# Extraction of Synovial Fluid from the Non-Effusive Pathologic Knee with Pneumatic Compression

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**Abstract**

**Objectives** –Aspiration of synovial fluid from non-effusive joints is undertaken for the diagnosis of crystal-associated arthritis, biomarker analysis, and to confirm intraarticular positioning. We hypothesized that pneumatic compression of the non-effusive knee would mobilize occult synovial fluid and improve arthrocentesis success.

**Methods** – The absence of a knee effusion was determined by physical examination, imaging, and exclusion of confounding disease. Conventional arthrocentesis was performed in 111 consecutive non-effusive knees and arthrocentesis volume (milliliters) determined. Pneumatic compression was then applied, and arthrocentesis was resumed.

**Results** – Pneumatic compression improved fluid yield: conventional: 0.4±1.0 ml, compression: 1.8±2.5 ml (319% increase, 95% CI -1.9<-1.4<-0.9; p=0.0001). Pneumatic compression reduced arthrocentesis failure (< 0.1 ml) from 74.8% (83/111) to 41.4% (46/111) (p=0.0001) and improved successful arthrocentesis in terms of adequate synovial fluid yield: 1) [?] 0.1 ml from 25.2% (28/111) to 58.5% (65/111) (+132%, p=0.0001), 2) [?] 0.5 ml from 22.5% (25/111) to 57.7% (64/111) (+156%, p =0.0001), 3) [?] 2.0 ml from 11.7% (13/111) to 47.7% (53/111) (+300%, p =0.0001), and 4) [?] 3.0 ml from 5.4% (6/111) to 36.0% (40/111) (+319%, p =0.0001).

**Conclusions:** Pneumatic compression of the non-effusive knee improves the extraction of synovial fluid of various requisite volumes for conventional and biomarker analysis.

## Introduction

Successful needle placement for diagnostic arthrocentesis of the obviously effusive knee is straightforward for the skilled proceduralist, and thus, successful arthrocentesis of the clinically effusive knee ranges from 96-100%, depending primarily on the amount of intraarticular fluid, the positioning of the knee, the local pathology of the knee (osteophytes, deformity, tophi, etc.), the anatomic approach, and technique including image-guidance [1-21]. However, previous studies have demonstrated a high failure rate of 38% to 68% of conventional arthrocentesis in unselected pathologic knees [1,12,20-22]. This high failure rate of arthrocentesis is primarily due to large proportion of "dry" or non-effusive knees; that is, knees without conventionally extractable fluid resulting in an arthrocentesis failure rate in non-effusive knees ranging between 82 -100% [1,10,19,20].

As reviewed by Pascual et al indications for aspirating the non-effusive knee are the following: 1) to diagnose crystal-associated disease (gout and pseudogout) during the intercritical period when there is no obvious effusion, 2) to confirm intraarticular needle positioning by synovial fluid return before injecting a joint with

a medication, and 3) to obtain synovial fluid for biomarker analysis [1-12,22-25]. As recently reviewed by Kraus et al biomarkers to classify and monitor the pathologic joint are an important area of research and new therapeutics [25]. For the diagnosis of crystal disease often only a few drops of synovial fluid are required; however, special analyses may require 0.1 ml or more and conventional analysis usually requires at least 2 ml [1-26]. To obtain adequate synovial fluid yield from the non-effusive knee, ultrasound guidance, stress maneuvers, joint lavage, and external compression may be used to obtain adequate synovial fluid volumes [12,20-29].

The present study specifically addressed the utility of ***pneumatic circumferential compression of the non-effusive knee*** to enhance arthrocentesis success by permitting extraction of resident occult synovial fluid.

