Continuous infusion pain pumps following joint arthroscopy

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2010
Dedication

This review is dedicated to my fiancée, parents, and friends. They have all helped, guided, and supported me throughout not only this process, but throughout my entire education. I could not have completed it without them.
Acknowledgements

I want to especially acknowledge Jay Peterson, PA-C, my advisor for this project. I appreciate his guidance, focus, and willingness to work around my schedule to make this project a success.
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**Introduction**

As recently as the early 1980s, nearly every surgical procedure was performed in a hospital setting, with patients generally spending several postoperative days recovering in the hospital (Ambulatory Surgery Center Association). At that time, only about 400,000 surgeries were performed in an outpatient setting annually. However, surgeries that require lengthy hospital admissions are becoming a thing of the past. For example, during the year 2000 approximately 8.3 million (75%) surgeries performed in the United States occurred in ambulatory or outpatient operating rooms (Ambulatory Surgery Center Association). Accordingly, there has been an 8.3% average annual increase in the number of ambulatory centers accredited by JCAHO (Ambulatory Surgery Center Association).

The increase in outpatient surgeries is especially common within orthopedic medicine, as many of the diagnostic and therapeutic procedures they perform are able to be done via arthroscopy. For instance, repairs of rotator cuff tears alone account for a great deal of arthroscopic procedures. It is estimated that complete supraspinatus tears are found in up to 20% of those over 32 years of age, up to 30% of patients over age 40 years, and as many as 80% of those over age 60 years, demonstrating the commonality of such injuries (Wheeless, III). Sherman et al. further states that rotator cuff repairs rose from 6,656 in 1997 to 10,128 in 2002 (Sherman, Lyman, Koulouvaris, Willis, & Marx, 2008). At one point, these repairs would have been done through open surgery, and although the effectiveness was well established, significant postoperative pain and morbidity led to the need for arthroscopic procedures. As such, outpatient rotator cuff repairs rose from 57% to 82% between 1997 and 2002 (Sherman, et al., 2008).

Arthroscopy is a very common surgical technique that is used for a wide array of musculoskeletal pathology. It is not only important for reconstruction of the shoulder, but is also
commonly used for knee procedures, as well as other joint reconstructions. For example, meniscal tears are among the most common injuries of the knee, occurring in approximately 61 individuals per 100,000, resulting in nearly 850,000 meniscal reconstructions per year (Baker, Peckham, Pupparo, & Sanborn, 1985). As with rotator cuff repairs, open reconstruction is a reasonable choice for repair, but since this procedure results in a great deal of postoperative pain and longer rehabilitation, most orthopedic surgeons are choosing to perform arthroscopic repairs.

Due to the drastic increase in the number of annual outpatient surgeries, a change in postoperative patient management had to change as well. Inpatient procedures provide the opportunity for continuous care by trained medical staff throughout much of the postoperative course, resulting in a much broader spectrum of pain management choices, such as intravenous medications. Patients undergoing similar procedures through an outpatient setting, however, do not receive care from trained medical staff beyond the one to two hours following surgery while recovering from anesthesia. As such, the focus of care for outpatient procedures is becoming centered on proper management of pain; specifically, management that does not require medical decision making or surveillance by those with advanced medical training.

Management of postoperative pain is of such importance because it serves as one of the key indicators of surgical outcomes. Severe postoperative pain is associated with delays in discharge and recovery due to inability to participate in rehabilitation programs (Rawal, 2007). Additionally, untreated severe pain has deleterious effects on neuroendocrine function, respiration, GI function, circulation, and autonomic activity. Therefore, better control of pain results in better surgical outcomes (Rawal, 2007).

Many gains have been made in the field of pain control research. For example, recent developments have led to the development of new classes of pain medication, like non-opioid
pain medications and local anesthetic medications (Rawal, 2007). Also, medications that have been used for decades are now being used in new, more effective combinations (Rawal, 2007). There are also new developments in the way that pain medications are being delivered. One of the most popular delivery systems currently in place involves the use of intra-articular pain pumps. These pumps utilize catheter tubing that is implanted directly into the surgical area and function to deliver continual pain medication in the days following surgery (Rawal, 2007).

**Intraarticular Pain Pump Mechanics**

The continuous pain medication delivery systems, known as pain pumps, are being used in multiple areas throughout the body. For many years they have been used for procedures in the foot and iliac crest, and have recently gained popularity for use in the glenohumeral and knee joints (Barber & Herbert, 2002).

The pumps consist of an external reservoir for the medication that is to be infused and tubing that extends from the device to the surgical site. The tubing catheters are placed under direct visualization at the completion of the surgery, but are easily removed by the patient in their home, in the medical office by medical assistants, or by physical therapists at the initial therapy session (Busfield & Romero, 2009).

There are different varieties of pumps, allowing the surgeon to choose the one that best fits individual patient needs. Pain pumps differ on total capacity of the reservoir, thus dictating the total amount of medication that can be delivered, generally between 100 mL and 300 mL of medication. They also differ on the rate of medication infusion, ranging from 2 mL/hr to 6 mL/hour. Additionally, some pumps offer a patient-controlled feature that gives them the option for additional boluses of medication every one to two hours as needed. This regimen of pain
control ensures the patient is always receiving a controlled amount of pain medication, while still allowing them flexibility to increase the dosage as their pain dictates (lmana.com/pain-management/pain-care-3000.php).

Once inserted, the pumps are able to infuse a range of medications, making them effective in a variety of settings. Bupivacaine and lidocaine, two forms of amide local anesthetics, are two very commonly infused medications through the pumps. Epinephrine, a vasoconstrictor, may also be added to the local anesthetic as an adjunct medication to extend the duration of action of the primary medication (Dragoo, Korotkova, Kanwar, & Wood, 2008). These medications may also be delivered in different concentrations, with bupivacaine most commonly delivered in either the 0.25% or 0.5% concentrations and lidocaine in the 1% or 2% concentrations (Dragoo, et al., 2008). Based on the different needs of individual patients, the surgeon is able to choose the safest and most effective form of treatment. For example, following a very labor-intensive surgery that generally yields a high level of postoperative pain, such as arthroscopic or mini-open rotator cuff repair, a pump infusing 0.5% bupivacaine and epinephrine may be warranted (Fontana, et al., 2009). Conversely, a surgeon may choose to use a pump infusing 0.25% bupivacaine without epinephrine following a surgery that generally results in less postoperative pain, such as following knee arthroscopy (Marchal, Delgado-Martinez, Poncela, Valenzuela, & de Dios Luna, 2003)

**Physiology of Amide Local Anesthetics**

Local anesthetics function through blockage of nerve conduction along action potentials (McLure & Rubin, 2005). Specifically, they work on voltage-gated ion channels which are dependent on differences in membrane potential dictated by sodium, potassium, and calcium ions.
Membranes are composed of two functional gates, an inner h gate and outer m gate. Under resting conditions, the outer m gate is closed and the inner h gate is open, allowing the membrane to function between -70mV to -90mV, known as the resting membrane potential. When stimulated, the membrane undergoes a conformation change that opens the outer m gate and allows an influx of positive sodium ions. This influx causes the membrane potential to rise, making the membrane more positively charged. Once the membrane reaches -60mV, an even larger influx of ions is allowed into the cell, resulting in an overshoot of the membrane and causing it to reach +20mV. Then, once the membrane charge is positive, the inner h gate is forced to close, inactivating the sodium channels and preventing further ion influx.

Each ion channel consists of pore-forming α-subunits and β-subunits, and the α-subunit is further divided into four domains (D1-4) that each contains six helical transmembrane segments (S1-6). Local anesthetics stop nerve conduction by reversibly binding to the D4-S6 part of the α-subunit. This binding occurs intracellularly, so the medication must cross the lipophilic lipoprotein membrane in order to enter the nerve cell. To cross, the medication must be in a neutral, unionized form. However, the drug is only active in the ionized, soluble form, so local anesthetics must be administered in an acidic solution. Then, once inside the cell, the lower intracellular pH allows the anesthetic to return to its original ionized form. At this point, the receptor within the sodium channel is blocked, thus stopping the upsurge of the membrane potential and conduction of the action potential. Therefore, the resting membrane potential is never altered and impulse conduction cannot continue.

The degree to which an impulse is blocked depends on the diameter of the nerve, such that larger diameter nerves require higher concentrations of local anesthetic to achieve a given block. Large diameter nerves are those responsible for touch, pressure, and motor fibers.
Conversely, small diameter fibers, like pain afferent fibers, require a lower concentration of local anesthetic to achieve the same degree of block as high concentration local anesthetic on large diameter fibers. Due to this difference in nerve diameters, sensory modalities are lost in sequential order, with pain disappearing first, temperature sensation next, followed by touch sensation, deep pressure sensation, and finally motor function.

Further, the degree of block is also dependent upon the affinity of the local anesthetic for its respective binding site. This affinity is based both on the state of conformation change as well as the individual properties of each local anesthetic. Specifically, when sodium channels are open, the affinity of local anesthetics for sodium channels is high because more binding sites are revealed. However, during the deactivated or resting phases, sodium channels are closed and the binding sites for the local anesthetics are hidden. This property can be used advantageously through increasing the frequency of nerve stimulation, causing the sodium channels to be in their activated states more often, thus resulting in a greater degree of neuronal block. However, different local anesthetics bind more tightly than others, so this too alters the amount of block. For example, lidocaine binds and dissociates from the channel quickly, while bupivacaine binds rapidly but dissociates more slowly, allowing the nerve blocking potential to last longer than that of lidocaine.

**Continuous Infusion Amide Local Anesthetic Side Effects**

Opioid-type medications have been used as a mainstay of pain relief for centuries, with their use being documented as far back at 3400 B.C. Opioid medication use, however, is not without potential side effects (Benyamin, et al., 2008). Most notably, opioid administration can cause immunologic suppression, opioid-induced hormonal changes, hyperalgesia, sedation, sleep
disturbances, nausea and constipation, bladder dysfunction, as well as respiratory depression. Additionally, these medications are also associated with a high degree of addiction and dependency with their use. However, they continue to be prescribed for many types of chronic and acute pain episodes, including in pre-, intra-, and post-operative settings (Benyamin et al. 2008). As such, continuous infusion pain pumps have gained popularity as a means of both controlling pain and limiting the use of opioid medications.

Although their side effect profile may be different than that of opioid type medications, continuous infusion pumps do carry their own set of risks. Recently, research has raised questions about whether or not they truly are a safe from of postoperative pain management. Local anesthetics have been used for decades in short-term, low-dose single injections, but are now only recently being used for longer durations and in larger doses. As such, their side effects are just now becoming apparent. The FDA recently became aware of possible problems associated with the continuous infusion of local anesthetics via pain pumps. In November 2009, the FDA issued the following warning: “Local anesthetics are approved as injections for the production of local or regional anesthesia or analgesia. The approved drug labels for local anesthetics do not include an indication for continuous intra-articular postoperative infusions or use of infusion devices, such as elastomeric pumps. The FDA has not cleared any infusion devices with an indication for use in intra-articular infusion of local anesthetics. Health care professionals are encouraged to follow the instructions for use of elastomeric infusion devices, and to not use these devices for continuous intra-articular infusion of local anesthetics after orthopedic surgery.” (US Food and Drug Administration).

Due to the popularity and rapid increase in the use of pain pumps and the recent FDA warning regarding potential hazards of pain pump use, the purpose of this clinical review is to
determine whether or not the pumps are a safe and effective alternative to the traditional methods of pain control. Specifically, the aim of this review is to outline the circumstances in which the infusion of local anesthetics has adverse effects that outweigh the advantages of their use.

