ISSN: 2634 - 680X

Journal of Clinical Case Studies Reviews & Reports

SCIENTIFIC Research and Community

Research Article

Open Access

# Subchondroplasty Bone Substitute Material (BSM) Histological Analysis after Total Knee Arthroplasty: A Case Series

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**ABSTRACT**

In our series of 227 patients who underwent prior Subchondroplasty of the knee wiht bone substitute material (BSM) we had the opportunity to review 4 cases which returned for conversion to Total Knee Arthroplasty (TKA). The average time to convert to a TKA was 23.5 months (18-35 months).

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**Received:** August 06, 2021; **Accepted:** August 13, 2021; **Published:** August 19, 2021

**Keywords:** Subchondroplasty, Bone Marrow Lesions, Bone Substitute Material

## Introduction

Bone marrow lesions (BMLs) are alterations of bone marrow signal intensity in subchondral bone that is identified on magnetic resonance imaging (MRI). Subchondral bone marrow signal changes can be seen in conjunction with trauma, trabecular necrosis, cyst formation, fibrosis, cartilage fragments, and osteoarthritis [1,2]. These lesions, more specifically in the pathologic process of osteoarthritis, are described as non-cystic subchondral areas of ill-defined hyper intensity on T2, proton density (PD), and Short-TI Inversion Recovery (STIR) weighted images, with high signal intensity on fluid-sensitive sequences which signify bone marrow edema [2]. In osteoarthritis, it has been well described that BML's can lead to cartilage defect formation with deterioration, and overall bone volume loss [3]. This disease process is likely secondary to repetitive stress loading, and overtime leads to subchondral bone attrition and progressive deformity from increased subchondral bone remodeling [4]. Naturally, these lesions can be a source of knee pain, decreased function, and rapid osteoarthritis progression and in some cases necessitates joint replacement surgery [5, 6]. Scher observed that BML's associated with osteoarthritis demonstrate a nine times increase in the likelihood that disease progression will necessitate total knee arthroplasty (TKA) within 3 years [2]. TKA or Unicondylar knee arthroplasty (UKA) are both surgeries that can ameliorate knee pain and increase function from osteoarthritis. However, despite the historical success of joint arthroplasty, they can be associated with various complications such as continued knee pain, hardware failure, and even prosthetic joint infections, which can ultimately necessitate revision surgery.

Subchondroplasty is an emerging less invasive surgical procedure designed to specifically address BML's by improving the structural integrity of the subchondral bone, preventing cartilage degeneration, and further joint collapse with the aim for pain reduction. In the subchondroplasty procedure, calcium phosphate bone substitute material (BSM) is directly injected into the prior identified BML and compromised subchondral bone under fluoroscopic guidance [7]. The goal of the procedure is to ameliorate knee pain as well as delay the progression of osteoarthritis, with the overall goal of native joint preservation. It has been proven in animal models that at both a cellular and molecular level the BSM will form a macroporous nanocrystalline matrix similar to native bone and overtime, through cell mediated remodeling, the BSM will be resorbed allowing new bone deposition [8]. Within the literature, however, there are mixed results on its efficacy [5,9,10]. To our knowledge there is no study that provides a histological analysis of bone after subchondroplasty in human subjects to evaluate its claims for BSM resorption and bone deposition at a histological level, as this can correlate with the procedures overall efficacy and patient improvement.

This case series describes two patients who originally had knee pain secondary to osteoarthritis with MRI's positive for BMLs. These patients both underwent subchondroplasty procedures to address these BMLs, and subsequently within two years were converted to total knee arthroplasties due to continued knee pain. These patients were specifically chosen for histological analysis because of their early conversion to TKA. Here we use histological analysis to evaluate the BSM's after subchondroplasty.

## Methods

A retrospective chart review was performed on two patients who had previous subchondroplasty procedures for BMLs and

subsequently underwent TKA. Preoperative imaging was reviewed as well as the gross and microscopic examination of bone from the regions of the prior subchondroplasties.