# Methods

This Arthrocentesis Quality Improvement Program and data analysis was formalized in the Division of Rheumatology, Department of Internal Medicine, University of New Mexico Health Science Center. This was not a clinical trial, but rather a retrospective analysis of quality improvement data and was approved by Institutional Review Board (IRB) (approval Study ID: 20-662; approval end date: 10/26/2022) by the Human Research Review Committee of the Office of Human Protections at the University of New Mexico Health Sciences Center, Albuquerque, New Mexico, USA compliant with US law (US 45 CFR 46.110 category 5). The procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000. Patient confidentiality was protected according to the U.S. Health Insurance Portability and Accountability Act (HIPAA) and all data has been de-identified. All patients provided written consent to all examinations and procedures. As a Quality Improvement intervention, this project assessed the immediate improvement of knee arthrocentesis outcome before and after introduction of the quality intervention of pneumatic compression applied by a pneumatic blood pressure thigh cuff providing robust compression of peri- and intraarticular tissues of the knee during arthrocentesis without manual compression [30-32]. To provide greater statistical power, the retrospective study was designed as a paired study where each knee functioned as both baseline control and measure of intervention effect. Thus, each knee first underwent 1) standard arthrocentesis in the flexed knee position, and then 2) additionally, with the arthrocentesis needle left on place, underwent pneumatic compression-assisted arthrocentesis to obtain additional occult extractable synovial fluid, and differences in the volume collected were then determined. One hundred eleven non-effusive osteoarthritic (OA) knees were included in this study. Grade I-III OA of the knee was confirmed using radiography with exclusion of confounding syndromes by physical examination and laboratory testing [33]. The presence or absence of a knee effusion was determined clinically by palpation for suprapatellar bursa distention, ballottement of a floating patella, and fluid shift with asymmetric compression confirmed by physical examination. Inclusion criteria included: 1) a person 18 years old or older, 2) the presence of painful grade I-III OA of the knee, 3) the lack of the presence of a clinically palpable effusion, 4) indications for therapeutic-diagnostic arthrocentesis, and 5) formal signed consent of the patient to undergo the procedure. Exclusion criteria: 1) presence of confounding disease (inflammatory arthritides, aseptic necrosis, osteomyelitis, etc.), 2) an asymptomatic knee, 3) the presence of a palpable effusion, 4) a person less than 18 years old, or 5) vulnerable individuals including children, pregnant women, prisoners, or persons unable to provide consent.

### Arthrocentesis and Joint Injection Technique

A thigh blood pressure leg cuff (HCS 9029LF, Cuff and Bladder Latex-Free, Thigh Size, Sphygmomanometer, Dyad Medical Sourcing, LLC, 2101 Waukegan Road, Suite 208, Bannockburn, IL USA 60015) was placed around the superior flexed knee where it surrounded the upper leg and the suprapatellar bursa **(Figure 1).**

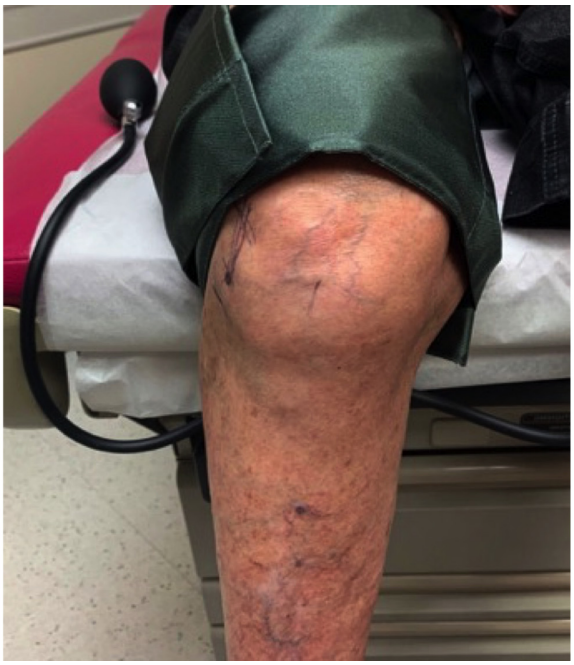

**Figure 1. Knee with Pneumatic Compression (front view). The pneumatic thigh blood pressure cuff is put snuggly over the superior knee in the flexed position.**

The patient was kept in the sitting position; the anterolateral portal was defined by the adjoining structures of anterolateral border of the patella, the lateral inferior border of the patellar tendon, and the lateral superior tibial plateau and marked by punctate skin depression using the front of a retractable pen with the point retracted [14,19,26]. The skin was first cleaned with chlorhexidine 2% for antisepsis. The one-needle multiple-syringe technique was used where 1) one needle is used for both anesthesia and arthrocentesis; and 2) a first syringe is used to anesthetize the synovial membrane and completely aspirate any effusion employing subsequent syringe exchanges as required if the effusion were large. A 22 gauge 2 inch needle (4710007050 – 22 GX2" (0.7X50 mm), FINE-JECT, Henke Sass Wolf, Kettenstrasse 1 D-78532 Tuttlingen, Germany) was mounted on a 3 ml syringe (3 ml Luer Lok syringe, BD, 1 Becton Drive, Franklin Lakes, NJ 07417, website: http://www.bd.com) filled with 3 ml of 1% lidocaine (Xylocaine® 1%, AstraZeneca Pharmaceuticals LP, 1800 Concord Pike, P.O. Box 15437, Wilmington, DE 19850-5437). With the knee in the flexed position, the 22 g needle was introduced through the skin and through the anterolateral portal of the knee, anesthetizing tissues during this introduction, directed towards the medial femoral condyle to the synovial membrane overlying the medial femoral condyle [19]. Arthrocentesis success and fluid yield were recorded. The needle was left intraarticularly, and the pneumatic thigh blood pressure cuff was then inflated to a pressure of 100 mm Hg so that the suprapatellar bursa and patellofemoral joint were compressed, but not the inferior knee **(Figure 2).**

