# Utility of positron emission tomography in biochemically recurrent prostate cancer: A comparison of carbon-11 acetate & 68Ga-prostate specific membrane antigen radiotracers

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## BACKGROUND

- Biochemical recurrence (BcR) after primary therapy represents a difficult clinical decision-making node.
- Prostate cancer-specific radiotracers have allowed better characterization of recurrent disease and now regularly influence treatment modality selection.
- Carbon-11 acetate and 68Ga-prostate specific membrane antigen radiotracers are commonly used radiotracers. Ga PSMA is small molecule that is prostate-specific at a molecular level, while C11 acetate relies on a pattern of rapid uptake and metabolism common in several cancers [1].
- Reports exist correlating magnitude of PSA at scan and ADT use at scan with a positive PSMA PET [2][3].
- We sought to: Determine whether our institution's application of these radiotracers corroborated previous findings regarding rate of positive scans for graded PSA categories, quantify lesion-specific positive predictive value for C11 acetate and Ga PSMA based on post-scan follow up data, and directly compare C11 PET and 68Ga PSMA PET performance.

## ABSTRACT

**INTRODUCTION & OBJECTIVE**: Carbon-11 acetate (C11 ac) and 68Ga-prostate specific membrane antigen (Ga PSMA) based PET/CT are often used to assess biochemical recurrence (BcR). We retrospectively analyzed 230 BcR patients who received PET/CT scans. 160 used C11 ac and 70 used Ga PSMA. Our objectives were to quantify how pre-scan PSA influenced the probability of a positive scan and determine the validity of radiotracer-based lesion characterization.

**METHODS**: A database of BcR patients was queried for PET/CT scans and sufficient post-scan data. All scans were read by a board-certified radiologist and PET-specific findings suggestive of malignancy were characterized separately from non-PET findings. Site-specific radiotracer avidity was recorded. Pre-scan PSA range categories (i.e. .0 – .5 ng / mL) were chosen. The outcomes (positive or negative) within these categories were subjected to Pearson's chi$^2$ test regarding percent of scans read as positive to assess for significant variance between radiotracers. Positive scans were classified as true or false and a lesion-specific positive predictive value (PPV) was calculated for each radiotracer. Three methods were used to confirm a positive site: 1) histology, 2) non-confounded, post-targeted therapy PSA trend, and 3) non-PET imaging. False positives were confirmed by histology.

**RESULTS**: The rate of positives was greater in higher PSA categories for both radiotracers. At PSAs < 2 ng / mL, no significant difference was observed at any PSA category or when considering PSAs < 2 as a group. At PSAs of 2 – 4, Ga PSMA begins to demonstrate a significantly (p = .041) higher rate of positives. For PSAs 2 – 20, Ga PSMA was positive in 35/36 vs. 62/79 with C11 ac (p = .01).

C11 ac PPVs were 93.9% and 88.4% for all cases and biopsy-confirmed cases, respectively. Ga PSMA PPVs were 97.4% and 92.9%.

**CONCLUSION**: Ga PSMA demonstrates a high positive read-rate (nearly 100%) above 2 ng/mL. C11 ac demonstrates a slower climb in positive read-rate as PSA increases. C11 ac and Ga PSMA both demonstrate high PPVs for prostatic malignancy at avid sites, with Ga PSMA demonstrating fewer false positives relative to C11 ac.

## METHODS

- A patient cohort of 230, where each patient received a C11 (n=160) or PSMA PET (n=70) and post-scan follow up was established.
- PSA at scan and scan outcome (positive or negative) was recorded for every patient
- Three methods were used to determine a true positive: 1) histologic confirmation, 2) PSA trend following targeted therapy, and 3) characteristic non-PET imaging modality findings in conjunction with PSA trend.
- False positives were confirmed by negative histology

## METHODS

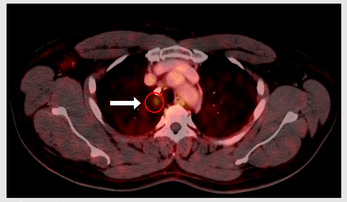

**Figure 1**

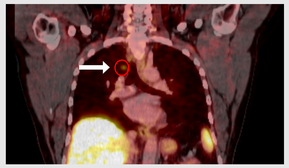

**Figure 2**
Ga PSMA – CT fusion images demonstrating a single right upper lobe lesion that was targeted with radiation. No concurrent systemic therapy was applied. Subsequent biopsy confirmed prostatic origin.

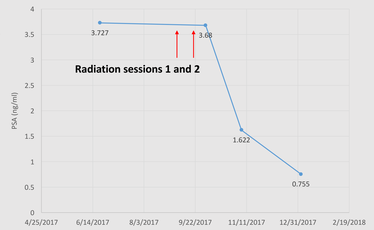


**Figure 3**
The patient received a total of 5000 cGy in two sessions targeted to the Ga PSMA identified lung lesion. The treatments are shown correlated temporally with PSA trend.