Patient one, R.C. a 69 year old male, obtained an MRI of the right knee which revealed a BML of the medial proximal tibia [Figure 1 (a,b)]. He subsequently underwent a subchondroplasty procedure on 3/3/2016 [Figure 1 (c,d,e)]. Twenty one months later, on 12/13/17, a right TKA was performed. The bone was carefully excised as part of the TKA in a single wafer specimen and sent to pathology department as per normal protocol. Analysis was performed in the hospital pathology department by an ASCP certified pathology assistant using standard preparation protocol.

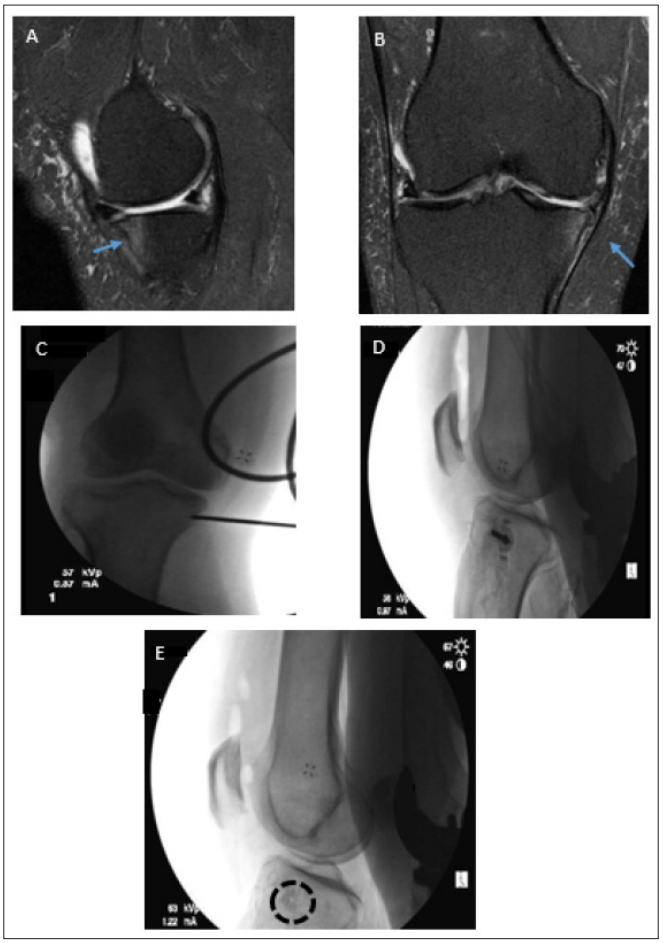


**Figure 1:** Bone marrow lesions on MRI and intraoperative fluoroscopic images. (A) Sagittal T2 Fat Sat MRI demonstrating bone marrow lesion (arrow) in anterior proximal tibial plateau. (B) Coronal T2 Fat Sat MRI demonstrating bone marrow lesion (arrow) in medial tibial plateau. (C) Intraoperative AP fluoroscopic image demonstrating placement of cannula in medial tibial plateau. (D) Intraoperative lateral fluoroscopic image with cannula injecting BSM. (E) Intraoperative Lateral fluoroscopic Image after injection of BSM (diffuse gray-shaded region within highlighted circle) into the medial tibial plateau.

After preparation, the tibial specimen was observed to contain BSM of calcium phosphate from subchondroplasty procedure, as well as adjacent normal bone (Figure 2a). Nine representative areas of the proximal tibia were chosen and labeled zones one through nine, which helped to analyze the interface between the BSM and surrounding medullary bone (Figure 2b) [1-6,8,11,12]. Following a standard decalcification process, each area underwent multiple histologic sections. The sections were stained with hematoxylin and eosin and then analyzed by a board certified pathologist. The findings were then confirmed by an independent bone pathology specialist.