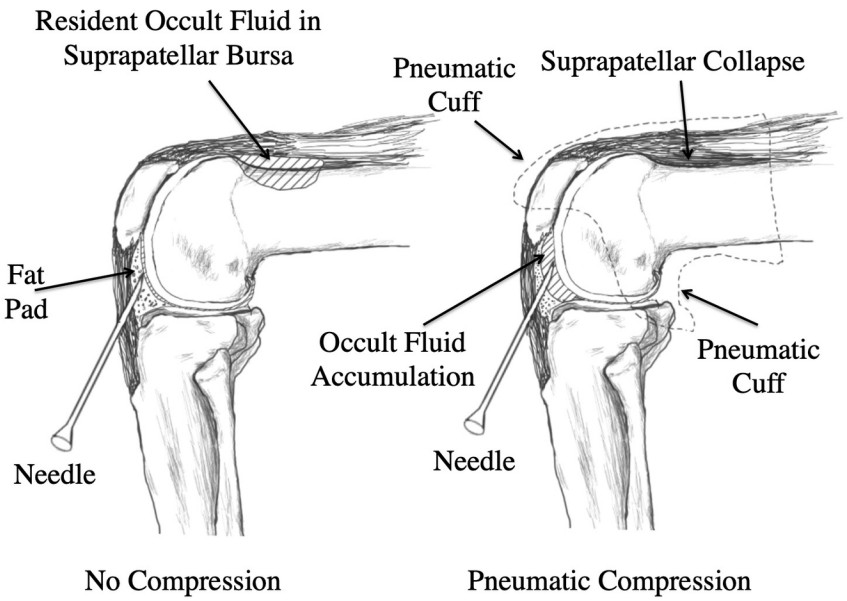


**Figure 2. Non-Effusive Knee with and without Pneumatic Compression (side view). The figure on the left is the flexed non-effusive knee with conventionally non-extractable occult synovial fluid in the suprapatellar bursa (diagonal hatch). The needle (Needle) does not access the synovial fluid because the fat pad (Fat Pad) (speckled area) puts pressure on the lower knee and forces any resident fluid to the suprapatellar bursa (diagonal hatch). The figure on the right represents the flexed non-effusive knee with the pneumatic thigh blood pressure cuff (Pneumatic Cuff) (broken line) that compresses the suprapatellar bursa that collapses (Suprapatellar Collapse) forcing the synovial fluid downward (Occult Fluid Accumulation) (diagonal hatch) over the cartilage surfaces of the femoral condyles and displacing the fat pad (speckled area). The synovial fluid (Occult Fluid Accumulation) over the femoral condyles can then be sampled by the needle (Needle).**

Placed this way, without the use of human hands susceptible to needle stick, the thigh cuff applies constant compression to the suprapatellar bursa, the synovial compartments of the superior medial and lateral knee, and patellofemoral joint, thus, collapsing these synovial compartments and forcing fluid inferiorly to the synovial reflections of the femoral condyles and cruciate ligaments where the fluid could be accessed **(Figures 2 and 3).**

