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Clinical Trials of ProxiScan™ Compact Gamma Camera in Prostate Cancer Diagnosis

Yonggang Cui

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Brookhaven National Laboratory
P.O. Box 5000
Upton, New York 11973
www.bnl.gov

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Brookhaven National Laboratory	Y. Cui, G. Camarda, G. De Geronimo, A. Hossain, K-H Kim G. Meinken, G. Mahler, P. O'Connor P. Vaska, G. Yang, R. Gul, and R. B. James
Hybridyne Imaging Technologies, Inc.	T. Lall
Radiological Associates of Sacramento	B. Franc, and T. Johnson
University of California at San Francisco	Y. Seo
Johns Hopkins University	M. Pomper, S. Cho, and B. Tsui
Midstate Hospital	K. Weisman

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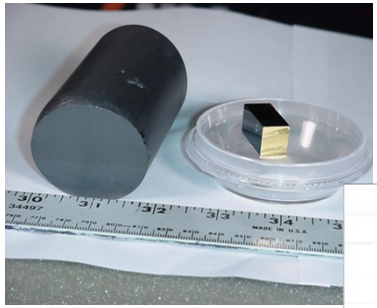
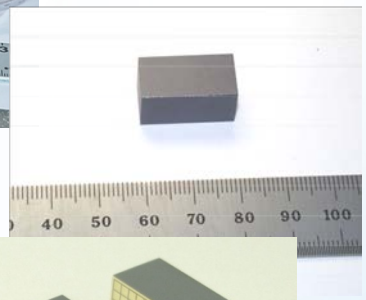
Outline

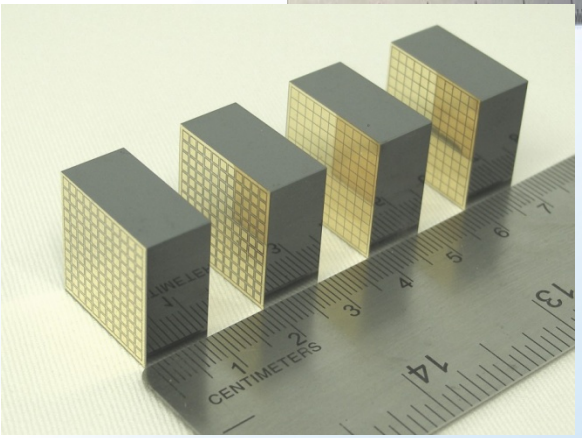
- CdZnTe detector
- ProxiScan™ gamma camera
  - Prostate cancer
  - Design of the gamma camera
- Clinical trials
  - General introduction of the trials
  - Images of selected patients
- Summary and future developments

CdZnTe Detector

- Good material properties for a radiation detection
  - High density and atomic number
    - High detection efficiency
    - Compact detector and system
  - High resistivity
    - Low leakage current
    - Room-temperature operation
  - High energy resolution
    - Spectroscopy
    - Energy resolved imaging
  - High spatial resolution
    - Easy fabrication of fine-pitch electrodes







Courtesy of Redlen, Acrorad and Yinnel Tech

Medical Applications of CdZnTe Detectors

- SPECT
  - Full ring system
    - Whole body imaging system and small animal imaging system
  - SPECT/MRI
  - SPECT / gamma camera for specific disease
    - Dental X-ray, cardiology and breast Imaging
- PET
  - Timing resolution needs to be improved before a practical system can be built
    - Better material, suitable detector design and ASIC development
- There are other fields that can make use of the advantages of CdZnTe: compact and low cost of the final systems
  - Intra-operative and endo-cavity imaging system
    - Prostate cancer
  - Low-cost flat camera for animal imaging
    - Animal research / clinics
    - Development of new drugs

Prostate Cancer

Background

- 1 in 6 will develop the disease
- 1 in 36 will die of the disease
- About 240,000 new cases in 2012 with 2 million patients living in the US

Problem – **Instruments available today cannot accurately image intra-prostatic cancer, and early detection of disease is disappointingly low**

- Significant numbers of cancers that could and should be treated at an early stage are missed due to high percentage of false negatives for biopsies
- Undiagnosed prostate cancer is highly prevalent
- Recurrent surgery after initial treatment due to inability to effectively localize and treat cancerous tissue
- Limitations in administering optimal therapeutic procedures (e.g., brachytherapy and cryo-surgery)
- Unnecessary and risky surgeries, including radical prostatectomy, commonly performed for non-lethal cases

