Subchondroplasty in the Treatment of Bone Marrow Lesions of the Knee: Preliminary Experience on First 15 Patients

Stefano Pasqualotto1, Andrea Vincenzo Sgroi1, Araldo Causero2, Paolo Di Benedetto2, Claudio Zorzi1

1 Divisione di Ortopedia e Traumatologia, IRCCS Ospedale Classiﬁcato Equiparato Sacro Cuore - Don Calabria, Negrar (Verona), Italy
2 DAME Università degli studi di Udine, Clinica Ortopedica, Azienda Sanitaria Universitaria Friuli Centrale, Udine, Italy

Address for correspondence Stefano Pasqualotto, MD, Divisione di Ortopedia e Traumatologia, IRCCS Ospedale Classiﬁcato Equiparato Sacro Cuore - Don Calabria, Via don A. Sempreboni, 5 - 37024 Negrar (Verona), Italy (e-mail: stefano.pasqualotto20@gmail.com).

Keywords
► bone marrow lesions
► subchondroplasty
► knee osteoarthritis
► calcium phosphate bone substitute

Abstract

Purpose The aim of this prospective study was to assess the effectiveness in terms of pain relief and functional improvement of the Subchondroplasty procedure in the treatment of osteoarthritis-related bone marrow lesions (BMLs) of the knee.

Methods The study included ﬁrst 15 consecutive patients undergone to Subchondroplasty procedure for the treatment of chronic degenerative BMLs in which previous conservative treatment have failed. Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores, Knee Injury and Osteoarthritis Outcome Scores (KOOS), and visual analog scale (VAS) pain scores were obtained preoperatively and at 1, 6, and 12 months of follow-up.

Results WOMAC scores signiﬁcantly improved from 39.7±20.2 before surgery to 26.8±16.1 at the 1-month follow-up (p = 0.045). A further signiﬁcant improvement to 15.5±12.7 (p = 0.02) and to 8.6±3.1 (p < 0.01) was obtained both at 6-month and at 1-year follow-up. KOOS scores improved signiﬁcantly from 47.5±16.6 before surgery to 65.4±14.9 at 1 month (p = 0.013) and to 80.4±15.1 at 6-month follow-up (p = 0.01). A further improvement to 85.6±15.1 was recorded 1 year postoperatively, although nonsigniﬁcant. VAS score showed a signiﬁcant improvement from 55.8±20.5 preoperatively to 36.2±16.9 at 1 month (p = 0.008) and to 18.2±17.3 at 6-month follow-up (p = 0.005). This further improved to 12.8±17.9 at 1-year follow-up, although not signiﬁcantly.

Conclusion Subchondroplasty procedure represents a safe and valid surgical option in the treatment of osteoarthritis-related BMLs of the knee, providing an improvement in terms of pain relief and functional recovery. Longer studies are required to evaluate how long these improvements may last.

Level of Evidence Therapeutic case-series, Level IV study.
Introduction

Knee osteoarthritis (OA) is a degenerative process, which affects not only the articular cartilage but the entire joint, including synovium, ligaments, menisci, and periaricular muscles and tendons.\(^1,2\) This process influences also the subchondral bone (SCB) and alterations are seen both from mechanical, morphological, and histochemical point of view.\(^3\)

SCB plays therefore a key role in the pathophysiology and progression of OA. The presence of bone marrow lesions (BMLs) in the setting of knee OA was correlated with pain, clinical deterioration, decreased quality of life,\(^4-7\) and with 6.5- and 7-fold greater probabilities of OA progression.\(^8\) Moreover, the presence of BMLs was associated with an accelerated progression to total knee arthroplasty (TKA).\(^9-11\)

BMLs, defined as high-signal-intensity alterations detected on magnetic resonance (MR) fluid-sensitive sequences \([T2/proton density with fat suppression and short tau inversion recovery]\) with a decreased bone marrow signal intensity on T1-weighted image, are a common feature of knee OA.\(^12\) Despite originally defined as bone marrow edema, several histological studies revealed that edema in the region of BML is minimal.\(^13,14\) In the osteoarthritic process, these areas are rather characterized by trabecular bone microdamages and microcracks\(^15-17\) associated with altered bone mineralization and increased bone remodeling.\(^18\) Moreover, vascular structure abnormalities,\(^14,15\) zone of fatty marrow, necrosis, and bone marrow fibrosis were detected.\(^13,19,20\)

