Using Prostate Biopsy Tissue Prints to Build an EDRN Reference Set for Molecular Biomarker Research

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Introduction and objectives: Tissue biopsies provide critical information about the molecular status of a patient's prostate cancer, but obtaining these valuable specimens from clinical trials is often challenging. Most clinical trials that include molecular biomarker studies of biopsy tissue rely primarily on formal fixed paraffin embedded (FFPE) specimens. However the limited amount of material remaining in the block after pathology diagnosis generally restricts the number and type of molecular studies that can be performed on these samples. Moreover, the processing of the FFPE tissue has a negative impact on both the yield and integrity of the RNA and DNA that can be recovered for analysis. One alternative to unstained FFPE tissue for molecular testing is nitrocellulose touch preps (tissue prints). Tissue prints are collected from the fresh tissue specimen and immediately snap frozen, providing a reliable source of high quality RNA and DNA from each biopsy core without compromising the tissue specimen for diagnostic H&E and immunohistochemistry (Gaston et al. 2005, 2018). Prostate biopsy tissue print collection has already been fully implemented at both academic medical centers and urology private practice sites for biomarker research. Our current objective is to integrate biopsy tissue print collection into a multi-center prostate cancer clinical trial sponsored by the NCI Early Detection Research Network (EDRN), the Prostate MRI Biomarker Study and Reference Set.

Specific Aims:

1. To develop protocols, training materials and tissue print collection kits that support the integration of prostate biopsy tissue print collection into the clinical workflow at the different EDRN study sites.
2. To confirm that the prostate biopsy tissue prints that are collected at the different study sites produce the expected yield and integrity of RNA and DNA.
3. For a subset of specimens, to compare gene expression profiles obtained from tissue prints and corresponding biopsy cores to benchmark the performance of the tissue print sampling technique for specific downstream applications.

Materials and Methods: Illustrated and video training materials have been developed to train study investigators and staff on how to collect nitrocellulose touch preps (tissue prints) from fresh prostate biopsy specimens as the core is transferred from the cutting needle to the formalin-fixation jar. The tissue print is then snap frozen and the core submitted for pathology as usual. To facilitate alignment with MR imaging, the prints and cores are oriented with an ink dot at the needle-point end. Double-sided tissue print techniques have been developed to obtain cells from both sides of the core. We have made site-specific adjustments as needed to smoothly integrate tissue print collection into the clinical workflow. For the EDRN Prostate MRI study, biopsy tissue prints are shipped on dry ice to a central biomarker analytic laboratory for processing. The expected median yields of purified RNA and DNA for tissue prints from biopsy cores that contain > 50% high-grade prostate cancer are approximately 480 and 940 ng, respectively. For tissue prints of cores with no cancer, the expected median RNA and DNA yields are approximately 250 and 920 ng, respectively.

Discussion and Conclusion: For clinical trials, tissue prints support molecular biomarker studies of valuable specimens that may otherwise be significantly limited or entirely unavailable for research.

References:

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