female patients, as well as baseline PROMs and hours of sleeve use with those at 2-week, 6-week, and 3-month time points. Significance was set to an α of 0.05.

Results

Patient Cohort Demographics

Fourteen patients enrolled in the study; however, several patients did not complete follow-up surveys, resulting in 13 patients at 2 weeks, 9 at 6 weeks, and 12 at 3 months. Patient demographics are shown in Table 1. Baseline PROMs between the sexes were

Table 2. Baseline patient-reported outcome scores

	Male, n = 4	Female, n = 10	*P*
KOOS-P	62.5 ± 6.6	43.4 ± 19.9	**0.047**
KOOS-Sy	53.6 ± 14.6	47.5 ± 11.4	0.393
KOOS-ADL	73.0 ± 11.1	48.4 ± 24.4	0.062
KOOS-Sp	43.8 ± 27.5	16.5 ± 18.1	0.075
KOOS-QOL	35.9 ± 12.9	29.8 ± 16.4	0.492
LKS	58.8 ± 16.4	39.6 ± 12.5	**0.031**
OKS	27.3 ± 9.6	22.4 ± 8.8	0.191
SANE	50.0 ± 31.6	55.0 ± 19.2	0.909
VAS	3.3 ± 3.3	5.4 ± 2.3	0.210
UCLA	5.5 ± 2.1	4.0 ± 1.2	0.164

Boldface values indicate statistical significance. KOOS, Knee Injury and Osteoarthritis Outcome Scores (ADL, activities of daily living; P, pain; Sp, sports and recreation; Sy, symptoms; QOL, quality of life); LKS, Lysholm Knee Score; OKS, Oxford Knee Score; SANE, Single Assessment Numeric Evaluation; UCLA, University of California at Los Angeles Score; VAS, Visual Analog Scale.

similar, with the exception of KOOS-Pain (P) ($P = 0.047$) and LKS ($P = 0.031$), which were lower in females (Table 2). The median KL classification was 3, ranging from 2 to 4. There was no correlation between PROMs and KL classification.

KOOS

The KOOS test is a validated survey that is composed of five sections: pain (P), symptoms (Sy), activities of daily living (ADLs), sports and recreation (Sp), and quality of life (QOL). During the 3-month study period, patients reported significantly greater KOOS scores in all five sections. KOOS-P, KOOS-Sy, KOOS-ADL, and KOOS-QOL scores were significantly higher at 2 weeks, 6 weeks, and 3 months compared with baseline. KOOS-Sp was only significantly greater after 3 months, however (Fig., A, and Table 3).

LKS

The average baseline score of 44.1 designated patients as "poor" function and ability. LKS scores rose with each follow-up survey. Statistical significance was reached at the 6-week and 3-month assessments, in which scores increased by 24.3 (55.1%) and 30.9 (70.1%) points, respectively. The