Diagnosis of Prostate Cancer

- Early screening
  - Prostate-specific antigen (PSA) blood test plus digital rectal exam (DRE)
  - High false-alarm rates for PSA tests
- Ultrasound
  - Determines prostate size and anatomy, portable, low cost, not ionizing, real time
  - Cannot distinguish benign from malignant tumors
  - Missing of small cancer tissues in ultrasound-guided biopsy
- Other imaging methods
  - CT – not specific to soft tissues
  - Traditional SPECT – large, expensive, modest spatial resolution due to prostate location in body and tissue between camera and gland
  - PET – large, expensive, tumors are not glucose dependent for ^{18}F-FDG, no specificity to cancerous tumors, modality not effective for PCa
  - MRI – good accuracy for staging, needs endo-rectal coil, expensive, magnetic environment complicates biopsy procedures

ProxiScan™ - A Compact Gamma Camera

Goal

Develop a compact digital gamma camera capable of insertion into the rectum as a probe, bringing it directly adjacent to the prostate gland for high-resolution localization and imaging of prostate cancer

To make this compact device

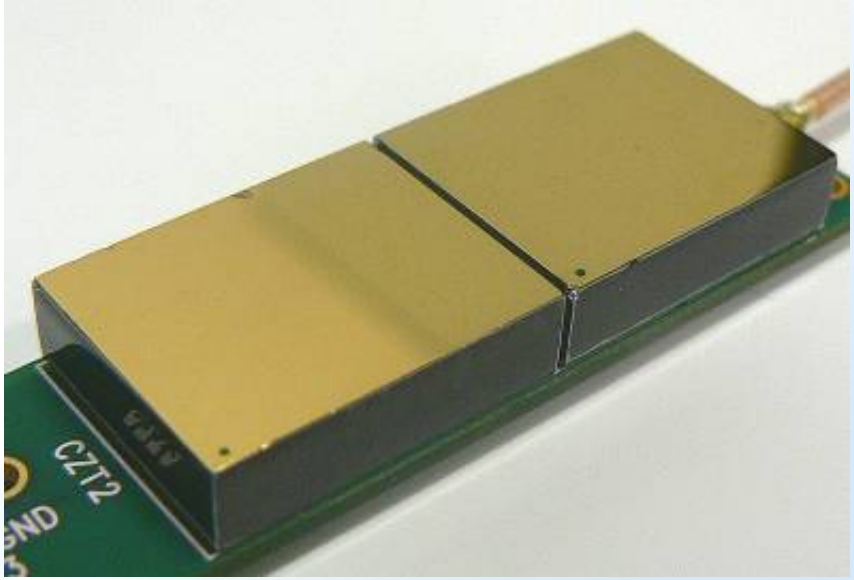
- Cadmium Zinc Telluride (CZT) detectors
- Application Specific Integrated Circuits (ASIC)

Features

- Compact and trans-rectal probe
  - Intra-body-cavity measurements
  - Close to the prostate
- High spatial resolution
  - High image quality
  - Detection of small tumors
- High sensitivity
  - Short imaging time and low injection dose
- Low cost