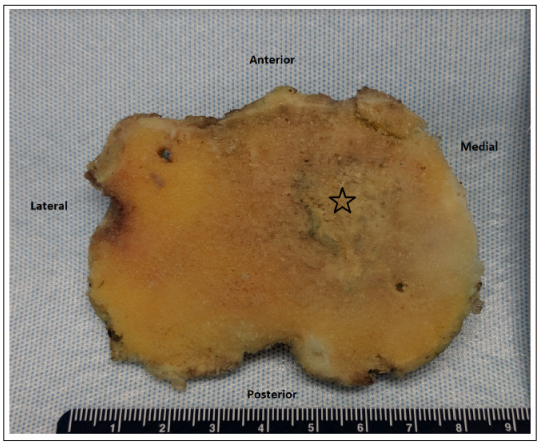


**Figure 2: (a):** BSM Visualized (star)

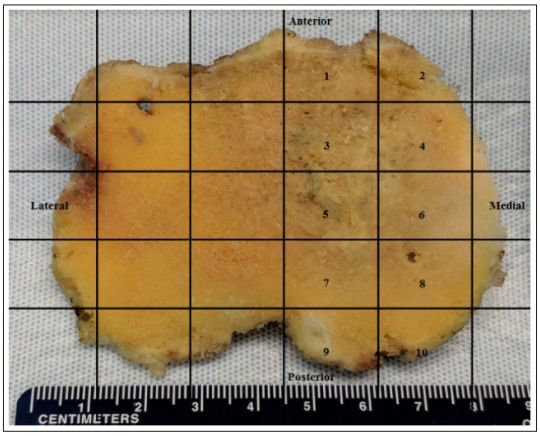


**Figure 2 (b):** key for corresponding histological analysis

**Figure 2 (a,b): Gross Specimen of Tibia**

Patient two, R.H. a 86 year old female, had left sided knee pain and underwent an MRI which revealed a BML of the medial femoral condyle [Figure 3 (a,b)]. She subsequently underwent a subchondroplasty procedure on 10/6/2016 [Figure 3 (c,d)]. Twenty-two months later, on 8/8/2018, a TKA was performed. The bone segment was then sent as a wafer specimen and analyzed in similar fashion as described in patient one [Figure 4 (a,b)].

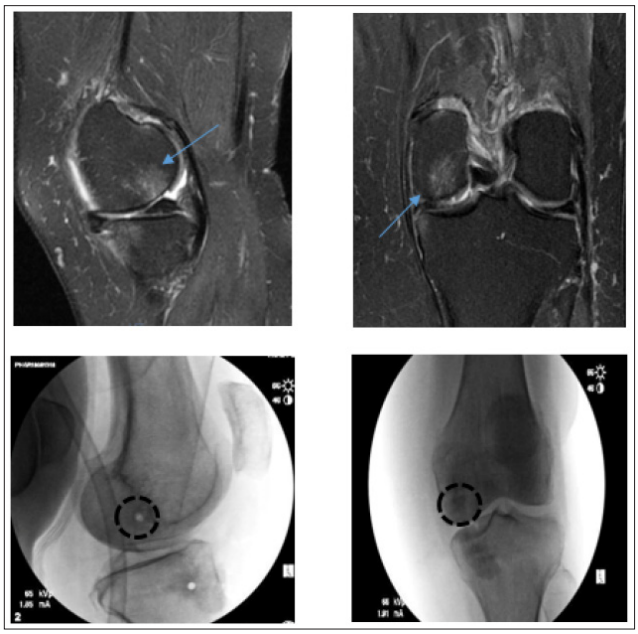

**Figure 3:** Bone marrow lesions on MRI and intraoperative fluoroscopic images. (A) Sagittal T2 Fat Sat MRI demonstrating bone marrow lesion (arrow) in posterior medial femoral condyle. (B) Coronal T2 Fat Sat MRI demonstrating bone marrow lesion (arrow) medial femoral condyle. (C, D)Intraoperative lateral and AP fluoroscopic image (respectively) after injection of BSM (diffuse gray-shaded region within highlighted circle) into the medial femoral condyle.

