

PRECISION IMAGING: QUANTITATIVE, MOLECULAR AND IMAGE-GUIDED TECHNOLOGIES



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Day
3

Lab Training Module 1: Introduction to the basics of human translation of a radiotracer

GOALS:

- **Interpret research Fluciclovine [18F] PET-CT cases**
- **Use rating system** to reach consensus after reviewing patient narratives and comparing findings to standard of truth
- **Compare results** with expert review
- **Calculate diagnostic performance** for prostate/bed and extraprostate

PRECISION IMAGING: QUANTITATIVE, MOLECULAR AND IMAGE-GUIDED TECHNOLOGIES

LAB TRAINING MODULE 1: INTRODUCTION TO THE BASICS OF HUMAN TRANSLATION OF A RADIOTRACER

[A] INTERPRET RESEARCH FLUCICLOVINE [18F] PET-CT CASES

You will be reading fluciclovine PET-CT images of 12 patients selected from 3 studies looking at the utility of fluciclovine PET-CT in recurrent prostate cancer patients. These are meant to be read blindly. Please do not proceed to PART B until PART A is completed.

**For research purposes, patients were imaged from below the
diaphragm to mid-thigh**

Process: Refer to case indications on page 5. Use criteria from reader training guide on SNMMI site (earlier completed)

1. On the MIM workstation, open the precision imaging folder located on the left hand-side of the screen
2. Select the case to be read (refer to case indications on page 5), highlight the CT image and PET image for the first time point [**TIP: Hold down CTRL button to select images**]
3. Select the protocol and click open
4. Review images and note suspicious lesions. **Hint: Window up and down as needed.**
5. Interpret your findings (malignant/positive or benign/negative) in keeping with the reader training guide on SNMMI online education site
6. Record your findings in the “read and final results” sheet (Appendix 1)

[B] DETERMINE YOUR FINAL INTERPRETATION BY USING THE RATING SYSTEM

The rating system is our research scale for finalizing decisions on the presence or absence of disease in the prostate/bed and extraprostate. **Refer to attached rating system table (Appendix 2).**

The rating system is from A-D/U for prostate/bed and A-E/U for extraprostate. This scale takes into account all clinical information including follow up PSA, therapy, biopsies/pathology reports, follow up CT/MRI/bone scans that were done after the fluciclovine PET-CT scan. In few cases, disease status remains “unknown” if there is insufficient information or systemic therapy was received making final decision on the location of disease difficult to reach.

There are no unknown cases in this training. All necessary information to reach a known and final consensus is provided to you

Process: Use attached “read and final results sheet” (Appendix 1) from before

1. Review **patient narratives** and pertinent clinical information provided
2. Make final decisions on reference standard of truth (disease or no disease) in the prostate/ bed and extraprostate locations and assign appropriate rating using the rating scale provided to show how you arrived at your final decisions i.e. TP/TN/FP/FN for each
3. In the prostate bed, default to biopsy for better or worse

Repeat Steps A and B for Each Case

After Completing All Cases, You Should Have Filled Out Table in Appendix 1

[C] CALCULATE DIAGNOSTIC PERFORMANCE OF FLUCICLOVINE [18F] PET-CT FOR PROSTATE CANCER IN THE PROSTATE/BED AND EXTRAPROSTATE

Why diagnostic performance?

This is to determine the ability of fluciclovine [18F] PET-CT to detect prostate cancer and differentiate this from benign prostatic diseases.

The aim is to determine the ability of fluciclovine PET-CT to determine the presence or absence of prostate cancer recurrence in the prostate/bed and in extraprostatic locations.

Tests of diagnostic performance

There are different methods to assess diagnostic performance of a test but we will be learning the following:

Diagnostic performance is an objective measure that can be used to compare different diagnostic techniques or modalities with one another

1. **Sensitivity:** The ability of the test to correctly determine patients who truly have the disease
 $TP / (TP+FN)$
2. **Specificity:** The ability of the test to correctly determine patients who do not have the disease
 $TN / (TN+FP)$
3. **PPV:** The probability that a patient who tests positive on the test has the disease
 $TP / (TP+FP)$
4. **NPV:** The probability that a patient who tests negative on the test does not have the disease
 $TN / (TN+FN)$
5. **Accuracy:** is a measure of the trueness of the test. The degree of closeness of the test to the truth
 $(TP+TN) / (TP+FP+FN+TN)$