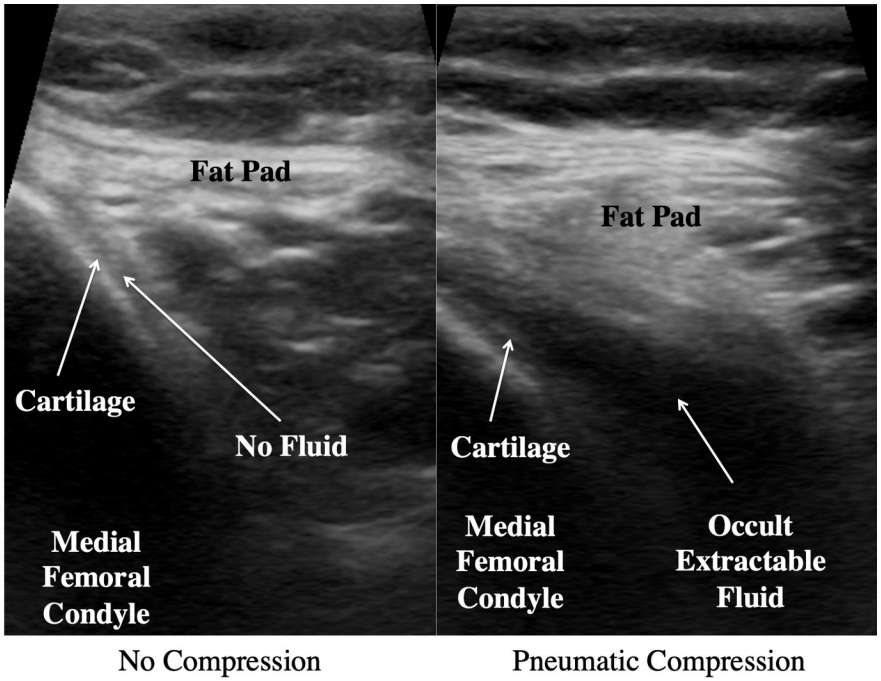


**Figure 3. Ultrasound Image of Non-Effusive Knee with and without Pneumatic Compression (medial knee). The figure on the left is the flexed non-effusive knee, where the needle (Needle) cannot access the synovial fluid because the fat pad (Fat Pad) forces fluid from the surface of cartilage to the superior knee (Cartilage). The figure on the right is non-effusive knee with the pneumatic compression that compresses the suprapatellar bursa and inducing collapse driving the occult synovial fluid (Occult Extractable Fluid) inferiorly where the fluid collects over the cartilage surfaces (Cartilage) of the medial femoral condyle (Medial Femoral Condyle) displacing the fat pad (Fat Pad). The synovial fluid (Occult Extractable Fluid) can then be accessed by the needle (Needle).**

After the pneumatic cuff was inflated to 100 mm Hg on the superior knee, 1-3 minutes were permitted to allow occult fluid to move from the superior knee to the inferior knee where it could be accessed **(Figure 3).** Arthrocentesis success, and fluid yield again were recorded. The needle was then extracted, and firm pressure applied to the puncture site.

**Outcome Measures:**

Patient pain was measured with the standardized and validated 0-10 cm Visual Analogue Pain Scale (VAS Pain Scale), where 0 cm = no pain and 10 cm = unbearable pain [28,34,35]. Pain by VAS was determined 1) prior to the procedure (baseline pain), 2) during arthrocentesis (procedural pain) and 3) immediately post procedure (post-procedural pain). Aspirated fluid volume was quantified in milliliters (ml). Arthrocentesis failure was defined as fluid yield as less than 0.1 ml. Diagnostic arthrocentesis success was defined in terms of adequate synovial fluid yield defined as the following requisite fluid yields: 1) [?] 0.1 ml, 2) [?] 0.5 ml, 3) [?] 2.0 ml and 4) [?] 3.0 ml. Patients were observed for serious adverse events.

***Statistical analysis*:** Data were entered into Excel (Version 5, Microsoft, Seattle, WA), and analyzed in Simple Interactive Statistical Analysis (Consultancy for Research and Statistics, Lieven de Keylaan 7, 1222 LC Hilversum, The Netherlands. A power calculation was made using preliminary data at this level where $\alpha$=0.0001, power = 0.9, and allocation ratio = 1.0 indicated that n=50 in each group would provide statistical power at the $p<0.05$ level, n = 75 in each group at the $p<0.02$ level, and n =100 at the $p<0.01$. Fisher's exact test with two by two table analysis was performed on categorical data calculating

both p values with significance reported at the P <0.05 level. Measurement data was analyzed using the Student t-Test calculating both p values and confidence intervals.