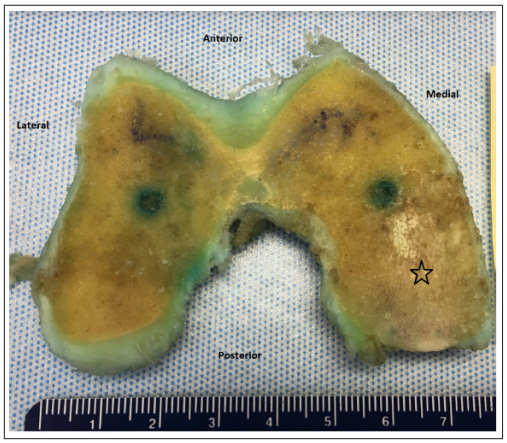


**Figure 4 (a):** Showing visible BSM (5 point star)

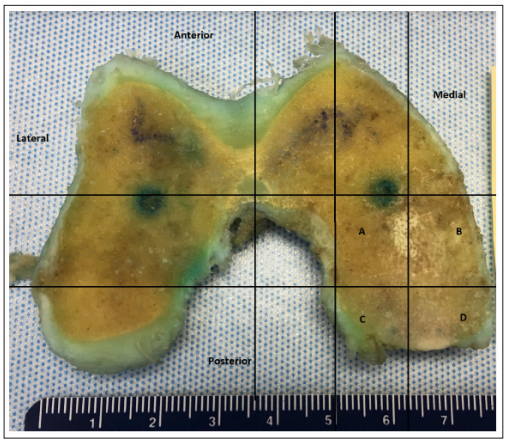


**Figure 4 (b):** Key for histological analysis (A, B, C, D)
**Figure 4 (a,b):** Gross specimen of distal femur

## Results

Patient One RC: After standard sample preparation the gross sample was further delineated with corresponding grid for histological analysis (Figures 2b and Figures 5a,b). In the gross specimen the BSM was clearly observed observed (Figures 2 a,b). Pathological analysis of the tibial segment demonstrated a variety of histopathologic features. Immediately subjacent to the articular cartilage, there was evidence of prominent osteosclerosis manifested by thickened lamellar bone plates (Figure 5a,b). Subjacent to this, there were histological features corresponding to the shape of the instilled cement material. The outer rim of the region consisted of prominent histiocytic infiltration including pigment laden histiocytes, which suggested an ongoing inflammatory reaction at the prior bone stimulating infusion. At the periphery of the infused region, there was evidence of remodeling of bone which created a pagetoid appearance. At the interface between viable bone and the histiocytic infiltrate, there was patchy lymphoplasmacytic infiltrate, likely a secondary phenomenon related to the aforementioned changes (Figure 5a). Bone inside the inflammatory rim showed evidence of osteonecrosis and necrosis of fatty marrow and some areas of the necrotic fragments of lamellar bone show evidence of resorption.

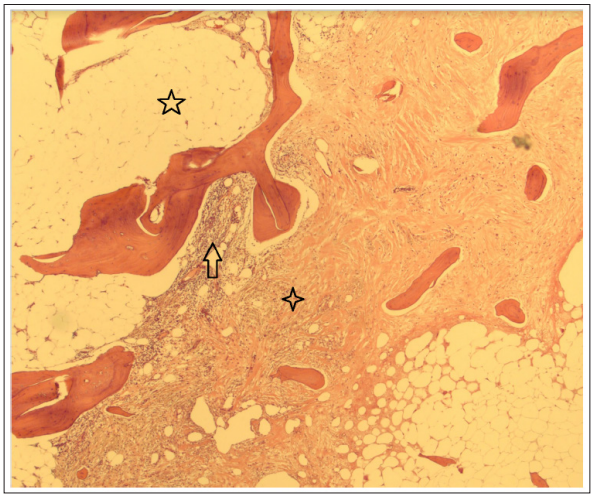

**Figure 5 (a):** 10x Magnification Showing Inflammatory Reaction of Lymphocytes (dark arrow), Histiocytes (4 point star) and Osteonecrosis (5 Point Star)

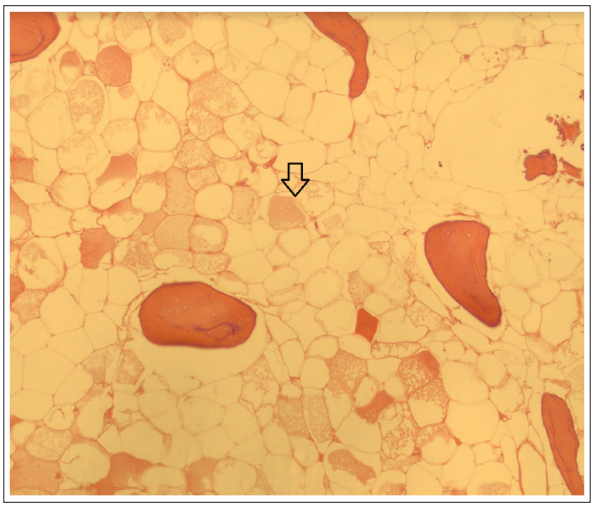

**Figure 5 (b):** 10x Magnification Show No Evidence of Bony Ingrowth and Remnant BSM (arrow) Figure 5 (a,b): Histological Slides from Section 3 of above key (Fig 2b)