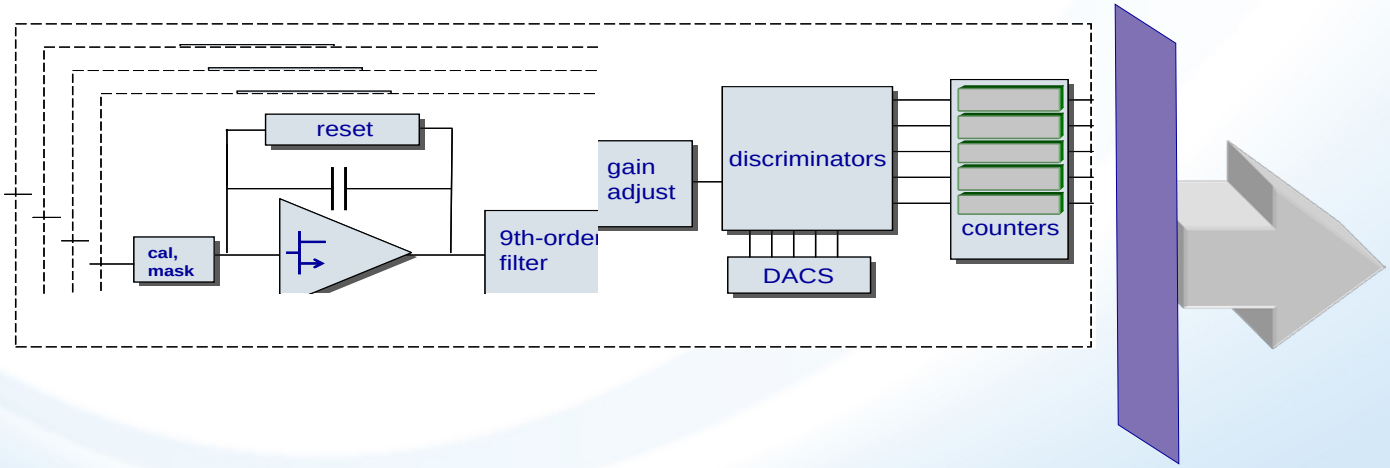
System Design – Detectors and Collimators

- First prototype
  - 2.5-mm pitch detectors
  - 6x8 pixel array
  - 15x40 mm^2 FOV
- Collimator
  - Parallel holes matching detector pixels
  - Monte-Carlo simulation (Geant4)
  - Tc-99m and In-111