**Effects of Local Amide Anesthetics on Chondrocytes**

Chondrolysis is defined as the “disappearance of articular cartilage as the result of lysis or dissolution of the cartilage matrix and cells” (Bogatch, et al., 2010). Although there is no proven etiology for chondrolysis following the use of intra-articular local amide anesthetics, there has been minimal research on the effect of pH. Due to the membrane properties discussed earlier in the review, local amide anesthetics must be delivered in an acidic solution and then use the basic intracellular properties to become active. A study done by Bogatch et al., however, showed that the more acidic the injected solution, the greater degree of cellular death. They used bovine chondrocytes for their study, harvesting fresh chondrocytes from 3-week-old calves and then allowing them to mature for no more than four weeks. They used a total of 300,000 cells, which were broken into different treatment groups. Groups were broken into commonly used concentrations for use in intra-articular pain pumps, and consisted of 1% lidocaine (pH 6.0), 0.25% bupivacaine (pH 5.9), 0.25% bupivacaine with epinephrine (pH 7.0 and pH 3.9), and 0.5% bupivacaine with epinephrine (pH 3.9). Treatment groups were compared to a control consisting of phosphate buffered saline (PBS) with a pH of 7.1. Other groups were also used to strictly determine the effect of pH, and these consisted of PBS solution treated with 1 M hydrochloride acid with pH values of 4.5, 3.8, 3.4, and 2.4. These values were chosen because many anesthetic and epinephrine injections have been shown to have pH values in those acidic ranges. All cells were treated for one hour at room temperature, washed with PBS immediately
after treatment, and then processed for flow cytometry analysis ((Bogatch, et al., 2010). Cells were analyzed through a staining technique that differentiated live from dead cells, such that dead cells stained fluorescent red due to uptake by a broken membrane, while live cells could not stain due to their intact membrane. A second, green stain was then used, which highlighted all cells and allowed for a total cell count to be determined.

The PBS control solution with a pH of 7.1 demonstrated an 8.4% chondrocyte death. Then, as the pH decreased, the percentage of dead cells increased as well. Their results yielded death in 13.3% of chondrocytes exposed to 1% lidocaine with pH 6.0 (p = 0.002), death in 11.8% of chondrocytes exposed to 0.25% bupivacaine with pH of 5.9 (p = 0.02), and death in 12.0% of chondrocytes exposed to 0.5% bupivacaine with epinephrine with pH 3.9 (p = 0.0006). Differing pH values of the same injected solution also yielded different results, such that 0.25% bupivacaine with epinephrine at a pH of 7.0 resulted in 11.8% death (p = 0.02) while the solution with a pH of 3.9 resulted in 12.0% death (p = 0.003).

Then, to solely determine the effect of pH on the chondrocytes, they exposed them to simple PBS solutions of differing pH values. They again compared them to the control PBS solution with a pH of 7.1. They again found that as the pH decreased, the percentage of cell death increased. Cells exposed to PBS with a pH of 4.5 resulted in the death of 8.1% of chondrocytes (p = 0.74), a pH of 3.8 resulted in the death of 7.5% of chondrocytes (p = 0.24), a pH of 3.4 caused death in 10.7% of chondrocytes (p = 0.03). while a pH of 2.4 resulted in 59.7% of chondrocytes death (p < 0.001) ((Bogatch, et al., 2010).
Methods

A systematic computerized literature search was conducted between November 2009 and October 2010 using PubMed and MD Consult databases with the following keywords used either singularly or in combination: intra-articular pain pumps, chondrolysis, knee, shoulder, glenohumeral, local anesthetics, bupivacaine, and lidocaine. Article inclusion criteria consisted of all journal articles published in English from 1985 to the present that pertained to the effects of intra-articular pain pumps utilizing bupivacaine and/or lidocaine on the knee and/or shoulder joints. If articles included information about other joints as well as the knee and/or shoulder they were included as long as the results for each joint were reported separately. Research on the effects of intra-articular pain pumps in both genders and in all ages, and results from both in vitro and in vivo studies were included. Research conducted on animal models were also included, but only if they pertained to research regarding the knee and/or shoulder. Articles were included if bupivacaine and/or lidocaine use via continuous infusion was compared to a different type of analgesic. For the purpose of the review, articles were stratified into the following non-mutually exclusive categories: animal models, intra-articular pain pump effects on the shoulder joint, and intraarticular pain pump effects on the knee joint. In total, 29 articles fit the given inclusion criteria and were analyzed in this review.
Literature Review

Animal Models

Chu et al. produced one of the sentinel studies dealing with the effects of continuous infusion of local anesthetics through use of animal models. (Chu, Izzo, Papas, & Fu, 2006). For their study, isolated articular bovine chondrocytes were encapsulated and placed in alginate beads for 1 week. Once allowed to grow in the media, chondrocytes were divided into three experimental and three control groups. The experimental groups were submerged in 1mL of 0.5% bupivacaine for 15, 30, and 60 minutes and the control group was submerged in 1mL of 0.9% normal saline for the same time intervals. Following immersion, all samples were washed and incubated in growth media. Through flow cytometry and histological analysis, chondrocytes were assessed at one hour, 24 hours, and one week. To ensure validity of results, the experiment was performed three separate times on three different animals samples.

A second arm of the study aimed to determine whether an intact articular surface provided a protective factor, so 18 bovine osteochondral cores were taken from the trochlear groove and assigned to six groups of three cores each. Three groups, encompassing nine total cores, were left completely intact, while three groups, also consisting of nine cores, had the top one millimeter of cartilage removed. One core from each of the six groups was then submerged in 0.9% normal saline, 0.25% bupivacaine, or 0.5% bupivacaine. After 30 minutes, the cores were removed and returned to growth media for 24 hours. To assess chondrocyte viability, cartilage pieces were analyzed through confocal microscopy.

Exposure to bupivacaine was found to be not only detrimental, but almost completely fatal to articular chondrocytes. The researchers found that after exposure to 0.5% bupivacaine less than 1% of the chondrocytes that were grown in the media were still viable after all lengths
of exposure. Further, the only particles remaining one week after exposure were empty lacunae. When the chondrocytes that were exposed to 0.9% normal saline were examined, however, an average of 69% of the chondrocytes was viable one week following exposure.

Intact articular cartilage appeared to provide some protection. When comparing the three osteochondral core sample groups with intact articular cartilage, the saline-exposed group resulted in more viable cells (74%+/11%) than the 0.5% bupivacaine-treated group (58%+/11%) (p<0.05). When compared to samples that had one millimeter of articular cartilage removed, the saline-treated group did not see a statistical change, with 76%+/9% cells remaining viable, but the bupivacaine-treated group fell to 25%+/14% viability (p<0.05). Also, the difference between the two bupivacaine experimental groups was significantly different, with cells whose articular cartilage was removed dropping to less than half of the viability of those whose cells retained intact articular cartilage (p<0.05).

In the bupivacaine experimental group that retained intact cartilage, nonviable cells were apparent to a depth of 200 microns, while in the group that had articular cartilage removed, nonviable cells were still present 1000 microns from the surface (p<0.05). As such, Chu et al. stated that 0.5% bupivacaine is cytotoxic to articular chondrocytes and osteochondral cores after 15 to 30 minutes. Even though their study was conducted on bovine chondrocytes, and as such cannot be generalized to humans with complete certainty, the authors noted that caution should be used when choosing to use continuous infusion of bupivacaine (Chu, et al., 2006).

As a follow up to this study, Chu et al. conducted a study in 2008 to determine if different concentrations of bupivacaine have different effects on bovine articular chondrocytes (Chu, Izzo, Coyle, Papas, & Logar, 2008). To do this they analyzed 0.5%, 0.25%, and 0.125% bupivacaine concentrations, and again used 0.9% normal saline as a control. Fresh bovine chondrocytes were
obtained and suspended in alginate-bead cultures for growth purposes, allowing ample time for their matrixes to mature before exposure to bupivacaine. After one week the beads were segregated into four groups of ten beads each, with each group exposed to one of the three bupivacaine concentrations or to the control solution. Beads were exposed for varying time intervals, either 15, 30, or 60 minutes, and then washed and incubated in growth media.

To assess viability, cells were removed from the growth media at 1 hour, 24 hours, or one week following exposure. After removal, beads were incubated in 1mL of cold 55mM sodium citrate to dissolve the alginate and release the chondrocytes. Each set of cells were then stained, such that apoptotic cells and the nuclei of dead cells would become apparent without altering the viability of live cells.

The experiment was conducted 72 times, resulting in over 3000 bovine chondrocyte beads. The authors found that 0.125% bupivacaine resulted in similar viability as normal saline, while the higher concentrations of bupivacaine yielded significantly less viability. Exposure to 0.25% bupivacaine demonstrated significantly higher viability than 0.5% bupivacaine, which resulted in nearly complete chondrocyte death in all time intervals, but was not without injury (p<0.05). The samples exposed to 0.25% bupivacaine for 15 minutes showed a time-dependent decrease when compared to normal saline, such that every increase in exposure time resulted in decreased viability. All time intervals revealed statistically significant decreases in cell viability when compared to the control, except at testing 1 hour following exposure of the 0.25% bupivacaine for 15 minutes (p<0.05) (Chu, et al., 2008).

Aside from bovine cartilage, other animal cartilage samples have been used to determine the effects of local anesthetics as well. Effects of continuous intra-articular infusion of bupivacaine on rabbit shoulders were studied in 2006 by Gomoll and colleagues (Gomoll, Kang,
Williams, Bach, & Cole, 2006). Thirty rabbits with a mean weight of 3.5 kg were divided into three groups receiving normal saline, 0.25% bupivacaine, or 0.25% bupivacaine with epinephrine. Each rabbit underwent the same procedure to introduce an infusion catheter into the joint space under direct visualization. Then, each catheter was connected to a 30 gram infusion disk filled with the appropriate testing material and set to run for 48 hours at a flow rate proportional to that of a 70 kilogram human infused with 4.16 mL/hour.

The rabbits were sacrificed five days following catheter removal and analysis was conducted through sulfate uptake, confocal laser microscopy, and cell histology. Sulfate uptake is a standard measure of cartilage proteoglycan metabolism, so this test serves as an indicator of cartilage anabolism. Confocal laser microscopy was used after the samples were stained, allowing the ratio of live cells to dead cells to be calculated. Two independent observers analyzed the samples, with the average of their results used for the final value. Finally, cell histology was assessed by two independent observers based on articular surface characteristics, Safranin O staining, clone formation, cellularity, and synovial membrane characteristics. Each observer rated each characteristic and then their scores were averaged to determine the final value.

Results for each of the three categories resulted in significant results. Sulfate uptake for the saline-treated group showed decreased uptake by 16%, while uptake was decreased by 58% for bupivacaine alone, and by 63% for combination bupivacaine and epinephrine (p<0.05). Comparison to the control group yielded a 50% reduction in uptake for the 0.25% bupivacaine group (p=0.02) and 56% reduction for the 0.25% bupivacaine with epinephrine group (p=0.09). There was no statistically significant difference between the two experimental groups (p=0.6).
Confocal microscopy analysis produced similar results. The saline control group did not cause any significant changes in viability after exposure (p=0.8), while the 0.25% bupivacaine group showed a 32% decrease in viability after exposure (p=0.02), but the 0.25% bupivacaine with epinephrine did not show a difference in viability (p=0.08) compared to the control. When the two experimental groups were compared, no significant difference was noted between them (p=0.35).

Finally, histologic analysis showed statistically significant differences between the experimental-infused group and the saline-infused group (p=0.007). When each of the five characteristics were analyzed separately, the control group showed some decreased proteoglycan content after exposure, but exposure to both experimental solutions yielded decreases in all five parameters. When compared to the control group, the 0.25% bupivacaine group and the 0.25% bupivacaine with epinephrine groups indicated worse pathology (p=0.004 and p=0.03, respectively). Again, no significant difference was noted between the two experimental groups.

