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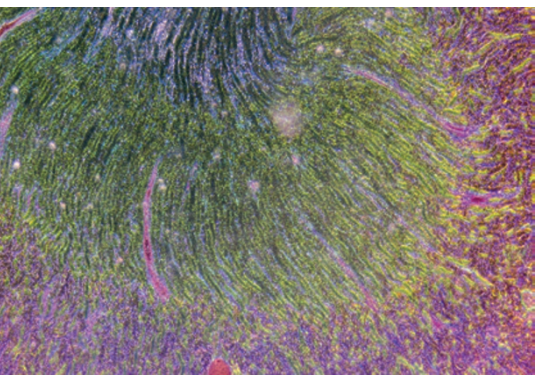
KIDNEY CANCER

Renal cortical neoplasm diagnosis? Go FISH

New research has further demonstrated the potential of fluorescence *in situ* hybridization (FISH) to complement core-needle biopsy histology in the diagnosis of renal masses. A series of FISH probes designed to detect genetic abnormalities involved in the most common subtypes of renal neoplasm improved overall diagnostic yield and accuracy in a set of 122 biopsies of resected renal masses, compared with histology alone.

Modern medical imaging techniques enable identification of increasing numbers of renal lesions, including small renal masses (<4 cm). These neoplasms require further characterization, to avoid overtreatment of benign oncocytomas and, for metastatic disease, to enable prompt initiation of differential therapies depending on tumour subtype—currently sunitinib for clear cell renal cell carcinoma (RCC) and temsirolimus for papillary RCC. By itself, histology of core-needle biopsy samples can lead to misdiagnosis, and is currently only recommended for elderly patients with comorbidities and for patients with contraindications for surgery. FISH is a promising candidate for an adjunctive diagnostic technique.



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The latest study compared the diagnostic yield and accuracy of core-needle biopsy histology, fine-needle aspiration FISH, and surgical specimen histology (the gold standard). The final FISH series included seven probe sets for 19 abnormalities across eight chromosomes. A four-step decision tree, with sequential analysis of nuclear fluorescence with these probe sets, was developed to enable categorization of samples as belonging to one of four neoplastic subtypes, or as having an unspecified abnormality, or no detected aberration.

Of 114 evaluable renal masses, 72 were clear cell RCC, 18 were papillary RCC, 13 were chromophobe RCC and 11 were benign oncocytoma on surgical specimen histology. More diagnoses were made using FISH (107) than biopsy histology (94), but concordance of the diagnosis with specimen histology was lower for FISH (79% versus 97%). Diagnostic accuracy —the number of concordant diagnoses as a percentage of the 114 biopsies with a diagnosis by either method—was 78% for FISH and 80% for histology, but rose to 96% when the two methods were combined. Notably, FISH had a high diagnostic yield for oncocytoma in small renal masses, and further validation of a marker of deletion at the 3p21 locus could confirm the improved ability to differentiate the benign oncocytoma from malignant chromophobe RCC.

> “Notably, FISH had a high diagnostic yield for oncocytoma in small renal masses...”

Challenges remain for the optimization of FISH in this setting. In cases of low levels of clonal aberrations, scoring additional cells should increase the diagnostic value. Integration of further genomic analyses, such as comparative genomic hybridization and massively parallel sequencing, is another goal “given the limited availability of specimen from core-needle biopsies,” says corresponding author Jane Houldsworth. “Such approaches will, at the same time, afford the simultaneous evaluation of additional discriminatory biomarkers to increase the accuracy of classification and improve the overall sensitivity with which the genomic aberrations can be detected.”

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Original article Gowrishankar, B. *et al.* Subtyping of renal cortical neoplasms in fine needle aspiration biopsies using a decision tree based on genomic alterations detected by fluorescence in situ hybridization. *BJU Int.* doi:10.1111/bju.12643