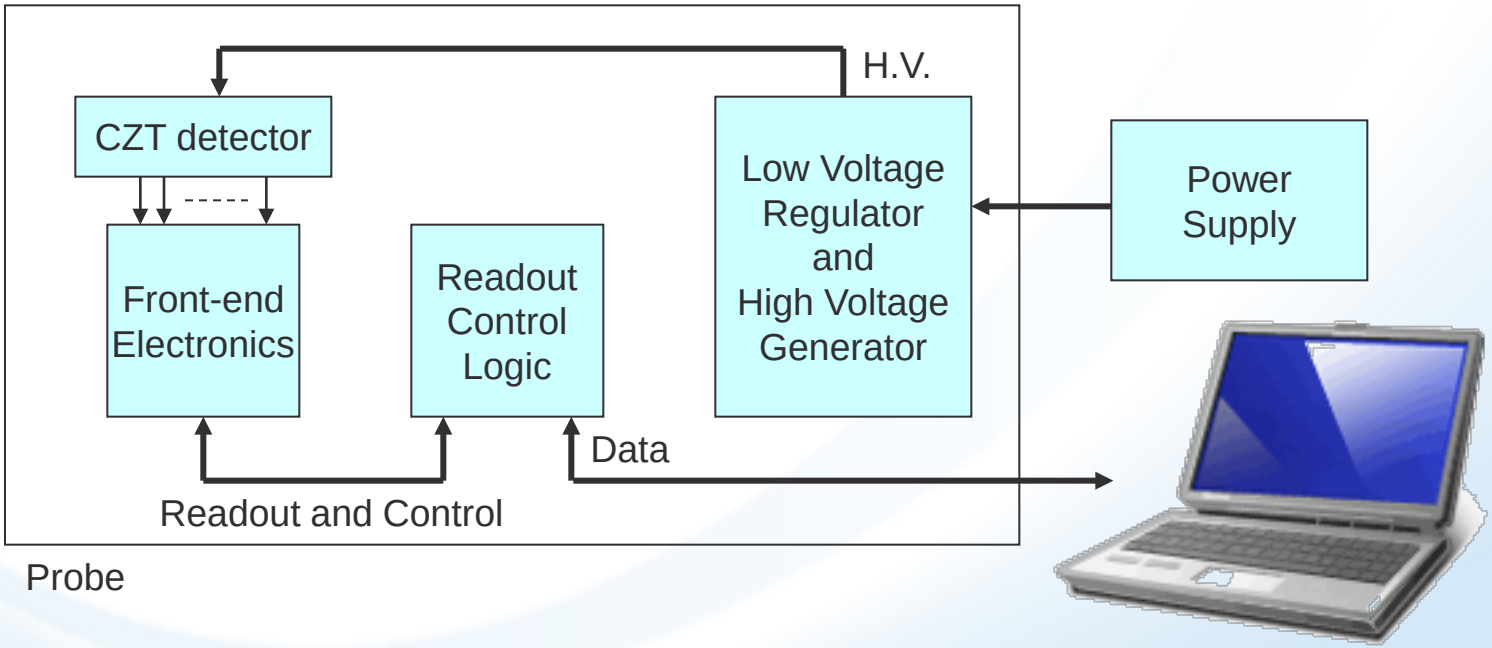
System Design – Readout Electronics

- Application-specific-integrated circuits (ASIC)
  - 64 channels, each channel has
    - Preamplifier
    - High-order shaper
    - Discriminators and counters
  - Low power (<5 mW/ch) and low noise (1.5 keV rms.)
  - High counting rate (2 MHz/ch)

