The Latest in Molecular Imaging

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The Radiologic Society of North America annual conference is the world's largest international medical conference with over 50,000 annual attendants in Chicago each year. I had the honor of giving a presentation as part of the "molecular imaging in prostate cancer" section and I wanted to share this information with the PCRI membership.

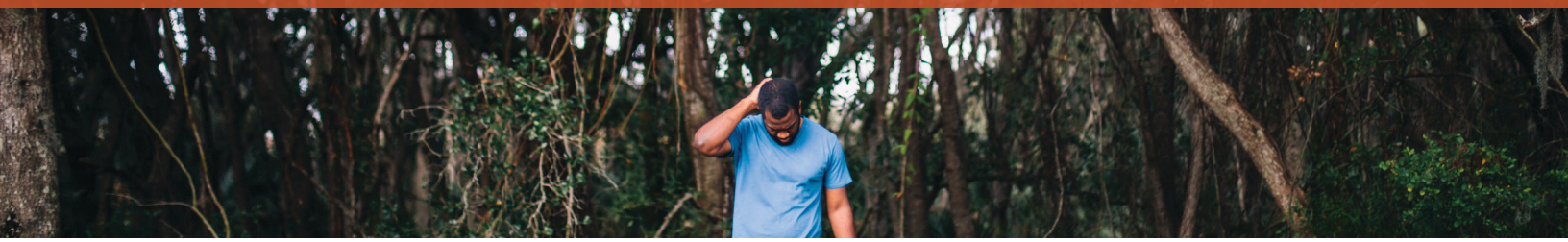
The treatment landscape for prostate cancer has been revolutionized by the arrival of multiple novel treatment approaches and agents over the last few years. After initial treatment with surgery or radiation however, up to 40% of patients will experience PSA relapse. Knowing the location of a cancer recurrence is important since recurrence in or near the pelvic lymph nodes may be amenable to additional curative focal therapy.

The primary difficulty is that standard imaging techniques such as *technetium bone scan*, CT scans and MRI are usually unable to see tiny recurrent tumors. On the other hand, **PET scans that work by exploiting various aspects of cancer metabolism, can often visualize and locate these small tumors.** In this article I will review some of the exciting new technology that is becoming available.

Growing Cancer Cells Need to Manufacture New Lipid Cell Membranes

Cell membrane synthesis and the building blocks—acetate and choline—are common structural elements in the cancer cell. Therefore, if these areas of the cancer cell are made radioactive with carbon-11 or fluoride-18 they will "light up" on a body scan.

In the study I presented at the meeting, 373 patients with PSA recurrence were evaluated with C11 Acetate PET scan. We found that the cancer detection rates co-related with the patient's level of PSA. For example, if the PSA was between 0.2-0.4 we had 50% cancer detection rate. If the PSA was between 0.41 – 1.0 the detection rate was 77%. When the PSA was over 1.1, detection was was 90%.



PSMA (Prostate Specific Membrane Antigen)

Some of the studies presented from other centers were also very interesting. For example, PSMA is a cell surface transmembrane glycoprotein that is over-expressed in prostate cancer cells and would appear to provide a rational target for diagnostic imaging and possible directed therapy. Multiple **Gallium (Ga68)** labeled PSMA probes (imaging agents) have been topic of study particularly in Germany for the last few years. Researcher from Germany, Dr. Frederick Giesel, presented his work on Gallium-PSMA PET in pre-treatment staging prior to radiation therapy. His study found that in 26 of 56 (46.4%) patients the treatment plan was changed after Gallium-PSMA PET imaging. This study demonstrates the significant impact that PET imaging probes can have on the treatment selection of patients with primary prostate cancer.