In recent years, therefore, interests were focused on interventions directed toward the SCB to prevent or reverse BMLs. Among these, Subchondroplasty (SCP) (Zimmer Knee Creations, West Chester, Pennsylvania, United States) is a procedure that utilizes an injectable, synthetic, calcium phosphate (CaP) bone void filler to treat chronic BMLs in which previous conservative treatment failed.\(^21\) The goal of this procedure is to improve the structural properties of the affected SCB and stimulate SCB remodeling, with the aim of preventing bone collapse and OA progression.\(^21,22\)

Purpose of this preliminary study was to evaluate clinical and functional outcomes of the treatment of OA-related knee BML with SCP combined with arthroscopy.

Methods

This prospective 1-year follow-up case-series was conducted on first 15 consecutive patients prospectively enrolled from February 2018 to October 2018 to undergo SCP for the treatment of OA-related BML of the knee. The study was approved by the institutional review board and written informed consent was obtained from each patient included.

Inclusion criteria were age between 40 and 75 years, atraumatic and localized knee pain for at least 6 months with failure of previous conservative treatments, and an MR imaging (MRI) showing a BML located in the subchondral region of the tibial plateau and/or femoral condyle, in correspondence to the location of knee pain (\(\uparrow\) Fig. 1).

Exclusion criteria were: generalized knee pain, known autoimmune disorders, active malignancies or infections, OA > grade 3 according to Kellgren–Lawrence,\(^23\) patellofemoral OA > grade 3 according to Iwano classification\(^24\) associated with symptoms related to patellofemoral joint, and varus or valgus malalignment of the lower limb more than 10 degrees.

MRI images were analyzed with RadiAnt DICOM Viewer (Medixant, Poznan, Poland) and BMLs were mapped in axial, sagittal, and coronal view to measure the distance from the joint line and the nearest cortex and to plan the direction of the cannula.

Anteroposterior, lateral, and Merchant views were performed to grade osteoarthritic changes whereas full-length lower limb X-rays were performed to assess lower limb alignment.

All the patients underwent the same clinical and radiological evaluations and were assessed preoperatively and at 1, 6, and 12 months with Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and Knee injury and Osteoarthritis Outcome Score (KOOS) whereas pain was measured using the visual analog scale (VAS).

All the patients underwent X-rays evaluations immediately after the procedure and at 1, 6, and 12 months postoperatively whereas MRI evaluations were performed at 6 and 12 months. Intra- and postoperative complications were also recorded.
Surgical Technique and Postoperative Management

After the preoperative planning, the SCP procedure was performed with the patient in supine position under spinal anesthesia.

According to preoperative planning, the entry point of the cannula was marked on the skin with the aid of fluoroscopy on both frontal and lateral view. A skin incision was then performed and the cannula introduced until the bone. A second check with the aid of the fluoroscopy was done to identify the proper entry point. The cannula was then introduced and drilling was continued until it reached the lesion. A fluoroscopic check was done to control the exact position of the cannula and to assess that all the three holes of the side-delivery cannula were deep to the cortex and oriented in the desired direction.

The AccuFill Bone Substitute Material (ETEX Corporation, Cambridge, Massachusetts, United States) was then prepared until the proper viscosity was reached and introduced into the injured area, checking its distribution with the aid of fluoroscopy (►Fig. 2).

After the SCP procedure, arthroscopy was performed to check the intra-articular leakage of the bone substitute and to evaluate and address intra-articular pathology such as chondral flaps, loose bodies, and degenerative meniscal tears.

The postoperative management consisted of partial weight-bearing with the aid of crutches for 1 week and then full weight-bearing was allowed without any restrictions in terms of range of motion. Return to daily-life activities was encouraged as soon as tolerated.