**Patient Two RH:** After standard sample preparation the gross sample was further delineated with corresponding grid for histological analysis [Figure 4 (a,b) and Figure 6 (a,b)]. In contrast to the previous case, a well defined circular region with ingrowth of inflammatory tissues was not identified. There was a focus of medullary fibrosis with fibroblastic proliferation and associated new cartilage formation (Figure 6a). Surrounding bone showed prominent cement lines consistent with previous remodeling. The amorphous basophilic medullary material was not present in the previous specimen but may represent cement material which has not been dissolved during processing. (Figure 6b)

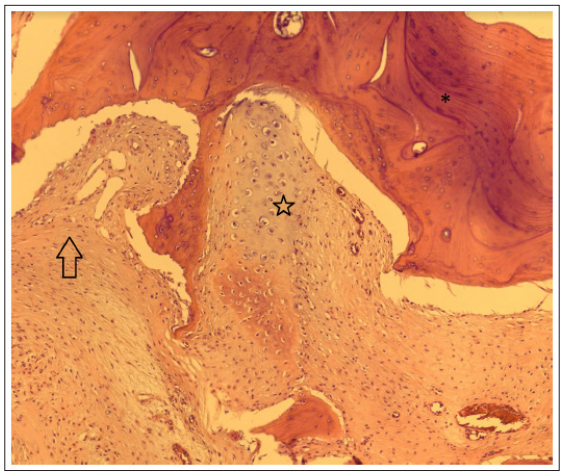

**Figure 6 (a):** 10x Magnification Fibroblastic Ingrowth (black arrow) with Cartilage Formation (5 point star) and Cement Lines (Sterisks)

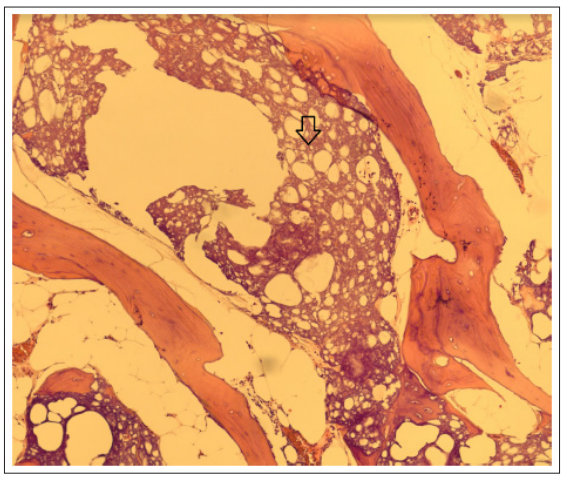

**Figure 6 (b):** Amorphous BSM (black arrow)
**Figure 6 (a,b):** 10x Magnification Histological Slides from Section A (See Figure 2b)

## Discussion

Various modalities for conservative treatment exist for the management of primary osteoarthritis of the knee, with the ultimate goal of native joint preservation, patient satisfaction, and maintenance of overall function until TKA is necessary. Though conservative management such as weight loss, medications, and physical therapy (PT) may aid in decreasing symptoms and delay the need for surgery, they are reported to have poor efficacy and are unlikely to reverse the clinical and radiographic disease progression [13,14]. Once non-operative interventions have been exhausted, minimally invasive joint preserving surgical options can be explored, and one such option described is the use of subchondroplasty.

