

# Postoperative Pain and Length of Stay Lowered by Use of Exparel in Immediate, Implant-Based Breast Reconstruction

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**Background:** Patients undergoing mastectomy and prosthetic breast reconstruction have significant acute postsurgical pain, routinely mandating inpatient hospitalization. Liposomal bupivacaine (LB) (Exparel; Pacira Pharmaceuticals, Inc., Parsippany, N.J.) has been shown to be a safe and effective pain reliever in the immediate postoperative period and may be advantageous for use in mastectomy and breast reconstruction patients.

**Methods:** Retrospective review of 90 immediate implant-based breast reconstruction patient charts was completed. Patients were separated into 3 groups of 30 consecutively treated patients who received 1 of 3 pain treatment modalities: intravenous/oral narcotic pain control (control), bupivacaine pain pump, or LB injection. Length of hospital stay, patient-reported Visual Analog Scale (VAS) pain scores, postoperative patient-controlled analgesia usage, and nausea-related medication use were abstracted and subjected to analysis of variance and multiple linear-regression analysis, as appropriate.

**Results:** Subjects were well-matched for age ( $P = 0.24$ ) regardless of pain-control modality. Roughly half (53%) of control and pain pump-treated subjects had bilateral procedures, as opposed to 80% of LB subjects. Mean length of stay for LB subjects was significantly less than control (1.5 days vs 2.00 days;  $P = 0.016$ ). LB subjects reported significantly lower VAS pain scores at 4, 8, 12, 16, and 24 hours compared with pain pump and control ( $P < 0.01$ ). There were no adverse events in the LB group.

**Conclusion:** Use of LB in this group of immediate breast reconstruction patients was associated with decreased patient VAS pain scores in the immediate postoperative period compared with bupivacaine pain pump and intravenous/oral narcotic pain management and reduced inpatient length of stay. (*Plast Reconstr Surg Glob Open* 2015;3:e391; doi: 10.1097/GOX.0000000000000355; Published online 7 May 2015.)

Current postoperative pain relief protocols for breast reconstruction patients consist of intravenous patient-controlled analgesia (PCA) transitioning to oral opioids. This approach focuses

only on the central aspects mediating pain control. Multimodal anesthesia, where local analgesia and intravenous analgesics are combined, is a preferred method for curtailing postsurgical pain due to advantages over monotherapies (ie, lower pain scores

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with subsequent reduction in opioid usage and, therefore, opioid-related adverse effects).<sup>1,2</sup>

In breast surgery, mastectomy surgical site local infiltration with bupivacaine is employed by some surgeons as a form of multimodal anesthesia.<sup>3</sup> However, the transient analgesic effect of such local anesthetics (6–8 hours for bupivacaine) has created the need for depot formulations, which release the drug slowly over time at sufficient doses to induce analgesia. Exparel (Pacira Pharmaceuticals, Inc., Parsippany, N.J.) is an extended-release, multivesicular liposomal formulation of bupivacaine administered as a depot injection.<sup>4,5</sup>

The aim of this study was to evaluate the efficacy of multimodal therapy comparing 3 different techniques: liposomal bupivacaine (LB) versus nondepot bupivacaine (NDB) pain pumps versus a control group (who received either no regional anesthesia or intraoperative lidocaine or bupivacaine) on postoperative analgesia in immediate implant-based (tissue expander or direct-to-implant) breast reconstruction. We hypothesize that the liposomal suspension of bupivacaine will produce prolonged analgesia, decrease postoperative supplemental narcotic use, and subsequently, increase patient quality of recovery after surgery.

## METHODS

The Institutional Review Board at NorthShore University HealthSystem approved this retrospective chart review. All patients who underwent mastectomy and immediate implant-based breast reconstruction, with or without lymph node dissection, from January 1, 2011, to January 31, 2014, were included in the initial chart review. Inclusion criteria for the study: Patients who had an immediate, implant-based breast reconstruction performed by 1 of 2 board-certified plastic surgeons. They also had the same postoperative pain control regimens with a hydromorphone hydrochloride (Dilaudid; Abbott Pharmaceutical, North Chicago, Ill.) PCA or morphine PCA if they had an allergy or contraindication to hydromorphone. All patients were transitioned to oral narcotics (typically hydrocodone/acetaminophen, 5/325 mg) on the first postoperative day. All patients received the same postoperative orders, including as needed antiemetic medications (ondansetron and metoclopramide), pruritus medication (diphenhydramine and hydroxyzine), and scheduled cyclobenzaprine.

