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PCa Commentary

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THE AXUMIN PET/CT SCAN: ITS CLINICAL UTILITY — AN UPDATE

This article benefited from the review by Dr. David Djang, Seattle Nuclear Medicine, Swedish Cancer Institute PET/CT.

It has been one year since the Commentary featured the Axumin PET/CT in the November 2017 issue *[control+click link to follow]*. A great deal of new research about this scan performance has been published since then. The material in this issue is based on this research. The overall theme of the studies is that the Axumin scan is providing clinically relevant information at PSA levels that lead to significant changes in treatment plans for a majority of men.

In brief, the Axumin PET/CT scan (generic name, 18F-fluciclovine) is a total body metabolic scan identifying tumors based on their proliferation rates. Currently, the FDA approved indication applies to cases of PSA relapse (suspected recurrent disease) after primary therapy. The National Comprehensive Cancer Network guidelines (NCCN) Version 4, 2018 mention "consider F-18 fluciclovine PET/CT for detection of biochemically recurrent disease after initial treatment".

The Axumin PET/CT scan is available at over 400 locations throughout the USA. Locations can be viewed at the Axumin Imaging Center Location Directory www.Axumin.com *[control+click link to follow]*.

❖ *The Axumin scan's tumor detection rate varies in relation to the PSA, Gleason score, and PSA doubling time.*

The Axumin scan's detection of prostate cancer is determined by the metabolic activity of target tissue, i.e. the rate of uptake of the ersatz amino acid lysine. The sensitivity of the scan will depend on the size of the potential lesion in relation to its proliferation rate. For example, two lesions of similar size will offer different likelihoods of detection depending on their associated PSA, Gleason score, and PSADT. Consequently, any data about detection rates must be considered generalizations without additional details. The decision to obtain an Axumin scan should be informed by these factors.

That said, research papers do give important information about detection rates usually in relation to PSA. An effort has been made in this Commentary to compress the extensive data detailed in these articles by focusing on detection rates at low PSA values, i.e., < 2 ng/mL, the range where clinically significant management decisions are most times made.

❖ *Detection Rate Data from Parent and Schuster, J Nuc Med, 2018 Mar.*

The detection rates with the Axumin scan for recurrent disease post-prostatectomy for PSA values of <1, 1-2, and ≥ 2 ng/ml were 72.0%, 83.3%, and 100%, respectively (cited from Akin-Akintayo, see below). In a mixed post-prostatectomy and radiotherapy study the detection rates for the same PSA values were lower: 37.5%, 91.7%, and 83.3%.

The difference in the rates at the <1 ng/mL level, i.e., 72% v 37.5% could likely be explained by the different mean PSA doubling times: 4.4 +/- 13.0 months in the prostatectomy cohort v. 13.9 +/- 19.9 months in the mixed group.

❖ *Major publications addressed the impact of the Axumin scan on disease management at two disease stages:*

1) The impact of the Axumin scan at biochemical recurrence (BCR) post-prostatectomy on the decision to administer salvage radiotherapy and the configuration of the target field.
2) The broader issue of the clinical usefulness of the Axumin scan when performed at *any point* of PSA recurrence during the course of the disease and the scan's influence on management.

Example #1 - Study of Salvage Radiation after Prostatectomy:

The article: "Change in Salvage Radiotherapy Management Based on Guidance with FACBC (Fluciclovine [Axumin]) PET/CT in Postprostatectomy Recurrent Prostate Cancer," Akin-Akintayo et. al., Emory University, Clin Nucl Med, 2017. [Clinical Trial - NCT01666808]

The schema: "After an initial provider-determined radiotherapy plan based on conventional imaging, 44 of 87 patients were randomized to additionally undergo a fluciclovine PET/CT. Pre-and post-fluciclovine radiotherapy decisions were compared and changes noted."

Patient characteristics: Median PSA 2.1 +/- 2.96 ng/ml; Gleason score ≤3 + 4 in 42.9%; ≥4 + 3 in 57.1%. The mean time to PSA recurrence (>0.2 ng/mL) after prostatectomy was 2.5 yrs at which time the Axumin scan was performed in the group assigned to that arm of the study.

Findings: In the 42 men in the Axumin arm 81% (34/42) of scans were positive. Of these 40.5% had their management changed based on the scan results. In 11 men the change was from planned radiation treatment of the prostate bed only to a new plan of including the pelvic lymph nodes; 4 men experienced the reverse change, i.e. whole pelvis radiation changed to prostate bed only. Two men were changed from radiation to systemic therapy.

