Fluorescence in situ Hybridization (FISH) and Array-Comparative Genomic Hybridization (a-CGH) from Percutaneous Needle Biopsy Compared to Renal Mass Histology

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OBJECTIVE

To correlate the two novel assays Fluorescence In Situ Hybridization (FISH) and Array-Comparative Genomic Hybridization (a-CGH) with the histologic findings of kidney tumor biopsies.

INTRODUCTION

Image-guided, percutaneous biopsy of kidney tumors is increasingly utilized, particularly in patients at higher risk of adverse outcomes;

Biopsy results may facilitate decision-making in the management of small renal masses;

Despite improved biopsy techniques, low yield and disrupted tissue architecture may make histologic diagnosis impossible;

Specific genetic alterations have been identified in kidney tumors;

Accurate detection of genetic alterations may improve the diagnostic capabilities of percutaneous kidney biopsy;

Selected patients may avoid extirpative treatment if benign or indolent tumors are determined by biopsy.

MATERIALS

Specimen acquisition:

• Percutaneous 18-22 Gauge core biopsies from 25 renal masses prospectively collected from 22 patients (9/2011–12/2011)

• Excluded cases:
  - Clinical data (1 patient);
  - Cystic fluid only (1 patient);

• Technique:
  - 1-4 core biopsies/renal tumor
  - 1 core fixed for FISH
  - 2-cores: DNA extraction for a-CGH

Study Patient Characteristics:

• 12 Men, 6 Women
• Median Age: 70 (IQR: 61, 74)
• Median Tumor Size: 3.1 cm (IQR: 2.0, 5.9)

Histologic Analysis:

• Diagnosis from pathology reports of biopsy tissue
• Surgical pathology assessment used when available.

METHODS & RESULTS

FISH (Fluorescence in Situ Hybridization) Analysis:

• Probe combinations used
• Up to 3 colors per combination
• Minimum of 100 cells scored using epifluorescence microscopy per hybridization
• 10 Normal kidney specimens used to determine cut-off values

Histologic Classification:

• FISH decision tree (developed using an independent dataset of core biopsies)

FISH:

• Total of 23 biopsies
• 6 Biopsies used for optimization of fixation procedure
• 5 Biopsies classified as clear cell RCC (ccRCC)
• 4 Biopsies classified as papillary RCC (pRCC)
• 6 Non-diagnostic biopsies
  - Lack of sufficient cells to generate score
• 2 Biopsies unclassifiable

• A decision tree not consistent with the four cortical neoplasms included in the decision tree

Method & Results:

• Array-CGH:
  - DNA extraction resulted in yields >500ng after Qc
  - Reference DNA: Sex-matched DNA (Promega)
  - Digitized and labeled DNA hybridized to targeted oligonucleotide microarray and analyzed according to manufacturer (Agilent Technologies)
  - Identification of genomic aberrations:
    - Nexa Copy Number Analysis v 1.1 (BioDiscovery Inc.)
  - Histologic classification:
    - a-CGH decision tree (developed using publicly available data)
  - Copy number aberrations not related to four studied renal cortical neoplasms identified as Unclassifiable-RCC
  - Biopsies exhibiting no aberrations (28%) classified as normal

Array-CGH Cases:

• Total of 23 biopsies
• 21 Biopsies analyzed
• 7 Biopsies classified as clear cell RCC (ccRCC)
• 8 Biopsies classified as papillary RCC (pRCC)
• 1 Biopsy classified as oncocytoma
• 3 Biopsies were unclassifiable
• 2 Biopsies: non-diagnostic

CONCLUSIONS

• Kidney biopsy can yield sufficient material for FISH and a-CGH studies.

• In this initial experience, the a-CGH method provided:
  - A more robust and interpretable assay than FISH;
  - Tumor classification with better correlation to pathologic assessment than FISH;
  - Less non-diagnostic results compared to FISH.

• Larger experience with these novel diagnostic tools is needed to determine their utility for the genonomic classification of kidney tumors from kidney needle biopsies.

REFERENCES


CONFLICTS OF INTEREST

B.G., C.M. and J.H. are full time employees of Cancer Genetics, Inc.

Table 1. FISH and a-CGH vs. Biopsy or Nephrectomy Histology

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<tr>
<td>a-CGH</td>
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Non-diagnostic results affected both FISH and a-CGH