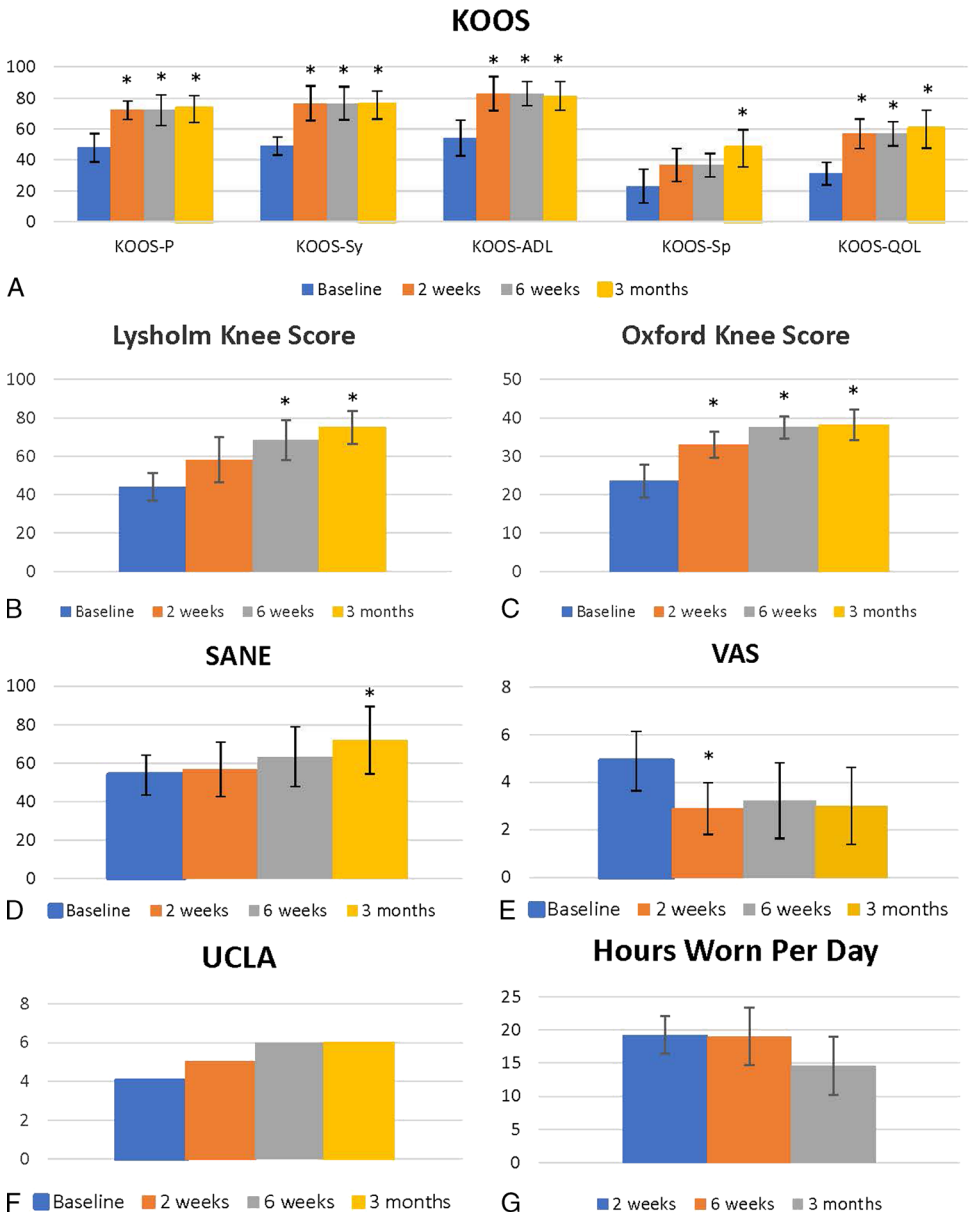

Fig. Comparison of patient-reported outcome measures. (*A*) KOOS, Knee Injury and Osteoarthritis Outcome Scores; (*B*) Lysholm Knee Score; (*C*) Oxford Knee Score; (*D*) SANE, Single Assessment Numeric Evaluation; (*E*) VAS, Visual Analog Score; (*F*) UCLA, the University of California at Los Angeles Activity Score; (*G*) hours worn per day. The asterisk indicates $P < 0.05$.

Table 3. Comparison of patient-reported outcome scores

	Baseline, n = 14	2 wk, n = 13	6 wk, n = 9	3 mo, n = 12
KOOS-P	47.9 ± 19.4	64.3 ± 11.1	72.2 ± 15.3	72.9 ± 15.2
P		**0.025**	**0.015**	**0.019**
KOOS-Sy	48.9 ± 12.0	63.5 ± 20.6	76.6 ± 16.3	75.6 ± 16.1
P		**0.025**	**0.011**	**0.002**
KOOS-ADL	54.2 ± 24.2	70.7 ± 20.1	82.8 ± 11.6	81.37 ± 16.0
P		**0.028**	**0.011**	**0.006**
KOOS-QOL	31.3 ± 15.5	46.2 ± 17.6	56.9 ± 11.9	59.9 ± 21.6
P		**0.021**	**0.007**	**0.007**
KOOS-Sp	22.9 ± 23.0	30.4 ± 19.6	36.7 ± 11.5	47.5 ± 21.3
P		0.720	0.574	**0.010**
LKS	44.1 ± 15.4	58.1 ± 21.7	68.4 ± 16.0	75.0 ± 15.3
P		0.080	**0.028**	**0.003**
OKS	23.5 ± 9.0	32.9 ± 6.3	37.6 ± 4.4	38.2 ± 7.0
P		**0.001**	**0.008**	**0.003**
UCLA Score	4.4 ± 1.5	5.0 ± 1.2	5.4 ± 1.4	5.4 ± 1.4
P		0.399	0.158	0.063
VAS	4.9 ± 2.6	2.9 ± 2.0	3.2 ± 2.4	3.0 ± 2.9
P		**0.011**	0.057	0.066
SANE	53.8 ± 21.6	56.8 ± 25.9	63.3 ± 23.7	72.0 ± 31.0
P		0.679	0.246	**0.020**
Hours worn per day	—	19.3 ± 4.9	19.0 ± 6.7	13.8 ± 7.5
P			0.770	0.124