Statistical Analysis

Statistical analyses were performed using RStudio v. 1.1.383 software (RStudio, Inc., Boston, Massachusetts, United States) and a $p$-value of $\leq 0.05$ was considered statistically significant. The Kolmogorov–Smirnov and Shapiro–Wilk tests were performed to assess the normality of the distributions. Descriptive statistics were calculated: paired Student’s $t$-test and the Wilcoxon matched-pairs signed rank test were used to test for significant differences between baseline and outcome score measurements.

Results

Ten of the 15 patients were male whereas 5 were female with a mean age at the time of surgery of $53.6 \pm 9.4$ years (range: 40–72). In seven cases, BML was located at the medial tibial plateau, in three cases at the medial femoral condyle, and in five cases both medial tibial plateau and medial femoral condyle were involved. At the preoperative X-rays evaluations, two patients had a grade 1 tibiofemoral OA, eight patients had a grade 2, and five patients had a grade 3 according to Kellgren–Lawrence, whereas according to Iwano classification five patients did not show any sign of patellofemoral OA, seven patients had grade 1, and three patients had grade 2. Six of the 15 patients have had previous surgery on the same knee; among these, four have undergone medial meniscectomy, one patient to an anterior cruciate ligament (ACL) reconstruction associated with a medial meniscectomy, and one patient has had a tibial tubercle osteotomy (►Table 1).

Table 1 Demographic data of patients treated with subchondroplasty

| No of patients | 15 |
|----------------|----|
| Mean age       | 53.6 years (range 40–72) |
| Sex            | 10 male |
|                | 5 female |
| Side of knee (%) | 9 right (60) |
|                | 6 left (40) |
| Location of BML (%) | 7 MTP (46.6) |
|                | 3 MFC (20) |
|                | 5 MTP and MFC (33.3) |
| Kellgren–Lawrence | Grade I: 2 patients (13.33%) |
|                | Grade II: 8 patients (53.33%) |
|                | Grade III: 5 patients (33.33%) |
| Iwano          | Grade 0: 5 patients (33.33%) |
|                | Grade I: 7 patients (46.66%) |
|                | Grade II: 3 patients (20%) |
| Previous surgery (%) | Partial medial meniscectomy |
|                | ACL reconstruction |
|                | Tibial tubercle osteotomy |
|                | 6 patients (40) |
|                | 4 patients |
|                | 1 patient |
|                | 1 patient |

Abbreviations: ACL, anterior cruciate ligament; BML, bone marrow lesion; MFC, medial femoral condyle; MTP, medial tibial plateau.

Fig. 2 Intraoperative fluoroscopic anteroposterior (AP) image showing the placement of the cannula and the diffusion of the calcium phosphate (CaP) in the medial femoral condyle.
Preoperative evaluations showed a mean WOMAC of 39.7 ± 20.2, a mean KOOS total score of 47.5 ± 16.6, and a mean VAS score of 55.8 ± 20.5 mm.

At follow-up assessments, significant increases were recorded in both WOMAC score, KOOS subscales, and VAS scale as detailed below (Table 2).

In comparison to preoperative values, WOMAC score 1 month postoperatively was 26.8 ± 16.1, showing a significant improvement (p = 0.045) which was maintained at 6-month follow-up when a mean value of 15.5 ± 12.7 was obtained (p = 0.02) and also at 1-year follow-up when a mean value of 8.6 ± 3.1 was recorded (p = 0.004).

KOOS score recorded 1 month postoperatively revealed a significant improvement in comparison to preoperative values (p = 0.013) and this improvement was also recorded 6 months after the procedure when a mean value of 80.4 ± 15.1 (p = 0.01) was obtained. KOOS at 1-year follow-up revealed a little improvement with a mean score of 85.6 ± 15.1 but no statistically significant differences were found with the 6-month mean value. Fig. 3 shows the distribution of KOOS subscales at the different evaluations.

