



Date: 11/21/2022

Drug Affected: Exparel (Liposomal Bupivacaine)

Dear Providers,

Exparel (liposomal bupivacaine) will no longer be stocked at Our Lady of the Lake Regional Medical Center. We have provided a list below of alternative cocktails derived from evidence-based practices. Please review the choices below, and select the cocktail of choice to allow for pharmacy to stock the correct medications in the appropriate operating room dispensing areas. Other medication options or strengths may be written on the blank spaces provided below.

Please check all that apply per specific cocktail:

- Bupivacaine 0.5%
- Bupivacaine 0.25%
- Bupivacaine + Meloxicam (Zynrelef) *
- Clonidine
- Dexamethasone
- Epinephrine 1:100,000
- Ketorolac
- Lidocaine 1%
- Lidocaine 2%
- Ropivacaine
- Tetracaine
- _____
- _____
- _____

***May only be used for FDA approved indications** (foot and ankle procedures, small to medium open abdominal procedures, lower extremity total joint arthroplasty procedures)

Abdominal Surgery

Alternatives Studied	
Bupivacaine	Bupivacaine + Meloxicam (Zynrelef)

Summary of Use for Abdominal Surgery Data

- **Key Points:** Use of intraoperative liposomal bupivacaine did not reduce length of stay, post-operative opioid use, or intra-operative complications.

Trial Design	Patient Population	Interventions	Outcomes	Conclusion
Fafaj 2020 ¹ <i>Location:</i> U.S. <i>Design:</i> single-center, double-blind, placebo-controlled, prospective N=164	Adult patients undergoing open, elective, ventral hernia repairs with mesh placed in the retromuscular position	<ul style="list-style-type: none"> • LB 266 mg + Bup HCl 150 mg (+ 40 mL NS) TAP (n=57) • Bup HCl 150 mg (+ 60 mL NS) TAP (n=55) • Placebo (120 mL NS) TAP (n=52) 	<u>Mean postop opioid use, MME:</u> <ul style="list-style-type: none"> • 0-72 hours: 310 vs 325 vs 350, p=0.725 • POD 0 to discharge: no difference between groups <u>Median length of stay, days:</u> 5.0 vs 5.0 vs 5.0, p=0.48 <u>Intraoperative complications:</u> 5.3% vs 7.3% vs 3.9%, p=0.952	<ul style="list-style-type: none"> • Median age: 59 years <u>Conclusion:</u> no apparent benefits of using LB vs Bup HCl TAP blocks in ventral hernia repair

1. Fafaj A, Krpata DM, Petro CC, et al. The efficacy of liposomal bupivacaine on postoperative pain following abdominal wall reconstruction: a randomized, double-blind, placebo-controlled trial. *Ann Surg.* 2020. Epub before print. doi:10.1097/SLA.0000000000004424

Bariatric Surgery

Alternatives Studied
Bupivacaine

Summary of Use for Bariatric Surgery Data

- **Key Points:** Use of intraoperative liposomal bupivacaine did not reduce pain scores, length of stay, or decrease use of post-operative opioids

Trial Design	Patient Population	Interventions	Outcomes	Conclusion
Ma 2019 ¹ <i>Location:</i> U.S. <i>Design:</i> RCT N=231	Patients who underwent laparoscopic bariatric surgery	LB 266 mg diluted with 20 mL NS + Bup HCl 150 mg (n=89) Bup HCl 150 mg diluted in 60 mL NS (n=90)	<u>Median postop pain scores (scale 0-10)</u> • POD 1: 3.5 vs 3.8, p=0.13 • Total in hospital: 3.5 vs 3.6, p=0.21 <u>Median daily opioid consumption, MME</u> • POD 1: 8.0 vs 7.5, p=0.94 • Total in hospital: 8.3 vs 7.5, p=0.85 <u>Length of hospital stay, days:</u> 1.3 vs 1.2, p=0.32	Mean age: 39.2 years <u>Conclusion:</u> LB + Bup HCl did not provide a significant reduction in opioid consumption in patients who underwent laparoscopic bariatric surgery
Wong 2020 ² <i>Location:</i> U.S. <i>Design:</i> retrospective review N=219	Patients undergoing laparoscopic Roux-en-Y gastric bypass, sleeve gastrectomy, or sleeve-to-bypass conversion	LB 266 mg + Bup HCl 75 mg + 100 mL NS TAP (n=75) Bup HCl 125 mg + 100 mL NS TAP (n=73) No TAP (n=71)	<u>Mean fentanyl PCA usage, mcg:</u> 351.4 vs 360.7 vs 353.9, p=0.97 <u>Mean total PCA usage, mcg:</u> 424.1 vs 432.2 vs 427.5, p=0.98 <u>Patients who required additional opioids:</u> 83.9% vs 95.9% vs 70.5%, p>0.05 <u>Mean NSAID usage, mg:</u> 14.2 vs 42.5 vs 21.3, p=0.37 <u>Mean acetaminophen usage, mg:</u> 486.4 vs 501.0 vs 353.4, p=0.15 <u>Mean pain scores (scale 1-10):</u> 4.3 vs 4.7 vs 4.7, p=0.35	• Mean age: 39-42 years <u>Conclusion:</u> use of intraoperative LB did not decrease the use of postop opioids, reduce pain scores, or reduce length of stay