# Results

The demographics and characteristics of the study population and results are summarized in **Table 1**.

| | Conventional Arthrocentesis | Pneumatic Assisted Arthrocentesis | | | |
|---|---|---|---|---|---|
| Number of Knees | 111 | 111 | Percent Difference | 95% CI of difference (Wald) | P Value |
| Age* | 60.3±11.9 | 60.3±11.9 | 0 | false | 1 |
| Female Gender** | 78.4% (87/111) | 78.4% (87/111) | 0 | Not applicable | 0.13 |
| Pre-Procedural Pain* | 7.3±1.6 cm | 7.3±1.6 cm | 0 | false | 1 |
| Pre-Procedural Pain* | 3.9±2.5 cm | 3.9±2.5 cm | 0 | false | 1 |
| Pre-Procedural Pain* | 1.6±1.4 cm | 1.6±1.4 cm | 0 | -0.4¡0¡0.4 | 1 |
| Failed diagnostic arthrocentesis (¡ 0.1 ml)** | 74.8% (83/111) | 41.4 (46/111) | -0.45 | Not applicable | 0.0 |
| Successful arthrocentesis ([?] 0.1 ml) with compression** | 25.2% (28/111) | 58.5% (65/111) | 1.32 | Not applicable | 0.0 |
| Successful arthrocentesis ([?] 2.0 ml) with compression** | 11.7% (13/111) | 47.7% (53/111) | 3 | Not applicable | 0.0 |
| Successful arthrocentesis ([?] 3.0 ml with compression** | 5.4% (6/111) | 36.0% (40/111) | 5.67 | Not applicable | 0.0 |
| *Mean± **Standard Deviation, two-tail t-test** | | | | | |
| ****Fisher Exact Test** | | | | | |

Table 1: **Arthrocentesis of the Non-Effusive Knee with and without Pneumatic Compression**

The mean age of the cohort was 60.3±11.9 years. Male:female ratio was 24:87 (78.4% female). Pre-procedural pain according to the 10 cm VAS was 7.3±1.6 cm indicating a significant degree of pre-procedural knee pain. Procedural pain according to the 10 cm VAS was typically low at 3.9±2.5 cm, and post-procedural pain was 1.6±1.4 cm.

There were no serious adverse events encountered by the 111 patients in the cohort including but not limited to septic joint, reaction to local anesthesia, pseudoseptic arthritis, needle-stick, infection, hemarthrosis, deep venous thrombosis, dermal atrophy, significant bruising, hemorrhage or post-injection visits to emergency facilities.

Synovial fluid analysis usually requires two milliliters for conventional analysis, larger amounts for cellular assays, but very small amounts are generally required for crystal examination or biomarker analysis (as little as 0.1 ml or less), thus, segregating successful requisite yields for a particular assay is important [1-7,22-25].

Pneumatic compression improved successful arthrocentesis in terms of adequate synovial fluid yield defined as follows: 1) [?] 0.1 ml from 25.2% (28/111) to 58.5% (65/111) (+132%, p=0.0001), 2) [?] 0.5 ml from 22.5% (25/111) to 57.7% (64/111) (+156%, p =0.0001), 3) [?] 2.0 ml from 11.7% (13/111) to 47.7% (53/111) (+300%, p =0.0001), and 4) [?] 3.0 ml from 5.4% (6/111) to 36.0% (40/111) (+319%, p =0.0001) **(Table 1).**

In the non-effusive OA knee pneumatic compression improved mean arthrocentesis yield from 0.43+-0.85 ml to 1.8+-2.5 ml with pneumatic compression (319% increase, 95% CI of difference: -1.9 <-1.4< -0.9; p=0.0001) (**Figures 4 and 5**).