P values represent comparison of baseline to 2-week, 6-week, or 3-month follow-up scores. Boldface values indicate statistical significance. KOOS, Knee Injury and Osteoarthritis Outcome Scores (ADL, activities of daily living; P, pain; Sp, sports and recreation; Sy, symptoms; QOL, quality of life); LKS, Lysholm Knee Score; OKS, Oxford Knee Score; SANE, Single Assessment Numeric Evaluation; UCLA, University of California at Los Angeles; VAS, Visual Analog Scale.

3-month average of 75.3 placed patients into "fair" function and ability (Fig., B, and Table 3).

OKS

With an average baseline OKS score of 23.5, patients were initially graded as having "moderate to severe" OA symptoms. Significant improvements in OKS were noted at each time point, with an average score increase of 9.4 (40%), 14.1 (60%), and 14.7 (62.6%) points at 2 weeks, 6 weeks, and 3 months, respectively. By 3 months, the average score of 38.2 is considered to constitute "mild to moderate" OA symptoms (Fig., C, and Table 3).

SANE

Subjective functional assessment did not reveal a statistically significant difference until the 3-month evaluation ($P = 0.02$). At that time, SANE scores increased on average by 18.2 (38.8%) percentage points, from 53.8% to 72% perceived function (Fig., D, and Table 3).

VAS

The average subjective pain at baseline was 4.9, which is considered moderate severity. VAS scores were lower at each follow-up survey relative to baseline; however, only the 2-week follow-up reached statistical significance, with a 2-point (40.8%) decrease in pain (Fig., D, and Table 3).

UCLA Score

At baseline, patients had a median score of 4, which indicates "regular participation in mild activities." No statistically significant changes in UCLA Scores were noted between time points. The median, however, increased to 5 ("sometimes participates in moderate activities, such as swim or could do unlimited housework") at 2 weeks and 6 ("Regularly participate in moderate activities, such as swimming and unlimited housework or shopping") by 6 weeks and 3 months (Fig., E, and Table 3).

Hours Worn per Day

Patients consistently wore their bioactive sleeves throughout the duration of the study, averaging 19.3, 19.0, and 13.8 hours per day at 2 weeks, 6 weeks, and 3 months, respectively. Although there was a decrease between week 6 and month 3, this difference was not statistically significant (Fig., F, and Table 3).

Complications

Most commonly, patients described that the sleeve did not fit properly and would fall down their leg. Three patients described knee swelling after 2 weeks, but there were no reports of this at 6 weeks or 3 months. Skin irritation was reported at 2 weeks (n = 2) and 6 weeks (n = 1), but not at 3 months. Lower leg and foot swelling also was reported in a patient at 6 weeks; however, this patient had a history of lower extremity edema without previous concern for clotting, deep vein thrombosis, or symptoms of pulmonary embolism.

Discussion

In this cohort study, we evaluated patient-reported outcomes in individuals using a bioactive knee sleeve for conservative knee OA management. We found significant improvements in patient-reported outcomes after 2 weeks, 6 weeks, and 3 months of sleeve use. These results are promising, given the improvements in this often difficult-to-treat population of obese patients (average body mass index 33.8) with moderate-to-severe knee OA (median KL grade of 3).

A previous study by Marino et al[9] investigated the effects of germanium-embedded bioactive knee sleeves for knee OA. The group performed a nonrandomized controlled trial, following patients during a period of 6 months. They demonstrated significant improvements in LKS, VAS, and OKS scores in the bioactive sleeve group. In their study, however, patients with KL scores of 3 to 4 did not show statistically significant improvements. In contrast, our study showed improvements in KL scores of 2 to 4, with no correlation between PROMs and KL scores. The proposed mechanisms of the germanium sleeves are similarly credited to semiconductor physics: as the temperature of the embedded metalloid increases, its resistance decreases, freeing available electrons. These photons are reflected by the sleeve at a wavelength near infrared, which has been shown to penetrate tissues and promote cell metabolism and circulation, thereby improving nutrient delivery and reducing ischemic damage incurred by degenerative processes.[9,10] It is unclear as to why the previous study did not show improvements in patients with higher KL scores.