### Table 2 Clinical scores preoperative and at 1 month, 6 months, and 1 year postoperative

| Clinical score | Preop Mean ± SD | 1 mo Mean ± SD | 6 mo Mean ± SD | 1 y Mean ± SD |
|---------------|----------------|---------------|---------------|---------------|
| WOMAC         | 39.7 ± 20.2    | 26.8 ± 16.1   | 15.5 ± 12.7   | 8.6 ± 3.1     |
| VAS           | 55.8 ± 20.5    | 36.2 ± 16.9   | 18.2 ± 17.3   | 12.8 ± 17.9   |
| KOOS–Pain     | 56.6 ± 19.6    | 61.3 ± 13.8   | 81.2 ± 14.6   | 88.1 ± 17.6   |
| KOOS–Symptoms | 56.5 ± 18.9    | 68.7 ± 14.6   | 81.2 ± 14.1   | 90.9 ± 11.3   |
| KOOS–ADL      | 64.1 ± 23.3    | 70.4 ± 16.3   | 85.6 ± 11.5   | 92.0 ± 13.6   |
| KOOS–Sports   | 23.7 ± 23.2    | 44.8 ± 24.8   | 66.5 ± 23.9   | 66.9 ± 20.9   |
| KOOS–QoL      | 30.3 ± 17.1    | 38.6 ± 21.5   | 65.3 ± 22.8   | 70.0 ± 24.0   |

Abbreviations: ADL, activity of daily life; KOOS, Knee Injury and Osteoarthritis Outcome Scores; QoL, quality of life; SD, standard deviation; VAS, visual analog scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

![Line graphs of Knee Injury and Arthritis Outcome Score subscales preoperatively and at 1-, 6-, and 12-month follow-up.](image_url)
In comparison to preoperative value, mean VAS significantly decreased to 36.2 ± 16.9 mm after 1 month (p = 0.008) and a further improvement was seen at 6-month follow-up with a mean value of 18.2 ± 17.3 mm (p = 0.005). At 1-year follow-up, VAS score showed a little progression with a mean value of 12.8 ± 17.9 without reaching a statistically significant difference from the value obtained at 6 months.

X-rays imaging in the postoperative period revealed increased density in the site where the CaP were introduced (Fig. 4A–D) whereas MR images showed an area of low signal intensity at the injection site (Fig. 5B, C).

In terms of complications, only one patient underwent an intraoperative complication with leakage of part of the CaP outside the tibia, which was immediately removed by enlarging the skin incision without any adverse outcome for the patient. None of the 15 patients showed a progression of the disease with a collapse of the joint surfaces.

Discussion

The most important finding of this prospective study was that SCP was able to provide a significant improvement in terms of pain relief and knee functional capacity in patients with chronic OA-related BMLs of the knee in which previous conservative treatment have failed.

At 1-year follow-up, pain improvement was 43 points on the VAS scale, in which the minimal clinically important differences (MCIDs) is 20 mm. Similarly, mean functional improvement on the WOMAC was 31.1 points for which MCID is 9.1, whereas KOOS showed a mean improvement of 38.1 points with a MCID of 8 to 10 points.

Traditionally, treatment of BMLs was based on nonsteroidal anti-inflammatory drugs, analgesics, and restricted weight-bearing especially in case of small lesions (< 3.5 cm²). More recently, pulsed electromagnetic fields and extracorporeal shockwave therapy.
achieved good results in the treatment of BMLs of the knee, though evidences are limited and long-term results have not been investigated yet.

Likewise, intravenous bisphosphonates\textsuperscript{34–36} and prosta-
cyclin analogs\textsuperscript{37–39} showed promising results in the treat-
ment of OA-related BMLs and early stage osteonecrosis in
terms of both functional recovery and BML area reduction.
However, further studies are needed to clarify indications,
safety, and posology of these drugs.

In case of failure of conservative treatment, surgical
approach is recommended and SCP is a recently developed
procedure in which a bone substitute material composed of
CaP is employed to treat chronic nonhealing BMLs.\textsuperscript{40} The
results of the present study are largely consistent with some
of the other studies that evaluated the effect of SCP in the
treatment of BMLs of the knee.