It is projected that by year 2030, patients younger than 65 will be undergoing the majority of TKA surgeries, and the demand for these procedures will grow the fastest in the 40 to 54 age range [15]. This number is expected to increase by 17 fold and exceed almost 1 million arthroplasties per year [15]. With this surge in primary TKA surgeries in patients younger than 65, subsequently, the inherent risk for complications increases. Of these complications, including periprosthetic fractures and periprosthetic joint infections, aseptic loosening is the most common [16]. Jorgensen et al. found a 7.8% revision rate for aseptic loosening after 15 years for patients undergoing TKA less than 55 years old, compared to only 1% for patients older than 75 years old [17]. This elevated rate of aseptic loosening is likely attributed to the greater activity level in the younger patient and greater stress levels on the implant and soft tissues overtime.

Complications after TKA that lead to revisions can becomes a large medical and fiscal burden to the patient, surgeon and health system. Prosthetic joint infection and subsequent revisions are inherently morbid procedures with historically poor outcomes as compared to primary arthroplasty, which have been reported to exceed $1.62 billion by 2020 for both TKA and THA [7]. Petis recently described an overall increased risk of mortality of 11% at 2 years following reimplantation for revision total hip arthroplasty [18]. The most common reason for revision is due to aseptic loosening, which is mechanical failure of the prosthesis that leads to osteolysis, structural changes to the knee, instability, and ultimately hardware failure. As patients are receiving TKA's at a younger age, the increased activity levels these prosthetic designs undergo increases the risk for aseptic loosening. Revision surgery after aseptic loosening leads to increased operating room time, larger incisions for exposure, more technically demanding prosthetic designs in order to balance the knee, and these contribute to increased morbidity to the patient [19,20].

Subchondroplasty (SCP), developed in 2007, is a less invasive procedure compared to TKA procedure to treat osteoarthritic changes about the knee that utilizes an orthobiologic composed of calcium phosphate (CaP) bone substitute material (BSM). This BSM is designed to mimic the structure of human bone in order to facilitate cell mediated remodeling. The BSM structure is designed to be osteoinductive, highly porous and high in compressive strength, which are physical properties comparable to cancellous bone [8]. It is this similarity to bone that is said to allow for resorption and new bone deposition over time. The subchondroplasty procedure is performed under fluoroscopic guidance to aid in proper placement of BSM. It is also typically performed in conjunction with arthroscopy to improve accuracy of the injection, as well as, to diagnose and treat any intra-articular pathologies that could be causing pain. Sharkey performed a subchondroplasty in patients with primarily grade 3 or 4 OA changes diagnosed by arthroscopy [5]. At 2 years follow up patients demonstrated a significant decrease in subjective pain scores performed a mid-term follow up study of 32 months on patients who recently underwent subchondroplasty diagnosed BMLs on MRI. Patients demonstrated a significant decrease in pain post-operatively [9]. Also, the average time to conversion to a TKA was 2.5 years for 25% of the patients in the study. In a level IV case series analysis by Chatterjee, they recommended against the use of subchondroplasty in patients with grade III or IV chondral lesion due to fair to poor results in 10 of 22 patients. However, when analyzing the raw data, 20 of 22 patients (91%) actually demonstrated improvement from baseline in their Knee Injury and Arthritis Outcome Scores and Tegner Lysholm Knee Scoring Scale [10]. The authors attributed this improvement to the

concomitantly performed arthroscopy prior to subchondroplasty.

Our results show that in patient R.C. there was no evidence of bony ingrowth, however, in patient R.H. there was evidence of beginning bony ingrowth. These results, though mixed, demonstrate that failure of subchondroplasty procedure may be related to lack of bony ingrowth. We specifically wanted to review samples from cases in which the subchondroplasty was performed on a tibia and a femur, to see if the different locations might be a factor in determining the bioinductive nature of the BSM. Additionally it may be that these particular cases out of our series of over 200 subchondroplasties over a 5 year period, were having persistent pain at less than 2 years because the process of remodeling and bony ingrowth failed. The authors also suggest that the BSM and histologic response to the material is more closely related to the typical reaction of the body to a biocompatible implant. The value of the subchondroplasty in joint preservation may be in the BSM ability to act as a structure support for the surrounding bone not just as a biologic scaffold. Future studies can look at including larger cohorts, increased time from the index procedure for further determination of its efficacy and to analyze what factors may contribute to patient outcomes based on histological analysis [21-23].

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