**Background**

Molecular residual disease (MRD) testing can detect cancer recurrence months to years earlier than the current standard of care, enabling earlier treatment of recurrence and improved patient outcomes. Tumor-informed MRD assays typically utilize formalin-fixed paraffin-embedded (FFPE) tumor tissue, which is available in limited quantities for some patients, for example, following core needle biopsy (CNB), after neoadjuvant treatment, or when patients need multiple tests from the same tumor sample.

**Methods**

To assess the lower limit of tissue input, we evaluated our MRD assay performance across a range of extracted tumor volumes. Thirty-seven sections from resected primary and metastatic tumors from 5 patients with renal cell carcinoma were H&E stained and macro-dissected. Tumor gDNA was extracted, quantified, prepared into libraries and sequenced. Sequenced libraries were aligned and evaluated for depth of coverage, variation of coverage and duplication rate. Somatic calling was performed on matched tumor and normal samples and a personalized panel with up to 1000 target sites was designed for each tumor section. The performance of each panel was evaluated by orthogonal validation of somatic target sites.

**Conclusions**

Patient-specific tumor-informed MRD assays have immense potential for increasingly sensitive treatment response and recurrence monitoring that can inform better treatment decisions. FFPE tumor tissue is a critical input into MRD assays but is a limited resource. This study supports a minimum DNA input of 10ng, corresponding to a tissue volume of 0.5mm³ or two 10µm slide with a 25mm² area, representing one of the lowest tissue input requirements for an MRD assay. Low FFPE tissue requirements expand the patient population that may benefit from MRD testing by utilizing samples that have low tumor content, are post-neoadjuvant therapy, or do not meet the tumor volume requirements of competing MRD offerings.