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Author's reply: Use of discard pleural fluid in molecular research

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We thank Grannis for his comments and interest in our article—The ethical use of mandatory research biopsies. *Nat. Rev. Clin. Oncol.* **8**, 620–625¹ (Use of discard pleural fluid in molecular research. *Nat. Rev. Clin. Oncol.* doi:10.138/nrclinonc.2011.114-c1).² We agree that when research biopsies are included in clinical trials involving patients with metastatic cancer, the most accessible location of the disease is the preferred site of tissue collection. In patients with lung and breast cancers, malignant pleural effusions are common, and cytologically positive cancer cells can be readily collected from these effusions and analyzed in translational studies. Genomic, transcriptomic, methylation and proteomic studies can be performed on both fresh specimens and formalin-fixed paraffin-embedded (FFPE) blocks prepared with the cells collected from these effusions.^{3–4} Importantly, molecular analyses of lung adenocarcinoma cells from pleural fluid have been used to predict response to targeted agents.^{6,7} Investigations about the biological aspects of metastatic cells in the pleural fluid can be incorporated into the clinical trial protocols, and via serial pleural thoracenteses, the molecular characteristics of these cells and potential mechanisms of acquired resistance to investigational agents can be analyzed.

The internal review boards will likely approve the protocols in which pleural fluid—that would have otherwise been discarded—is collected for scientific analysis. This approach adds minimal additional risk for the patients undergoing a clinically indicated thoracentesis. However, safety issues will arise if a protocol proposes serial or a single thoracentesis for only research purposes. Iatrogenic pneumothorax is more likely to occur after therapeutic thoracentesis and frequently requires insertion of a chest tube.⁸ Nevertheless, as outlined by Grannis, in patients with indwelling pleural catheters there is a unique opportunity to regularly collect tumor cells without the need for repeated biopsies.

Competing interests

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References

1. Olson EM, Lin NU, Krop IE, Winer EP. The ethical use of mandatory research biopsies. *Nat Rev Clin Oncol*. 2011; 8:620–625. [PubMed: 21808265]
2. Grannis FW Jr. Use of discard pleural fluid in molecular research. *Nat Rev Clin Oncol*. 10.138/nrclinonc.2011.114-c1
3. Sriram KB, et al. Diagnostic molecular biomarkers for malignant pleural effusions. *Future Oncol*. 2011; 7:737–752. [PubMed: 21675837]
4. Stancel, GA., et al. Identification of tissue of origin in body fluid specimens using a gene expression microarray assay. *Cancer Cytopathol*. <http://dx.doi.org/10.1002/cncy.20167>
5. Cheng M, Chen Y, Yu X, Tian Z, Wei H. Diagnostic utility of LunX mRNA in peripheral blood and pleural fluid in patients with primary non-small cell lung cancer. *BMC Cancer*. 2008; 8:156. [PubMed: 18513434]
6. Soh J, et al. Usefulness of EGFR mutation screening in pleural fluid to predict the clinical outcome of gefitinib treated patients with lung cancer. *Int J Cancer*. 2006; 119:2353–2358. [PubMed: 16921488]
7. Soh J, et al. EGFR mutation status in pleural fluid predicts tumor responsiveness and resistance to gefitinib. *Lung Cancer*. 2007; 56:445–448. [PubMed: 17335935]
8. Gordon CE, Feller-Kopman D, Balk EM, Smetana GW. Pneumothorax following thoracentesis: a systematic review and meta-analysis. *Arch Intern Med*. 2010; 170:332–339. [PubMed: 20177035]