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From this initial cohort, we collected 30 consecutive charts in each of 3 pain-management modalities: control (patient-controlled intravenous/oral narcotics), NDB pain pump, and LB. The pain pump was placed in the subpectoral plane underneath the implant and in a separate pocket than the drain.

### LB Injection Technique

To provide an adequate field block, the third to fifth lateral and medial intercostal nerves are targeted. In unilateral breast reconstruction, 20 mL (13.3 mg/mL) of Exparel is injected via a 25- or 27-gauge needle. However, in bilateral breast reconstruction, Exparel is diluted with 10 mL of 0.9% normal saline for a total volume of 30 mL. Each breast is then injected with 15 mL (8.86 mg/mL). For patients who receive implantation of acellular dermal matrix (ADM), the injection is performed after the ADM is sutured into position.

Initially, the medial third to fifth ribs are palpated, and 1 mL of LB is injected in the soft tissue just inferior to the rib to block the medial intercostal nerves. Care is taken to inject superficially to avoid an iatrogenic pleural or lung parenchymal injury. The syringe plunger is pulled back to ensure no blood return and extravascular injection. An additional 3 mL is used to infiltrate around the ADM suture sites inferiorly, if ADM was used. The third to fifth lateral intercostal nerves are blocked in a similar fashion as the medial intercostal block. Finally, a drain site is chosen in the lateral anterior axillary line, and 1 mL is injected into the subcutaneous tissue where the drain and suture will be placed.

### Analysis

Data collected from the chart review included postoperative PCA usage, nausea-related medication use, hospital length of stay (LOS), and patient reported Visual Analog Scale (VAS) pain scores at defined time intervals (30 minutes, 2 hours, 4 hours, 8 hours, 12 hours, 16 hours, 24 hours, and at time of discharge). For comparison, pain medications were converted to morphine equivalents to calculate total narcotic usage per hospital stay. To evaluate LB injection safety, all adverse outcomes were collected in the LB group, such as hematoma, pneumothorax, gastrointestinal, cardiac, and neurologic complications.

Statistical analyses were performed with IBM SPSS Statistics (Version 19.0.0; IBM, Armonk, N.Y.). All data are reported as mean  $\pm$  SD. Mean medication (analgesic and antiemetic) use and patient-reported pain scores were compared by analysis of variance. LOS was calculated in hours and then converted into days. LOS was also compared as the categorical value of 1-day

discharge. Categorical values or Pearson's chi-square tests were subject to assess significance. Multiple linear regression analysis was made to assess impact of identified factors (pain scores, analgesia modality, bilateral procedures, and ADM usage) on LOS.

## RESULTS

Subject demographics are reported in Table 1. As a whole, the cohorts were relatively homogenous. Mean subject age was  $55 \pm 11.2$  years, with no significant difference when charts were separated based on pain-control modality ( $P = 0.24$ ). Nearly all patients were white (82%). Fifty-seven patients (62%) underwent bilateral reconstruction ( $P = 0.014$ ), and 74 (82%) had ADM placed at the time of reconstruction ( $P = n/a$ ). Of note, ADM was placed in all subjects in the control and LB groups but in only 47% of NDB subjects. Despite the high use of ADM in control and LB subjects, the intraoperative fill

volumes across all groups were not significantly different ( $P = 0.71$ ). Also, there was no significant difference in morphine equivalents, VAS pain scores, or LOS between the ADM and non-ADM subjects in the NDB group.

Table 2 reflects the clinical course of the study subjects in terms of LOS and inpatient medications. Subjects received intraoperative and postoperative analgesics and antiemetics (fentanyl, morphine, dilaudid, decadron, zofran, and reglan) in various forms and doses depending on patient-specific drug allergies. All narcotics were converted into morphine equivalents and summed throughout the subject's inpatient stay. Likewise, all antiemetic medications were summed. The mean values of these medications indicate that there was no significant difference in the administration of either analgesics or antiemetics between groups (Table 2). However, the LB group had a significantly shorter LOS when