			<u>Mean time to ambulation, days:</u> 1.7 vs 1.6 vs 2.0, p=0.79 <u>Mean length of stay, days:</u> 1.6 vs 1.5 vs 1.4, p=0.32 <u>Patients with nausea:</u> 35.7% vs 57.8% vs 46.5%, p=0.03	
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Bariatric Surgery Data

1. Ma P, Lloyd A, McGrath M, et al. Efficacy of liposomal bupivacaine versus bupivacaine in port site injections on postoperative pain within enhanced recovery after bariatric surgery program: a randomized clinical trial. *Surg Obes Relat Dis.* 2019;15(9):1554-1562. doi:10.1016/j.soard.2019.06.004
2. Wong KA, Cabrera AG, Argiroff AL, et al. Transversus abdominis plane block with liposomal bupivacaine and its effect on opiate use after weight loss surgery: a randomized controlled trial. *Surg Obes Relat Dis.* 2020;16:886-93.

Cardiac Surgery

Alternatives Studied
Bupivacaine

Summary of Use for Cardiac Surgery:

- **Key Points:** Liposomal bupivacaine did not decrease opioid consumption on pain scores in those undergoing elective coronary artery bypass surgery.

Trial Design	Patient Population	Interventions	Outcomes	Conclusion
Lee 2019 ¹ <i>Location:</i> U.S. <i>Design:</i> prospective, randomized N=79	Patients undergoing elective coronary artery bypass grafting through a median sternotomy performed on or off cardiopulmonary bypass	<ul style="list-style-type: none"> • LB 0.53% parasternal nerve blocks (n=38) • NS parasternal nerve blocks (n=41) 	<u>Median postop pain scores (scale 0-10)</u> <ul style="list-style-type: none"> • 12 hours: 1.5 vs 2.0, p>0.05 • 24 hours: 2 vs 4, p>0.05 • 48 hours: 1.5 vs 2.0, p>0.05 • 72 hours: 1 vs 0, p>0.05 <u>Median postop morphine consumption, MME</u>	<ul style="list-style-type: none"> • Mean age: 65 years • <u>Conclusion:</u> LB did not decrease pain scores or opioid consumption in patients undergoing elective coronary artery bypass surgery

			<ul style="list-style-type: none"> • 4 hours: 5.0 vs 8.4, p>0.05 • 12 hours: 13.0 vs 16.0, p>0.05 • 24 hours: 11.5 vs 18.0, p>0.05 • 48 hours: 4.17 vs 3.33, p>0.05 • 72 hours: 2.50 vs 3.33, p>0.05 <p><u>Median ICU length of stay, hours: 22.8 vs 25, p=0.846</u></p> <p><u>Median hospital length of stay, days: 5 vs 5, p=0.140</u></p>	
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Cardiac Surgery Data

1. Lee CY, Robinson DA, Johnson Jr CA, et al. A randomized controlled trial of liposomal bupivacaine parasternal intercostal block for sternotomy. *Ann Thorac Surg.* 2019;107:128-34.

Colorectal Surgery

Alternatives Studied
Bupivacaine

Summary of Use for Colorectal Surgery

- **Key Points:** Use of intraoperative liposomal bupivacaine did not reduce length of stay, post-operative opioid use, or intra-operative complications.

Trial Design	Patient Population	Interventions	Outcomes	Conclusion
McKeown 2020 ¹ <i>Location:</i> U.S. <i>Design:</i> retrospective cohort N=154	Patients undergoing elective ileostomy reversal or colostomy reversal	<ul style="list-style-type: none"> • LB 266 mg (n=87) • Bup HCl 0.25% (n=67) 	<p><u>Total daily opioid consumption, MME:</u> 75.7 vs 78.8, p=0.66</p> <p><u>Mean length of stay, days:</u> 3.45 vs 4.27, p=0.009</p>	<ul style="list-style-type: none"> • Mean age: 52-55 years <p><u>Conclusion:</u> LB has the potential to lower the length of stay in ileostomy reversal or colostomy reversal but did not decrease opioid consumption</p>



<p>Felling 2018² <i>Location:</i> U.S. <i>Design:</i> open-label, prospective, RCT N=179</p>	<p>Patients undergoing elective colorectal surgery</p>	<ul style="list-style-type: none">• LB 133 mg (on each side) TAP (n=92)• Epidural analgesia with Bup HCl 0.0625% + fentanyl at 6-8 mL/hr (n=87)	<p><u>Mean pain score (scale 0-10):</u> 2.32 vs 2.12, p=0.387 <u>Mean overall benefit of analgesia score:</u> 0.37 vs 0.48, p=0.091 <u>Mean postop opioid use (excluding fentanyl from epidural), MME</u> • POD 0: 54.64 vs 27.55, p<0.001 • POD 1: 13.34 vs 0.87, p<0.001 • POD 2: 2.61 vs 1.73, p=0.706 • POD 3: 0.22 vs 0.26, p=0.845 • Total: 98.29 vs 54.70, p<0.001 <u>Median length of stay, days:</u> 3.267 vs 3.268, p=0.846 <u>Overall complications:</u> 32.6% vs 33.3%, p>0.99 <u>30-day readmission:</u> 13% vs 16%, p=0.846</p>	<ul style="list-style-type: none">• <u>Conclusion:</u> TAP with LB reduces early opioid use but shows little difference in reducing scores compared to Bup HCl
<p>Torgeson 2018³ <i>Location:</i> U.S. <i>Design:</i> prospective, randomized N=83</p>	<p>Patients undergoing elective laparoscopic or open colorectal surgery</p>	<ul style="list-style-type: none">• LB 266 mg (+ 60 mL NS) TAP (n=44)• Bup HCl 0.0625% + fentanyl epidural (n=39)	<p><u>Mean time to discharge, days:</u> 2.8 vs 3.3, p=0.023 <u>Patients with nausea:</u> 31.7% vs 13.5%, p=0.057</p>	<ul style="list-style-type: none">• Mean age: 59-62 years• <u>Conclusion:</u> LB TAP allowed for a ~0.5 day earlier discharge compared to Bup HCl epidural in patients undergoing colorectal surgery