Bupivacaine is not the only local anesthetic commonly used, however, so Karpie et al. conducted a study in 2006 to determine the effects of continuously infused lidocaine (Karpie & Chu, 2007). Karpie and Chu isolated bovine articular chondrocytes and exposed them to 1% lidocaine, 2% lidocaine, or 0.9% normal saline (control). After isolation, samples were encapsulated in alginate beads for 1 week to allow proper maturation, and then divided into 15 groups of 10 beads each. Experimental groups were submerged in 1mL of their respective solution for 15 minutes, 30 minutes, or 60 minutes. After exposure was complete, samples were washed and incubated in growth media. Viability was assessed using flow cytometry one hour, 24 hours, and one week following exposure.
Exposure to lidocaine, like bupivacaine, proved to be cytotoxic when compared to 0.9% normal saline. For the experimental group exposed to 1% lidocaine for 15 minutes, viability decreased to 77% +/-4.5% by one hour, while viability decreased to 87% +/-4% when exposed to normal saline (p=0.0009).

Additionally, 2% lidocaine proved to be more toxic than 1% lidocaine. For the experimental groups submerged for 60 minutes, viability of cells exposed to 2% lidocaine fell to 28%+-13% after one hour, while those exposed to 1% lidocaine fell to 66%+- 5% (p=0.037). For each of the exposure times, both 1% and 2% lidocaine groups resulted in significant decreases in cell viability when compared to the control (p<0.05).

**Continuous Infusion into the Knee Joint**

**Efficacy of continuous intra-articular pain pumps following ACL reconstruction.**

With the transition from inpatient surgical procedures to outpatient, many studies have been conducted to determine the best source of postoperative pain relief. Multiple studies have been done in an attempt to determine whether or not continuous infusion of local anesthetic postoperatively can effectively manage postoperative discomfort.

Alford et al. conducted a study that included 49 consecutive patients aged 15-50 who underwent anterior cruciate ligament (ACL) repair (Alford & Fadale, 2003). All patients received the same pre-operative and intra-operative anesthesia, and all underwent an autologous ipsilateral bone-patellar tendon-bone graft with a single midline incision and two anterior portals. Finally, all patients had an infusion catheter inserted into the anterior joint space through the lateral puncture at the completion of the procedure. For post-operative pain management, the patients were divided into three groups. The placebo group received an infusion catheter that
delivered 0.9% saline (placebo), the experimental group was given an infusion catheter that delivered 2.08 mL/hr of 0.25% bupivacaine, and the control group did not have any infusion catheter inserted. The study was both randomized and double-blinded, ensuring neither the investigators nor the patients were aware of the catheter contents or the group assignment.

Adjunct post-operative pain medication was given to all patients in the form of hydrocodone/acetaminophen 5mg/500mg by mouth every four hours as needed for pain and ibuprofen 800 mg by mouth scheduled three times per day. Patients were also instructed to ice regularly, keep their leg elevated, and stay immobile during the postoperative period. Twice per day, patients were told to document their pain levels via the 10 centimeter visual analogue scale (VAS) and their adjunct pain medication consumption for the first four days following surgery. Catheters were then removed on postoperative day number four, and one of three certified physical therapists recorded patients’ initial physical therapy performance based on range of motion and ability to perform straight leg raises. Finally, patients were instructed to continue documenting their pain levels via the VAS and medication consumption for the next four days.

Patient demographics in all groups were matched with regard to age, gender, and side of injury. The control group consisted of eight males and six females with a mean age of 29.6 +/-11 years. The placebo group contained six males and six females with a mean age was 30.7 +/-11 years. Finally, the experimental group consisted of nine males and seven females with a mean age of 29.8 +/-11 years. There was no difference between groups in regards to the sides of injury either.

When comparing VAS scores, the group receiving 0.25% bupivacaine had significantly lower maximum pain scores while the catheters were in place compared to the placebo and control groups, with a mean rating of 4.3 (p<0.03). Then, during the four days following catheter
removal, the experimental group reported higher maximum pain levels than the placebo and control groups, rating pain at approximately 5.1 out of 10. When comparing median pain levels while catheters were in place, both the experimental and placebo group showed lower pain levels than the control group (p<0.05). This trend was not seen after the catheters were removed.

When comparing narcotic consumption, the placebo groups showed significantly decreased consumption than the control group (p<0.05), while the experimental group has similar narcotic use compared to the control group. All patients adhered to taking the ibuprofen every eight hours regardless of pain level. Physical therapy data showed that significantly higher percentages of the experimental (72%) and placebo (70%) group were able to perform straight leg raises on the first physical therapy session on postoperative day four compared to the control group (50%) (p<0.05) (Alford & Fadale, 2003).

A similar study was conducted using 26 patients undergoing ACL reconstruction using a patellar tendon autograft through a single anterior incision. These patients were divided into two groups, an experimental group that was infused with 2mL/hr of 0.25% bupivacaine intra-articularly for 48 hours, and a the control group that received 2mL/hr of normal saline continuously for 48 hours (Hoenecke, Pulido, Morris, & Fronek, 2002). Patients were randomly assigned to their respective group, and both groups received a 25 mL bolus consisting of 0.25% bupivacaine and 5 mg morphine at the completion of their surgeries. Under direct visualization, every patient had a 20 gauge catheter placed into the donor site of the patellar tendon and anterior fat pad. Patients were instructed on proper use of their pain pumps and told to remove the catheter after 48 hours or completion of the medication.

To determine pain levels, a nurse in the Post Anesthesia Care Unit (PACU) had subjects rate their pain immediately upon awakening via the 10 cm VAS and pain descriptors, and then
instructed the subjects to continue pain ratings at 2, 4, 12, 18, 24, 36, and 48 hours postoperatively. Patients were also asked to rate their pain relief and narcotic use as well. A scoring tool similar to the 10 cm VAS was used to document pain relief, with the far left indicating “no relief” and the far right indicating “complete relief.” Narcotic use was documented through a dose equivalency (DE) system based on conversion factors from Drug Facts and Comparisons, such that all supplemental and rescue narcotics could be equally compared.

After analysis, no differences were found in the demographics between groups. When comparing differences in pain levels and pain relief levels, however, the groups did have significant differences. The subjects in the experimental group reported average VAS scores of 2.7 versus 4.0 for the control (p<0.05). The pain relief scores also indicated that the experimental group had significantly more pain relief compared to the control group (7.2 vs. 5.6, respectively, p<0.05). Subjects in the experimental group also showed a trend toward less narcotic use, consuming 37% less than those in the control group, but this was not significant (p=0.08).

Parker et al. compared the effects of continuous infusion of 0.25% bupivacaine (experimental) versus 0.9% normal saline (placebo) and to no catheter (control) using methods similar to the study by Alford et al. (Parker, Streem, Schmitz, Martineau, & Marguerite, 2007). The study included 63 total patients. The experimental group consisted of 18 patients with ages ranging from 19-49 years, the placebo group consisted of 21 patients with ages ranging from 18-46 years, and the control group consisted of 21 patients with ages between 20-37 years. Demographics, consisting of sex, age, affected side, chronicity of ACL insufficiency, and type of procedure conducted, showed no significant differences among the groups. All patients required ACL reconstruction and underwent the same procedure, a quadruple bundle autograft ipsilateral
semitendinosus hamstring intra-articular endoscopic ACL reconstruction, performed by the same surgeon. Patients requiring additional intervention, like chondroplasty or meniscal repair, also received that procedure at the time of the ACL reconstruction as well. At completion of each procedure, the surgeon was instructed as to which patients were to receive a catheter (those in the experimental and placebo groups), and inserted them arthroscopically through the superior lateral pouch and positioned them intra-articularly in the intercondylar notch.

To assess pain, patients were instructed to document pain upon arrival to the PACU, then hourly for six hours, every six hours for the following 24 hours, and then every 12 hours for the next 96 hours. Patients were also instructed to document all narcotic and NSAID use. The only statistically significant finding occurred when comparing pain levels between 48 and 72 hours postoperatively, such that the experimental group documented less pain than the control group (p=0.015).

DeWeese et al. wanted to determine how intra-articular pain pumps compared to other postoperative pain management techniques, so they conducted a retrospective study comparing postoperative pain levels for 86 patients (91 knees) who received continuous infusion pumps and 82 patients (91 knees) who received patient-controlled epidural anesthesia. (DeWeese, Akbari, & Carline, 2001). Intra-articular infusion catheters delivered 50 mL of 0.5% bupivacaine at a constant rate of 2 mL/hour and the catheter was removed on the first postoperative day. The patient-controlled epidural anesthesia consisted of 2 micrograms/mL of fentanyl combined with 0.125% or 0.2% bupivacaine at a maximum rate of 15 mL/hour, with an on-demand bolus of 5 mL every 30 minutes. Like the infusion catheter, the epidural was discontinued on the first postoperative day, at which point patients were offered supplemental pain relief throughout the day. Patients were given on-demand morphine sulfate or meperidine by intramuscular injection
for the infusion catheter group and through intravenous delivery in the epidural group. Additionally, all patients were offered Toradol 15 mg or 30 mg IM every six hours as needed for pain and Propoxyphene napsylate 100 mg or acetaminophen 650 mg one or two tablets orally every four to six hours as needed for pain.

Demographics for both groups were statistically similar, except that more women received the continuous infusion pump than the patient-controlled epidural anesthetic (62% vs. 45%, p<0.05). When comparing the use of additional analgesics between groups, those receiving continuous infusion of 0.5% bupivacaine used significantly more analgesics than those receiving the patient-controlled epidural anesthesia. Total acetaminophen consumption was 1816 +/-1206 vs. 1130 +/- 820 (p=0.00001), total toradol consumption was 20.1 +/- 27.0 vs. 10.7 +/- 12.5 (p=0.003), and total Propoxyphene napsylate consumption was 247 +/- 184 vs. 135 +/- 116 (p=0.00003)

**Safety of continuous intra-articular pain pumps following ACL reconstruction.**

Chu et al. conducted research on the effects of exposure to different concentrations of bupivacaine using ten fresh articular cartilage samples from tissue donors and from the tissue of osteoarthritic knees whose specimens were macroscopically healthy (Chu, et al., 2008). The specimens were harvested and the articular cartilage was isolated and suspended in alginate beads for maturation. Like previous experiments, the samples were allowed to mature for seven days, at which point they were divided into four groups. The experimental groups consisted of 0.5% bupivacaine, 0.25% bupivacaine, and 0.125% bupivacaine, and the control group was made of 0.9% saline. The samples were exposed for 15 minutes, 30 minutes, or 60 minutes, and then washed three times and allowed to incubate in chondrocyte growth media. Cell viability was then assessed at different intervals, including one hour, 24 hours, and one week following exposure.
To help assess viability, beads were removed at their designated time intervals and incubated in 1mL of cold 55mM sodium citrate to dissolve the alginate and release the chondrocytes. Cells were then stained such that apoptotic cells and the nuclei of dead cells would be visible with flow cytometry.

The 0.5% bupivacaine group demonstrated cytotoxicity to human articular chondrocytes after 30 minutes of exposure, whereas the cells exposed to normal saline remained mostly intact following the same exposure time (p<0.05). Even when examined at a depth of 100 micrometers below the surface, the chondrocytes exposed to bupivacaine displayed cellular death at a 1.7-fold increased rate compared to those exposed to normal saline (p<0.001). Further, there appeared to be a dose-dependent chondrotoxicity as evidenced by significantly different results found with the 0.25% bupivacaine sample compared to the placebo but not to the 0.125% solutions. For the cells exposed to 0.5% bupivacaine, 41% remained viable after 15 minutes of exposure, 4% remained after 30 minutes, and no living chondrocytes were present after 60 minutes of exposure. The 0.25% bupivacaine returned 100% of the cells viable after 15 minutes of exposure, 92% viable after 30 minutes, and 23% viable after 60 minutes of exposure. Cells exposed to normal saline, conversely, showed little difference among exposure times, revealing 65% viability after 15 minutes, 64% after 30 minutes, and 67% after 60 minutes.

