Commentary: Leveraging operative exposure—Future "targeted" opportunity or disappointment?

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Disclosures: Author has nothing to disclose with regard to commercial support.

Received for publication Sept 9, 2019; revisions received Sept 9, 2019; accepted for publication Sept 10, 2019; available ahead of print Nov 4, 2019.

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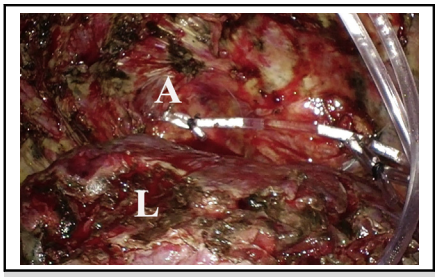
J Thorac Cardiovasc Surg 2020;159:344-5

0022-5223/$36.00

https://doi.org/10.1016/j.jtcvs.2019.09.051



Intraoperative photo after thoracoscopic radical pleurectomy and decortication.

Central Message

During routine exposures and anatomic manipulations, thoracic surgeons could introduce other long-acting cancer therapies to increase overall effectiveness of their operative interventions.

See Article page 330.

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The article in this issue of the *Journal* by Opitz and colleagues[1] is important because it describes a practical way to enhance local control of a frustrating malignancy, and extrapolations from it suggest additional promising opportunities for our specialty. The fibrin-cisplatin compound that they describe is applied to the area of the macroscopically complete pleural resection assumed to have microscopic residual disease. Many investigators target microscopic residual disease with such intraoperative adjuvants as heated chemotherapy or other cytotoxic agents, such as povidone-iodine.[2] Another example is shown in Figure 1, where a post thoracoscopic radical decortication space is about to receive photodynamic therapy.

Because of tumor biology, single intraoperative adjuvant applications have less ability to aggregate cell death that occurs by repeated therapy cycles used by our medical and radiation oncology colleagues. Because of advances in nanotechnology and biomaterials, however, prolonged release of antitumor agents is possible. We are familiar with drug-eluting coronary artery stents and hepatic tumor embolization beads, but the fibrin glue used by Opitz and colleagues[1] is clever, because it is also a product favored by surgeons for its hemostatic properties. Of interest, research with fibrin glues indicates that they can be engineered to release their payloads selectively into certain types of tumor stroma.[3] In addition, they can be filled with other specific chemotherapeutic nanoparticles, or even virus payloads that target biofilm-producing bacteria to reduce infections.[4,5]

Even as we embrace minimally invasive surgery, our colleagues similarly have been developing competitive, less toxic, and more targeted chemotherapy and radiation, which we offer to our patients as their general thoracic oncology disease managers. During our operative exposure, we routinely control ventilation, pulmonary blood flow, and pleural drainage selectively. That capability can be harnessed for additional selective airway and vascular therapies, which are beyond the scope of this commentary.[6] They should all be considered, however, as opportunities for surgeons to augment further medical and radiation therapies that are proving more and more efficacious, as well as to prevent new malignancies. For instance, the technology proposed in the article of Opitz and colleagues[1] might be useful for lung cancers with visceral pleural invasion at risk for occult pleural seeding.

Sadly, regional thoracic therapies have had long, complicated, and frequently disappointing track records. There is

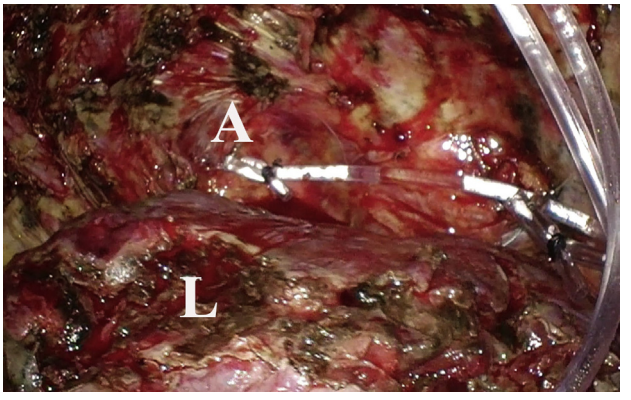

FIGURE 1. Intraoperative photograph of the right pleural space after thoracoscopic pleurectomy and decortication and before photodynamic therapy. *A*, Apex of chest with photodetector catheter sutured nearby; *L*, right lung.

good reason to hope that upcoming iterations will do better, however, because of more nuanced, targeted use by which systemic chemotherapy has evolved for lung cancer. Therefore, rather than using cisplatin for all mesothelioma patients, optimal fibrin glue drugs might be selected on the basis of initial thoracoscopic pleural biopsy genomic data or pleural catheter fluid biomarker samples during induction therapies.

If we are to succeed, we will need to expand our working knowledge of chemotherapies, immunotherapies, and biomaterials. There is a surgical precedent for this; gynecologic oncologists understand chemotherapy well, because they prescribe it routinely. We may need to expand thoracic surgery residency and postgraduate chemotherapy curricula similarly to give surgeons the tools to conceive of hybrid therapies that work actively past our routine perioperative period. Diversification of our services through adoption of other successful treatment modalities will further multidisciplinary integration and the relative importance of surgical therapies.

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