Colorectal Surgery Data:

1. McKeown DG, Sokas C, Isenberg G, Goldstein S, Phillips B. Effectiveness of liposomal bupivacaine in ostomy reversal: a retrospective review. *Am Surg*. 2020. Epub ahead of print. doi:10.1177/0003134820951434
2. Felling DR, Jackson MW, Ferraro J, et al. Liposomal bupivacaine transversus abdominis plane block versus epidural analgesia in a colon and rectal surgery enhanced recovery pathway: a randomized clinical trial. *Dis Colon Rectum*. 2018;61(10):1196-204.
3. Torgeson M, Kileny J, Pfeifer C, Narkiewicz L, Obi S. Conventional epidural vs transversus abdominis plane block with liposomal bupivacaine: a randomized trial in colorectal surgery. *J Am Coll Surg*. 2018;227:78-83.

Neurosurgery/Spinal Surgery

Alternatives Studied	
Bupivacaine	Bupivacaine
	Epinephrine

Summary of Use for Neurosurgery/Spinal Surgery

- **Key Points:** Many studies found little to no difference in opioid use, post-operative pain scores, or length of stay with liposomal bupivacaine when compared to bupivacaine. Of note, some studies below showed that both groups received peri-incisional bupivacaine + epinephrine followed by liposomal bupivacaine versus bupivacaine.

Trial Design	Patient Population	Interventions	Outcomes	Conclusion
Chung 2020 ¹ Location: U.S. Design: retrospective cohort N=159	Adult patients undergoing either elective primary or revision long instrumented fusion to correct a spinal deformity	Both groups received peri-incisional 30 mL Bup HCl 0.5% + epi (5 mg/mL) • LB 266 mg in 120 mL NS (n=90) • Bup HCl 0.5% 30 mL in similar volume (n=96)	<u>Mean postop pain scores (scale 0-10)</u> • POD 1 = 4.8 vs 5.7, p=0.02 • POD 2 = 5.4 vs 5.4 • POD 3 = 5.6 vs 5.7 • POD 4 = 5.6 vs 5.6 • POD 5 = 5.8 vs 5.7 • POD 6 = 6.5 vs 7.0 • POD 7 = 6.1 vs 7.0 <u>Mean postop opioid use, MME</u> • POD 1 = 59 vs 61 • POD 2 = 39 vs 49 • POD 3 = 12 vs 25, p=0.01 • POD 4 = 6 vs 12 • POD 5 = 3 vs 7 • POD 6 = 5 vs 1 • POD 7 = 3 vs 5	• Mean age 54 years • <u>Conclusion:</u> use of LB in spinal deformity surgery does not appear to offer benefit over Bup HCl



			<p><u>Mean length of stay, days</u></p> <ul style="list-style-type: none"> • 4.7 vs 4.8 <p><u>Complication rates</u></p> <ul style="list-style-type: none"> • Overall: no differences • Ileus: 7.8% vs 4.3%, p=0.216 • Superficial wound infection: 1.1% vs 0.0%, p=0.189 	
<p>Katsevman 2020² <i>Location:</i> U.S. <i>Design:</i> retrospective cohort N=122</p>	<p>Neurosurgical patients who underwent PLIF or TLIF procedures through an open midline approach</p>	<ul style="list-style-type: none"> • LB 266 mg + Bup HCl 150 mg Bup HCl (total 40 mL) (n=97) • Bup HCl 150 mg (n=25) 	<p><u>Mean total opioid consumption, MME</u></p> <ul style="list-style-type: none"> • 0-12 hours: 17.6 vs 16.2, p=0.5895 • 12-24 hours: 12.5 vs 11.7, p=0.3042 • 24-36 hours: 10.4 vs 12.7, p=0.5158 • 36-48 hours: 10.8 vs 13.6, p=0.4536 • 48-60 hours: 6.8 vs 11.1, p=0.2833 <ul style="list-style-type: none"> ○ IV opioids: 0.3 vs 1.2, p=0.0494 • 60-72 hours: 9.6 vs 12.8, p=0.6035 <p><u>Mean postop pain scores (scale 0-10)</u></p> <ul style="list-style-type: none"> • 0-12 hours: 5.2 vs 3.9, p=0.0079 • 12-24 hours: 4.3 vs 3.4, p=0.1493 • 24-36 hours: 3.4 vs 2.7, p=0.3701 • 36-48 hours: 3.2 vs 3.2, p=0.9606 • 48-60 hours: 1.8 vs 2.4, p=0.5565 • 60-72 hours: 2.7 vs 2.6, p=0.9389 <p><u>Median length of stay, days</u></p> <p>1.94 vs 3.08, p=0.0043</p>	<ul style="list-style-type: none"> • Mean age 57-58 years • 90% PILF procedure; 5% TLIF procedure, 5% had both <p><u>Conclusion:</u> little difference in opioid use or postop pain scores between LB and Bup HCl groups, but lower hospital stay in LB group</p>
<p>Roh 2020³ <i>Location:</i> U.S. <i>Design:</i> retrospective cohort N=210</p>	<p>Adults who underwent posterior lumbar spinal fusion surgery</p>	<p><i>All patients received initial local injection of Bup HCl 0.25% + epi</i></p> <ul style="list-style-type: none"> • LB 266 mg in 100 mL NS (n=105) • Bup HCl (n=105) 	<p><u>Mean postop pain scores (scale 0-10)</u></p> <ul style="list-style-type: none"> • Day 1, with activity: 4.8 vs 4.8, p=0.9 • Day 1, at rest: 3.9 vs 3.9, p=0.9 	<ul style="list-style-type: none"> • Mean age 60 years • Primary author of trial is a consultant for Pacira Pharmaceuticals