Chu et al. also concluded that cellular death occurred faster in humans than in bovine samples, as it required 34 minutes for 50% of bovine samples exposed to 0.5% bupivacaine to die, while it took only 13 minutes for 50% of human samples to lose viability. The same held true for 0.25% bupivacaine, as it took 60 minutes for the bovine sample viability to be reduced by 50%, but only 47 minutes for the human chondrocyte samples (Chu, et al., 2008).
A similar study was conducted by Dragoo and colleagues to evaluate the effects of bupivacaine and lidocaine with and without epinephrine (Dragoo, et al., 2008). Peripheral intact articular cartilage was taken from two patients during total knee arthroplasty. The samples underwent enzymatic digestion, filtration, and were grown in chondrocyte growth media for seven days. Samples were then infused with their respective experimental solution directly into the treatment area using doses similar to those used for postoperative pain management. Samples were exposed for 24 hours, 48 hours, or 72 hours. Results were compared to a control group that was exposed to chondrocyte growth media only.

To determine viability after exposure, cells were exposed to a two-color fluorescence assay that allowed viability to be determined as a function of membrane integrity. The total number of cells in the culture was first determined through a staining process where all cells in the culture stained green, and then a second dye was added that identified all non-viable cells through uptake of red dye by the damaged membrane. After 24 hours, cultures exposed to 0.25% bupivacaine with epinephrine, 0.5% bupivacaine with epinephrine, and 1% lidocaine with epinephrine showed a significant decrease in chondrocyte viability for groups when compared to the control (p<0.05). 1% lidocaine with epinephrine demonstrated the most chondrotoxicity, with an almost 60% necrosis rate. When comparing 1% lidocaine, 0.25% bupivacaine, and 0.5% bupivacaine without epinephrine, however, there were essentially no differences in viabilities when compared to the control (p>0.05). After 48 hours, all samples exposed to medications combined with epinephrine again showed significant decreases in viability when compared to the control (p<0.05), with the 1% lidocaine with epinephrine group again having the highest degree of cytotoxicity when compared to the control (p<0.05). After 48 hours of exposure to both concentrations of bupivacaine and 1% lidocaine, the lidocaine again resulted in the highest
degree of cell death, with an approximately 60% necrosis rate. The group exposed to 0.5% bupivacaine resulted in about 33% of cells becoming non-viable, while those exposed to 0.25% bupivacaine demonstrated the least chondrotoxicity, with about a 23% necrosis rate. After 72 hours of exposure, all medications combined with epinephrine, as well as the group exposed to 0.5% bupivacaine without epinephrine, demonstrated significantly more cytotoxicity than the control (p<0.05).

Microscopic evaluations were also done on all samples to help determine viability. As with the staining trials, all cultures perfused with a local anesthetic with epinephrine showed significantly decreased viability when compared with the control media at all trial times. The groups exposed to 1% lidocaine with epinephrine resulted in the largest decrease in cell viability for all time intervals (p<0.001). However, those exposed to an anesthetic without epinephrine yielded similar cell death rates to the control, including the groups exposed to 1% lidocaine at 24 hours, 0.25% and 0.5% concentrations of bupivacaine at 24 and 48 hours, and 0.25% bupivacaine at 72 hours. The group exposed to 0.5% bupivacaine without epinephrine, however, did show significantly decreased rates of cell viability at 72 hours (p<0.05).

Multiple case studies have also been conducted in order to determine effects of continuous intra-articular infusions of local anesthetics into the knee. A 21-year-old female suffered a knee injury and had a pre-operative MRI that showed a complete ACL tear with no damage to the menisci or articular cartilage (Fester & Noyes, 2009). The patient underwent a semitendinous/gracilis autograft repair using a LINX-HT implant for femoral fixation with a bioabsorbable interference screw for tibial fixation. After completion of the surgery, a bolus of bupivacaine with epinephrine and morphine was injected intra-articularly, followed by the
placement of a bupivacaine pain pump that delivered an undocumented dose and volume of medication, which was removed 48 hours postoperatively.

During the initial postoperative period the patient progressed as expected, with pain gradually decreasing and the ability to perform physical therapy increasing. Rehabilitation progressed well for the first seven months, but shortly after, the patient began to experience generalized knee pain. Over time, the pain continued to worsen, it ceased to respond to NSAIDs, and it began to limit activities of daily living (ADLs). The patient denied re-injury to the knee or episodes of instability since surgery, and a KT-1000 arthrometer test demonstrated an intact, functional ACL.

An MRI was then taken 12 months postoperatively, revealing an intact ACL graft, but partial to full thickness tricompartmental cartilage loss. To check for the presence of infection, a joint aspiration was conducted, revealing clear fluid and a negative workup. Further, serum studies were also conducted to determine the presence of infection, but the findings again yielded negative results. Seventeen months following the index procedure she was referred for a second opinion, where the patient presented with continually increasing pain that limited ADLs. The patient reported 4/10 knee pain and gave a history of transient knee effusions associated with activity. Physical examination revealed full range of motion within the knee, mild crepitus of the patellofemoral joint, and negative Lachman and pivot-shift tests. Following the exam, radiographs were taken and revealed mild narrowing of the medial and patellofemoral joint spaces with associated sclerosis. The patient received an intra-articular injection into the knee containing two mL of methylprednisone and lidocaine. The injection did not provide relief, so an arthroscopic evaluation was performed, revealing diffuse partial to full thickness delaminating cartilagenous lesions in all three knee compartments. During the arthroscopy, the fragmented
cartilage was debrided from all compartments and a biopsy specimen was taken. Biopsy revealed no sign of infection and showed dense fibroconnective tissue that was consistent with scar formation.

Another case involved an 18-year-old female who was injured during a basketball competition. MRI demonstrated a complete tear in the ACL, a bone bruise of the lateral femoral condyle, and the absence of menisci or cartilage damage (Fester & Noyes, 2009). The patient underwent diagnostic arthroscopy and a complete ACL tear was confirmed, along with the absence of both meniscal and cartilage damage. At one month following the injury, the patient underwent reconstruction with a semitendinous/gracilis autograft repair with LINX-HT implants for femoral fixation and a bioabsorbable interference screw for tibial fixation. At the completion of surgery a bolus of morphine and bupivacaine with epinephrine was injected into the knee, and a bupivacaine-infusing pain pump that delivered an undocumented volume and flow rate of medication was inserted and instructed to be removed 48 hours postoperatively.

The patient’s initial recovery was unremarkable and rehabilitation followed a standard physical therapy protocol. Then, at ten months postoperatively, the patient began to experience pain and swelling in the knee, with symptoms persisting despite consistent use of NSAIDs. At 19 months following the index procedure, radiographs were taken that revealed mild narrowing of the medial compartment. A follow up MRI demonstrated an intact ACL graft, a small area of edema in the lateral femoral chondyle, no meniscal damage, and diffuse thinning of cartilage in all three knee compartments. Pain persisted despite using various modalities to relieve the pain, so at 20 months postoperatively the patient underwent diagnostic arthroscopy. The procedure revealed an intact ACL reconstruction with no loose hardware or fragments. However, tricompartmental chondral defects were noted, with full-thickness defects of the patella, trochlea,
medial femoral condyle, and medial tibial plateau with large chondral flaps and a delaminating appearance. Microfracture was performed on the areas of exposed bone in the medial femoral condyle and medial tibial plateau. The patient experienced some pain relief, but a few months after the procedure the pain and swelling returned. The patient was therefore referred for a second opinion five months following the microfracture procedure. On examination, a small knee effusion, mild tenderness to palpation of the patellofemoral and medial compartments was appreciated with a negative Lachman and pivot-shift tests. Radiographs showed narrowing of the patellofemoral and medial compartments, at which point the patient was diagnosed with chondrolysis. The patient never fully recovered from the pain, continuing to rate it a 5/10, despite medical management for joint arthrosis, including a course of viscosupplementation injections.

The next case involves a 41-year-old female who suffered a knee injury during a skiing accident (Fester & Noyes, 2009). Pre-operative radiographs showed mild (<50%) articular cartilage narrowing and sclerosis of all three compartments, and an MRI showed a complete ACL tear, horizontal medial and lateral meniscal tears, and a mild amount of articular cartilage thinning throughout the knee. Diagnostic arthroscopy confirmed the presence of complete ACL tear, and showed no articular cartilage lesions. The patient underwent semitendinous/gracilis autograft reconstruction with bioabsorbable interference screws for fixation. At the completion of the procedure, the knee was injected with 0.5% bupivacaine and a bupivacaine pain pump set to infuse an undocumented volume and flow rate of bupivacaine was introduced to the knee joint and removed 48 hours postoperatively.

No complications were encountered during the initial postoperative period or rehabilitation periods, and the patient returned to her previous activity level without any pain or problems. No re-injuries of the knee were noted, but at 21 months following the index procedure
the patient developed significant pain that interfered with her ADLs. At 23 months postoperatively, the patient saw another specialist, at which time she rated her pain a 4/10, had a positive Lachman test, and a grade 2 pivot shift test. Radiographs demonstrated diffuse tricompartment changes with near bone-on-bone appearance of the medial compartment and greater than 50% loss of joint space in the lateral compartment. An MRI was then taken and revealed an ACL graft disruption, tricompartment articular cartilage lesions, and full-thickness chondral defects throughout the knee, particularly in the medial compartment.

A 17-year-old female soccer player suffered an injury during a competition, and a diagnostic MRI demonstrated a complete ACL tear with an associated lateral meniscal tear, but pristine articular cartilage (Slabaugh, Friel, & Cole, 2010). The patient underwent ACL reconstruction with quadruple hamstring autograft with bioabsorbable fixation implants and a lateral meniscus repair. At the completion of surgery, a bupivacaine pain pump was placed in the suprapatellar pouch that delivered an undocumented volume and flow rate of medication to be removed 48 hours following the surgery.

During the immediate postoperative period, the patient progressed normally. At eight weeks following surgery, the patient noted a decrease in knee flexion and at that point the patient underwent manipulation under anesthesia, resulting in full flexion. Then, at four months following the index procedure, crepitus was noted by the patient in the medial aspect of the knee, with associated pain and swelling. Upon physical examination, early degeneration was suspected, and MRI confirmed the presence of tricompartmental chondrolysis with an intact ACL graft. The patient underwent arthroscopy and the presence of diffuse articular cartilage damage was confirmed, consisting of Outerbridge classification grades III and IV. The patient was then referred for a second opinion. Physical exam revealed an intact ACL with no evidence
of meniscal tear. Radiographs showed tricompartmental narrowing that was most significant on the medial aspect, with varus alignment of the limb. To rule out an infectious etiology, blood tests were done and interpreted as negative. After examination of her case, all causes of her severe chondrolysis were excluded aside from use of the bupivacaine pain pump.

Continuous Infusion into the Glenohumeral Joint

Safety of continuous intra-articular pain pumps following shoulder arthroscopy.

Much like intra-articular knee infusions, pain relief following shoulder arthroscopy is often attempted through the use of intra-articular pain pumps.

A prospective, double-blinded, randomized study to evaluate the effectiveness of intra-articular pain pumps in the glenohumeral joint was published in 2002. The study included 49 patients who all underwent outpatient arthroscopic rotator cuff repair, arthroscopic SLAP lesion repair, subacromial decompression, or arthroscopic capsular reefing (Barber & Herbert, 2002). Patients were divided into two groups, with 24 receiving continuous infusion of normal saline and 25 receiving continuous infusion of 0.5% bupivacaine. Pumps were set to flow at a rate of 2.08 mL/hour over the course of 48 hours, resulting in a total volume of 99.84 mL. Additionally, patients were given adjunct pain control through an intra-articular or intrabursal injection of 10 mg of morphine sulfate, bupivacaine injections into all portal sites before they were created, and 30 mg of intravenous ketorolac tromethamine postoperatively.

Patients were interviewed at 1, 2, and 8 hours postoperatively, and then every 24 hours for the next eight days. Patients were asked to rate their pain according to the 10 cm VAS and four point Likert categorical pain scales, and additional questions were asked regarding the effectiveness of the fluid-delivery system. Each patient received home prescriptions for
hydrocodone with acetaminophen and given strict instructions to only use them when they perceived pain, not in anticipation of pain. Patients documented their pain levels and use of adjunct medication in home diaries.