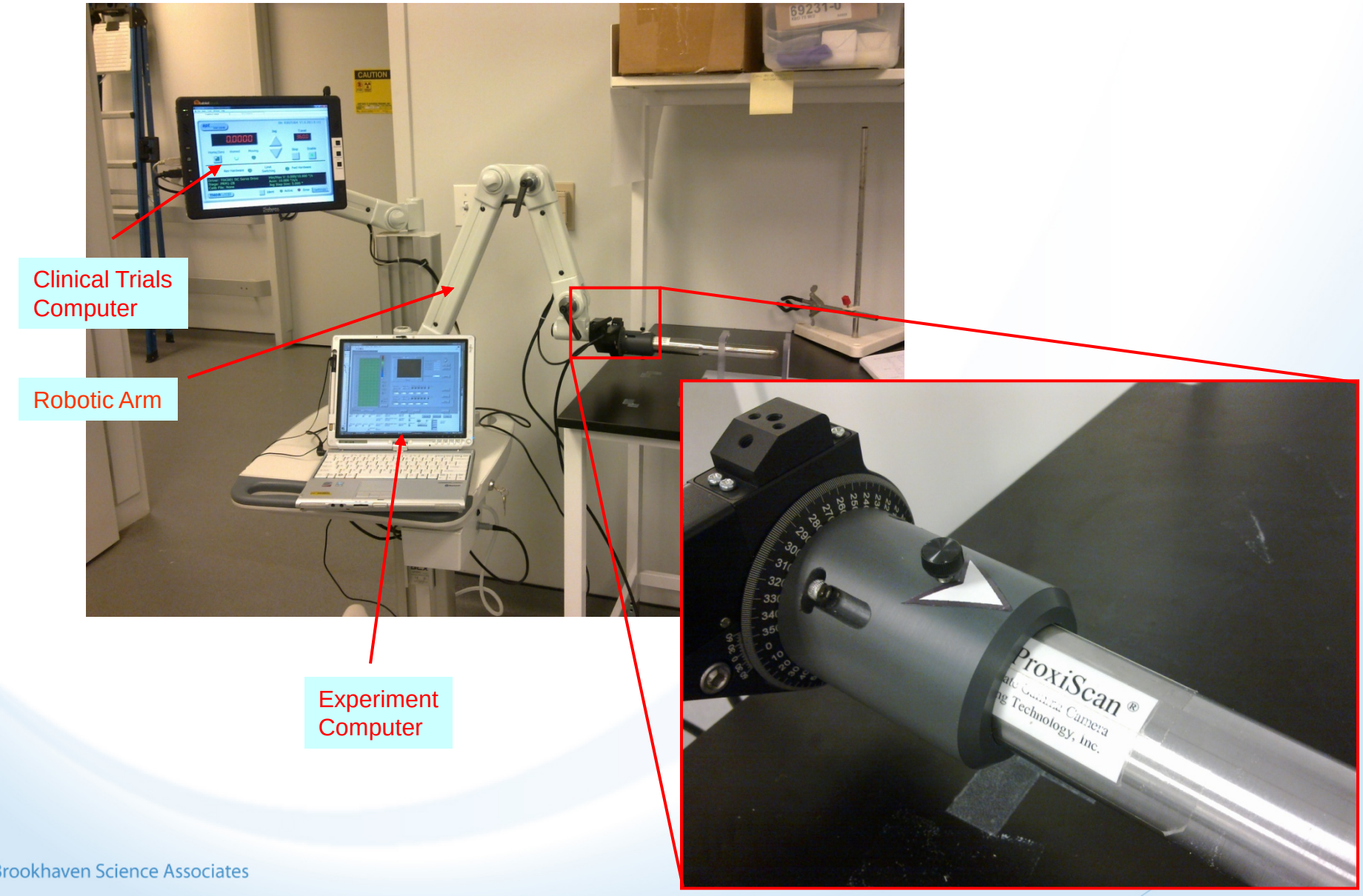


System Design - Data Acquisition System

- Highly integrated design
- USB communication
- Low power consumption: ~600 mW
- ML-EM image processing



System Photo



Clinical Trials of ProxiScan™

- FDA 510(k) clearance was granted in 2010.
- Two clinical trial sites
  - Johns Hopkins Hospital (JHU)
  - Radiological Associates of Sacramento (RAS)
- Clinical trials started in May 2011 and finished in April 2012.
- 14 patients were seen in this study. Among them, 10 have confirmed disease indicated by biopsy procedure.

ProxiScan™ Imaging Procedure

- Radioactive tracer - ProstaScint®
  - In-111 based radiopharmaceutical
  - Sole tracer approved by FDA for prostate cancer imaging by the time the trials started
- Procedure
  - Selected patient has biopsy and MRI scan before ProxiScan™ procedure
  - Patient is injected 5-mCi ProstaScint 5 days before ProxiScan™ imaging
  - On the day of ProxiScan™ imaging, the patient has whole body SPECT/CT first.
  - ProxiScan™ imaging procedure
    - 4 images, 1 for each quadrant
    - 5-min acquisition time for each image
  - Pathology data generated for several patients
  - Image data are processed off-line
- Whole data set has been processed and is being reviewed by physicians

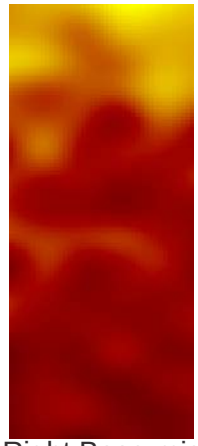
Patient 1

Patient Info

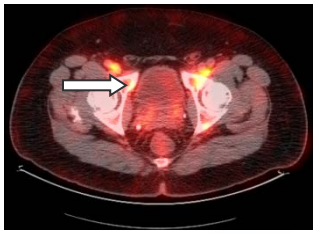
- Biopsy results
  - Right base-mid: 8 mm
  - Left base-mid: focal high grade prostatic intraepithelial neoplasia (PIN)
- Surgical pathology results
  - Right base-mid: 18 mm
  - Left base-mid: 2 mm

Image Interpretation

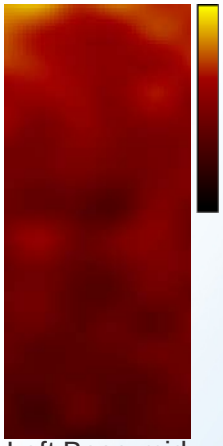
- High uptake in both right and left base-mid regions
- In the right base-mid region, the ProxiScan™ result (estimated 15 mm) is in agreement with SPECT-CT, biopsy and pathology results
- In the left base-mid region, foci (estimated at 5 mm) is small
  - Missed in biopsy
  - Result agrees with SPECT/CT and pathology results
- The measurement of small tumor sizes was limited by the resolution of the current system