			<ul style="list-style-type: none"> • Cumulative, with activity: 4.8 vs 4.7, p=0.5 • Cumulative, at rest: 3.8 vs 3.5, p=0.1 • <u>Mean postop opioid usage, MME</u> • Day 0: 102.7 vs 152.1, p<0.001 • Day 1: 49.0 vs 81.4, p<0.001 • Day 2: 29.6 vs 48.7, p<0.001 • <u>Patient ambulation post-surgery</u> • <12 hours: 61.2% vs 3.0%, p<0.001 • 12-24 hours: 33.0% vs 90.0%, p<0.001 • >24 hours: 5.8% vs 7.0%, p=0.73 • <u>Median walk distance on first mobilization, feet</u> • 150 vs 175, p=0.02 • <u>Mean length of stay, days</u> • 1.8 vs 2.7, p<0.05 	<ul style="list-style-type: none"> • <u>Conclusion</u>: no difference in postoperative pain scores but lower opioid use and length of stay in LB group
<p>Brown 2019⁴ <i>Location</i>: U.S. <i>Design</i>: randomized, placebo-controlled, un-blinded, pilot study N=59</p>	<p>Adults undergoing primary, 1-, or 2-level elective open posterior lumbar decompression and instrumented fusion for degenerative spondylosis</p>	<p><i>Injections made prior to wound closure</i></p> <ul style="list-style-type: none"> • LB 266 mg in 60 mL NS (n=33) • NS 60 mL (n=26) 	<p><u>Mean length of stay, days</u></p> <ul style="list-style-type: none"> • 3.9 vs 3.9, p=0.92 <p><u>Adverse events</u></p> <p>No statistically significant difference in any adverse events</p>	<ul style="list-style-type: none"> • Mean age 60 and 63 years in LB and NS groups • Trial funded by Pacira Pharmaceuticals • <u>Conclusion</u>: no difference in length of stay or adverse events between NS and LB
<p>Grieff 2016⁵ <i>Location</i>: U.S. <i>Design</i>: retrospective, matched cohort N=116</p>	<p>Adults who underwent posterior-approach primary decompression and fusion, cervical and lumbar spinal surgeries for spondylotic pathologies</p>	<ul style="list-style-type: none"> • LB 266 mg + up to 40 mL NS (n=51) • Bup HCl 0.5% 20 mL (n=65) • *Further comparison between cervical (n=52) and lumbar (n=64) spinal surgery 	<p><u>Mean analgesic requirements, MME/day</u></p> <ul style="list-style-type: none"> • Cervical: 2.7 vs 5.7, p=0.27 • Lumbar: 7.1 vs 17.3, p=0.30 <p><u>IV rescue pain medication requirements, MME/day</u></p> <ul style="list-style-type: none"> • Cervical: 0.39 vs 1.0, p=0.31 	<ul style="list-style-type: none"> • Mean age 62 years • <u>Conclusion</u>: no difference in LB vs Bup HCl groups in terms of analgesic requirements, rescue pain medications, length of stay,

			<ul style="list-style-type: none"> • Lumbar: 0.37 vs 1.0, p=0.08 <p><u>Mean length of stay, days</u></p> <ul style="list-style-type: none"> • Cervical: 4.9 vs 4.7, p=0.78 • Lumbar: 5.9 vs 5.6, p=0.49 <p><u>Complication rate</u></p> <ul style="list-style-type: none"> • Cervical: 16.6% vs 8.8%, p=0.92 • Lumbar: 26.5% vs 18.4%, p=0.41 	or complication rates
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Neurosurgery/Spinal Surgery data:

1. Chung AS, Crandall D, Revella J, Adeniyi B, Chang YHH, Chang MS. Does local administration of liposomal bupivacaine reduce pain and narcotic consumption in adult spinal deformity surgery? *Global Spine J.* 2020; online ahead of print. doi:10.1177/2192568220931053
2. Katsevman GA, Allison AA, Fang W, et al. retrospective assessment of the use of liposomal bupivacaine in lumbar fusions in immediate postoperative hospital care. *World Neurosurg.* 2020;S1878-8750(20)31307-3.
3. Roh MS, Kucher OA, Shick KM, Knolhoff DR, Mcgarvey JS, Peterson SC. Intramuscular liposomal bupivacaine decreases length of stay and opioid usage following lumbar spinal fusion. *Clin Spine Surg.* 2020;33(8):e359-63.
4. Brown L, Weir T, Koenig S, et al. Can liposomal bupivacaine be safely utilized in elective spine surgery? *Global Spine J.* 2019;9(2):133-137.
5. Grieff AN, Ghobrial GM, Jallo J. Use of liposomal bupivacaine in the postoperative management of posterior spinal decompression. *J Neurosurg Spine.* 2016;25(1):88-93.