An interesting departure from the PET agents discussed in this session was a presentation regarding *trofolastat*, which is a small molecule PSMA ligand. This agent is labeled with **Technetium-99m** which is a SPECT radiotracer. This study reviewed the ability of trofolastat to detect prostate cancer in 54 high risk patients within the prostate gland and found correlation for the detection of the primary cancer in 91% of patients. Problematic was that all patients in this study had high risk disease with large prostate cancers and/or extra-prostatic extension (T3 or greater). Yet in 6 of the study patients, the primary prostate cancer was not identified at all! In this setting, one would hope for a near 100% detection rate for the primary cancer.

Amio Acid PET Scans

A synthetic non-metabolized amino acid analog (**anti-18F-FACBC**) accumulates in prostate cancer cells due to over-expression of multiple amino acid transport systems. A recent Italian study suggests that anti-18F-FACBC scans may be superior to C11-choline for localization of disease in PSA recurrence. At the meeting Dr. Oluwaseum Odewole from Emory University presented results of a study comparing the accuracy of anti-18F-FACBC with the accuracy of a standard CT scan. Seventy of 86 patients (81.4%) were positive for detecting cancer with anti-F18-FACBC versus only 16 of 86 (18.6%) on the CT examinations. PSA level was also important in the detection rate for anti-18F-FACBC with the positivity rate at a PSA <1 ng/mL for anti-18F-FACBC of 38.5%, while for PSA ≥ 1 scan positivity rate was 89.0%. The results of this study appear to be fairly comparable to that of C11-Acetate and Choline, especially when the PSA is > 1 ngmL.

Bony Matrix

Sodium Flouride (F18-NaF) is readily absorbed into the matrix of bone and has very high affinity for bone metastasis. F18-NaF PET/CT has been shown to provide higher sensitivity and specificity than technetium based planar and SPECT bone imaging for detection of osseous (bone) metastases in prostate cancer. With all of the molecular imaging probes thus far discussed, the consensus from the conference was that bony metastasis can be identified more readily with these PET imaging probes compared to conventional imaging. There was general agreement from the various presenters, however that all of these probes missed very small bony lesions which had only a very small volume of cancer cells, but these lesions were often seen on F18-NaF PET. In a separate session at the meeting, I presented the results of a direct comparison study of C11-Acetate PET to F18-NaF PET in 185 patients. F18 showed a slightly higher rate of detection of bony metastasis (41%) compared with C11-Acetate (32%). Overall however, the best detection rate came with using both C11 and F18.

Conclusion

For evaluation of the intact prostate gland as part of initial diagnosis, under active surveillance, and for targeted biopsy, multiparametric MRI is becoming the imaging study of choice. PET scans are not likely to compete with MRI in this area in the immediate future. However, they may be complimentary, especially in patients with higher risk disease to rule out the presence of local and distant metastatic disease.

With the plethora of these different types of PET scans (and particularly with

Dr. Almeida will be speaking at the **2015 Moyad and Scholz Mid-Year Update**, see page 11 for more details.

the many variations on PSMA probes), the question however remains which is the best? The following characteristics appear important: 1) a fluorine (F18) tag would be optimal as this is the most widely used cyclotron produced isotope, is readily available throughout the US, and would result in the most cost effective agent, 2) low radiation dose to the patient and to those who work with the agent, 3) rapid clearance from the background, 4) high specificity and 5) little or no urinary excretion.

Unfortunately, none of the imaging probes to date meet all of the optimal characteristics. The point regarding urinary excretion is important, as high urinary excretion in the ureters and urinary bladder cause significant interference with detection of lesions in the nearby areas (i.e the prostate, prostate bed and adjacent lymph nodes). The PSMA probes have the potential to have the highest specificity, but unfortunately, all these probes to date demonstrate high urinary excretion and high background in the blood pool, which may hamper the overall usefulness of these agents. C11-Acetate and C11-Choline offer several of the desired characteristics, but the short half-life of the C11 isotope requires more costly dedicated equipment. Of these probes, F18-FACBC perhaps comes closest to having the optimal characteristics and will be of keen interest for further evaluation as a first line imaging study for detection of metastatic prostate cancer and in the evaluation of PSA recurrence. ☐