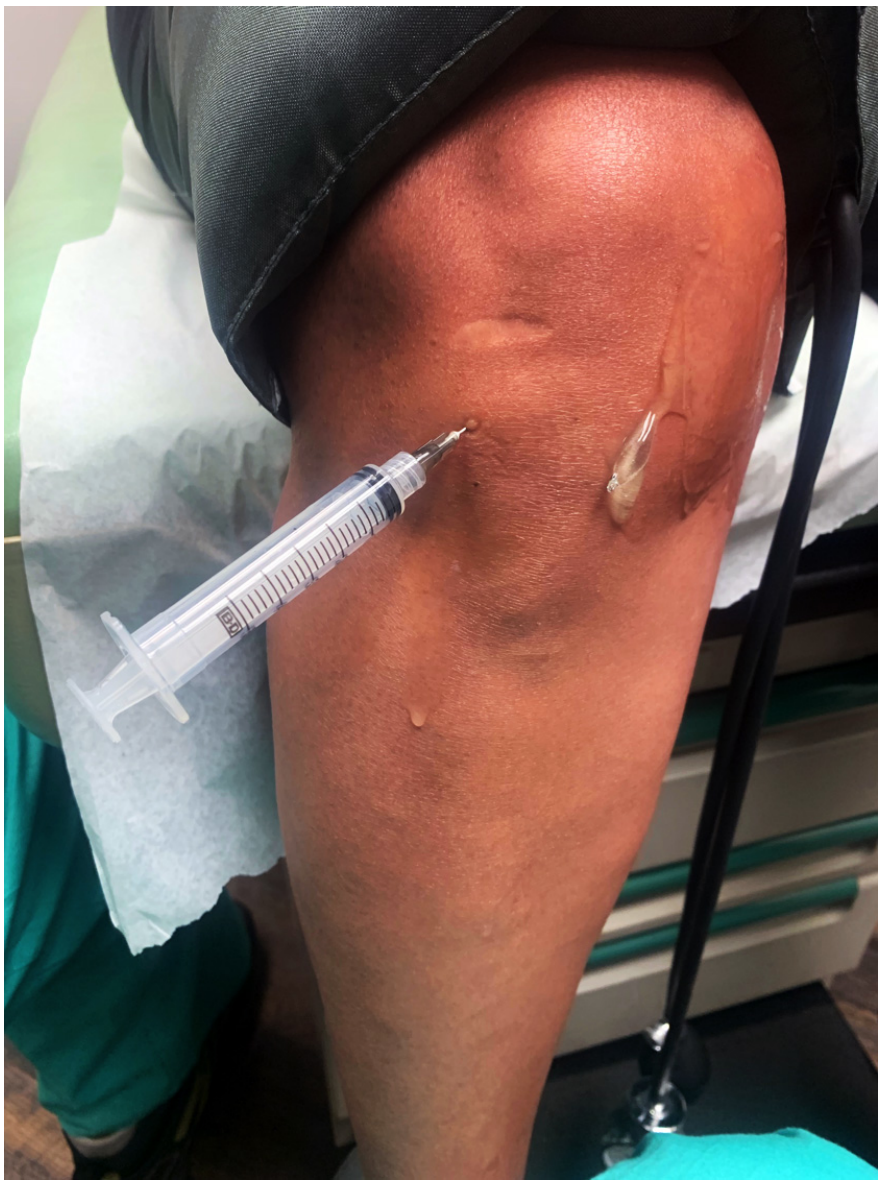

**Figure 4. Arthrocentesis in the Knee with Pneumatic Compression. After pneumatic compression at 100 mm Hg is applied to the patellofemoral joint and suprapatellar bursa with the pneumatic compression cuff, fluid flows down into the lower knee where it can be accessed by the anterolateral portal.**

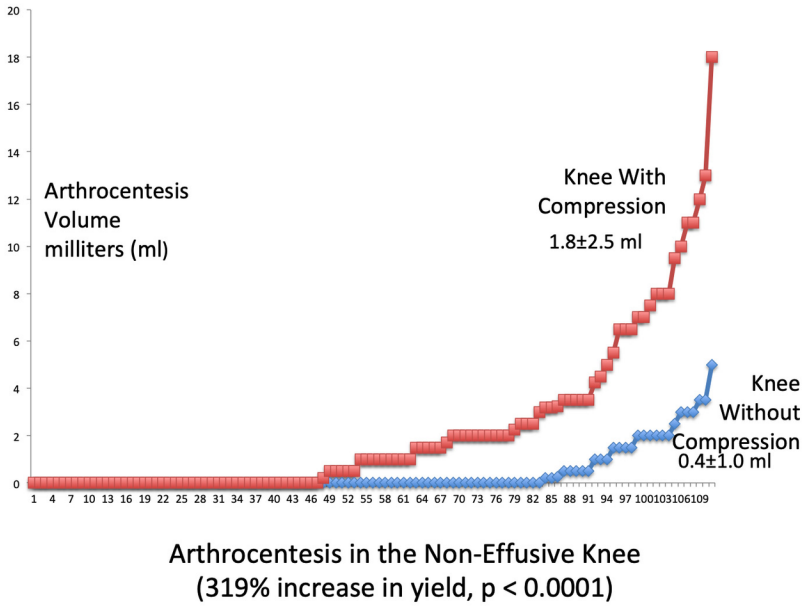


**Figure 5. Arthrocentesis Volume with Pneumatic Compression of the Flexed Knee. This graph demonstrates the fluid yield with and without pneumatic compression of the flexed knee using the anterolateral portal. Pneumatic compression resulted in a 312% increase in fluid yield (p<0.0001).**

Thus, pneumatic compression as a quality improvement measure markedly improves the success rate and yield of extraction of synovial fluid in the dry, non-effusive knee.