Orthopedic Surgery

Alternatives Studied			
Ropivacaine	Bupivacaine	Ropivacaine	Bupivacaine + Meloxicam (Zynrelef)
Epinephrine	Lidocaine	Tetracaine	
Clonidine	Epinephrine	Epinephrine	
Ketorolac			

- **Key Points:**
 - Knee: LB does not appear to decrease pain scores, reduce length of stay (LOS), increase range of

motion (ROM), or reduce postoperative nausea and vomiting (PONV) compared to femoral nerve blocks (FNB) or traditional periarticular injections (PAI) in patients undergoing total knee arthroplasty. Some meta-analyses found decreased opioid consumption from 0-72 hours postoperatively, while others showed no difference.

- **Hip:** Data from three meta-analyses was inconsistent, with one finding significant reductions in pain scores and opioid use up to 48 hours, while two found little to no difference. Similarly, two found a reduced LOS in the LB group, though clinical significance is uncertain, and one showed no difference. Two reported on PONV, finding a significant reduction with LB.
- **Shoulder:** No difference was found in pain scores, opioid consumption, LOS, or PONV in patients undergoing total shoulder arthroplasty.
- **Ankle:** In a single study evaluating the use of LB vs a continuous popliteal sciatic nerve block, no difference was found between groups in pain score, narcotic use, or complications/readmissions throughout the study period. In ankle fracture, a case series showed variable response to LB and prospective trial showed lower pain scores from 4-72 hours.
- **Elbow:** At 24 hours, more opioids were required in the LB group, but the difference did not remain at 12 weeks. No difference in pain scores were reported throughout the study period. Higher complication rates were seen in the interscalene catheter (ISC) group, with the majority being directly related to the catheter/pump.
- **Hand:** Little to no difference in pain score or opioid consumption was noted in patients treated with LB.

*Please refer to separate document for Orthopedic data

Peripheral nerve blocks (all comers)

Alternatives Studied	
Lidocaine	Ropivacaine
Epinephrine	Dexamethasone

Summary of Use for Peripheral Nerve Blocks (all comers)

- **Key Points:** In various surgeries with peripheral nerve blocks, liposomal bupivacaine was not superior to ropivacaine or bupivacaine in reducing functional or analgesic outcomes, but may reduce pain scores in the first 72 hours.

Trial Design	Patient Population	Interventions	Outcomes	Conclusion
Hussain 2021 ¹ <i>Location:</i> U.S. <i>Design:</i> meta-analysis N=9 trials	Trials evaluating adult patients undergoing any type of surgery with peripheral nerve blocks comparing LB with non-LB anesthetics	<ul style="list-style-type: none"> ● LB, 88-266 mg (n=316) ● No LB (ropivacaine or Bup HCl) (n=303) 	<u>AUC pain scores over 24-72 hours: 6.6 vs 7.6, MD 1.0 (99% CI 0.5, 1.6)</u> <u>Mean postop pain scores at rest (scale 0-10)</u>	Surgery types included: shoulder surgery (major, rotator cuff, arthroscopic), THA, TKA,

		<ul style="list-style-type: none"> • 1 hour: 2.8 vs 3.2, MD 0.4 (99% CI -0.2, 0.9) • 24 hours: 3.0 vs 3.2, MD 0.2 (99% CI -0.4, 0.8) • 48 hours: 3.4 vs 4.1, MD 0.5 (99% CI -0.2, 1.2) • 72 hours: 3.4 vs 4.0, MD 0.3 (99% CI -0.3, 0.8) <p><u>Mean postop oral morphine consumption, mg</u></p> <ul style="list-style-type: none"> • 0-24 hours: 22 vs 27, MD 1 (99% CI -3, 6) • 25-48 hours: 21 vs 29, MD 7 (99% CI -3, 16) • 49-72 hours: 15 vs 21, MD 4 (99% CI -2, 10) <p><u>Mean time to analgesic request, hours:</u> 19.4 vs 17.7, MD -1.3 (99% CI -5.3, 2.7)</p> <p><u>Opioid related side effects:</u> OR 1.5 (99% CI 0.6, 3.9)</p> <p><u>Mean length of hospital stay, days:</u> 3.9 vs 3.6, MD -0.1 (99% CI -0.3, 0.2)</p>	<p>video-assisted thoracoscopic surgery, minimally invasive lung resection, inflatable penile prosthesis placement, and total mastectomy</p> <p><u>Conclusion:</u> LB vs non LB did not provide benefit in analgesic or functional outcomes, but may reduce pain scores over the first 72 hours post-surgery</p>
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Peripheral nerve blocks (all comers) data:

1. Hussain N, Brull R, Sheehy B, et al. Perineural liposomal bupivacaine is not superior to nonliposomal bupivacaine for peripheral nerve block analgesia. *Anesthesiology*. 2021;134:147-64.