A screening test is expected to be highly sensitive while a confirmatory test is expected to be highly specific. ROC analysis finds the best trade-off between sensitivity and specificity

To calculate diagnostic performance

Create a table (see below) and fill in the appropriate information. **Extract the required information for your calculations from your read and result summary sheet in Appendix 1.**

PROSTATE/BED		DISEASE		
FLUCICLOVINE PET-CT		YES	NO	TOTAL
	POSITIVE	TP =	FP =	
	NEGATIVE	FN =	TN =	
	TOTAL			
EXTRAPROSTATE		DISEASE		
FLUCICLOVINE PET-CT		YES	NO	TOTAL
	POSITIVE	TP =	FP =	
	NEGATIVE	FN =	TN =	
	TOTAL			

Use formulae on page 3 to calculate your sensitivity, specificity, accuracy, PPV and NPV.

Record your statistics in table below.

	Prostate	Extraprostate
Sensitivity		
Specificity		
PPV		
NPV		
Accuracy		

[D] COMPARE RESULTS WITH EXPERT REVIEW

Please see attached expert reviews and consensus results on each case at the end of this document to determine how this was done by our expert analysis **[Be sure to complete parts B and C first]**. Note that you may or may not have a better eye or judgement than our experts!

CASE INDICATIONS

CASE 1

67yr old diagnosed with Gleason 6 prostate cancer presenting with rise in PSA up to 5.37ng/ml post-cryotherapy

CASE 2

73yr old with Gleason 7 prostate cancer with PSA rise up to 8.32ng/ml post-brachytherapy and EBRT

CASE 3

68yr old diagnosed with Gleason 6 prostate cancer presenting with rising PSA up to 11.4ng/ml post-brachytherapy

CASE 4

69yr old with Gleason 8 prostate cancer with rising PSA up to 7.53ng/ml post-prostatectomy and adjuvant EBRT

CASE 5

80yr old patient with rising PSA up to 1.59ng/ml post EBRT, brachytherapy and cryoablation.

CASE 6

74yr old with Gleason 7 disease with rising PSA up to 4.79ng/ml post- cryoablation and hormone therapy.

CASE 7

69yr old with Gleason 9 disease presenting with rising PSA up to 12.46ng/ml post-radiotherapy.

CASE 8

61yr old with Gleason 6 prostate cancer now with rising PSA up to 2.71ng/ml post- brachytherapy and EBRT.

CASE 9

71yr old with Gleason 8 prostate cancer with rising PSA up to 6.4ng/ml post- brachytherapy and EBRT.

CASE 10

78yr old with Gleason 7 (4+3) disease presenting with rise in PSA up to 8.39ng/ml post- HT and EBRT.

CASE 11

77yr old with Gleason 7 disease presenting with rising PSA up to 8.90ng/ml post-brachytherapy, EBRT, cryotherapy and TURP.

CASE 12

75yr old with Gleason 7 (3+4) prostate cancer now having rising PSA up to 1.31ng/ml post-cryotherapy and hormone therapy.

PATIENT NARRATIVES

Use this information to determine your own final consensus on prostatic / extraprostatic disease for each case

Case 1

Positive prostate biopsy. Follow up PSA post-cryotherapy = < 0.05 and remained low for more than 1 year

Case 2

Negative prostate biopsy and positive lymph node dissections of right and left external iliac LN. Post LND, PSA dropped from 8.32ng/ml to 3.02ng/ml. He then commenced hormone therapy and PSA dropped to < 0.06 ng/ml.

Case 3

Positive prostate biopsy and positive left obturator lymph node with extension.

Case 4

Prostate biopsy was negative. Bone scans and MRI confirmed metastasis to the 10th rib. Commenced hormone therapy and PSA dropped from 10.88ng/ml to nadir.

Case 5

Prostate biopsy was positive. Patient then had cryotherapy. Follow up PSA was 0.01 and remained low

Case 6

Positive prostate biopsy and had salvage cryotherapy. PSA dropped from 4.79ng/ml to 0.06ng/ml and remained low (PSA= 0.02ng/ml) after 1yr

Case 7

Positive prostate biopsy and negative left inguinal node biopsy. Has diffuse uptake in the hip consistent with inflammation and bilateral ilio-femoral grafts. Post-FACBC, patient had high dose rate brachytherapy and PSA was controlled. CT abdomen was negative.