# Discussion

Extraction of synovial fluid for crystal examination and cellular, immunologic, biomarker and metabolic analysis is presently an important area of clinical care and research integral to current and future joint preservation strategies and therapies [1-10,12,22-25]. Thus, obtaining at least a minimal volume of synovial fluid from a painful or pathologic knee is important diagnostically, prognostically, for accurate injection of therapeutics, and scientifically, especially for research and development of precision arthritis therapies [20-27]

In the current study we report significant improvement in terms of arthrocentesis fluid yield and diagnostic success from pneumatic compression of the non-effusive knee **(Table 1, Figure 5).** Using the flexed knee positioning, 111 consecutive clinically non-effusive OA knees underwent arthrocentesis using a standard anterolateral portal. Subsequently, the superior knee and suprapatellar bursa were compressed with a pneumatic blood pressure cuff to 100 mg Hg, arthrocentesis was again attempted with marked improved arthrocentesis success. Unlike previous reports that used a specialty compression cuff, the present study demonstrates that a widely available, inexpensive conventional thigh blood pressure cuff can be used to provide circumferential pressure to effectively extract fluid from the non-effusive knee [12,20,21,26,27].

The inability to fully extract synovial fluid from the non-effusive knee is due to minimal resident synovial fluid, the thin synovial fluid layer over the cartilage surfaces, mistargeting by the needle, and the complex foldings of the villi and discrete intraarticular synovial compartments that retain viscous occult synovial fluid [9,10,21-29,36,37]. The present study demonstrates that external pneumatic compression of the non-effusive knee **(Figure 1)** mobilizes occult synovial fluid, dilates the joint space target with displaced occult

fluid **(Figure 2)** and permits fluid flow to the femoral condyles where the synovial fluid can be accessed using the anterolateral portal **(Figure 3)** [19,37-42].

The subset of clinically "dry" non-effusive knees without objective fluid have a high conventional arthrocentesis failure rate ranging between 82%-100% [1,10,19,20]. In the present study, we confirm a high failure rate (defined as <0.1 ml) of 74.8% with conventional arthrocentesis of the non-effusive knee **(Table 1)**. Because of this high arthrocentesis failure rate, ultrasound guidance and joint lavage - where fluid is injected in the joint and then aspirated - have been increasingly used in the non-effusive knee to obtain adequate synovial fluid for conventional and biomarker analysis [11,22-25]. Kraus et al have described an effective technique of joint lavage with a dilution correction to obtain samples from the non-effusive joint for biomarker analysis [23]. The present study without lavage or ultrasound guidance demonstrated marked improvement of arthrocentesis success in the non-effusive knee using pneumatic compression compared to conventional arthrocentesis **(Table 1)**.

An important aspect of performing arthrocentesis using the anterolateral portal is that at least a 2-inch (5.1 cm) needle is required so that the needle can predictably access the fluid layer over the femoral condyle [19]. Also, despite pneumatic compression forcing synovial fluid from the suprapatellar bursa and superior knee to the femoral condyles where the fluid could be accessed, the fluid over the femoral condyle was layered quite thin dimensionally due to the restricted compressibility of adjacent fat pad **(Figures 2 and 3)**. Thus, the needle often had to be rotated in the long axis so that the needle bevel was properly positioned in the fluid layer (**Figure 3**).

When the pneumatic thigh cuff was inflated to 100 mm Hg and compressed the suprapatellar bursa, synovial fluid flow was typically languid, often requiring 1 to 3 minutes to flow from the suprapatellar bursa to the lower compartments of the knee where the fluid was accessible for aspiration. Therefore, because of the viscous properties of synovial fluid, it was useful to inflate the cuff and wait several minutes until the fluid had completely been displaced [23-25,36-38]. Further, during the extraction process the operator should realize that additional synovial fluid will accumulate at the extraction point with time and that the procedure should not be aborted prematurely.