Thoracic Surgery

Alternatives Studies	
Bupivacaine	Bupivacaine
Epinephrine	Lidocaine

Summary of Use for Thoracic Surgery Data

- **Key Points:** Liposomal bupivacaine may reduce opioid use within the first 24 hours post-surgery, but not after.

Trial Design	Patient Population	Interventions	Outcomes	Conclusion
<p>Louis 2019 <i>Location:</i> U.S. <i>Design:</i> prospective, observational N=82</p>	<p>Patients undergoing a uniportal thoracoscopic lobectomy</p>	<ul style="list-style-type: none"> • LB 266 mg diluted with 20 mL NS (n=50) • Bup HCl + epi (1 mL/kg) (n=32) 	<p><u>Median postop opioid consumption, MME</u></p> <ul style="list-style-type: none"> • POD 0: 22 vs 60, p=0.001 • POD 1: 39 vs 68, p=0.03 • POD 2: 21 vs 25, p=0.58 Total: 112 vs 192, p=0.01 	<ul style="list-style-type: none"> • Mean age: 68-69 years • <u>Conclusion:</u> LB has the potential to decrease pain and lower narcotic consumption
<p>Kelley 2018⁴ <i>Location:</i> U.S. <i>Design:</i> retrospective review N=47</p>	<p>Adult patients who underwent video-assisted thoracoscopic surgery for any benign or malignant neoplasms of the lung and mediastinum, bleb resections, effusions or sympathectomy</p>	<ul style="list-style-type: none"> • LB 266 mg (+ 20 mL NS) intercostal block (n=21) • Bup HCl 50 mg + lidocaine 100 mg intercostal block (n=26) 	<p><u>Mean opioid use, MME</u></p> <ul style="list-style-type: none"> • 0-6 hours: 15.62 vs 52.41, p=0.01 • 7-24 hours: 29.98 vs 65.17, p=0.001 • 24-48 hours: 33.33 vs 37.17, p>0.05 • 48-72 hours: 19.64 vs 23.40, p>0.05 <p><u>Mean IV acetaminophen use, mg</u></p> <ul style="list-style-type: none"> • Intraoperative: 476.19 vs 444.44, p=0.80 • 0-6 hours: 285.71 vs 185.19, p=0.50 • 7-24 hours: 428.57 vs 259.26, p=0.45 <p><u>Mean IV ketorolac use, mg</u></p>	<ul style="list-style-type: none"> • Mean age: 63 (LB) vs 58 (Bup HCl) years • <u>Conclusion:</u> use of LB in intercostal block reduces opioid use within the first 24 hours post-surgery but not after

			<ul style="list-style-type: none"> • Intraoperative: 1.43 vs 1.11, p=0.85 • 0-6 hours: 0.00 vs 7.78, p=0.025 • 7-24 hours: 1.43 vs 15.56, p=0.035 <p><u>Mean length of stay, days:</u> 4.3 vs 4.2, p=0.94</p>	
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Thoracic Surgery Data:

1. Parascandola SA, Ibanez J, Keir G, Anderson J, Plankey M, Flynn D ~ et al. Liposomal bupivacaine versus bupivacaine/epinephrine after videoassisted thoracoscopic wedge resection. *Interact CardioVasc Thorac Surg* 2017;24:925–30
2. Kelley TM Jr, Bailey DW, Sparks P, Rice R, Caddell E, Currier H et al. Intercostal nerve blockade with ExparelVR results in lower opioid usage during the first 24 hours after video-assisted thoracoscopic surgery. *Am Surg* 2018;84:1433–8
3. Louis SG, King C, Baral P, Veeramachaneni N. Liposomal bupivacaine enhances the pain-control benefits of uniportal thoracoscopic lobectomy. *Ann Thorac Surg* 2019;108:1514
4. Kelley TM, Jr, Bailey DW, Sparks P, et al. Intercostal Nerve Blockade with Exparel® Results in Lower Opioid Usage during the First 24 Hours after Video-Assisted Thoracoscopic Surgery. *Am Surg* 2018;84:1433-8.

Urologic/Gynecologic Surgery

Alternatives Studied			
Bupivacaine	Lidocaine	Bupivacaine	Ropivacaine
	Epinephrine	Lidocaine	

Summary of Use for Urologic/Gynecologic Surgery:

- **Key Points:** A majority of studies found no significant reduction in opioid consumption or post-operative length of stay in urologic or gynecologic surgery patients.

Trial Design	Patient Population	Interventions	Outcomes	Conclusion
Meyer 2021 ¹ <i>Location:</i> U.S. <i>Design:</i> RCT N=102	Patients who underwent laparotomy for gynecologic surgery	<ul style="list-style-type: none"> • LB 266 mg diluted in NS to 60 mL + Bup HCl 150 mg (n=48) 	<p><u>Median daily opioid consumption, MME</u></p> <ul style="list-style-type: none"> • POD 0: 6.9 vs 10, p=0.71 • POD 1: 7.5 vs 7.5, p=0.68 	<p>Mean age: 60 years</p> <p><u>Conclusion:</u> LB + Bup HCl did not provide a significant</p>