**Table 1. Demographic Profile of the Subjects Denotes Similar Characteristics**

	LB (n = 30)	NDB (n = 30)	Control (n = 30)	Total (n = 90)	P
Age					
Mean $\pm$ SD	53.2 $\pm$ 11.5	54.7 $\pm$ 11.9	58.0 $\pm$ 10.0	55.3 $\pm$ 11.2	0.24*
Range	36–84	38–77	31–73	31–84	
Race					
White	22	26	26	74 (82.3%)	0.490†
Asian	2	3	3	8 (8.9%)	
African-American	3	0	1	4 (4.4%)	
Hispanic	3	1	0	4 (4.4%)	
Surgery					
Unilateral	6	14	14	24	0.014†
Bilateral	24	16	16	56	
% Bilateral	80%	53.30%	53.30%		
ADM use					
Yes	30	14	30	74	NA
No	0	16	0	16	
Intraoperative fill volume (mL)					
Mean $\pm$ SD	231 $\pm$ 76	252 $\pm$ 113	235 $\pm$ 101	239 $\pm$ 97	0.71*
Range	100–420	60–480	60–420	60–480	

\*Determined by 1-way analysis of variance.

†Determined by Pearson's chi-square.

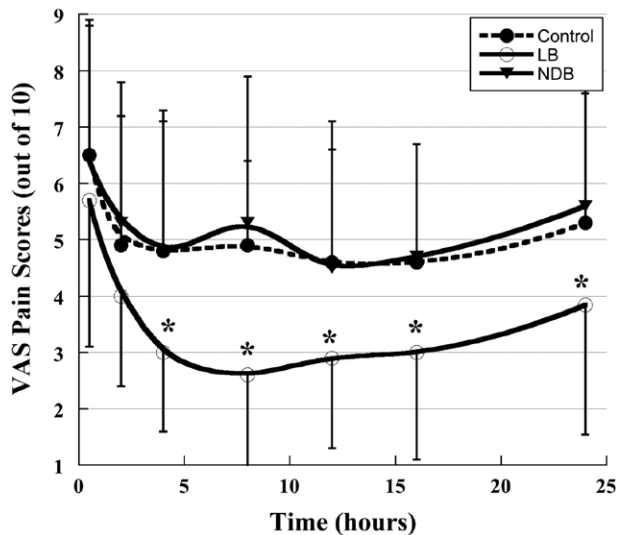
NA, not available.

**Table 2. Shorter LOS for Patients Receiving Liposomal Bupivacaine, despite Having Similar Narcotic and Antiemetic Use Profiles**

	LB (n = 30)	NDB (n = 30)	Control (n = 30)	Total (n = 90)	P
LOS (h)					
Mean $\pm$ SD	34.2 $\pm$ 16.2	41.5 $\pm$ 21.4	45.2 $\pm$ 18.4	40 $\pm$ 19.2	0.074*
LOS (d)					
Mean $\pm$ SD	1.5 $\pm$ 0.8	1.9 $\pm$ 0.9	2.0 $\pm$ 0.8	1.8 $\pm$ 0.9	0.062*
1-d discharge	20	13	9	42	0.016†
Morphine equivalents (mg)					
Mean $\pm$ SD	1137 $\pm$ 508	1275 $\pm$ 580	1205 $\pm$ 500	1206 $\pm$ 528	0.605*
Antiemetic medications (mg)					
Mean $\pm$ SD	13.7 $\pm$ 7.3	12.0 $\pm$ 9.2	12.7 $\pm$ 7.3	12.8 $\pm$ 7.9	0.72*

\*Determined by 1-way analysis of variance.

†Determined by Pearson's chi-square.



**Fig. 1.** Mean VAS pain scores are significantly lower in patients treated with LB.

measured by days. There was a significant increase in the number of LB patients being discharged within 1 day when compared with both NDB and controls ( $P = 0.016$ ). Multiple linear regression of factors that influenced 1-day discharge found a significant effect when comparing pain-control modality ( $P = 0.02$ ) and VAS pain score at 24 hours ( $P < 0.01$ ).

Patient-reported VAS pain scores for the LB group reflected significantly lower pain at 4, 8, 12, 16, and 24 hours postoperatively ( $P < 0.01$ ; Fig. 1). Again, these subjects had equivalent narcotic profiles to the control and NDB groups, with delivery of analgesia being different. Considering the effect of bilateral procedures on overall VAS pain score reporting, multiple-linear regression was undertaken for pain scores at 12 and 24 hours with pain control modality and bilateral procedures as factors. There was no significant interaction ( $P = 0.81$ ). There were no adverse events in the LB group, including pneumothorax, hematoma, or medication toxicity.