Unloader braces are another modality used to conservatively manage OA. These braces are designed to exert a valgus or varus force to unload the affected compartment and reduce pain.[19] Multiple studies have reported their efficacy, noting 7- to 15-point increases in KOOS scores and decreased VAS scores following at least 1 year of use.[20] Because of a variety of factors, including skin irritation, improper fit, bulkiness, and ease of use, patients do not consistently adhere to wearing these braces. One study indicated regular use in roughly one-fourth (21%–28%) of patients prescribed an unloader brace.[21] Another group demonstrated that by 1 year, 42% of subjects discontinued brace use, with 88% of those individuals stopping within the first 6 months.[22] Although few patients in our study voiced skin irritation and swelling, those issues were viewed as minor and still permitted consistent sleeve use. In addition, improvement in KOOS scores within our cohort were greater, averaging at least 25 points within each subsection by 3 months.

Intra-articular corticosteroid injections (IACIs) are another frequently used therapy for nonoperative OA management. The analgesic properties of IACI are believed to be the result of decreased synovial blood flow, local leukocyte, and inflammatory cytokine response.[23] Although they are common practice, this therapy is not universally efficacious. Several studies have demonstrated that IACIs are less potent for individuals with higher grade OA (KL 3 or 4) and obese individuals (body mass index >30).[24,25] Similar to the bioactive sleeve, IACIs provide the greatest degree of pain relief within the first 3 to 6 weeks[24]; however, the 20% to 27% improvement in VAS scores described by Matzkin et al was less pronounced than our 34% to 41% reduction, even in an obese population with grades 3 and 4 OA. Furthermore, IACIs do pose potential negative adverse effects, including glucose spikes in diabetics, infection risk, and chondrotoxicity.

Physical therapy is another conservative modality for knee OA that is geared toward patients with functional limitations and focuses on quadriceps strengthening and joint stability by using a variety of progressive isotonic, isometric, and isokinetic exercises.[26,27] Lund et al[28] measured KOOS scores in patients with knee OA following 8 weeks of formal physical therapy. The group demonstrated clinically significant score improvements, with 13- to 23-point increases in KOOS-Sy, KOOS-P, and KOOS-ADL; however, our KOOS improvements were more substantial, with at least 25-point increases in all five subsections by 6 weeks and 3 months.

In late-stage OA that is recalcitrant to conservative therapies, total knee arthroplasty (TKA) often is offered as a treatment. Although this procedure can provide significant pain relief and functional improvement and last for several decades,[29] it is not without potential complications. Some of the frequently noted complications including neural deficit, vascular injury, joint instability, malalignment, stiffness, deep joint infection, fracture, and extensor mechanism disruption, among others.[30] The literature indicates a 10% acute complication rate and nearly 50% complication rate following TKA within the first 6 months after discharge, as well as discontentment in 20% of patients by 1 year.[31,32] As such, modalities, such as a bioactive sleeve, that may help avoid or delay a TKA are important in the treatment algorithm.

In this study we demonstrated statistically significant improvements in numerous PROMs with the use of a bioactive knee sleeve for OA. A common method of conveying statistical results in a more clinically tangible form is to compare them with previously reported MDCs. The MDC refers to the minimal change outside of error that reflects true change by a patient between two time points and is often used for clinical significance. When compared with previously reported MDCs for PROMs in knee OA, our average net change in scores for each significant KOOS and OKS value surpassed the 90% confidence interval for the MDC (MDC90).[18,33–35] For the LKS and VAS, however, the MDC90 was surpassed at all time points for each survey, despite statistical significance only being found at 6 weeks and 3 months

for LKS and 2 weeks for VAS.[36,37] UCLA also was found to surpass the minimal clinically important difference by 6 weeks and 3 months, despite no statistically significant difference.[38] These findings indicate clinically significant improvements in patient knee pain, satisfaction, and function with consistent bioactive sleeve use.

This study is not without limitations. The sample size was small, and we had several patients not follow up at each time point; however, our power analysis indicates that we were sufficiently powered to detect clinically important differences between baseline and follow-up measurements. Of the patients who enrolled, the majority (71.4%) were female, which may be perceived as a sampling bias; however, previous meta-analyses demonstrated that the majority (60%) of patients with knee OA are female.[39,40] In addition, the lack of a control group makes it difficult to assess for potential placebo effects. Our outcome measurement improvements are comparable to the previously referenced placebo-controlled trial, however.[9] Lastly, our follow-up period was brief and thus additional studies are needed to assess long-term outcomes.

Conclusions

These data suggest that a bioactive sleeve may improve patient reported pain, symptoms, and function in the setting of knee OA. Further research is needed to better understand the role of bioactive sleeves for patients with knee OA.

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