		<ul style="list-style-type: none"> Bup HCl 150 mg in total volume of 60 mL (n=64) 	<ul style="list-style-type: none"> POD 2: 0 vs 0, p=0.42 POD 3: 0 vs 0, p=0.76 Cumulative: 21.3 vs 33.8, p=0.36 <p><u>Length of hospital stay, days: 2 vs 3 p=0.64</u></p>	reduction in either opioid consumption or postop length of stay in laparotomy for gynecologic surgery patients.
Aboukhshaba 2020 ² [abstract only] Location: U.S. Design: N=50	Patients undergoing surgical sperm extraction	<ul style="list-style-type: none"> LB (n=25) Bup HCl (n=25) 	<p><u>Mean AUC of postop pain scores</u></p> <ul style="list-style-type: none"> 48 hours: p=0.38 60 hours: p=0.53 72 hours: p=0.84 <p><u>Patients who did not require supplemental narcotics: 695 vs 56%, p=0.46</u></p>	<u>Conclusion:</u> use of LB in surgical sperm extraction did not alter pain scores or opioid consumption
Amasyali 2020 ³ [abstract only] Location: U.S. Design: prospective, randomized N=45	Patients undergoing harvest and placement of rectus fascia sling or levator plasty	<ul style="list-style-type: none"> LB 266 mg (n=21) Bup HCl 20 mL (n=24) 	<p><u>Mean subjective pain scores (scale 0-10): 7.3 vs 6.3, p=0.284</u></p> <p><u>Mean postoperative opioid use in PACU, MME: 9.7 vs 7.2, p=0.309</u></p> <p><u>Mean length of stay, hours: 17.6 vs 20.0, p=0.159</u></p>	Mean age: 58 (LB) and 68 (Bup HCl) years <u>Conclusion:</u> LB is not superior to Bup HCl for controlling pain in vaginal reconstructive surgery
Chu 2020 ⁴ Location: U.S. Design: prospective, single-blinded, randomized N=43	Adult males requiring urethroplasty with buccal mucosal graft harvesting	<ul style="list-style-type: none"> LB 266 mg (n=21) Lidocaine 2% + epi (n=22) 	<p><u>Mean postop pain scores (scale 0-10)</u></p> <ul style="list-style-type: none"> POD 1: 1.84 vs 2.75, p=0.162 POD 2: 1.69 vs 2.67, p=0.153 POD 3: 1.93 vs 2.83, p=0.190 1 month: 1.471 vs 1.429, p=0.959 <p><u>Mean postop narcotic usage, MME</u></p> <ul style="list-style-type: none"> POD 1: 12.833 vs 21,409, p=0.017 POD 2: 9.571 vs 15.109, p=0.066 Total: 22.405 vs 36.518, p=0.025 	Mean age: 54 years <u>Conclusion:</u> use of LB decreased narcotic use over first 24 hours but did not reduce pain scores compared to lidocaine group



			<p><u>Patients reporting oral numbness</u> POD 2: 87.5% vs 44.4%, p=0.013</p>	
<p>Chua 2020⁵ <i>Location:</i> U.S. <i>Design:</i> single-center, retrospective cohort N=109</p>	<p>Patients who underwent open radical cystectomy with any type of urinary diversion</p>	<ul style="list-style-type: none"> • LB 266 mg + Bup HCl 75 mg + NS 100 mL (n=53) • Epidural, with ropivacaine 0.0625% + fentanyl 2 mcg/mL given at 12 mL/hr (n=56) 	<p><u>Mean opioid use, MME</u></p> <ul style="list-style-type: none"> • Intraoperative: 65.2 vs 99.8, p<0.001 • POD 1: 18.6 vs 132.8, p<0.001 • POD 2: 22.9 vs 124.4, p<0.001 • POD 3: 24.3 vs 83.6, p<0.001 • POD 4: 16.4 vs 56.6, p=0.003 • POD 5: 9.9 vs 36.1, p=0.007 • Total: 188.3 vs 612.2, p<0.001 <p><u>Mean postop pain score (scale 0-10)</u></p> <ul style="list-style-type: none"> • POD 1: 4.6 vs 3.3, p=0.009 • POD 2: 3.5 vs 3.4, p=0.85 • POD 3: 3.7 vs 2.5, p=0.012 • POD 4: 3.1 vs 2.7, p=0.47 • POD 5: 3.2 vs 2.7, p=0.52 <p><u>Mean time to ambulation, hours:</u> 24.0 vs 30.3, p=0.18</p> <p><u>Mean length of stay, days:</u> 5.1 vs 6.8, p<0.001</p> <p><u>30-day readmission:</u> 17% vs 16%, p=0.90</p>	<p>Mean age: 66-69 years 45% of LB patients were completed opioid-free postop <u>Conclusion:</u> use of LB in radical cystectomy reduced length of stay and opioid use</p>
<p>Dengler 2020⁶ <i>Location:</i> U.S. <i>Design:</i> single-blinded, randomized N=108</p>	<p>Pregnant adults eligible to deliver vaginally and required perineum repair following delivery</p>	<ul style="list-style-type: none"> • LB 266 mg (n=53) • Bup HCl 50 mg (n=55) 	<p><u>Median postpartum vaginal pain scores (scale 0-11)</u></p> <ul style="list-style-type: none"> • PPD 1: 2 vs 2, p=0.82 	<p>Mean age: 30 years 94% also received epidural</p>