A conventional pneumatic thigh blood pressure cuff to compress the knee during arthrocentesis has a number of advantages. Pneumatic thigh blood pressure cuffs are usually available in most clinics and offices, and therefore the technology is already at hand, obviating the need for ordering and stocking an expensive specialized compression cuff [27,29]. Further, using the anterolateral portal and the flexed knee sitting positioning, blood or extravasated synovial fluid from the puncture wound tends to stream down the leg, not up, thus the cuff remains uncontaminated by patient fluids (**Figure 4**). There are also commercial covers made for blood pressure cuffs that may be used between patients and then disposed.

A potential limitation to this study is that ultrasound guidance was not used to target the synovial fluid [11,16,18,27,28]. However, it is anticipated that with ultrasound guidance pneumatic compression will be even more effective to provide synovial fluid samples [27,28]. In this study the anterolateral portal was utilized instead of the lateral suprapatellar or lateral midpatellar approaches [13-19]. In the non-effusive knee, the suprapatellar approach to arthrocentesis generally fails because the suprapatellar bursa is collapsed and inaccessible and thus the needle is driven into adjacent soft tissues including the fascia, quadriceps muscle and tendon, adipose tissues or patella [18]. Another approach to the noneffusive knee is the lateral midpatellar approach with the patellofemoral joint targeted; however, although the needle can usually be accurately placed in the joint, this approach generally fails for arthrocentesis because fluid does not pool in the patellofemoral joint due to pressure of the patella on the anterior femur driving fluid to other areas [17].

In contrast, the anterolateral approach uses the cartilage surface of the medial femoral condyle to define the joint surface with a palpable "hard-stop" where the needle cannot go further defining the cartilage surface [19,38-42]. Using the anterolateral portal approach in the non-effusive knee, multiple studies have demonstrated excellent accuracy of intraarticular needle placement in respectively 97.1%, 93%, 89%, 87.8%, and 87.4% of knees and this approach is less painful than the traditional superolateral or lateral midpatellar

approaches [19,38-42].

There are further potential limitations to this study. This study did not use an randomized controlled design, but rather used a paired-study design where each knee served as it's own control that, although providing a robust structure for determining improvements in individual extractable fluid and arthrocentesis yield, could not eliminate a consistent bias. However, this paired sample design is a standard practical study design for quality improvement studies in all institutions [12,30,31]. Although pneumatic compression markedly reduced arthrocentesis failure in the non-effusive knee, volumes of synovial fluid >0.1 ml were still obtained from only 58.5% of non-effusive knees even with compression. Thus, if larger volumes of synovial fluid were absolutely required for analysis, another additional technique such as ultrasound guidance or injection lavage would be required in the remaining 41.4% of arthrocentesis failures in the non-effusive knee [2,21,22]. Further, we did not report volumes <0.1 ml (**Table 1**), thus, in the majority of the cases with <0.1 ml yields, a few drops of synovial fluid were still obtained and these were probably adequate for crystal analysis [1-7]. Injection lavage to obtain synovial fluid, although very effective to obtain diluted samples, involves extra time, more procedural steps, more costs, and more manipulation of the joint – thus with compression fewer of these lavage procedures may be necessary [1-7,22,23]. On the other hand, the present pneumatic compression technique could also be combined with the injection lavage technique to permit more complete fluid extraction of injected lavage fluids [21].

## Conclusions

Pneumatic compression with a thigh blood pressure cuff improves the success rate of arthrocentesis and the yield of occult extractable synovial fluid volume in the typically arthrocentesis-resistant dry, non-effusive knee. This inexpensive and widely available pneumatic compression technology used alone or in combination with ultrasound guidance or lavage should be useful for providing adequate synovial fluid return from non-effusive pathologic knees for confirmation of intraarticular needle placement during intraarticular procedures and for crystal, biomarker and conventional diagnostic analyses.

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## Conflict of Interest:

None of the authors declare a conflict of interest. The authors have full control of all primary data and that they agree to allow the journal to review their data if requested.

## Ethical Standards:

This research was approved by Institutional Review Board (IRB). The procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000. Patient confidentiality was protected according to the U.S. Health Insurance Portability and Accountability Act (HIPAA) and all data has been de-identified. All patients provided written consent to all examinations and procedures.

## Clinical Trial:

This was not a clinical trial but a retrospective analysis of quality improvement data.

## Data Availability:

Summary data are presented in the article. However, raw deidentified data can be provided on request but must be attributed in any publication.

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