

whether they speed discharge readiness⁴ compared to femoral nerve block.

When we conducted our study, there were no randomized clinical trials that evaluated combinations of peripheral nerve block with periarticular injection. There is thus little evidence to support the assertion of Webb *et al.* that combining peripheral nerve blocks with periarticular injection offers advantages over other modalities. In fact, the reference they provide to support their assertion is a review article rather than original research.⁵

We restricted our rehabilitation analyses to passive range of motion because it was the only functional outcome reported sufficiently often to be analyzed. We agree that there are probably better methods of assessing functional recovery, and this point was conceded in the limitations section of our discussion. That said, it remains unknown which “newer” rehabilitation outcomes best predict good long-term recovery.

Including multiple analgesic approaches in recovery pathways is prudent and increasingly routine; however, it is also clear that peripheral nerve blocks substantially reduce the need for systemic analgesics and should be included in multimodal pathways when practical. For example, a recent cohort study found that patients given peripheral nerve blocks (including major plexus and femoral nerve blocks) for knee arthroplasty had shorter hospital stays and fewer readmissions, with no differences in emergency department visits or falls.⁶

Our network meta-analysis included multiple sensitivity analyses, such as excluding low-quality studies. It was based on the balance of pain control, opioid use, and passive range of motion of the prosthetic joint throughout the initial 72 postoperative hours and not at just at 72 h or any single time point.¹ We were thus able to strongly conclude that “the combination of femoral and sciatic nerve block appears to be the overall best approach,” whereas “rehabilitation parameters remain markedly understudied.”

Competing Interests

The authors declare no competing interests.

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Solvent Matters!

To the Editor:

We gladly read the article by Xing *et al.*¹ suggesting that lidocaine may exert potent antitumor activity in hepatocellular carcinoma. We would like to congratulate the authors for this *in vitro* and *in vivo* trial bringing new information to the subspecialty of onco-anesthesia.

However, we would like to point out a bias in the methodology. According to the Materials and Methods section, the authors purchased Lidocaine from Sigma-Aldrich (USA). The authors did not specify how it was diluted. It can be assumed that they followed the product specification sheet indicating that the powder is soluble in ethanol, absolute. This solvent could have an effect on cancer cells, *per se*. Indeed, percutaneous ethanol injection therapy is commonly used to treat hepatocellular carcinoma,^{2,3} and ethanol is also combined with transarterial chemoembolization.⁴ Ethanol causes tumor destruction by dehydrating tumor cells, thereby denaturing the structure of cellular proteins. As lidocaine must be solubilized at a maximal concentration of 0.21 M, ethanol is present in a range varying from 0.00446 to 4.46% in the *in vitro* experiments of Xing *et al.* Moreover, according to preclinical and clinical studies, quantifying ethanol regimens depending on the tumor size improves its curative effect.³ Therefore, the effects shown by the authors could be a consequence of the addition of ethanol to the lidocaine. To be strictly rigorous in terms of methodology, the authors should have added another control group using only the solvent.

Furthermore, as onco-anesthesia is an emergent research field, we believe it is important to promote exhaustive and clean methodology to enhance reproducibility of experiments for further research in this area.

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Competing Interests

The authors declare no competing interests.

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In Reply:

We thank Chamaraux-Tran and Beloeil for their letter and concern about our article.¹ Since the lidocaine used in our experiment was water soluble, ethanol was not required as a solvent. Therefore, there was no effect of ethanol in our experiment.

Competing Interests

The authors declare no competing interests.

Wei Xing, M.D., Ph.D., Dong-Tai Chen, M.D., Jia-Hao Pan, M.D., Yong-Hua Chen, M.D., Yan Yan, M.D., Qiang Li, M.D., Rui-Feng Xue, M.D., Yun-Fei Yuan, M.D., Wei-An Zeng, M.D., Ph.D. Sun Yat-Sen University Cancer Center, Guangzhou, China (W.-A.Z.). zengwa@mail.sysu.edu.cn

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Distal Subclavian Cannulation and Extravasation

To the Editor:

In reading “Examining the Edges of Extravasation”¹ I noticed that the subclavian catheter enters the skin quite laterally. A more lateral cannulation often tunnels through the pectoral musculature, the tail of the breast in a female patient, and a thicker portion of adipose tissue than would a more medially placed catheter. These structures are mobile and allow for the distance from the skin to the vessel to change as patients are positioned, bathed, perform physical therapy, or move of their own volition. Such motion may result in a significant portion of the proximal catheter, and thus the proximal port, leaving the vessel and causing the subsequent extravasation.

The authors do not specify the method of cannulation, but a subclavian catheter that is placed *via* landmarks is usually located quite medially while a more lateral approach is preferred with the use of ultrasound guidance so that the vein is not in the shadow of the clavicle. Technically, ultrasound guidance often results in cannulation of the axillary vein rather than the subclavian vein proper. A systematic review and meta-analysis² and a prospective study³ of ultrasound guidance for subclavian cannulation concluded that ultrasound guidance reduced the frequency of complications, such as artery puncture and hematoma, hemothorax, pneumothorax, and nerve injury relative to internal jugular vein cannulation. Ultrasound is also a means to check for a pneumothorax without the costs associated with a traditional chest roentgenogram. Although the ultrasound technique does purport many benefits, Bronshteyn and Bittner's case demonstrates one specific complication that can also occur with a more lateral cannulation, such as often occurs with the use of ultrasound guidance.

Competing Interests

The author declares no competing interests.

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This letter was sent to the author of the original article referenced above, who did not respond.—Evan D. Kharasch, M.D., Ph.D., Editor-in-Chief.