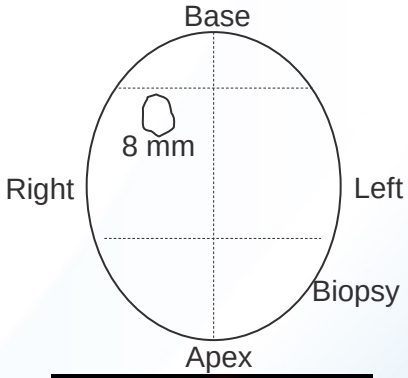
Right Base-mid

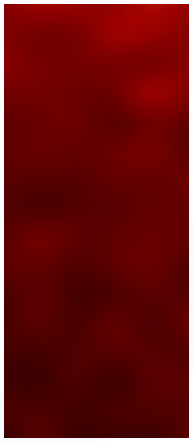


Transaxial view of mid-base region

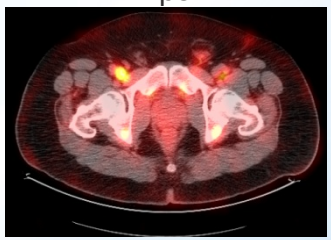


Left Base-mid





Right Apex



Transaxial view of apex region

Left Apex

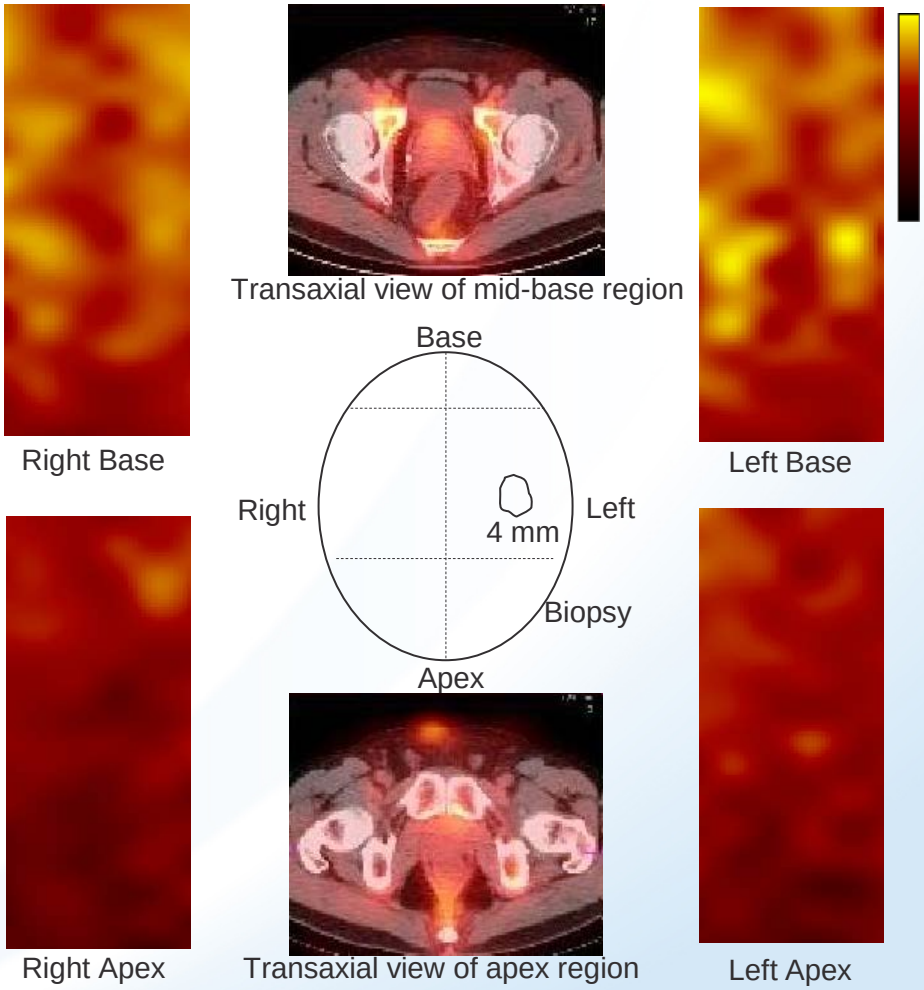
Patient 2

Patient Info

- Biopsy results
  - Right base-mid: scattered high-grade PIN
  - Left mid: 4 mm
- Pathology results
  - Right base-mid: 5 mm
  - Left base-mid: 12 mm

Image Interpretation

- High uptake foci were seen in ProxiScan images of all the regions.
- In the left base-mid region, the estimated high uptake foci are about 13 mm, in agreement with SPECT-CT, biopsy and pathology results.
- In the right base-mid region, the contrast is lower; estimated size is smaller. The result was missed in biopsy.
- The result is repeatable between patients 1 and 2.