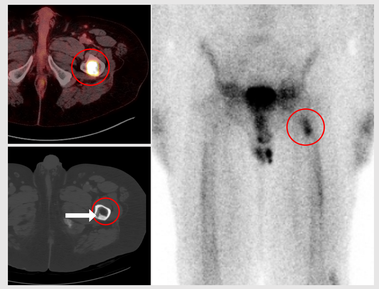

**Figure 4**
These images, Ga PSMA-CT fusion (top left), CT (bottom left), and bone scan (right) were obtained within a 60 day period. Although no biopsy of this PSMA-avid lesion was obtained, characteristic findings on these other imaging modalities in conjunction with PSA trend were considered to provide sufficient evidence for confirmation.

## RESULTS

| | Scans PSA (0 - 20) | Mean PSA (0 - 20) | T test P value | Fisher's exact for positive / negative scan ratio |
|---|---|---|---|---|
| Ga PSMA | 66 | 4.568 | 0.7192 | 0.2785 |
| C11 acetate | 147 | 4.318 | | |

| | Scans PSA (2 - 20) | Mean PSA (2 - 20) | T test P value | Fisher's exact for positive / negative scan ratio |
|---|---|---|---|---|
| Ga PSMA | 35 | 8.084 | 0.39 | 0.0122 |
| C11 acetate | 79 | 7.316 | | |

**Table 1**
When excluding PSA values below 2 ng/mL, the increased read rate for Ga PSMA relative to C11 acetate is significant.

**Figure 5**
Percentage of positive reads

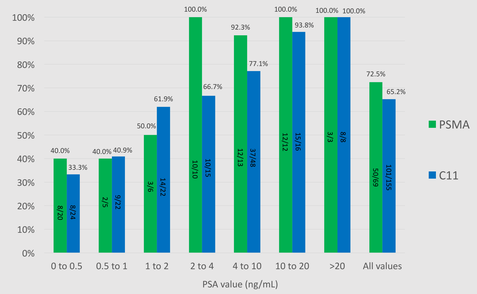


**Table 2**
Positive predictive value data

| | C11 acetate | Ga PSMA |
|---|---|---|
| Total scans | 160 | 70 |
| Scans read as positive | 105 | 50 |
| Verification data present | 82 | 38 |
| **Confirmed TRUE POSTIVES** | | |
| Histologic | 38 | 13 |
| PSA trend after focal therapy | 18 | 2 |
| Non-PET imaging | 20 | 22 |
| Alternative PET radiotracer | 1 | 0 |
| **Confirmed FALSE POSTIVES** | | |
| Histologic | 5 | 1 |
| **Positive predictive values** | | |
| All cases | 93.9% | 97.4% |
| Biopsy-confirmed cases only | 88.4% | 92.9% |

## REFERENCES

1. Jaden D. Evans, MD, Krishan R. Jethway, MD, Brian J. Davis, MD, PhD, et al: Prostate cancer-specific PET radiotracers: A review on the clinical utility in recurrent disease. Practical Radiation Oncology 2017 Jul; 28 – 39.

2. Ali Afshar-Oromieh, John W Babich, Clemens Kratochwil, et al: The Rise of PSMA Ligands for Diagnosis and Therapy of Prostate Cancer. The Journal of Nuclear Medicine 2016 Oct; 79 – 89.

3. Ali Afshar-Oromieh, Tim Holland-Letz, Frederik L Giesel, et al: Diagnostic performance of 68 Ga-PSMA-11 PET/CT in patients with recurrent prostate cancer: Evaluation in 1007 patients. Eur J Nucl Med Mol Imaging 2017 May; 1258 – 68.

## LIMITATIONS

- A portion of the patients with positive scans were lost to follow up or the scan was obtained too recently for sufficient post-scan confirmatory data.
- A binary "positive" or "negative" designation was assigned to scan readings. At times radiology reports indicated graded levels of suspicion. These nuances remained below the resolution of our data collection and reporting.

## CONCLUSIONS

- Ga PSMA increases the rate of positive reads relative to C11 acetate at PSA values greater than 2 ng/mL, with 37/38 scans read positive.
- Our positive read rate for PSA categories less than 2 ng/mL was slightly less than rates cited elsewhere [2][3]. We hypothesize that this may be due to a greater number of hormone naïve patients in our cohort.
- C11 and Ga PSMA radiotracers demonstrate high PPVs for prostatic malignancy, with Ga PSMA producing fewer false positives than C11 acetate.
- Further study regarding ideal application and limitations of Ga PSMA is warranted. Additionally, study to determine the significance of a negative scan in the context of a rising PSA should be assessed with longer term clinical outcome follow up.