## DISCUSSION

In patients undergoing immediate implant-based breast reconstruction, use of LB injection lowered postoperative pain scores and shortened inpatient LOS compared with subjects on bupivacaine pain pumps or PCA narcotic delivery. LB is a relatively new analgesic drug that has been found to be safe and effective in other surgical applications.<sup>6,7</sup> It provides 48–72 hours of pain control without the need of additional catheters or injections.<sup>8</sup> We note no complications in the LB-treated group, which is in accordance with previous reports.<sup>3,6,9</sup>

Intraoperative blocks with lidocaine or bupivacaine have traditionally been used to control pain in mastectomy and breast reconstruction patients; however, there are significant instances of breakthrough pain, which can result in increased patient morbidity and increased LOS. Our data show an increase in VAS pain scores for patients receiving PCA pain control, compared with patients in LB group. Although pain pumps are effective, disadvantages such as the burden of another catheter and heavy pump, kinking or malfunction of the catheter, and infections have limited their use.<sup>10,11</sup> Further, the analgesic is infused into a pocket where drains are placed, which may cause drug loss via egression through the drains. Our data demonstrated that in this series, pain pumps provided a limited improvement in the pain control compared with the control, PCA narcotic group, but LB was superior.

The control group received no intraoperative local anesthetic, lidocaine, or bupivacaine. Many surgeons still perform breast reconstruction without any intraoperative regional anesthetic and rely on intravenous narcotics postoperatively to manage pain. This study did not have enough subjects to identify any difference between patients receiving no intraoperative local and those receiving lidocaine or bupivacaine. All 3 groups had similar pain scores at 30 minutes and 2 hours. The control group and the pain pump group continued to have similar pain trends, whereas the LB group had improved pain scores in the immediate postoperative period, which may have significantly affected LOS. It is clear that subjects who received LB reported lower pain scores and had a greater likelihood of discharge after 1 day.

Adequate postoperative pain control is essential for the acute and long-term wellbeing of the patient. Postmastectomy pain syndrome (PMPS) has been reported to occur in 20–52% of patients undergoing mastectomy, but immediate breast reconstruction has not been shown to increase the incidence of PMPS.<sup>12,13</sup> Severe postoperative pain has been associated with the development of PMPS.<sup>12,14</sup> This pain can add to an already psychologically devastating experience and negatively impact quality of life.<sup>15</sup>

Second, there has been an emphasis on reducing the hospital LOS to diminish the risk of nosocomial infections, deep vein thromboses, and overall medical care cost. The average LOS of the LB group was less than that of pain pump patients and control group. Furthermore, the cost of LB and pain pumps is similar (approximately \$300), and there is no immediate cost savings in using one versus the other. However, the decreased LOS could represent significant cost savings.

This retrospective chart review is limited by the small sample size and differences in subjects' clinical management. All LB and control subjects had ADM implanted, whereas only half of the NDB subjects had ADM. Considering the VAS pain scores were similar between control and NDB subjects, it is possible that ADM implantation did not affect pain scores. All patients received preoperative counseling, which included expectations for pain and its management. Furthermore, LB patients were made aware of its use, which may have influenced pain score reporting. Studies have shown that having realistic preoperative expectations regarding postoperative pain can improve pain control in general.<sup>14,16</sup> Patients with severe preoperative anxiety and emotional instability are also more likely to have pain issues regardless of treatment modalities.<sup>14</sup> It is interesting to note that although the majority of LB subjects had bilateral procedures, the reported VAS pain scores were lower. Increased LOS was also not associated with bilateral reconstructions. One would expect bilateral reconstruction to negatively impact VAS pain score and LOS reporting, so the actual difference in analgesia may be greater. A prospective, randomized controlled study would overcome these limitations and strengthen the overall conclusion.

## CONCLUSIONS

This study supports the use of LB for postoperative pain management in immediate, implant-based breast reconstruction patients. Reductions in VAS pain scores and LOS are favorable results. LB is also more convenient for the patient by removing the additional catheter burden of the pain pump systems.

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