Case 8

Patient had repeated negative prostate biopsies. He had lymph right pelvic lymph node dissections of the right common iliac and obturator nodes that were positive. Bone scan = negative. Patient now on hormone therapy with PSA nadir.

Case 9

Negative biopsy of the prostate and positive biopsy of the ischiorectal fossa mass. Had CT guided cryoablation of the perirectal mass on account of pain and commenced ADT. PSA is now nadir.

Case 10

Positive prostate biopsy and positive laparoscopic dissection of the right obturator lymph node.

Case 11

Positive prostate biopsy. Had cryotherapy but PSA kept rising up to 20.25ng/ml. Positive non-fluciclovine avid sclerotic densities in the spine but a positive L3 bone lesion (that appears like schmorl's node). All were confirmed as positive bone metastasis on bone scan and CT.

Case 12

Prostate biopsy showed high grade PIN (treat as benign). PSA dropped spontaneously 0.34ng/ml and stayed < 1 ng/ml for 1 year without any therapy.

EXPERT REVIEW

Compare your final consensus to this expert review on prostatic / extraprostatic disease.

Case 1

Positive prostate (A); Negative extra-prostate (B)

Case 2

Negative prostate (B); Positive extra-prostate (A)

Case 3

Positive prostate (A); Positive extraprostate (A)

Case 4

Negative prostate (B); Positive extra-prostate (A)

Case 5

Positive prostate (A); Negative extra-prostate biochemical (B)

Case 6

Positive prostate (A); Negative extra-prostate biochemical (B)

Case 7

Positive prostate (A); Negative extra-prostate (B)

Case 8

Negative prostate (B); Positive extra-prostate (A)

Case 9

Negative prostate (B); Positive extra-prostate (A)

Case 10

Positive prostate (A); Positive extra-prostate (A)

Case 11

Positive prostate (A); Positive extra-prostate (A)

Case 12

Negative prostate (D); Negative extra-prostate (D)

APPENDIX 1: FLUCICLOVINE PET-CT READ & FINAL RESULTS SHEET

Cases	Prostate read (P/N)	Truth in Prostate/bed (P/N) & scale (A-D)	(TP/FP/TN/FN)	Extraprostate read (P/N)	Location (Extraprostate)	Truth in extraprostate (P/N) & scale (A-D)	(TP/FP/TN/FN)
Case 1							
Case 2							
Case 3							
Case 4							
Case 5							
Case 6							
Case 7							
Case 8							
Case 9							
Case10							
Case11							
Case12							

P = Positive; N = Negative

APPENDIX 2: FLUCICLOVINE PET-CT CONSENSUS RATING SYSTEM

PROSTATE			
Scale	Explanation	Truth	Notes
A	Biopsy positive	DISEASE	
B	Biopsy negative with no clinical override	NO DISEASE	
C	Biopsy negative but with clinical override	DISEASE	Clinical override: PSA controlled after local therapy and meets criteria for no extraprostatic disease
D	Findings not consistent with disease in prostate/bed or extraprostatic	NO DISEASE	PSA remained stable or decreased without prostate/bed therapy
U	Lost to follow up of insufficient data	UNKNOWN	
EXTRAPROSTATE			
A	Biopsy positive and/ or imaging positive (bone only)	DISEASE	Node, bone or other extra-prostate confirmed positive on biopsy or characteristic appearance for bone metastasis on 2 or more imaging modalities
B	PSA controlled after local therapy and / or PSA course not consistent with extraprostatic disease	NO DISEASE	For radical prostatectomy, absolute PSA<0.2ng/ml; for other local therapy, PSA<nadir+2ng/ml
C	Biochemical failure without prostate/bed disease to explain PSA rise or possibility of seeding	DISEASE	Includes negative prostate biopsies without local therapy or negative subsequent biopsies after local therapy
D	Findings not consistent with disease in prostate/bed or extraprostatic	NO DISEASE	PSA remained stable or decreased without prostate/bed therapy
E	Biochemical failure with proven or suspected active local disease to explain PSA course and or disease seeding in interim	UNKNOWN	
U	Lost to follow up of insufficient data	UNKNOWN	