Results of the study demonstrated significantly lower pain scores overall in the bupivacaine-infused group when compared to the saline-infused group (p<0.05), but no overall difference between groups was noted in the use of comedication (p>0.05). Pain scores were not significantly lower in the bupivacaine-infused group for days two and three (p>0.05), and had a coinciding greater use of comedication on those days. To determine whether the differences in pain scores were due to differences in the study groups, the authors attempted to identify all potential cofactors, including: age and sex of the patient and whether or not the procedure was performed on the patient’s dominant or non-dominant shoulder. Their model indicated that procedures performed on the dominant shoulder yielded significantly higher pain scores than those conducted on the non-dominant limb over the first three days (p<0.05). Further, results of medication use paralleled perceived pain scores, indicating that patients used medication only for perceived pain and not for anticipated pain. See table 3 for a summary of the results.

Efficacy of continuous intra-articular pain pumps following ACL reconstruction.

Since pain pumps continuously infusing local anesthetics into the glenohumeral joint are a common choice of pain management following shoulder arthroscopy, many studies have surfaced regarding the safety of their use.

Hansen et al. conducted a retrospective study of ten patients (12 shoulders) who presented with symptoms of chondrolysis following arthroscopic shoulder stabilization procedures (Hansen, et al., 2007). All patients presented with increasing pain both at rest and
during mobilization, crepitus, and decreasing active range of motion due to pain when compared to ROM documented at previous visits. Glenohumeral joint space narrowing was documented with AP and Grashey view radiographs. All patients then underwent joint aspiration, serologic studies, and MRIs to rule out other causes of the pain. Basic patient exam demographics and initial surgical information was examined to determine commonalities among the patients. Once these cases were analyzed and similarities determined, the records of 152 patients (177 shoulders) who underwent arthroscopic surgery from August 2003 to March 2005 by the same surgeon were analyzed for the same characteristics. Of these surgeries, 125 were procedures isolated to the bursal space, including subacromial decompression, distal clavicle resection, rotator cuff repair, or some combination of the surgeries. Eighteen of the 177 shoulders underwent procedures involving both the bursal space and the glenohumeral joint, including instability repair and rotator cuff repair, and 34 of the shoulders underwent instability procedures alone. Of the 34 instability procedures, 30 underwent an arthroscopic repair while the remaining 4 received an open repair.

For the initial 12 shoulders studied that developed chondrolysis, it was found that they all belonged to group of 30 that received arthroscopic shoulder stabilization. The indications for the patient to undergo the procedure were then identified, revealing that three had symptomatic multidirectional instability that did not improve with conservative treatment and nine presented with posttraumatic instability.

The similarities and differences of the 12 surgical procedures were then analyzed. From this, the authors determined that all but one of the surgeries was performed with the patient in the lateral decubitus position. Also, four surgeries involved use of a thermal radiofrequency probe to augment the capsular shift effect of the labral repair. The authors noted, however, that thermal
radiofrequency probes were also used intra-articularly in 51 other shoulders that did not result in any signs or symptoms of chondrolysis. When analyzing sutures and anchors used throughout the procedures, no consistency was noted. Of the patients that did have anchors, one patient presented with a broken anchor inserter tip that required a second procedure for removal after the diagnosis of chondrolysis was made. Regarding anesthesia, all 12 patients received preoperative and postoperative intra-articular injections of 25 mL of 0.25% bupivacaine with epinephrine and 5 mg of morphine sulfate. Also all 12 shoulders that subsequently developed chondrolysis received post-surgical pain pump catheters that delivered a total of 250 mL of 0.25% bupivacaine with epinephrine at a constant drip rate of 4.16 mL/hour over 48 hours. Nine of the twelve patients also received an additional 30 mg of ketorolac for adjunct postoperative pain control. Finally, all patients progressed through a similar post-operative pattern, making significant gains in motion initially following surgery, and all appeared to be recovering as expected after four weeks of immobilization. During postoperative weeks 5-12, the charts of all 12 shoulders indicated continued progression in motion and function during physical therapy sessions, so all were subsequently prescribed a home or gym exercise program. Then, within the year following the index procedure, all patients presented with complaints of new onset atraumatic pain, stiffness, and increasing pain and crepitus during motion. The mean time for the onset of symptoms was 4.3 months following the index procedure, ranging from 3 to 13 months, and the mean age at the time of surgery was 28.9 years, ranging from 16 to 47 years. Patients were followed closely after new onset of symptoms, as all presented with radiographic evidence of glenohumeral joint space narrowing. Further, physical exams of all shoulders were noted to have significantly decreased active range of motion when compared to earlier follow-up exams.
Other possible cofactors among the patients affected by chondrolysis were examined, but none produced any significant correlation. These included rheumatology studies, serology studies, and needle aspirations. All rheumatology and serology tests were normal in the patients with chondrolysis, and all but one needle aspiration was negative for an infectious process. For the patient that had the positive needle aspiration, however, it was determined that the positive test was due to a contaminant from the laboratory because the patient did not present with any further evidence of infection and the aspiration was only positive on one of three agar plates.

Additional chart reviews were then conducted on 104 of the 152 patients who were treated with the same preoperative and postoperative protocols, including intra-articular injections and pain pumps, as the 12 shoulders studied, but the pain pumps in those 104 patients were placed superficial to the rotator cuff tendons, making them extra-articular. Of the 104 patients, none experienced chondrolysis symptoms. A second subset, including 13 additional patients who were treated with arthroscopic stabilization, did not receive pain pumps at the conclusion of their surgeries. Of the 13, none developed chondrolysis symptoms.

At the conclusion of the analysis, 12 of the 177 shoulders evaluated (6.8% of the total procedures) resulted in chondrolysis. Thirty of those 177 shoulders were treated with arthroscopic stabilization and 19 of the 30 shoulders were given intra-articular pain pump catheters. Twelve of the 19 (63%) shoulders treated with intra-articular pain pumps developed chondrolysis confirmed by radiographic narrowing and symptoms.

A case study following an otherwise healthy right hand-dominant 18-year-old female who was injured while playing softball was conducted following development of shoulder pain postoperatively (Petty, Jazrawi, Estrada, & Andrews, 2004). After the injury, standard radiographs were performed that revealed a type II acromion, and a subsequent MRI showed a
small articular margin partial tear of the supraspinatus tendon. Conservative treatment was attempted, but the patient failed to achieve significant improvement. The patient then underwent shoulder arthroscopy with subacromial decompression and undersurface rotator cuff debridement, with intra-operative findings revealing smooth articular surfaces of both the humeral head and glenoid cavity with healthy-appearing cartilage. At the completion of the surgery, the patient had a pain pump inserted into the glenohumeral joint set to deliver 0.5% bupivacaine with epinephrine at an undocumented flow rate and duration.

The immediate postoperative course was unremarkable, yet three months following the index procedure, the patient was still unable to resume normal throwing activities due to limited external rotation and pain with active shoulder motion. The patient received an intra-articular cortisone injection, but experienced minimal relief. At five months postoperatively, the patient sought a second opinion. Standard shoulder radiographs showed marked narrowing of the glenohumeral joint and an MRI showed the presence of joint space narrowing and subchondral cystic changes of both the glenoid and humeral head. Approximately 6 months following the index procedure a second arthroscopy was performed, revealing severe glenohumeral degenerative changes. Complete (type IV) loss of the glenoid cartilage and significant loss of humeral head cartilage was noted. Extensive fraying of the anterior glenohumeral ligaments and labrum were also apparent, while the rotator cuff was noted to be intact. During the procedure, the subacromial space was decompressed and a biopsy and culture of the synovium were taken. Culture results were negative for both aerobic and anaerobic bacteria, acid-fast bacilli, and fungus. Stain for urate crystals was positive and gross histologic examination of the biopsies revealed focal degenerative changes with microlcalcifications consistent with a foreign body inflammatory reaction.
Following the arthroscopy, the patient was referred for a third opinion, about 8 months after the index procedure, for a complete rheumatologic exam. The workup revealed negative rheumatoid factor and negative ANA, and serum uric acid and complete blood count results were within normal limits. With these additional negative findings, the patient was given the presumptive diagnosis of glenohumeral chondrolysis.

With the increase in published articles dealing with shoulder chondrolysis, two case series were conducted in 2009 to further investigate possible causes. Bailie et al. followed 23 participants from 2005 to 2006 who presented to the office with a delayed increase in shoulder pain following arthroscopy (Bailie & Ellenbecker, 2009) and McNickle et al. followed 20 patients who were referred to their office after symptoms consistent with glenohumeral chondrolysis following an index shoulder arthroscopic procedure (McNickle, L'Heureux, Provencher, Romeo, & Cole, 2009).

Symptoms in the first case series began an average of 9.1 months, ranging from 8 to 12 months, following the index procedure. All patients that presented with symptoms denied intervening injury following their surgery, and review of pre- and intra-operative notes did not indicate evidence of degenerative arthritis, infection, or inflammatory condition in any of the patients (Bailie & Ellenbecker, 2009). Procedures conducted in the 23 cases studied included 14 labral repairs using bioabsorbable fixation devices, five Bankart-type tear repairs, and 9 SLAP lesion repairs. Seven cases had documented use of thermal probes to treat capsular laxity, and 17 cases involved use of intra-articular pain pumps that delivered between 250 and 300 mL of 0.25% bupivacaine over 48 hours at an undocumented flow rate. In the cases that used pain pumps, one was placed into the subacromial space following a mini-open rotator cuff repair while the other 16 were placed into the glenohumeral joint. Additionally, six of the cases
involved use of adjunct epinephrine in the pump. Finally, four cases did not have any reported use of fixation anchors, thermal probes, or continuous infusion pumps.

Clinical presentation of the 23 cases followed a similar course, with the initial postoperative period resulting in nearly complete resolution of symptoms. Most of the patients had completed a rehabilitation program and returned to their baseline activity levels without limitations. The patients noticed an increase in pain at an average of 9.1 (range, 8-12 months) months following their respective procedure, that rapidly escalated over the next four to six weeks. Nine patients also noticed a rapid loss of function and range of motion, while 14 only reported increased pain. At that time, radiographs were taken of all patients and compared to initial preoperative images. All patients demonstrated diffuse loss of glenohumeral joint space, ranging from one millimeter to complete loss. However, none presented with evidence of substantial bone loss or osteophyte development. Some patients also had subsequent MRIs, which confirmed the presence of profound articular cartilage loss and revealed symmetric subchondral cysts on both sides of the joint.

As an initial treatment, all patients were given an unsuccessful trial of injected and/or oral corticosteroids, oral NSAIDs, and/or physical therapy. Nine patients, who initially presented with more severe loss of motion and function and who had more diffuse loss of articular cartilage, ultimately underwent cementless humeral head resurfacing arthroplasty. Six of those nine patients underwent arthroscopic debridement and capsular release prior to the arthroplasty that did not ultimately result in increased range of motion or decreased pain. The remaining 14 of the 23 patients underwent successful arthroscopic debridement and/or capsular release, with 11 receiving hyaluronic acid injections beginning six weeks after the procedure.
Through these subsequent arthroscopies, additional findings were noted. Among the 23 shoulders, a small number of loose bodies were present, nearly complete dissolution of articular cartilage on the glenoid was noted, and central cartilage erosion of the humeral head was also present. None of the shoulders demonstrated mechanical abrasion by the infusion catheter or had broken labral fixation devices. Finally, the intra-articular soft tissue surrounding the areas of chondral involvement remained unaffected in all cases, localizing the problem specifically to the articular cartilage.

The case series conducted by McNickle et al. revealed similar results. Of the 20 cases included in their analysis, all patients were younger than 35 years old, had undergone glenohumeral arthroscopy with capsular or labral involvement, had documented intact glenohumeral cartilage at the index procedure, and had ongoing postoperative symptoms of shoulder pain at the time of referral (McNickle, et al., 2009).