Sharkey et al\textsuperscript{21} were the first to describe the use of SCP in a
51-year-old woman with a chronic OA-related BML associ-
ed with disabling knee pain resistant to previous conserva-
tive treatment. The follow-up at 31 months showed excellent
clinical and functional outcomes and a complete resolution
of subchondral BML.

Farr and Cohen\textsuperscript{41} in a cohort of 59 patients with chronic
localized knee pain associated with subchondral BML
reported a significant pain reduction and functional im-
provement in 75% of patients at a mean follow-up of 14.8
months after SCP. However, the study showed a failure rate of
25% with 15 out of 59 patients who underwent a unicomp-
partmental knee arthroplasty or a TKA at a mean follow-up
of 10.1 months.

Chatterjee et al\textsuperscript{42} in a retrospective study on 22 patients
with OA-related BML reported a significant functional im-
provement \((p < 0.001)\) on the KOOS and Tegner–Lysholm
Knee Scoring Scale at a minimum follow-up of 6 months
after SCP associated with knee arthroscopy. Despite these
promising results, the authors advised against the use of SCP
since 10 out of 22 patients were considered clinical failure
according to clinical outcome categories of Tegner–Lysholm
Knee Scoring Scale, which was originally developed to eval-
uate ACL reconstruction and, therefore, not indicated in the
evaluation of the success rate of this treatment.\textsuperscript{43}

Cohen and Sharkey,\textsuperscript{22} in a study on 66 patients, demon-
strated at 2-year follow-up a significant improvement of 4.5
point on the VAS scale and of 17.8 points on the International
Knee Documentation Committee Subjective Knee Evaluation
Form. Moreover, at 2-year follow-up, the authors registered
a failure rate of 30%, since 18 patients underwent TKA.
Cohen’s failure rate was higher in comparison with that of
the current study. However, it should be noted that patient
selection was different with Cohen’s cohort including
patients with moderate to severe OA, initially presented
for arthroplasty consultation who, to the contrary, were
excluded from the present study.

Bonadio et al,\textsuperscript{44} in a case-series of 5 patients with OA-
related BMLs treated with SCP, reported a significant pain
relief with a reduction of 7.2 points on the VAS scale and a
significant functional improvement of 32.8 points on the
KOOS. However, these results referred to a short-term fol-
low-up of 24 weeks.

More recently, Chua et al\textsuperscript{45} reported very good results in a
cohort of 12 patients with chronic localized knee pain
associated with a traumatic or degenerative subchondral
insufficiency fracture detected with MRI. The authors dem-
strated immediate postoperative pain relief that persisted
up to 1 year with a reduction of 5.4 points on the VAS scale.
Moreover, as in the present study, a significant functional
recovery with an early return to activity of daily living was
evidenced by an improvement of 34.7 points on the KOOS
and of 33.5 on the WOMAC scale at 1-year follow-up.

Despite the good results, the present study has some
limitations. First, the follow-up period is limited to 1 year
whereas a study with a longer follow-up would be able to
better evaluate the durability of the improvement. Second,
arthroscopic treatment of intra-articular pathologies could
represent an important limitation since the relative contri-
bution of each procedure could not be evaluated. However,
it should be noted that several studies in patients with knee OA
showed that arthroscopic debridement was not able to
provide a durable relief of OA symptoms.\textsuperscript{46–48} Third, we
acknowledge that our results refers to a small, nonrandom-
ized cohort without a control group.

In conclusion, based on the results of the present study
and literature considerations, it is possible to claim that SCP
in the treatment of OA-related BMLs provide a significant
improvement in terms of pain relief and functional recovery
although on short-term follow-up. This safe, mini-invasive,
and joint-sparing procedure could represent a valid second-
line therapeutic option in the treatment of chronic OA-
related BMLs in which previous conservative treatment has
failed. Anyway, randomized controlled studies with broader
cohort and longer follow-up are needed to confirm these
promising results and to detect real benefits that SCP could
provide in the treatment of BMLs of the knee.

Conflict of Interest
None declared.

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