Of the 34 positive scans 12 were positive in the prostate bed only, 2 beyond the pelvis, and 20 were prostate + extraprostatic regions.

The men not receiving the Axumin scan underwent a radiation treatment plan based clinical history, pathology findings, PSA trajectory, and conventional imaging only, i.e., CT or MRI and bone scan. The comparative outcomes of the two groups will be the subject of a later report.

Example #2: Salvage radiation after prostatectomy and radiotherapy - The FALCON Trial (NCT02578940).

The report: Presented in abstract form at ASCO GU 2018 Meeting: "Impact of 18F-fluciclovine PET/CT on Clinical Management Choices for Men with Biochemically Recurrent Prostate Cancer."

The schema: "Men [n-85] being considered for curative-intent salvage therapy following BCR were recruited at 6 different UK sites. Management plans were documented prior to and following 18F-fluciclovine PET/CT imaging."

Patient characteristics: Median PSA was 0.63 ng/mL. The mean time for scanning after initial diagnosis was 4.8 yrs. Initial Gleason score was ≤6 in 12 men, GS 7 in 60, and ≥8 in 13.

Findings: The majority, 61.2% (52 of 85) of those imaged had a post-scan change of management. A change from planned salvage radiotherapy to hormone therapy was made in 34.6% and in 25% management was changed from salvage radiotherapy to observation. These were considered 'major changes.' The planned radiation field was altered in 40.4% and this was considered a 'minor change'. Of the 41 positive scans 34 were positive in the prostates bed, 19 were extraprostatic, 12 in pelvic lymph nodes and 9 were positive in bone.

Example #3 - The LOCATE trial: (NCT92680041)

The article: "The Impact of Positron Emission Tomography with 18F-Fluciclovine on Management of Patients with Biochemical Recurrences of Prostate Cancer: Results of the LOCATE Trial." Andriole *et al, J. Urol.* 2018.

The schema: The LOCATE trial compared the management plans prior to and after an Axumin scan in 213 men who exhibited biochemical progression *at any time* in the course of disease after primary therapy with prostatectomy or radiation.

Patient characteristics: Median PSA 1.0 ng/mL (range 0.2-93.5). The mean time after initial diagnosis for scanning evaluation was 54 months. Gleason score at diagnosis was ≤6 in 27 men, 7 in 134, and ≥8 in 50. Of the 213 men, 164 had a prostatectomy and 46 had radiation. To be eligible for this study, conventional imaging with CT, MRI, and bone scan *had to have been negative* (or equivocal, 16%).

Findings: "Overall, 126/213 (59%) had a change in management post-scan; 78% of these changes were considered 'major'. The Axumin scan identified lesions in 57% of patients with some overlap in several regions: prostate bed, 52%; pelvis 47%, and bone, 9.7%. Detection rate relative to PSA value: "For patients of PSA >0.5-1.0 ng/mL, positivity was 50%, rising to 66% for PSA >1.0-2.0 ng/mL."

The most frequent major changes were from planned salvage radiation or from planned systemic therapy to observation only (25%); from planned systemic therapy to salvage radiation (24%); and from planned salvage radiation to systemic therapy (9%).

Their conclusion: "18F-Fluciclovine-PET/CT detected one or more sites of recurrence in the majority of men with BCR, frequently resulting in major changes to their management plans. Future studies will be planned to determine if change of management leads to improved outcome."

❖ ***BOTTOM LINE:*** (A bit of editorializing)

No current imaging technique captures minimal and unseen microscopic disease. The molecularly targeted PSMA PET/CTs probably come closest, with the metabolic Axumin PET/CT one step behind. The sensitivity of the venerable tech99m bone scan and conventional CT scans have been far surpassed. Multiparametric MRI offers the most detailed examination of the prostate gland but is not a total body survey. The examples cited in this Commentary provide short-term evidence of greater disease detection than can be achieved with conventional imaging, resulting in consistently high rates of changes in treatment plans. However, the long term benefit measured by improved progression-free survival or freedom from metastases resulting from these changes has yet to be demonstrated.

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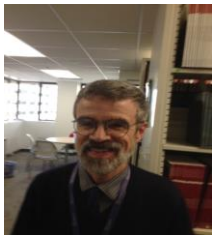
Your comments and requests for information on a specific topic are welcome e-mail ecweber@nwlink.com.

Please also visit https://prostatecancerfree.org/prostate-cancer-news for a selection of past issues of the PCa Commentary covering a variety of topics.



Mike Scully, Librarian

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