Factors analyzed as possible causative agents for the development of the symptoms were similar to the previous case series. Sixteen patients (80%) received intra-articular glenohumeral pain pumps with catheters that delivered either continuous 0.25% or 0.5% bupivacaine for 48 to 72 hours at undocumented flow rates. Two patients had metal anchors placed along the anterior glenoid for Bankart repair that were prominent and required removal, both of which were removed within one year of placement. Eight other patients had fixation anchors placed, but did not experience any loose, prominent, or displaced devices. Radiofrequency capsular shrinkage was used during surgery in five patients, two of which received it as primary treatment and three received it as an adjunct to anchor placement. No patient experienced wound dehiscence, nerve paresthesias, or superficial or deep infection following surgery.
Following the index procedure all 20 patients reported increasing pain at an average of 5.7 months following the procedure, ranging between 2 and 20 months. Fifteen of the 20 (75%) patients also reported a decreased range of motion at an average of 6.2 months, ranging from 2 to 20 months, following surgery. Additionally, seven patients (35%) reported persistent stiffness and four patients (20%) reported weakness. At the referral visit following symptom return, decreased range of motion was a common finding, with mean passive shoulder flexion of 119 degrees (range from 40 degrees to 175 degrees), external rotation of 42 degrees to the side (range from 0 degrees to 90 degrees), and mean internal rotation to the L2 level (range from greater trochanter to T4 level). Radiographic studies demonstrated degenerative changes of the glenohumeral joint with joint space narrowing in 13 of 20 (65%) shoulders, including six patients who presented with complete obliteration of cartilage that resulted in bone-on-bone contact. Bony changes were also present in those six patients, including subchondral cysts, collapse, and osteophyte formation.

Eighteen of the 20 (90%) patients presenting for referral were ultimately scheduled for revision surgery at a mean of 33 months, ranging from 8-78 months, following the index procedure. At the time of revision surgery, all shoulders demonstrated large focal diffuse chondral changes to the humeral head, glenoid, or both, and had grade IV humeral head cartilage loss, extending between 50% and 100% of the surface area. Additionally, 95% presented with diffuse cartilage involvement, ranging from 20% to 100% involvement (McNickle, et al., 2009).

Another case series was conducted from May 31, 2004 to December 7, 2005 by Anderson et al. that retrospectively analyzed 18 charts from patients diagnosed with chondrolysis during the given time frame (Anderson, Buchko, Taillon, & Ernst, 2010). They discovered that of the 18 patients, all underwent arthroscopic labrum repair surgery for symptomatic glenohumeral
instability and all received intra-articular pain pumps that infused 0.5% bupivacaine with epinephrine for postoperative pain relief. Patients either received a high-flow pump that infused a total volume of 275 mL at a flow rate of 5 mL/hour or a low-flow pump that infused a total volume of 100 mL at a flow rate of 2 mL/hour. Patients were also given intra-articular boluses, ranging from 15 mL to 60 mL, of 0.25% or 0.5% bupivacaine at the completion of surgery.

Average age of the 18 patients was 23.83 years, and the study was comprised of 15 males and two females. Surgeries were performed by one of two surgeons conducting the case series, and procedures included 15 anterior Bankart repairs, one posterior Bankart repair, one combined anterior and posterior Bankart repair, and one combined posterior Bankart repair and SLAP lesion repair. Repairs were completed through tack placement and/or suture anchors, but no cases involved the use of thermal energy. Also, there were no postoperative findings or clinical suspicion of shoulder infections or wound complications.

Mean time to diagnosis was 9.5 months, ranging between 2 to 27.5 months. However, the wide range in time to diagnosis may be skewed, as early in the process neither surgeon understood that chondrolysis was the cause of their patients’ pain, so diagnosis required a greater length of time. Towards the end of the study period, however, they were able to diagnosis the condition rather easily. Of the 18 patients studied, 14 underwent a second shoulder arthroscopy once the diagnosis of chondrolysis was suspected. All arthroscopic evaluations confirmed the presence of chondral changes consistent with the diagnosis. None showed evidence of suture anchor failure or mechanical irritation from suture anchors.

Additionally, they then went on to study charts from all patients within the surgeons’ practices who underwent arthroscopies during the given time-frame, resulting in a total of 113 charts. In total, there were 82 anterior Bankart repairs, four posterior Bankart repairs, six SLAP
lesion repairs, and multiple combination procedures consisting of anterior and posterior Bankart repairs, SLAP repairs, and rotator cuff repairs. Including the 18 aforementioned patients, 45 patients received either a high-flow pain pump (32 patients) or a low-flow pump (12 patients). An additional patient received a pump, but the flow rate was not documented. Of those who received the high-flow pump, 16 later developed chondrolysis (50%), and two of the patients that received the low-flow pump eventually developed chondrolysis (17%). During the same time-frame, no patients that underwent the same types of procedures but did not have a pain pump placed ever developed chondrolysis. Further, since ceasing to use pain pumps following arthroscopies, no patients of the two surgeons have developed chondrolysis following their procedures.

A rather unique study was conducted by Saltzman et al., where a single individual underwent bilateral shoulder arthroscopy and had pain pumps placed in both shoulders at the conclusion of their surgeries (Saltzman, Mercer, Bertelsen, Warme, & Matsen, 2009). The patient was a 37-year-old female law enforcement agent injured both shoulders three years before presentation. She underwent conservative therapy for two months but did not find any relief in the right shoulder, so went to her healthcare provider and was diagnosed with a partial thickness rotator cuff tear, subacromial bursitis, impingement, and a SLAP lesion. Therapy began with a corticosteroid injection but she found no relief, so four months following the injury underwent arthroscopic SLAP repair, Bankart repair, capsulorrhaphy, acromioplasty, and distal clavicle excision of the right shoulder. No thermal devices were used in the procedure. At the completion of the arthroscopy, an intra-articular pain pump was placed in the glenohumeral joint that was set to deliver 2% lidocaine continuously at a flow rate of 2 mL/hour. However, the pain pump never functioned correctly and the patient never received any medication, as evidenced by
leakage outside of the shoulder. Despite physical therapy, the patient never gained full range of motion in the shoulder, so she underwent manipulation and arthroscopic subacromial decompression, debridement of the glenohumeral joint, and lysis adhesions three months following the index procedure.

Then, one month later, she returned to the surgeon for discomfort of the left shoulder. At that time, she was diagnosed with rotator cuff tendonitis, a SLAP lesion, and bicipital tendonitis of the left shoulder. She was again initially treated with a subacromial corticosteroid injection, but did not find sufficient relief, as her symptoms persisted for four months. Therefore, she underwent an arthroscopic SLAP repair, capsulorrhaphy, acromioplasty, and distal clavicle excision of the left shoulder. Again, there was no documentation of thermal devices used in the procedure. At the completion of the arthroscopy, an intra-articular pain pump was placed in the left glenohumeral joint and set to deliver 2% lidocaine continuously at a rate of 2 mL/hour. Unlike the pain pump used on the right side, however, this pain pump functioned properly, did not leak any medication outside of the body, and functioned for several days following the arthroscopy.

Much like the right side, she again developed right shoulder stiffness and decreased range of motion. She therefore underwent arthroscopic lysis of adhesions four months after the index procedure. However, despite this, the left shoulder remained stiff, so nine months following the index procedure she underwent manipulation and repeat arthroscopic subacromial decompression, acromial decompression, and adhesion lysis. Intraoperatively, it was noted that the humeral head and glenohumeral joint were nearly completely devoid of articular cartilage. Further, the procedure did not provide any relief, so over the following seven months she
received multiple cortisone injections, five viscosupplementation injections, physical therapy, and narcotic pain medication, but nothing sufficiently relieved the pain.

She was then referred for another opinion, where she presented with severe left shoulder pain and stiffness and a mostly asymptomatic right shoulder. On the “Simple Shoulder Test,” she answered “no” to all 12 questions for the left shoulder and to 3 of the 12 questions for the right side. On physical examination, her left shoulder showed 30 degrees of forward flexion, 0 degrees of external rotation, and internal rotation to her buttock, while the right shoulder was able to reach 140 degrees of forward flexion, 60 degrees of external rotation, and internal rotation to T12. Radiographs were taken of bilateral shoulders, revealing significant left glenohumeral joint space narrowing but normal-appearing joint spaces on the right. At that point, the surgeon diagnosed the patient with left shoulder postsurgical chondrolysis and offered possible treatment plans.
Discussion

Animal Models

Although animal models cannot necessarily be generalized to human models, identifying the effects of local anesthetic on cartilage of any species is a key starting point to understanding the negative consequences that may ensue with their use in humans. In 2006, Chu et al. explained the importance of determining the long term consequences of continuously infusing local anesthetics. Continued exposure to 0.5% bupivacaine was toxic to bovine chondrocytes. Although human chondrocytes do not mimic bovine chondrocytes entirely, by determining that exposure is toxic in one species, it is reasonable to believe it is toxic to other species. When comparing 0.5% bupivacaine to 0.9% normal saline, it was determined that only empty lacunae were remaining one week after exposure to bupivacaine, while 69% of chondrocytes exposed to 0.9% normal saline were still viable.

The second arm of their study demonstrated that intact articular cartilage may serve as a protective factor against the use of continuous local anesthetics. However, the purpose of pain pumps is to reduce the amount of perceived pain following an arthroscopic procedure, and as such, they are often used in an area where very little intact cartilage may still exist. Therefore, although their study illustrated that continuously infused local anesthetic may not be completely detrimental to chondrocytes under this circumstance, it is not a condition that is necessarily present.

Chu et al. did not stop there, also investigating whether the concentration and/or duration of exposure affected the extent of cartilage damage. Through this arm of the study they again demonstrated that bupivacaine was toxic to bovine chondrocytes, stating that exposure to all concentrations yielded a time-dependent decrease. They showed that for every increase in
exposure duration, the amount of chondrocyte death increased proportionally, with the greatest loss noted one week following exposure for 60 minutes. This is important to understand when integrating the animal models into human data, as it shows an increased degree of cell death with increased time of exposure. Even though the cells were only exposed for 60 minutes, the degree of cell death continued far beyond the exposure time. When used for human pain relief, the joint is typically exposed to the local anesthetic for 48 to 72 hours, but as illustrated by the animal models, effects may continue far beyond that timeframe.

Following the work of Chu et al., Gomoll et al. chose to infuse bupivacaine with and without epinephrine into the glenohumeral joints of rabbits. This provided data on the effects in a different species in addition to analyzing effects in live animals. Their results again suggested that local anesthetics affected chondrocytes in a negative manner.

Since similar results were demonstrated in different species, the likelihood of detrimental effects to human chondrocytes becomes more probable. Further, since testing on human chondrocytes cannot be conducted due to ethical standards, testing on animals serves as the best opportunity to determine the severity of damage. In order to analyze the effects of local anesthetics on live, human joints, retrospective series and case reports are the only option.

Finally, it is also important to look at different local anesthetics, so Karpie et al. chose to determine effects resulting from exposure to continuous lidocaine in 1% and 2% concentrations. Much like the bupivacaine studies, continuous infusion of lidocaine also showed significant toxicity, and the higher concentration proved to be more detrimental. Therefore, animal models provide many insights into the effects of local anesthetics: 1) they are shown to be toxic among two different animal species, making the likelihood of them being toxic in other species higher, 2) their effects are time-dependent, such that even when exposure is complete, their effects may
be appreciated for a much greater length of time, and 3) bupivacaine and lidocaine, the two local anesthetics used in human pain pumps, demonstrated dose-dependent chondrotoxicity, such that higher concentrations yielded worse results.