Patient 3

Patient Info

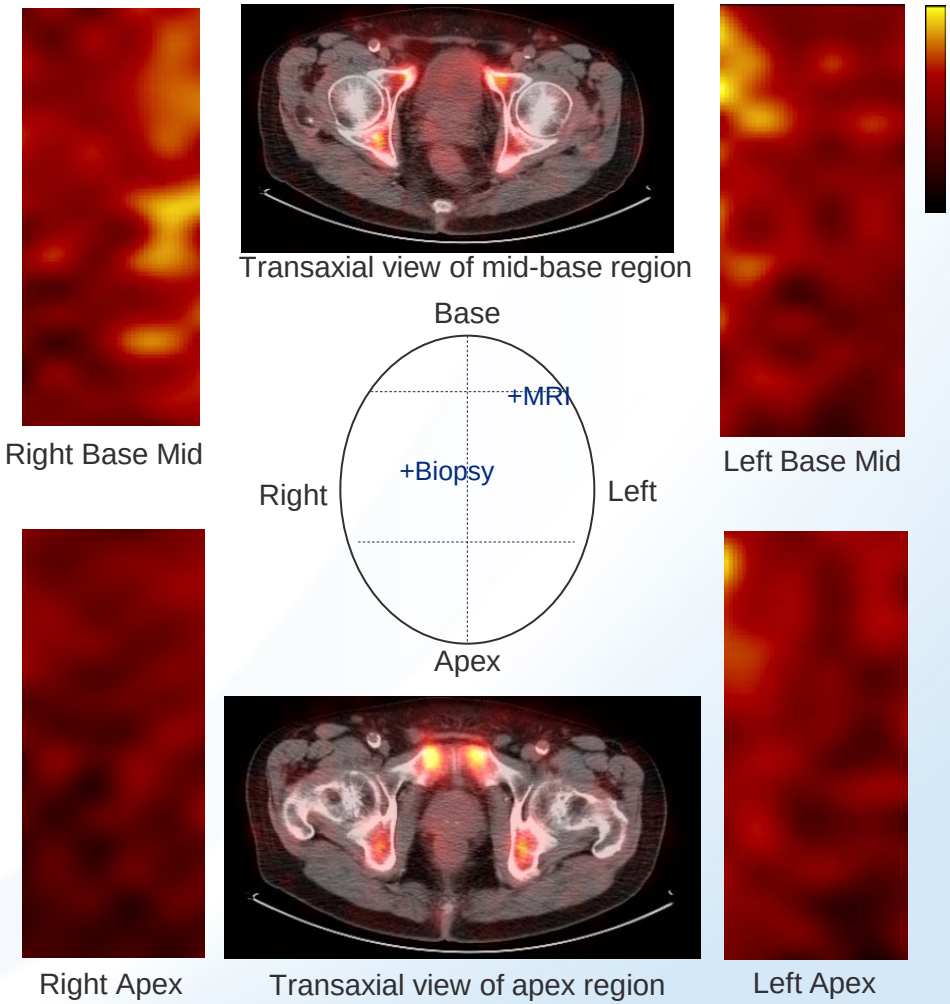
- Cancer tissues detected by biopsy procedures
- SPECT/CT
  - Right lobe: mild but focal accumulation
  - Left base: faint tiny focus

Image Interpretation

- Both right and left regions have high uptake areas

ProxiScan™ vs. SPECT

- SPECT
  - Weak signal
  - Low local contrast
  - Tracer has immune-based sequestration in the hepatic parenchyma
- ProxiScan™
  - Higher contrast
  - Clearer foci (better image quality)



Conclusions

- We developed a compact gamma camera
  - High resolution, high efficiency and low cost
  - Capable of trans-rectal measurements
  - Allowing (for the first time) capture of gamma-ray image for the prostate at very close distance
  - FDA 510(k) clearance granted
- Phase I clinical trials of ProxiScan™ were completed successfully.
  - In most cases, ProxiScan™ results are in agreement with biopsy and pathology results.
  - In some cases, small tissues were missed in biopsy procedure, but were seen by ProxiScan™.
  - ProxiScan™ is more sensitive than SPECT, esp. when the patient has lower uptake of tracer in prostate gland due to the immune-based sequestration in the hepatic parenchyma.
- Next generation of ProxiScan™ is being developed that combines ultrasound transducer into the same probe, allowing better interpretation of the images and ability to pinpoint the position of the tumor within the gland.

Acknowledgments

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