Deciding site of biopsy at metastatic relapse

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To the editor,

The problem of tumour heterogeneity has been noted since the earliest use of targeted therapy, hormonal therapy for endocrine responsive breast cancer, and biopsy of the metastatic site is now an accepted procedure to assess receptor discordance. It is recommended that the biopsy site 'should be selected considering easy access, low risk of complications' [Foukakis *et al.* 2012]. Similarly, Janku suggests that 'liquid biopsies' using cell free DNA in plasma/serum can be used to monitor tumour heterogeneity at multiple time points, being a noninvasive approach with less risk to patients and at a lower cost [Janku, 2014].

Both recommendations ignore that fact that all metastases are not created equal. For example, brain metastases in breast cancer have graver prognostic significance (survival measured in months) than lymph node or bone metastases (survival measured in years). Thus, it is not surprising that there are no reports that altering treatment based on biopsy of most accessible metastasis, lead to improvement in survival. If the plan is to use targeted therapy, and with the knowledge that tumour heterogeneity exists [Hoefnagel *et al.* 2013], it is imperative that the clinically important metastasis be biopsied, irrespective of its accessibility.

Thus, the decision on biopsy site should be based on clinical significance rather than accessibility. Visceral metastases with graver prognostic significance (brain, liver, lungs) should be biopsied rather than those easily accessible, especially if

targeted therapy is planned. In future, molecular imaging of targets should soon replace invasive biopsies [Sörensen *et al.* 2014; Fleuren *et al.* 2014].

Conflict of interest statement

The author declares no conflict of interest in preparing this letter.

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