Pain Pump Use in Knees

Pain pumps have become a common choice for pain relief following arthroscopic knee surgeries, but studies suggest they may not be the best choice for pain relief. After analyzing efficacy studies, continuous intra-articular infusion into the knee following ACL reconstruction provides marginal, if any, pain relief. Through a study conducted by Alford et al., intra-articular pain pumps demonstrated efficacy while the bupivacaine pain pumps were in place and for 24 to 48 hours after removal that may have been statistically significant, but was not necessarily clinically significant. However, those who were given the bupivacaine pain pump actually reported higher pain scores than those infused with normal saline once the catheters were removed on postoperative day four. Pain levels were further analyzed through documentation of adjunct oral pain medication consumption by the patients. If pain pumps were truly effective for pain relief, it would be expected that those given the pain pump would use a significantly lower amount of oral analgesics. However, the data from their study did not demonstrate any significant difference between those given the pain pumps and those exposed to normal saline. As such, the study provides further evidence to suggest that pain pumps provide only marginal pain relief following ACL reconstruction.

Similarly, results from a study by Hoenecke et al., showed significantly lower average pain scores for those given pain pumps (2.7 versus 4, p<0.05) that further resulted in higher pain relief scores (7.2 versus 5.6, p<0.05). However, although both numbers are statistically
significant their clinical relevance is rather marginal, as the difference between the given numbers is rather unimpressive. Moreover, the patients given intra-articular pain pumps did not consume a significantly lower amount of oral opioid medication use when compared to the control group, further indicating the little benefit gained from the pain pumps.

Pain scores were again compared between groups exposed to either continuous infusion of 0.25% bupivacaine or 0.9% normal saline in a study conducted by Parker et. al (Parker, et al., 2007). From their data, it was determined that exposure to 0.25% bupivacaine did provide some pain relief, but only between postoperative hours 48 to 72 (p=0.015). Again, when looking at the results from a broad, clinical point of view, lessened pain relief over a mere 24 hour period does not warrant the pain pumps as effective. Similarly, DeWeese et al. conducted a retrospective study comparing patients either infused with 0.5% bupivacaine continuously or given a patient-controlled epidural anesthesia which again demonstrates the marginal pain relief provided by the intra-articular pain pumps. Their data showed that patients given intra-articular pain pumps required a significantly greater amount of adjunct pain medication (p=0.00001 for acetaminophen, p=0.003 for toradol, and p=0.000003 for Propoxyphene napsylate) than those with the epidural anesthesia.

From the currently published research, pain pumps are only providing marginal pain relief following ACL reconstruction. Going even further, literature is also surfacing about the potential safety concerns associated with their use. For example, Chu et al. not only analyzed the effects of continuous infusion of local anesthetics in animal models, but also went on to expose human knee chondrocytes to 0.125%, 0.25%, and 0.5% bupivacaine. They used a method similar to their studies on animal cells, and found similar results. Not only did they determine that continuous exposure to bupivacaine is detrimental, they also again illustrated the dose-dependent
effect of the medication, such that as the concentration increased the amount of viable cells decreased. Further, cellular death may actually occur faster in humans than in bovine models, solidifying the notion that the animal models can be loosely generalized to human models.

Pain pump safety concerns have also surfaced following analysis of case studies, with again, alarming results. All patients included in this clinical review demonstrated negative outcomes after use of intraarticular pain pumps following ACL reconstruction. Unfortunately, none of the case studies provided detailed information about things such as flow rates or total volume of local anesthetic infused through the pumps. As those are key components in determining the safety of these pumps, future case studies including such information would be beneficial. However, even though these concrete numbers do not currently exist in the literature, when the documented cases are analyzed in combination with the very marginal pain relief provided by the pumps, their use seems both futile and dangerous.

Also, all case studies presented involved female patients, which may be due to the well-established female predilection for ACL injuries. However, there is presently no way to statistically determine if gender plays a role in the toxicity of local anesthetics infused through pain pumps following ACL reconstruction. However, from the information gained from the animal and human studies, there is currently no data to support the intra-articular use of pain pumps following ACL reconstruction. Rather, there is strong data that indicates there is actually inherent danger when using pain pumps in such a situation.

**Pain Pump Use in Shoulders**

Pain pumps have been commonly used in the glenohumeral joint following shoulder arthroscopy. However, studies regarding the quality of pain relief gained through pain pump use
within the joint are inconclusive. For example, Barber et al. conducted a study on pain pump usage following shoulder surgery where patients infused continuously with 0.5% bupivacaine at a flow rate of 2.08mL/hr reported lower pain scores than did patients infused with normal saline at the same flow rate. However, the patients did not use a statistically significant less amount of comedication, indicating the decreased pain score reported by the patients infused with bupivacaine exhibited little clinical significance. Additionally, pain scores reported by the bupivacaine-infused group did not remain significantly lower for the duration of the study period, causing them to actually ingest a higher amount of comedication than the saline-infused group after the pain pumps were empty and removed during the later time points of the study. As such, the study demonstrates that pain pumps placed in the glenohumeral are only marginally effective for pain control following shoulder arthroscopy.

Like in the knee joint, numerous studies and case reports have documented glenohumeral chondrolysis to be a serious safety concern when pain pumps are used intra-articularly within the glenohumeral joint. For instance, a study by Hansen et al. provided more information on the effects of pain pumps by analyzing the charts of 177 shoulders that underwent arthroscopy performed by the same surgeon. Of the 177 shoulders studied, 12 (6.8%) resulted in chondrolysis. However, when all 177 shoulders were divided by procedure, it was found that 30 patients were treated with an arthroscopic stabilization procedure. Then, when broken further into pain management techniques, of the 30 shoulders that underwent stabilization arthroscopy, 19 were fitted with intra-articular pain pumps. Finally, when returning to the initial 12 shoulders that presented with chondrolysis, it was found that all 12 patients were in the 19 (63%) that underwent stabilization arthroscopy and were treated with intra-articular pain pumps for pain control (see figure 1).
Case studies have also been conducted recently to determine causes of chondrolysis following shoulder arthroscopy. Of the cases reviewed, all patients demonstrated a very similar postoperative course, initially doing well, but then returning to the office with decreased range of motion, pain, and radiographic changes. The one common factor among all cases was the use of intra-articular pain pumps that delivered bupivacaine (0.25% or 0.5%) via constant infusion following shoulder arthroscopy. Of the 23 patients followed by Bailie et al. who returned to the office suffering symptoms of chondrolysis that was later confirmed via radiographs, 17 (74%) were fitted with pain pumps either in the subacromial space (n=1) or into the glenohumeral joint (n=16). Of those 17, six were given epinephrine in the pain pump as an adjunct. Similarly, McNickle et al. followed 20 patients who suffered signs and symptoms of chondrolysis in their case series, revealing that 16 (80%) of those patients received pain pumps inserted under direct visualization into the glenohumeral joint. Anderson et al. analyzed 113 shoulder arthroscopies, reviewing cases where either high-flow or low-flow pain pumps were used following shoulder arthroscopies. These pumps delivered 0.5% bupivacaine at total volumes of 275 mL at flow rates of 5mL/hour or total volumes of 100 mL at flow rates of 2 mL/hour respectively (Anderson, et al., 2010). They determined that 50% of patients receiving high flow medication and 17% of those receiving low-flow medication developed chondrolysis. However, none of their patients that underwent the same types of procedures during the study timeframe but did not have an intra-articular pain pump placed for pain relief developed chondrolysis. This, therefore, helps to illustrate not only the dangerous link between intra-articular pain pumps and chondrolysis, but also helps to validate the dose-dependent nature of local anesthetics used intra-articularly, as a greater percentage of the individuals receiving the high-flow medication developed chondrolysis.
A single case study also provided a great deal of information about the resulting effects of intra-articular pain pumps (Saltzman, et al., 2009). Here, a single individual had bilateral intra-articular pain pumps inserted following bilateral shoulder arthroscopies. However, only one of the pumps functioned correctly and only that shoulder developed chondrolysis. Studies can be hard to compare to one another, as all individuals are different, thus making it impossible to exclude all intervening variables. In this case study however, all interpersonal variables can be excluded, as it simply compares a single individual’s bilateral joints. Through both clinical symptoms and radiographic illustrations, the authors deduced that only the shoulder that had a functioning intra-articular pain pump placed developed chondrolysis postoperatively, even though both shoulders underwent similar arthroscopic procedures. Although nothing can prove a causal relationship, this case study does provide a very effective illustration of the possible effects following use of intra-articular pain pumps.
Limitations with Current Research and Ideas for Future Research

The major limitations in the current research come from the inability to conduct live, prospective studies. Since chondrolysis has been documented following arthroscopic procedures, however, studies cannot be done on human subjects, as they would not comply with ethical guidelines. To gain the best understanding of the degree of detriment caused by intra-articular use of local amide anesthetics, however, prospective data gained from human models would provide the most optimal information. As such, we are unable to gain that information. Further, the prospective studies we do have are all based on information gained from animal models, and since human chondrocytes differ from animal models, we cannot generalize those results with complete confidence.

Additionally, the appearance of chondrolysis following arthroscopy is not an immediate side effect. It often takes months to years for symptoms to appear, so many people who will be affected may not be showing signs or symptoms yet. As such, it is difficult to understand the breadth of detriment caused by their use. Also, because this is a rather new topic, patients suffering with symptoms of chondrolysis may not realize the connection between their arthroscopic procedure and their current symptoms. Therefore, this is a topic that must continue to be researched and must become common knowledge among all healthcare professionals to ensure proper diagnoses are being made.

Aside from limitations in the types of research possible, the current research available now also has limitations. For example, many of the studies do not disclose the type of pain pump used, nor the doses and flow rates. Therefore, there is no way to determine the data gained thus far can be generalized to all pumps, doses, and other specific parameters. There may be variations among pump devices that have not been taken into consideration yet, so until all
variables are accounted for, there is no way to make a completely sound judgment on their safety. Again however, due to ethical guidelines this type of research should not be conducted because chondrolysis is becoming a known complication of intra-articular pain pumps.

Other important research surrounding the general use of pain pumps would be to ascertain whether or not they are effective under different circumstances. Although they have been shown to cause damage and provide little benefit when used intra-articularly, the theory behind them does show promise. New pain management techniques that do not require the use of narcotic pain medication should always be under research, as the side effects and chance for dependency is great with that class of medication. The side effects of the new techniques, however, cannot outweigh the benefits of their use, as is the case with intra-articular pain pumps. Therefore, further research should continue with pain pumps to determine whether or not they are both efficacious and safe in other circumstances. For example, there has been very minimal research on their use within the subacromial space of the shoulder, but from what has been ascertained to date, there is a possibility they may be both efficacious and safe when used in this particular circumstance (Boss, et al., 2004; Busfield, Lee, Carrillo, Ortega, & Kharrazi, 2008).

Lastly, research in postoperative use of pain pumps within the knee joint is currently strictly limited to use following ACL reconstruction, so use cannot necessarily be generalized to all intra-articular use within the knee following all intra-articular procedures. However, as evidenced by other research on the effects of local anesthetics on chondrocytes in animal models and on the effects within the glenohumeral joint, it stands to reason than any use within the knee joint will result in similar effects. It would therefore not only seem futile to conduct that research, it may also be considered unethical.
Conclusion

When considering the marginal pain relief provided by intra-articular pain pumps and their potential for serious detrimental effects within the glenohumeral and knee joints, they should not be used following shoulder arthroscopy or ACL reconstruction. Although there has been no research to provide complete statistical evidence regarding the ratio of intra-articular pain pumps used annually compared to the number of those that develop chondrolysis, of the small studies presented in this review, a large percentage of those given intra-articular pain pumps developed chondrolysis. Further, there is a great deal of research regarding the efficacy of intra-articular pain pumps, and there is no good evidence to prove that they even significantly decrease postoperative pain or reduce the amount of adjunct medication needed following surgery. Of course there is no perfect pain relief regimen, as all medications carry some sort of risk and may not completely eradicate postoperative pain. It is quickly becoming obvious, though, that the effects of intra-articular pain pumps are life-altering and lifelong. Moreover, because intra-articular pain pumps do not actually greatly decrease the need for adjunct medication, patients are not exempt from those side effects either, as narcotic consumption is often not decreased with use of intra-articular pain pumps. As such, the current research very strongly advises against the use of intra-articular pain pumps following shoulder arthroscopy and ACL reconstruction.