			<ul style="list-style-type: none"> • PPD 3: 2 vs 2, p=0.63 • Sum PPD 1-3: 4 vs 4, p=0.85 • PPD 7: 1 vs 1, p=0.47 <p><u>Mean ibuprofen usage, mg:</u> 3872 vs 3629, p=0.30</p> <p><u>Mean acetaminophen usage, mg:</u> 4175 vs 3678, p=0.15</p>	<p><u>Conclusion:</u> no proven benefit of LB over Bup HCl in postpartum vaginal pain scores or pain medication utilization</p>
<p>Schmidt 2020⁷ <i>Location:</i> U.S. <i>Design:</i> prospective/retrospective cohort N=62</p>	<p>Adult patients who underwent radical cystectomy (open or robotic)</p>	<ul style="list-style-type: none"> • LB 266 mg + 180 mL NS (n=34) • Bup HCl 250 mg + 150 mL NS (n=28) 	<p><u>Mean postop pain scores (scale 0-10)</u></p> <ul style="list-style-type: none"> • POD 1: 2.1 vs 2.6, p=0.23 • POD 2: 1.9 vs 2.4, p=0.19 • POD 3: 1.7 vs 1.9, p=0.69 <p><u>Mean postop opioid exposure, MME</u></p> <ul style="list-style-type: none"> • PACU: 6.5 vs 9.0, p=0.29 • Remainder of hospital stay: 42.1 vs 36.8, p=0.81 <p><u>Mean length of stay, days:</u> 4.9 vs 5.0, p=0.93</p>	<p>Mean age: 71 years 73% open procedures <u>Conclusion:</u> no difference in pain scores or opioid consumption between LB and Bup HCl in radical cystectomy</p>
<p>Iwanoff 2019⁸ <i>Location:</i> U.S. <i>Design:</i> RCT N=57</p>	<p>Patients who underwent retropubic midurethral sling placement surgery</p>	<ul style="list-style-type: none"> • LB 266 mg diluted with 60 mL NS (n=24) • Bup HCl 0.5% 30 mL plus lidocaine 1% 50 mL diluted with 100 mL NS (n=33) 	<p><u>Median postop pain scores (scale 100-mm Likert scale)</u></p> <ul style="list-style-type: none"> • POD 1: 20 vs 30, p=0.0459 • POD 2: 20 vs 20, p=0.58 • POD 3: 20 vs 20, p=0.78 • POD 4: 0 vs 15, p=0.92 • POD 5: 0 vs 5, p=0.39 • POD 6: 0 vs 0, p=0.76 • POD 7: 0 vs 0, p=0.97 	<p>Mean age: 51-53 years <u>Conclusion:</u> LB did not provide a significant reduction in postop pain in retropubic midurethral sling placement compared to Bup HCl</p>

			<p><u>Median daily opioid consumption, MME: 30 vs 0, p=0.83</u></p> <p><u>Median quality of recovery scores (QoR-15)</u></p> <ul style="list-style-type: none"> • POD 1: 124 vs 144, p=0.007 • POD 7: 139 vs 141, p=0.89 	
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Urologic/Gynecologic Surgery Data

1. Meyer LA, Corzo C, Iniesta MD, et al. A prospective randomized trial comparing liposomal bupivacaine vs standard bupivacaine wound infiltration in open gynecologic surgery on an enhanced recovery pathway. *Am J Obstet Gynecol.* 2021;224(1):70.e1-70.e11. doi:10.1016/j.ajog.2020.07.017
2. Aboukhshaba A, Hayden R, Hart K, Schlegel P. Post-operative pain control of testicular sperm extraction using liposomal bupivacaine, a randomized double blinded trial. *J Urol.* 2020;203(4S):Abstract PD58-10. [abstract only]
3. Amasyali AS, Feldkamp A, Groegler J, et al. Prospective randomized comparison of long-acting liposomal bupivacaine (exparel) versus standard bupivacaine (marcaine) for pain control following vaginal reconstructive surgery. *Neurourol Urodyn.* 2020. doi:10.1002/nau.24307 [abstract only]
4. Chu CE, Law L, Zuniga K, et al. Liposomal bupivacaine decreases postoperative length of stay and opioid use in patients undergoing radical cystectomy. *Urology.* 2020. Epub before print. doi: 10.1016/j.urology.2020.11.036
5. Chua ME, Zuckerman JM, Strehlow R, et al. Liposomal bupivacaine local infiltration for buccal mucosal graft harvest site pain control: a single-blinded randomized controlled trial. *Urology.* 2020;145:269-74.
6. Dengler KL, Simpson KJ, Strauchon CJ, Shaddeau AK, Brooks DI, Gruber DD. A randomized controlled trial of liposomal bupivacaine for pain following obstetrical laceration. *Am J Obstet Gynecol MFM.* 2020;2:100115.
7. Schmidt B, Bhambhani HP, Greenberg DR, et al. Bupivacaine local anesthetic to decrease opioid requirements after radical cystectomy: Does formulation matter? *Urol Oncol.* 2020. Epub before print. doi:10.1016/j.urolonc.2020.11.008
8. Iwanoff C, Salamon C. Liposomal bupivacaine versus bupivacaine hydrochloride with lidocaine during midurethral sling placement: a randomized controlled trial. *J Minim Invasive Gynecol.* 2019;26(6):1133-1138. doi:10.1016/j.jmig.2018.11.005