It is extremely important to weigh the risk-to-benefit ratio when making medical recommendations and to keep up to date with the current evidence-based medicine. Currently, the information surrounding intra-articular pain pumps that continuously infuse bupivacaine or lidocaine is not promising. Even the FDA recently issued a warning surrounding the use of continuously infused local anesthetics in pain pumps, saying “the approved drug labels for local
anesthetics do not include an indication for continuous intra-articular postoperative infusions or use of infusion devices, such as elastomeric pumps,” evidencing the need for cautious thought before use of intra-articular pumps for postoperative pain relief. Therefore, it is not recommended that these pumps should be the pain management technique of choice following knee or shoulder arthroscopy.
References


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<td>Alford et. al</td>
<td>49 Knees</td>
<td>P, Ra, DB, PC</td>
<td>ACL Repair</td>
<td>1) Exp: 0.25% BC @ 2.08 mL/hr 2) Placebo: 0.9% NS @ 2.08 mL/hr 3) Control: no catheter inserted</td>
<td>1) Exp VAS scores: lower while catheter in place (p&lt;0.03), higher after catheter removal (p&lt;0.05); no clinical significance 2) Narcotic consumption: placebo group with least usage (p&lt;0.05); no clinical significance 3) PT: higher percentage exp group able to perform activities at first session</td>
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<tr>
<td>Hoenecke et. al</td>
<td>26 Knees</td>
<td>ACL Repair</td>
<td>1) Exp: 0.25% BC @ 2.0 mL/hr 2) Placebo: 0.9% NS @ 2.0 mL/hr</td>
<td>1) Exp VAS: 2.7 v 4 (p&lt;0.05); no clinical significance 2) Exp Pain Relief Scores: 7.2 v 5.6 (p&lt;0.05); no clinical significance 3) Narcotic consumption: no statistical or clinical significance</td>
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<td>Parker et. al</td>
<td>63 Knees</td>
<td>P, Ra, DB, PC</td>
<td>ACL Repair</td>
<td>1) Exp: 0.25% BC 2) Placebo: 0.9% NS 3) Control: no catheter</td>
<td>1) Exp VAS: no statistical or clinical significance 2) Narcotic consumption: no statistical or clinical difference</td>
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<td>DeWeese et. al</td>
<td>182 Knees</td>
<td>Re</td>
<td>Total Knee Arthroplasty</td>
<td>1) Exp: 0.5% BC @ 2.0 mL/hr 2) Control: fentanyl PCA with 0.125% BC</td>
<td>1) Adjunct medication use: exp group consumed significantly more of each medication (p=0.00001, 0.003, 0.000003)</td>
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Table 1. Summary of reviewed articles pertaining to intra-articular pain pump efficacy in the knee joint; Key: P-prospective, Ra-randomized, DB-double blinded, PC-placebo controlled, BC – bupivacaine, NS – normal saline, PCA – patient controlled anesthesia
<table>
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<td>Fester et. al</td>
<td>21 y/o F</td>
<td>ACL repair w/ bioabsorbable screw and implant fixation</td>
<td>BC for 48 hours</td>
<td>1) Generalized knee pain beginning 7 months postop 2) MRI 12 mo postop showed tricompartmental cartilage loss 3) Repeat arthroscopy showed diffuse partial to full thickness delaminating cartilaginous lesions in all 3 compartments of knee</td>
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<tr>
<td>Fester et. al</td>
<td>18 y/o F</td>
<td>ACL repair with bioabsorbable screw and implant fixation</td>
<td>BC for 48 hours</td>
<td>1) Generalized knee pain and swelling 10 months postop 2) Radiographs 19 months postop revealed mild narrowing of medial compartment 3) MRI showed small area of edema in lateral femoral condyle and diffuse thinning of cartilage in all 3 knee compartments 4) Repeat arthroscopy at 20 months postop showed full-thickness defects of patella, trochlea, medial formal condyle, and medial tibial plateau with large chondral flaps and delaminating appearance</td>
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<tr>
<td>Fester et. al</td>
<td>41 y/o F</td>
<td>ACL repair with bioabsorbable screw fixation</td>
<td>BC for 48 hours</td>
<td>1) Generalized knee pain at 21 months postop 2) Radiographs at 23 months postop showed tricompartmental changes with near bone-on-bone appearance of medial compartment and &gt;50% of joint space in lateral compartment 3) MRI showed tricompartmental cartilage lesions, full-thickness chondral defects throughout knee</td>
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<tr>
<td>Slabaugh et. al</td>
<td>17 y/o F</td>
<td>ACL repair with bioabsorbable fixation and lateral meniscus repair</td>
<td>BC for 48 hours</td>
<td>1) Decrease in knee flexion at 8 weeks postop (underwent sedated manipulation) 2) Increased crepitus, pain, and swelling at 4 months postop 3) MRI showed tricompartmental chondrolysis 4) Repeat arthroscopy showed presence of diffuse articular cartilage damage (class III and IV) 5) Radiographs showed tricompartmental narrowing</td>
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Table 2. Summary of reviewed case series regarding the effects of intra-articular bupivacaine pain pumps. Key: BC – bupivacaine
<table>
<thead>
<tr>
<th>Authors</th>
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<th>Procedure</th>
<th>Study Groups</th>
<th>Results</th>
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<td>Barber et. al</td>
<td>49 Shoulders</td>
<td>P, Ra, DB</td>
<td>1) Arthroscopic rotator cuff</td>
<td>1) Exp: 0.5% BC @ 2.08 mL/hr</td>
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<td></td>
<td>Avg Age Exp: 47.4</td>
<td></td>
<td>2) Arthroscopic SLAP lesion</td>
<td>2) Control: NS @ 2.08 mL/hr</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Avg Age Control: 46.0</td>
<td></td>
<td>3) Subacromial decompression</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Statistically Similar</td>
<td></td>
<td>4) Arthroscopic capsular reefing</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1) Exp: significantly lower VAS scores (p&lt;0.05), but not on days 2-3</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2) Exp: did not use significantly less (p&gt;0.05) pain medication</td>
<td></td>
</tr>
</tbody>
</table>

*Table 3. Summary of article outlining efficacy of intra-articular pain pumps used within the glenohumeral joint (Barber & Herbert, 2002). Key: P-prospective, Ra-randomized, DB-double blinded, BC – bupivacaine, NS – normal saline*
<table>
<thead>
<tr>
<th>Authors</th>
<th>Demographics</th>
<th>Procedure</th>
<th>Pump Specs</th>
<th>Results</th>
</tr>
</thead>
</table>
| Petty et. al  | 18 y/o F     | Shoulder arthroscopy with subacromial decompression and rotator cuff repair | 0.5% BC with epi                                                           | 1) 3 months following procedure was unable to resume normal throwing activities  
2) Radiographs 5 months postop showed marked narrowing of glenohumeral joint  
3) MRI 5 months postop showed presence of joint space narrowing and subchondral cystic changes of glenoid and humeral head  
4) Repeat arthroscopy 6 months postop revealed severe glenohumeral degenerative changes with complete loss of glenoid cartilage and significant loss of humeral head cartilage |
| Baile et. al  | 23 Shoulders | 1) Bankart repair  
2) SLAP lesion repair  
3) Rotator cuff repair | 250-300 mL of 0.25% BC for 48 hours (used in 17 cases) Epinephrine used as adjunct in 6 | 1) At average 9.1 months postop noticed increase in pain that escalated over 4-6 week period (9 with rapid loss in ROM)  
2) Radiographs showed diffuse loss of joint space, from 1mm of loss to complete loss  
3) Repeat arthroscopies showed nearly complete dissolution of articular cartilage on glenoid and central cartilage erosion of humeral head |
| McNickle et. al | 20 Shoulders | 1) Bankart repair  
2) SLAP lesion repair  
3) Capsuoro-rraphy | 0.25-0.5% BC for 48-72 hours | 1) All patients experienced increasing pain at average 5.7 months postop  
2) All patients showed focal diffuse changes to humeral head, glenoid, or both on imaging  
3) 95% showed between 20-100% cartilage involvement on imaging  
4) 75% experienced decreased ROM at average 6.2 months postop  
5) 65% demonstrated joint space narrowing on imaging  
6) 35% experienced persistent stiffness  
7) 20% experienced weakness |
| Anderson et. al | 113 Shoulders | 1) Bankart repair  
2) SLAP lesion repair  
3) Rotator cuff repair | HF: 275 mL of 0.5% BC @ 5mL/hr  
LF: 100 mL of 0.5% BC @ 2mL/hr | 1) 32 patients given HF pumps and 16 later developed chondrolysis (50%)  
2) 12 patients given LF pumps and 2 later developed chondrolysis (17%)  
3) 69 patients did not receive pain pumps following their procedures and 0 have developed chondrolysis  
4) Since ceasing use of IAPP, no patients have since developed chondrolysis following shoulder arthroscopies |
<table>
<thead>
<tr>
<th>Authors</th>
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<th>Procedure</th>
<th>Pump Specs</th>
<th>Results</th>
</tr>
</thead>
</table>
| Saltzman et. al | 37 y/o F w/ bilateral IAPP | Bilateral SLAP repair, Bankart repair, acromioplasty, distal clavicle excision | Rt: 2% LC @ 2 mL/hour – malfunctionedLt: 2% LC @ 2 mL/hour – functioned | 1) Rt: experienced postop stiffness, so underwent manipulation, subacromial decompression, and lysis of adhesions – no damage to articular cartilage noted  
2) Lt: experienced postop stiffness and decreased ROM so underwent lysis of adhesions, but pain persisted  
3) Lt: required repeat arthroscopy 9 months postop where it was noted that the humeral head and glenohumeral joint were nearly completely devoid of articular cartilage  
4) Forward flexion: R – $140^\circ$, L – $30^\circ$  
5) External rotation: R – $60^\circ$, L – $0^\circ$  
6) Internal rotation: R – T12, L – buttock |

*Table 4.* Summary of reviews on intra-articular pain pump safety within the glenohumeral joint. Key: IAPP – intra-articular pain pump, BC – bupivacaine, LC – lidocaine, HF – high flow, LF – low flow
Figures

177 Arthroscopies

Procedure

30 (17%) Arthroscopic Stabilizations

Pain Management

19 (63%) Intra-Articular Pain Pumps

Outcome

12 (63%) Chondrolysis

7 (37%) No Chondrolysis

11 (100%) No Chondrolysis

147 Other Procedures

Pain Management

11 Other Techniques

Outcome

11 (100%) No Chondrolysis

0 Intra-Articular Pain Pumps

Outcome

147 (100%) No Chondrolysis

Figure 1. Graphic description of case series conducted by Hansen et al. (Hansen, Beck, Beck, & Townsley, 2007)
Abstract

Objective:
The objective of this clinical review was to determine whether intra-articular pain pumps are effective and safe for treatment of postoperative pain following knee and shoulder arthroscopy.

Methods:
A search of PubMed and MD Consult was conducted for articles published within the past 25 years using the following search terms: intra-articular pain pumps, chondrolysis, knee, shoulder, glenohumeral, local anesthetics, bupivacaine, and lidocaine. A total of 29 articles fit the criteria and were reviewed.

Results:
Intra-articular pain pumps demonstrate marginal efficacy following ACL reconstruction. Further, they are unsafe, as numerous links to knee chondrolysis exist. Intra-articular pain pumps also exhibit marginal efficacy following shoulder arthroscopy, and although limited, evidence supports a link to glenohumeral chondrolysis.

Conclusion:
Intra-articular pain pumps should not be used for postoperative pain management following ACL reconstruction or shoulder arthroscopy. More research is necessary regarding pain pump use following other circumstances, such as in the subacromial space.